

GUIDELINES

Pre-operative evaluation of adults undergoing elective noncardiac surgery

Updated guideline from the European Society of Anaesthesiology

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The purpose of this update of the European Society of Anaesthesiology (ESA) guidelines on the pre-operative evaluation of the adult undergoing noncardiac surgery is to present recommendations based on the available relevant clinical evidence. Well performed randomised studies on the topic are limited and therefore many recommendations rely to a large extent on expert opinion and may need to be adapted specifically to the healthcare systems of individual countries. This article aims to provide an overview of current knowledge on the subject with an assessment of the quality of the evidence in order to allow anaesthesiologists all over Europe to integrate – wherever possible – this knowledge into daily patient care. The Guidelines Committee of the ESA formed a task force comprising members of the previous task force, members of ESA scientific subcommittees and an open call for volunteers was made to all individual active members of the ESA and national societies. Electronic databases were

searched from July 2010 (end of the literature search of the previous ESA guidelines on pre-operative evaluation) to May 2016 without language restrictions. A total of 34 066 abstracts were screened from which 2536 were included for further analysis. Relevant systematic reviews with meta-analyses, randomised controlled trials, cohort studies, case-control studies and cross-sectional surveys were selected. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used to assess the level of evidence and to grade recommendations. The final draft guideline was posted on the ESA website for 4 weeks and the link was sent to all ESA members, individual or national (thus including most European national anaesthesia societies). Comments were collated and the guidelines amended as appropriate. When the final draft was complete, the Guidelines Committee and ESA Board ratified the guidelines.

This article is accompanied by the following Invited Commentary:

Lurati Buse G. Pre-operative evaluation of the adult patient undergoing elective noncardiac surgery: updated guideline from the European Society of Anaesthesiology. Direction and not directives. *Eur J Anaesthesiol* 2018; 35:405–406.

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LIST OF ABBREVIATIONS

| | |
|--------------------|--|
| ACC | American College of Cardiology |
| ACCP | American College of Chest Physicians |
| ACE | Angiotensin Converting Enzyme |
| ACS | American College of Surgeons |
| ADE | Adverse Drug Events |
| AHA | American Heart Association |
| AKI | Acute Kidney Injury |
| ALT | Alanine aminotransferase |
| ARB | Angiotensin Receptor Blocker |
| ARDS | Acute Respiratory Distress Syndrome |
| ASA | American Society of Anesthesiology |
| ASA-PS | American Society of Anesthesiology Physical Status |
| AUD | Alcohol Use Disorders |
| AUDIT | Alcohol Use Disorder Identification Test |
| BADL | Basal Activities of Daily Living |
| BiPAP | Bilevel Positive Airway Pressure |
| BMI | Body Mass Index |
| BNP | Brain Natriuretic Peptide |
| BUN | Blood Urea Nitrogen |
| CAGE | Cutting down, Annoyance by criticism, Guilty feeling, Eye opener |
| CDT | Carbohydrate Deficient Transferrin |
| CGA | Comprehensive Geriatric Assessment |
| CHADS ₂ | Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, Stroke [double weight] |
| CKD | Chronic Kidney Disease |
| CNS | Central Nervous System |
| COPD | Chronic Obstructive Pulmonary Disease |
| CPAP | Continuous Positive Airways Pressure |
| Cr | Creatinine |
| CYP | CYtochrome P |
| DECREASE | Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography |
| DI | Difficult Intubation |
| DL | Difficult Laryngoscopy |
| DM | Diabetes Mellitus |
| DMV | Difficult Mask Ventilation |
| DOACs | Direct Oral Anticoagulants |
| EBA | European Board of Anaesthesiology |
| ECG | ElectroCardioGraphy |

ENT Ear Nose Throat
ESA European Society of Anaesthesiology
ESC European Society of Cardiology
EU European Union
FEV Forced Expired Volume
FFP Fresh Frozen Plasma
FONA Front of Neck Access
FS Functional Status
FVC Functional Vital Capacity
GGT Gamma Gluteryl Transferase
GFR Glomerular Filtration Rate
GRADE Grading of Recommendations Assessment, Development and Evaluation
Hb Haemoglobin
hsTnT high sensitivity Troponin T
IADL Instrumental Activities of Daily Living
IMT Inspiratory Muscle Training
IMV Impossible Mask Ventilation
INR International Normalised Ratio
ISA Illicit Substance Abuse
IS Incentive Spirometry
LMWH Low Molecular Weight Heparin
MACE Major Adverse Cardiac Events
MAOI MonoAmine Oxidase Inhibitor
MELD Model of End-stage Liver Disease
MICA Myocardial Infarction and Cardiac Arrest index
6MWD 6 Minutes Walking Distance
NICE National Institute for Health and Care Excellence
NOAC Novel Oral non-VKA AntiCoagulant
NP Natriuretic Peptides
NSQIP National Surgical Quality Improvement Program index
OR Odds Ratio
OSAS Obstructive Sleep Apnoea Syndrome
OS-MRS Obesity Surgery Mortality Risk Score
PCC Prothrombin Complex Concentrates
PPC Postoperative Pulmonary Complications
PFA Platelet Functional Activity
PBM Patient Blood Management
PICOTS Populations, Interventions, Comparators, Outcomes, Timing, Setting

PI_{max} Maximal Inspiratory Pressure
POCD PostOperative Cognitive Dysfunction
POD PostOperative Delirium
POISE PeriOperative ISchemic Evaluation
PONV PostOperative Nausea and Vomiting
POSSUM Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity
PRF Postoperative Respiratory Failure
PSV Pressure Support Ventilation
RCRI Revised Cardiac Risk Index
RCT Randomised Controlled Trial
RRT Renal Replacement Therapy
SAVS-CRI the South African Vascular Surgical Risk Index score
SSRI Selective Serotonin Reuptake Inhibitor
TCA TriCyclic Antidepressants
THM Traditional Herbal Medicines
TIA Transient Ischaemic Attack
TTE TransThoracic Echocardiography
TUG Timed Up and Go
ULBT Upper Lip Bite Test
VC Vital Capacity
VKA Vitamin K Antagonist
VSG-CRI the Vascular Study Group of New England Cardiac Risk Index
VTE Venous ThromboEmbolism
WHO World Health Organisation

SUMMARY OF THE UPDATED RECOMMENDATIONS

| Recommendation | Grade | References |
|--|-------|-------------------------|
| 1. How should a pre-operative consultation clinic be organised? | | |
| 1.1. <i>How, when and by whom should patients be evaluated pre-operatively?</i> | | |
| • We suggest the use of computer-based pre-operative evaluation tools based on well conceived standardised questionnaires, whenever possible; their use may improve the quality of assessment. | 2B | 16–19 |
| • We recommend the implementation of functional measures such as level of independence, frailty and level of anxiety in pre-operative evaluation. | 2C | 20 |
| • We suggest that pre-operative evaluation is carried out with sufficient time before the scheduled procedure to allow for the implementation of any advisable pre-operative intervention aimed at improving outcome. | 1B | 21–27,31 |
| • Pre-operative assessment may be carried out by a nurse or other physician, but we recommend that it should be concluded by a physician anaesthetist. | 2C | 32 |
| • We suggest that pre-operative evaluation is carried out with sufficient time before the scheduled procedure to allow for the implementation of any advisable pre-operative intervention aimed at improving outcome. | 1C | 33,34 |
| 1.2. <i>How should the patient be informed about peri-operative risks?</i> | | |
| • We recommend the inclusion of information in every pre-operative consultation, as it is very important to patients. | 2B | 18,36–49 |
| • The preferred format of patient education appears to be multimedia presentations, for which we suggest a web-based approach due to feasibility and ease. | 2B | 18,39,44,45,48,49,53,54 |
| • We recommend that consistent effort is made to improve clinicians' communication skills. | 1B | 55 |
| 2. How should pre-operative assessment be performed? | | |
| 2.1. <i>Specific clinical conditions</i> | | |
| Cardiovascular disease | | |
| • We suggest that selected patients with cardiac disease undergoing low and intermediate-risk noncardiac surgery may be referred by the anaesthesiologist for cardiological evaluation and medical optimisation. | 2C | 6 |
| • We recommend the NSQIP model or the RCRI for peri-operative cardiac risk stratification. | 1B | 6 |
| • We suggest considering assessment of cardiac troponins in high-risk patients, both before and 48 to 72 h after major surgery. | 2B | 6 |
| • We suggest considering BNP measurements for obtaining independent prognostic information for peri-operative and late cardiac events in high-risk patients. | 2B | 6 |
| • We recommend peri-operative continuation of beta-blockers in patients currently receiving this medication. | 1B | 6 |
| • We suggest considering pre-operative initiation of beta-blockers in patients scheduled for high-risk surgery and who have at least two clinical risk factors or ASA status at least 3. | 2B | 6 |
| • We suggest considering pre-operative initiation of beta-blockers in patients who have known ischaemic heart disease or myocardial ischaemia. | 2B | 6 |
| • We suggest that when oral beta-blockade is initiated in patients who undergo noncardiac surgery, the use of atenolol or bisoprolol as a first choice may be considered. | 2B | 6 |
| • We suggest that continuation of aspirin may be considered in the peri-operative period, and should be based on an individual decision that depends on the peri-operative bleeding risk, weighed against the risk of thrombotic complications. | 2B | 6 |
| • We suggest discontinuation of aspirin therapy when haemostasis is anticipated to be difficult to control during surgery. | 2B | 6 |
| Respiratory disease, smoking, obstructive sleep apnoea syndrome | | |
| • We do not recommend pre-operative diagnostic spirometry in noncardiothoracic patients for evaluating the risk of postoperative complications in general. | 1C | 80–82 |
| • We do not recommend routine pre-operative chest radiographs because they rarely alter peri-operative management. | 1C | 78,79,81,82 |
| • We recommend that patients with obstructive sleep apnoea syndrome should be evaluated carefully for a potential difficult airway and that they receive special vigilance in the immediate postoperative period. | 1B | 94,95 |
| • We recommend the use of specific questionnaires to screen for obstructive sleep apnoea syndrome when polysomnography is not available (gold standard). The STOP-BANG questionnaire is the most sensitive, specific and best validated score. | 1B | 91,99–106 |
| • We suggest use of peri-operative CPAP in patients with obstructive sleep apnoea syndrome to reduce hypoxic events. | 2B | 95,96 |
| • We suggest that pre-operative inspiratory muscle training reduces postoperative atelectasis, pneumonia and length of hospital stay. | 2A | 108 |
| • We do not suggest that pre-operative incentive spirometry helps prevent postoperative pulmonary complications. | 2A | 110 |
| • We suggest correction of malnutrition. | 2C | 111 |
| • We suggest that smoking cessation for at least 4 weeks prior to surgery reduces postoperative complications. | 2A | 122,123 |
| • We suggest that there is insufficient evidence that short-term cessation (<4 weeks) of smoking decreases the rate of postoperative complications. | 2A | 121 |
| Renal disease | | |
| • We suggest taking known risk factors such as older age or obesity, into consideration to identify patients at risk of postoperative acute kidney injury (AKI). Additional caution is warranted when administering potentially nephrotoxic medication, adjusting the volume status and controlling blood pressure in this group | 2C | 142–144 |
| • We suggest taking into consideration test results (BUN/Cr ratio, pre-operative Hb concentration and peri-operative Hb decrease) in order to identify patients at risk of postoperative AKI. | 2B | 145,146,148 |
| • We suggest using calculated GFR instead of serum creatinine for renal function evaluation and prediction of postoperative morbidity and mortality in patients with impaired renal function undergoing noncardiac procedures. | 2B | 149–151 |
| • We suggest that adding pre-operative statin therapy does not have additional value in the preservation of renal function in patients undergoing noncardiac procedures. | 2B | 152,153 |

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| Recommendation | Grade | References |
|--|-------|---------------------|
| <i>Diabetes</i> | | |
| • We suggest that patients with known diabetes mellitus should be managed in accordance with guidelines on the management of patients with known or suspected cardiovascular disease. | 2A | 7,176,192,193 |
| • We suggest that blood sugar is not routinely measured at pre-operative assessment in otherwise healthy individuals scheduled for elective noncardiac surgery, except for patients undergoing major orthopaedic or vascular surgery. | 2A | 173,178 |
| • We recommend that patients at a high risk of disordered glucose homeostasis should be identified as needing specific attention to peri-operative glucose control. | 1C | 166,173 |
| • We suggest blood glucose testing and testing for HbA1c in patients with known diabetes mellitus and patients scheduled for major orthopaedic and vascular surgery. | 2A | 166,175,190 |
| • We suggest that patients with long-standing diabetes should undergo careful airway assessment. | 2C | 194 |
| <i>Obesity</i> | | |
| • We suggest that pre-operative assessment of the obese includes at least the STOP-BANG questionnaire, clinical evaluation, ECG, oximetry and/or polysomnography. | 2B | 103,202,209,255–262 |
| • We suggest laboratory examination in the obese in order to detect pathological glucose/HbA1c concentrations and anaemia. | 2C | 218,220,223 |
| • We suggest that neck circumferences at least 43 cm and a high Mallampati score are predictors for a difficult intubation in the obese. | 2C | 209 |
| • We suggest that the use of CPAP/PSV/BiPAP peri-operatively might reduce hypoxic events in the obese. | 2C | 255,264 |
| <i>Coagulation disorders</i> | | |
| • We recommend assessment of the bleeding history, including a physical examination, as the best tool for identification of patients with impaired haemostasis and/or an increased risk of bleeding complications during and after surgery. | 1B | 268 |
| • We suggest that, in addition to detailed history taking, laboratory tests can be used to improve identification of coagulation disorders. | 2C | 269,270 |
| • We suggest that simple laboratory tests such as platelet count may have a prognostic value and can be used in the evaluation. | 2A | 272,273 |
| • We suggest that cataract surgery with continued anticoagulant medication can be performed safely provided that topical anaesthesia is used and a clear corneal incision is made by a skilled surgeon. | 2B | 274 |
| • We suggest that noncardiac surgery may be safely performed in patients on single antiplatelet therapy after coronary stent implantation. | 2B | 277 |
| • We suggest that neither the history of platelet inhibitor-intake nor findings from the PFA-100 can predict peri-operative bleeding. Surgery in hip-fracture patients taking aspirin is considered well tolerated and withdrawal of clopidogrel for 3 days is considered sufficient to prevent major bleeding. | 2B | 269–271 |
| • We recommend that surgery can safely be performed in hip-fracture patients without discontinuing clopidogrel peri-operatively. | 1B | 278,279 |
| • We suggest that if reversal of warfarin-associated coagulopathy is necessary, primarily PCC should be used. In the absence of PCC, the combination of FFP and vitamin K is a possibility. | 2C | 282,283 |
| • We recommend an evidenced-based approach to the decision to withdraw clopidogrel in specific patient groups because of the potential risks. | 1C | 278 |
| • We suggest that elective surgical procedures can safely be performed while on clopidogrel without increased peri-operative bleeding risk. | 2C | 280 |
| <i>Anaemia and pre-operative blood conservation strategies</i> | | |
| • We recommend treating known iron deficiency anaemia with intravenous iron before elective procedures. | 1B | 288–292 |
| • We recommend using parenteral iron rather than oral iron supplements for iron deficiency anaemia before elective procedures. | 1C | 292 |
| • We suggest using erythropoietin supplements for anaemic patients before elective surgery and those who are at risk of postoperative anaemia if other causes of anaemia have been excluded or treated. | 2B | 293,295 |
| • For the best results in peri-operative anaemia management, we recommend using intravenous iron together with stimulants of erythropoiesis. | 1C | 296,297 |
| • We recommend implementing PBM principles and goal-directed transfusion policy into the daily practice of the hospital. | 1C | 298–301,303 |
| • We recommend using tranexamic acid for known anaemic patients or those at risk of postoperative anaemia undergoing elective joint arthroplasty procedures. | 1C | 304 |
| • We suggest using cell salvage for all patients having orthopaedic procedures with anticipated high blood loss. | 2B | 295,305 |
| • We suggest that pre-operative donation of autologous blood (or acute normovolaemic haemodilution) should be considered carefully and its use based on individual patient need and the type of surgery. | 2C | 306,308 |
| <i>The geriatric patient</i> | | |
| • Functional status can be impaired in the elderly and predicts functional outcome. We recommend the evaluation of functional status, preferably through comprehensive geriatric assessment to identify patients at risk and/or to predict complications. | 1B | 311,312,314,316–329 |
| • Levels of independence may be impaired which predicts complications. We recommended scoring the level of independence using validated tools such as the Basal and Instrumental Activities of Daily Life. | 1B | 312,314,330–332 |
| • Comorbidity and multiple morbidity become more frequent with ageing and are related to increased morbidity and mortality. We recommend the assessment of comorbidities by age-adjusted scores, such as the Charlson Comorbidity Index. | 1B | 312,314,333–337 |
| • Poly-medication and inappropriate medication (mostly anticholinergic or sedative-hypnotic drugs) are common and predict complications and mortality. We recommend the consideration of appropriate peri-operative medication adjustments. We recommend the evaluation of medication in a structured way, such as the Beers criteria. | 1B | 316,317,319,343 |

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| Recommendation | Grade | References |
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| <ul style="list-style-type: none"> • Cognitive impairment is frequent and often undervalued. It may affect comprehension, hampering appropriate informed consent. Cognitive impairment predicts complications and mortality. We recommend the evaluation of cognitive function based on validated tools. | 1B | 311,312,314,339–341 |
| <ul style="list-style-type: none"> • Depression is frequent in the elderly and is related to increased complications. We recommend that depression is assessed by validated tools. | 1B | 311,314 |
| <ul style="list-style-type: none"> • We recommend the evaluation and management of risk factors for postoperative delirium in accordance with the ESA evidence-based and consensus-based guidelines on postoperative delirium. | 1B | 311 |
| <ul style="list-style-type: none"> • Sensory impairment weakens communication and is associated with postoperative delirium. We recommend the assessment of sensory impairment and that time without sensory aids in the peri-operative setting is minimised. | 1B | 25,312,314 |
| <ul style="list-style-type: none"> • Malnutrition is frequent, often undervalued and predicts complications. Obesity is associated with increased risk for kidney injury. We recommend the assessment of nutritional status (preferably by Nutritional Risk Screening), to implement appropriate interventions in patients at risk and to minimise pre-operative fasting. | 1B | 143,312–314,343,344 |
| <ul style="list-style-type: none"> • Frailty is a state of extreme vulnerability. It predicts morbidity and mortality. We recommend the assessment of frailty in a structured, multimodal way such as Fried Score or Edmonton Frailty Scale, avoiding surrogate single measures. | 1B | 22,23,311,312,314,337,339,345–360 |
| Alcohol and drug misuse and addiction | | |
| <ul style="list-style-type: none"> • We recommend that for the pre-operative detection of AUD, a combination of the standardised CAGE questionnaires and laboratory tests such as GGT and CDT is superior to the sole use of laboratory tests or using a questionnaire alone. | 1B | 376 |
| <ul style="list-style-type: none"> • We recommend using only the combination of GGT and CDT as biomarkers for the pre-operative identification of AUD, as they provide the highest sensitivity. | 1C | 371 |
| <ul style="list-style-type: none"> • We recommend the use of a computerised self-assessment questionnaire, as it appears superior to an interview by an anaesthesiologist in the identification of patients with AUD and illicit substance use. | 1C | 370,374 |
| <ul style="list-style-type: none"> • We recommend that the AUDIT-C and the AUDIT score are not interchangeable for detection of AUD in pre-operative assessment. | 1C | 370 |
| <ul style="list-style-type: none"> • We suggest that the NIAAA-4Q tool can be used pre-operatively to identify AUD. | 2C | 375 |
| <ul style="list-style-type: none"> • We recommend pre-operative alcohol cessation, including pharmacological strategies for relapse prophylaxis and withdrawal symptoms, as they may significantly reduce postoperative complication rates. | 1B | 379,380 |
| <ul style="list-style-type: none"> • No suggestion can be given on the timing, duration and intensity of alcohol cessation. | 2A | 379 |
| <ul style="list-style-type: none"> • A positive pre-operative cocaine screen may not be associated with adverse intra-operative haemodynamic events. Therefore, when evaluating these patients, we suggest that clinical symptoms of cocaine abuse should be taken into account. | 2C | 377,378 |
| Neuromuscular disease | | |
| <ul style="list-style-type: none"> • We suggest early pre-operative consultation for patients with severe, poorly controlled or decompensated neurological disease, a recent stroke and those undergoing procedures with a high risk of neurological complications. | 2B | 381 |
| <ul style="list-style-type: none"> • We suggest an assessment of pulmonary function including vital capacity and FVC. For cardiac function assessment, we suggest an ECG and TTE for quantifying the degree of potential cardiomyopathy. | 2B | 384 |
| <ul style="list-style-type: none"> • We suggest that pre-operative optimisation and/or treatment may improve the patient's outcome. | 2C | 381 |
| 2.2. How to deal with the following concurrent medication? | | |
| Herbal medication | | |
| <ul style="list-style-type: none"> • We suggest asking patients explicitly about their intake of herbal drugs, particularly those that may cause increased bleeding in the peri-operative period and other drugs taken concomitantly that also may influence haemostasis such as NSAID. | 2B | 391 |
| <ul style="list-style-type: none"> • We suggest stopping herbal medicines 2 weeks prior to surgery. | 2B | 391,399 |
| <ul style="list-style-type: none"> • There is no evidence for postponement of elective surgery, but for high-risk surgery in 'closed compartments' such as intracranial procedures, we suggest that the possible impairment of haemostasis by these drugs is taken into account. | 2B | 391 |
| Psychotropic drugs | | |
| <ul style="list-style-type: none"> • We suggest that patients chronically treated with TCA should undergo comprehensive cardiac evaluation prior to anaesthesia. | 2B | 404,408 |
| <ul style="list-style-type: none"> • We recommend that antidepressant treatment for chronically depressed patients should not be discontinued prior to anaesthesia. | 1B | 424 |
| <ul style="list-style-type: none"> • We suggest that there is insufficient evidence for discontinuation of SSRI treatment peri-operatively. | 2B | 409,420,421 |
| <ul style="list-style-type: none"> • We recommend stopping irreversible MAOI at least 2 weeks prior to anaesthesia. In order to avoid relapse of underlying disease, medication should be changed to reversible MAOI. | 1C | 409 |
| <ul style="list-style-type: none"> • We suggest that antipsychotic medication is continued in patients with chronic schizophrenia peri-operatively. | 2B | 408 |
| <ul style="list-style-type: none"> • We suggest stopping lithium administration 72 h prior to surgery. | 2B | 408 |
| <ul style="list-style-type: none"> • It can be restarted if the patient has normal levels of electrolytes, is haemodynamically stable and able to eat and drink. We suggest that blood levels of lithium are controlled within one week. | 2B | 408 |
| <ul style="list-style-type: none"> • We suggest that lithium therapy is continued in patients undergoing minor surgery under local anaesthesia. | 2C | 408 |
| <ul style="list-style-type: none"> • We suggest stopping herbal medicine 2 weeks prior to surgery. | 2B | 399 |
| Peri-operative bridging of anticoagulation therapy | | |
| <ul style="list-style-type: none"> • In high-risk patients taking VKA, we recommend a 'bridging' strategy for the peri-operative period in accordance with existing ESA clinical guidelines. However, we suggest an individualised approach in determining the need for 'bridging anticoagulation' based on the patient's estimated thromboembolic risk and peri-procedural bleeding risk. | 2C | 397 |
| <ul style="list-style-type: none"> • In minor surgical procedures, such as cataract or minor soft tissue surgery, we recommend continuation of VKA instead of instituting 'bridging' therapy. | 1B | 397 |

(continued)

| Recommendation | Grade | References |
|--|-------|--|
| <ul style="list-style-type: none"> In pacemaker and defibrillator devices implantation, we recommend continuing VKA therapy in preference to 'bridging' therapy with LMWH. | 1B | 444,445 |
| <ul style="list-style-type: none"> We do not recommend 'bridging' with LMWH in patients receiving a DOAC agent for short DOAC interruptions. | 1C | 307 |
| 2.3. Which pre-operative tests should be ordered? http://www.nice.org.uk/guidance/ng45 | | 190 |
| 2.4. How should the airway be evaluated? | | |
| <ul style="list-style-type: none"> We recommend that screening for DMV and difficult intubation should be conducted, whenever feasible, in all patients potentially requiring airway management for anaesthesia and in the ICU. This screening includes a medical history, a surgical history, history of difficult airway management and, if available, examination of previous anaesthetic records. | | |
| <ul style="list-style-type: none"> Details of this should be documented in the patient chart. | 1A | 458 |
| <ul style="list-style-type: none"> We recommend that no single predictive sign for difficult airway management is sufficient by itself and the pre-anaesthesia assessment needs the combination of different validated evaluation criteria. | 1A | 467,470,475 |
| <ul style="list-style-type: none"> We suggest that although the Mallampati test has been validated in awake patients, lying, sitting or standing, there is poor correlation with glottic view by direct laryngoscopy | 2B | 464,465 |
| <ul style="list-style-type: none"> We recommend that the Mallampati classification alone should no longer be considered capable of predicting the laryngoscopic view with precision. | 1B | 461,464–467 |
| <ul style="list-style-type: none"> We recommend that the potential for DMV should be evaluated and should rely on the presence of two or more of the following factors: BMI of at least 30 kg m⁻²; jaw protrusion severely limited; snoring; beard; Mallampati classification 3 or 4; and age at least 57 years. | 1C | 458–460 |
| <ul style="list-style-type: none"> We suggest that the potential for impossible mask ventilation should be evaluated and should rely on the presence of three or more of the following factors: neck radiation changes, male sex, presence of OSAS, Mallampati class 3 or 4 and presence of a beard. | 2B | 460 |
| <ul style="list-style-type: none"> We suggest that the combination of the ULBT with the thyromental distance (threshold: 6.5 cm) and interincisor distance (mouth opening; threshold: 4.5 cm) is easy to perform and reliable as a predictor for difficult intubation. | 2A | 473,474 |
| <ul style="list-style-type: none"> We suggest that particular attention to the evaluation for possible difficult intubation should be paid in certain medical conditions such as obesity, OSAS, diabetes, fixed cervical spine, ENT diseases and pre-eclampsia. Neck circumference of more than 45 cm is another warning sign. | 2C | 480 |
| <ul style="list-style-type: none"> We suggest that difficult videolaryngoscopy cannot easily be predicted, as only a few studies have addressed this question so far. | 2C | 461,463,471 |
| <ul style="list-style-type: none"> We recommend the use of ULBT as a predictor for difficult intubation with GlideScope videolaryngoscopy. | 1B | 474 |
| 2.5. The place of risk indices and biomarkers | | |
| Risk indices | | |
| <ul style="list-style-type: none"> We recommend using ASA-PS to stratify mortality risk in patients undergoing noncardiac surgery. | 1B | 487,488,491–496 |
| <ul style="list-style-type: none"> We recommend using RCRI for assessing peri-operative cardiovascular risk in patients undergoing noncardiac, nonvascular surgery. | 1B | 64,487,498–502,505,506,509,511 |
| <ul style="list-style-type: none"> We recommend using ASA-PS, RCRI, NSQIP MICA for assessing peri-operative morbidity risk. | 1C | 64,489–491,496,498–502,505,506,509,511 |
| <ul style="list-style-type: none"> We suggest using the Nottingham Hip Fracture Score to stratify peri-operative mortality risk in patients undergoing surgery for hip fractures. | 2C | 517–522 |
| <ul style="list-style-type: none"> We recommend using the STOP BANG questionnaire to assess the risk of OSAS and postoperative complications. | 1C | 103–106 |
| Biomarkers | | |
| <ul style="list-style-type: none"> We suggest using pre-operative hsTnT measurement to aid risk assessment in patients at risk of coronary artery disease and in patients undergoing major surgery. | 2C | 507,552–559 |
| <ul style="list-style-type: none"> We recommend that pre-operative measurements of natriuretic peptides be used for risk stratification in intermediate and high-risk patients undergoing vascular or major thoracic surgery. | 1C | 546–551 |
| <ul style="list-style-type: none"> We suggest pre-operative measurement of natriuretic peptides for risk stratification in high-risk patients undergoing major general or orthopaedic surgery. | 2C | 549–551 |
| 2.6. Postoperative nausea and vomiting | | |
| <ul style="list-style-type: none"> We recommend implementing a PONV guideline according to the local clinical setting. | 1B | 569–571 |
| <ul style="list-style-type: none"> We recommend the inclusion of a pre-operative PONV score in the pre-anaesthetic evaluation. | 2B | 569 |
| <ul style="list-style-type: none"> According to the score, we recommend a risk-adapted multimodal approach to be used to reduce the PONV rate. | 1B | 563–565,570,572,595,596 |
| <ul style="list-style-type: none"> We recommend the measurement of the PONV rate in order to improve the guideline and to feedback to staff. | 1C | 570,572 |

Preamble

The present guidelines are an update of the 2011 European Society of Anaesthesiology (ESA) recommendations on pre-operative evaluation of adults undergoing noncardiac surgery.¹ The guidelines aim to present recommendations based on the available relevant clinical evidence on the topic. The information used may not only come from high-quality randomised clinical trials or meta-analyses but also from cohort studies and even statements of expert opinion. Ultimately, these recommendations should help physicians make decisions in their clinical practice.

Clinical practice over Europe may vary widely. Despite the availability of the same scientific information, the way in which healthcare services are organised and individual national jurisprudence may significantly determine how this scientific evidence will be implemented in the different practices throughout the countries of Europe. For instance, a Dutch study including 4540 adult surgical patients suggested that trained nurses, compared with anaesthesiologists, were perfectly capable of assessing pre-operative health status, providing a scientific basis for using nurses in pre-operative assessment.² Yet, in a number of European countries, nurses are not legally allowed to perform pre-operative evaluations of patients. Hence, this specific information might result, in some countries, in a recommendation to include nurses in a pre-operative assessment, whereas in other countries, local legislation will preclude such an initiative.

The ESA is committed to the production of high-quality, evidence-based clinical guidelines and recommendations. However, emphasis is also put on the practicability of reading and implementation. The Guidelines Committee of the ESA defines the topics to be treated, which are then referred to specific Task Forces to elaborate the question and propose guidelines based on a critical appraisal of the available literature. The Guidelines Committee also defines when an update of the guidelines is deemed necessary. Usually, new and additional studies and publications dictate that the evidence of recommendations needs to be updated every 5 years.

Few well performed randomised studies on the topic of pre-operative evaluation of the adult for noncardiac surgery are available. Many recommendations rely mainly on expert opinion and are specifically adapted to the healthcare systems in individual countries. The present contribution aims to provide an overview of the present knowledge on the subject with assessment of the quality of the evidence in order to allow anaesthesiologists all over Europe to integrate – wherever possible – this knowledge into their daily patient care.

Potential legal implications of publication of recommendations and guidelines seem to be a major point of concern among medical practitioners.³ It cannot be emphasised sufficiently that guidelines may not be appropriate for all clinical situations. The decision whether or not to follow a

recommendation from a guideline must be made by the responsible physician on an individual basis, taking into account the specific conditions of the patient and the available resources and local regulations, laws and good clinical practice recommendations of the particular country. Therefore, deviations from guidelines for specific reasons remain perfectly permissible and can certainly not be interpreted as the basis for a negligence claim.

Introduction

The present guideline deals with the pre-operative evaluation of *adults* undergoing *elective, noncardiac surgery*. The ultimate aim of this evaluation is twofold. First, it should allow identification of those patients for whom the peri-operative period may bring an increased risk of morbidity and mortality in addition to those risks associated with any underlying disease. Second, this identification should help to design peri-operative strategies that aim to reduce additional peri-operative risks.

Surgical risk may vary tremendously, depending on the duration of the procedure, estimated blood loss, estimated fluid shifts and the anatomical region involved.^{4,5} Surgical risk has been given either a two or three-part classification. The recent European Society of Cardiology (ESC)/ESA guidelines on cardiovascular assessment and management of the cardiac patient undergoing noncardiac surgery distinguish between low, intermediate and high-risk procedures.⁶ The recent parallel American Heart Association (AHA)/American College of Cardiology (ACC) guidelines, however, only distinguish between low and elevated surgical risk because recommendations for intermediate and high-risk procedures are similar and classification into two categories may simplify the recommendations without loss of fidelity.⁷ It should be noted, however, that with the increasing uptake of minimal invasive surgical techniques, the concept of surgical risk may have to be reconsidered.⁸

Risk factors are therefore not only related to individual, surgical, but also organisational factors. Not all of these can be covered by recommendations. In addition, reliable clinical evidence on many issues is scarce and of low quality or even absent. Therefore, where possible, recommendations will be provided based on the best available evidence and when this is not possible, the recent available evidence will be summarised.

For the present revision of the guidelines, the task force decided to follow the same framework as the original ESA guidelines on pre-operative evaluation of adults undergoing noncardiac surgery.¹ Therefore the following thematic questions were addressed:

How should a pre-operative consultation clinic be organised?

This organisational issue is addressed by assessing the evidence from the responses to the following questions:

How, when and by whom should patients be evaluated pre-operatively?

This first part of this question assesses the evidence about the different available tools for pre-operative screening, such as paper or website questionnaires to be completed by the patients, interviews by a nurse or a physician, and others.

The background for the second part of the question lies in the need to optimise the patient's condition when risk factors are identified. This implies that patients should be seen sufficiently in advance to allow for measures to be instituted. This question seeks to determine whether the timing of pre-operative assessment affects the outcome.

The third part of the question evaluates the evidence regarding the qualifications necessary for the performance of pre-operative evaluation: nurse, general practitioner, anaesthesiologist or others?

How should the patient be informed about peri-operative risks?

Patients have a moral and legal right to be informed about what is going to happen to them. Although the process of obtaining consent for anaesthesia and surgery varies between countries, a common principle is that the patient should understand enough about the risks and benefits of the proposed procedures in order to make an informed decision. In addition, providing information might be expected to have effects on patient anxiety, satisfaction with care and possibly compliance with therapy or instructions.⁹ Two related questions therefore arise. First, what information is needed and/or wanted by the patient? Second, how should this information be presented to the patient?

How should a pre-operative assessment of a patient be performed?

We decided to apply the same stepwise approach as previously using a number of successive topics for which the best available evidence was sought and assessed for quality. This practical aspect is addressed by assessing the evidence from the available responses to the following questions:

Specific clinical conditions

Every patient should be checked for specific conditions that might interfere with anaesthesia and surgery; each one should be evaluated and treated as necessary. Uncommon diseases and endocrinological disorders other than diabetes were not included in the present overview because they represent specific entities in which specialised diagnosis, treatment and advice on peri-operative support are always indicated.

Pregnancy was deliberately not included in the present guidelines, as it has its own comorbidities, risks and

associated physiological changes that deserve separate guidelines.

The following conditions are covered in the current guidelines:

- (1) cardiovascular disease
- (2) respiratory disease, smoking, obstructive sleep apnoea syndrome
- (3) renal disease
- (4) diabetes
- (5) obesity
- (6) coagulation disorders
- (7) anaemia and pre-operative blood conservation strategies
- (8) the geriatric patient
- (9) alcohol and drug misuse and addiction
- (10) neuromuscular disease

In contrast to the previous guidelines,¹ the task force decided not to include the topic 'allergy' in the present update, as it is a very specific, specialised topic that deserves separate guidelines. In this updated version of the guidelines, we have added neuromuscular disease because pre-operative preparation for these conditions requires specific attention.

How to deal with the following concurrent medication?

- (1) herbal medication
- (2) psychotropic drugs
- (3) peri-operative bridging of anticoagulation therapy

The topic 'Antithrombotic therapy and regional anaesthesia' has not been included in the present guidelines, as it is the subject of separate ESA guidelines, to which the reader is referred.¹⁰ These guidelines are currently in the process of being updated (<https://www.esahq.org/guidelines/guidelines/guidelines-in-development>).

Which pre-operative tests should be ordered?

Recommendations on which pre-operative tests should be used for elective surgery have recently been updated by NICE (<http://www.nice.org.uk/guidance/ng45>).

How should the airway be evaluated?

This part discusses the methods of pre-operative airway evaluation.

The place of risk indices and biomarkers

Postoperative nausea and vomiting

Several guidelines are available on the prevention and treatment of postoperative nausea and vomiting (PONV). However, in view of the importance of the problem, with a reported overall incidence of 25 to 30% and up to 70 to 80% among high-risk patients, the task force considered

it important to provide a concise clinical overview of the current principles for dealing with PONV.

Materials and methods

Selection of the task force

As is customary for an update of guidelines, members of the original task force were approached with regard to their willingness and availability to take part in the update process. Following the new policies and procedures of the ESA Guidelines Committee, appointed members of the European Board of Anaesthesiology (EBA) with specific interest and expertise in the topic were included and an open call to interested active ESA members was published.

Due to the variety of topics addressed by this guideline, we created the following six thematic clusters: organisation and patient information, clinical conditions, concurrent medication, airway management, indices and biomarkers, and postoperative nausea and vomiting. We developed separate key questions and inclusion and exclusion criteria according to the PICOTS scheme for each cluster. Support was obtained from Cochrane Austria at the Department for Evidence-based Medicine and Clinical Epidemiology of the Danube University Krems, Austria, for protocol development and literature search.

Literature search

We developed an electronic search strategy for each thematic cluster covered by this guideline in order to identify articles relevant to key questions. We focused on terms to describe the relevant patient groups and interventions of interest. Search terms were chosen on the basis of text analysis (PubMed PubReMiner,¹¹ TermMine¹²) of known relevant literature and in consultation with the members of the guideline development group responsible for each thematic cluster and its key clinical questions.

We searched Medline (Ovid), Cochrane Library (Wiley), Embase (Elsevier) and PubMed from 2010 (starting from the end of the searches of previous guidelines) until May 2016 by using Medical Subject Headings and title and abstract key keywords. Electronic literature searches were conducted by an experienced information specialist. We limited electronic searches to guidelines, systematic reviews, meta-analyses and controlled study designs. In addition, we restricted searches to human-only studies. Full details of each search strategy for each cluster and the number of hits are shown in the appendix (Supplemental Digital Content, <http://links.lww.com/EJA/A152>).

Eligibility criteria

For each cluster, we specified inclusion and exclusion criteria based on the PICOTS format. For this guideline, we included adults (18 years or older) undergoing elective noncardiac surgery. We included systematic reviews with

meta-analyses, randomised controlled trials (RCT) and observational studies. We did not include narrative reviews, editorials, case series or case reports.

We screened abstracts and selected articles that were relevant to the key clinical questions. Specifically, we selected articles that investigated interventions that might be implemented by an anaesthesiologist in the pre-operative period. We applied no limitation on study duration or length of follow-up.

Study selection

All titles and abstracts identified were assessed for eligibility and relevance for key clinical questions by two members of each thematic cluster. Disagreements were solved by consensus or by consulting a third reviewer. Studies included by title and abstract underwent subsequent full-text review. Final inclusions of the abstract review process were documented in an EndNote bibliographic database for each cluster.

An overview of the total number of abstracts screened and finally included for each cluster is summarised in Table 1 (Supplemental Digital Content, <http://links.lww.com/EJA/A153>). A total of 34 066 abstracts were screened from which 2536 were included for further analysis.

Table 1 Mean rankings and range of outcome rankings by participants

| Outcome | Responses (n) | Mean | Range |
|--|---------------|------|--------|
| Ranked as critical | | | |
| All-cause mortality | 10 | 8.90 | 8 to 9 |
| Failure to rescue | 10 | 8.50 | 6 to 9 |
| Major adverse cardiovascular events | 10 | 8.20 | 7 to 9 |
| Cardiopulmonary resuscitation | 10 | 8.10 | 6 to 9 |
| Acute kidney injury/failure | 10 | 7.80 | 7 to 9 |
| Heart failure | 10 | 7.50 | 6 to 9 |
| Postoperative pain | 10 | 7.40 | 6 to 9 |
| Hepatic failure | 10 | 7.40 | 7 to 9 |
| Pneumonia | 10 | 7.20 | 6 to 8 |
| Postoperative recovery | 9 | 7.11 | 5 to 9 |
| Infection | 10 | 7.00 | 5 to 9 |
| Postoperative respirator therapy | 10 | 7.00 | 6 to 8 |
| Ranked as important | | | |
| Delirium | 10 | 6.90 | 5 to 8 |
| Health-related quality of life (EuroQoL, EQ5D) | 10 | 6.80 | 5 to 8 |
| Mental state postoperatively | 10 | 6.70 | 4 to 8 |
| Bleeding | 10 | 6.60 | 4 to 9 |
| Postoperative mobility | 10 | 6.60 | 5 to 9 |
| Health and disability (12-item WHODAS 2.0) | 10 | 6.50 | 5 to 8 |
| Re-intubation rate | 9 | 6.44 | 4 to 8 |
| Coagulation disorders | 10 | 6.40 | 4 to 8 |
| Patient satisfaction | 10 | 6.30 | 4 to 8 |
| Atelectasis | 10 | 6.30 | 5 to 9 |
| Blood transfusions | 10 | 6.20 | 5 to 9 |
| Length of stay in intensive care unit | 10 | 6.10 | 4 to 8 |
| Additional surgical intervention | 10 | 6.00 | 5 to 8 |
| Discharge destination | 10 | 5.80 | 3 to 9 |
| Length of stay in hospital | 10 | 5.80 | 4 to 7 |

Table 2 Risk factors for postoperative pulmonary complications

| Risk factor | OR | CI |
|---|------|--------------|
| Age 60 to 69 years ^a | 2.09 | 1.70 to 2.48 |
| Age 70 to 79 years ^a | 3.04 | 2.11 to 4.39 |
| COPD | 1.79 | 1.44 to 2.22 |
| Smoking | 1.26 | 1.01 to 1.56 |
| Congestive heart failure | 2.93 | 1.02 to 8.43 |
| Total functional dependence | 2.51 | 1.99 to 3.15 |
| Partial functional dependence | 1.64 | 1.36 to 2.01 |
| Higher ASA classification and prolonged duration of surgery | 2.14 | 1.33 to 2.46 |

ASA, American Society of Anesthesiology; CI, 95% confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio. ^a Compared with patients aged <60 years.

Full-text review was performed by two members of each thematic cluster and assessment of evidence was performed according to the recommendations of the Cochrane handbook for systematic reviews of interventions.¹³ Disagreements were solved by consensus or consulting a third reviewer.

Strength of evidence

The ESA guidelines committee selected the GRADE system for assessing levels of evidence and grading recommendations, as outlined in Table 2 (Supplemental Digital Content, <http://links.lww.com/EJA/A154>).

The guideline development group was asked to nominate relevant outcomes across all clusters and rank the relative importance of outcomes following a process proposed by the GRADE group.¹⁴ We used SurveyMonkey for anonymous ranking of the relative importance of outcomes. Participants used a 9-point Likert scale (9 indicated greatest importance and 1 least importance) to rank outcomes into three categories: critical for decision making, important but not critical for decision making and of low importance for decision making. Table 1 summarises the outcomes respondents considered as either critical or important for decision making.

Review process

The ESA Guidelines Committee supervises and coordinates the preparation of guidelines. The final draft guideline underwent a review process previously agreed upon by the ESA Guidelines Committee. The draft was posted on the ESA website for 4 weeks, and the link sent to all ESA members, individual or national (thus including most European national anaesthesia societies). We invited comments within this 4-week consultation period. We also sent the draft for review to members of the scientific subcommittees and external experts with specific expertise in these areas.

We collated the comments from all these sources and amended the guidelines as appropriate. When the final draft was complete, the Guidelines Committee and ESA Board ratified the guidelines.

After final approval, the ESA is responsible for the publication of the guidelines and for implementation programmes at the different levels. Finally, application of the guidelines throughout Europe will be monitored and a regular update of the guidelines is planned.¹⁵

How should a pre-operative consultation clinic be organised?

How, when and by whom should patients be evaluated pre-operatively?

Introduction

To provide a structured compendium of recent evidence on this topic, the 'interrogation' used the same methodological aspects as the previous guidelines,¹ which were as follows:

- (1) tools to screen patient history and physical status;
- (2) timing of pre-operative assessment;
- (3) professional qualification needed to perform the assessment.

In addition, recent literature has shown an increasing interest in tools that define surgical risk such as functional (independence, nutrition, sensory impairment, frailty) and diagnostic measures.

The need for accuracy in defining computer-based methods and tools to obtain and register clinical data was also investigated. Four thousand three hundred and fifty-five abstracts were screened for relevance; 425 papers were selected for analysis and 19 of them were included in the current guideline.

Existing evidence

Results of the literature review substantially confirmed the majority of statements on which the previous recommendations were based. In addition to the evidence reported in the previous document, the following aspects should be added.

Question 1: Tools to screen patient history and physical status

Increased use of computer-based self-assessment questionnaires is testified by a number of studies, one of which is a systematic review.^{16–19} Their use improves workflow in pre-operative assessment.²⁰

Many studies concentrate on the importance of defining surgical risk through functional measures,²¹ the evaluation of patients' fitness,²² frailty,²³ nutritional status²⁴ and sensory deficits.²⁵ The Timed Up and Go (TUG) score predicts postoperative complications in patients over 74 years of age²⁶ and identifies patients who benefit from prehabilitation better than the ASA score.²⁷

A number of studies investigated the role of BNP in defining surgical risk assessment.^{28–30} The role of pre-operative investigations is covered elsewhere.

An aspect not covered by the previous guidelines is the assessment of patients' anxiety. A recent RCT claims that anxiety assessment should be incorporated in the pre-operative consultation.³¹

Question 2: Timing of pre-operative assessment

An RCT showed that pre-operative evaluation clinics reduce consultation time and increase patient satisfaction.³² Screening patients with TUG allows identification of patients who need time for prehabilitation.²⁷

Question 3: Professional qualification needed to perform the assessment

Two systematic reviews failed to establish that pre-operative evaluation was better done either by nurses or by doctors.^{33,34} There is no new evidence for the useful participation of pharmacy personnel in the process of pre-operative assessment. There is also no new evidence about the preferred model that a patient should be seen by the same anaesthetist from pre-operative assessment through to anaesthesia.

Updated recommendations

- (1) We suggest the use of pre-operative computer-based evaluation tools, based on well conceived standardised questionnaires, whenever possible **(2B)**^{16–19}; their use may improve the quality of assessment.²⁰ **(2C)**
- (2) We recommend the implementation of functional measures such as level of independence, frailty and level of anxiety in pre-operative evaluation.^{21–27,31} **(1B)**
- (3) We suggest a sufficient time lapse between pre-operative evaluation and the scheduled procedure to allow for the implementation of any advisable pre-operative intervention aimed at improving patient outcome.³² **(2C)**
- (4) Pre-operative assessment may be carried out by a nurse or physician, but we recommend that it should be concluded by a physician anaesthetist.^{33,34} **(1C)**

How should the patient be informed about peri-operative risks?

Introduction

An emerging area of interest is that of communication processes as intrinsic elements of the pre-operative assessment. This aspect was not extensively covered by the previous version of the guideline.¹

We investigated the issue under two separate headings. First, the amount and timing of information were questioned and second we addressed methods of dissemination.

Of the 4355 abstracts screened for relevance, 425 papers were selected for analysis and 26 of them were included in the current guidelines.

Existing evidence

During our literature search, it became clear that interest in this field was greater than was evident at the preparation of the previous version of the guidelines. This was supported by a Cochrane systematic review.³⁵

Question 1: amount and timing of information

There is no clear evidence that points to an ideal amount of information to give, nor the time to give it. How effective the information might be is also controversial,^{36,37} even if most observations find improved knowledge of anaesthetic procedures, compliance with prescriptions and overall satisfaction.^{18,38–49}

A great number of studies examine the effect of any form of information on pre-operative anxiety. Some show no effect,^{36,37,44} while others report a beneficial effect.^{31,40,49–54} These contradictory results are probably related to different techniques used and, particularly, different patient groups. One RCT reports the relationship between clinicians' communication skills and pre-operative anxiety reduction.⁵⁵

Question 2: Methods of dissemination

A variety of methods have been described in the literature, spanning traditional paper forms,^{31,46,56} to sophisticated psychological interventions.^{50,51} Web-based^{18,38,39,48} and generic multimedia approaches,^{44,45,49,54,57} particularly animated videos,^{47,53} appear very effective.

Updated recommendations

- (1) We recommend the inclusion of pre-operative information in every pre-operative consultation, as it is very important to patients.^{18,36–49} **(1B)**
- (2) The preferred format of patients' education appears to be multimedia presentations, for which we suggest a web-based approach due to feasibility and ease.^{18,39,44,45,48,49,53,54} **(2B)**
- (3) We recommend applying consistent effort to improve clinicians' communication skills.⁵⁵ **(1B)**

How should a pre-operative assessment of a patient be performed?

Specific clinical conditions

Cardiovascular disease

Introduction

Of the 200 million adults undergoing major noncardiac surgery worldwide each year, an estimated 100 million are at risk for peri-operative myocardial infarction or injury and more than 10 million actually suffer major cardiac adverse events in the first 30 postoperative days. Adverse cardiac events prolong hospitalisation, increase medical costs and account for at least 30% of peri-operative mortality.⁵⁸

Pre-operative identification of patients at risk for developing peri-operative cardiac problems and possible medical optimisation of the condition may therefore greatly improve outcome. Recently, the ESC/ESA recommendations on the cardiovascular assessment and management of patients undergoing noncardiac surgery have been updated.⁶ We refer to these guidelines and recommendations for all issues related to peri-operative cardiovascular concerns.

Existing evidence

Since the 2009 guidelines on the topic,⁵⁹ new evidence has become available on a number of different issues. The recommendations on peri-operative beta-blockade have been seriously challenged after the discovery of scientific unreliability in the DECREASE studies that provided much of the evidence in its support.⁶⁰ As a consequence, the evidence on peri-operative beta-blocking therapy was critically re-analysed and the existing recommendations were modified. The only remaining 1B recommendation with regard to peri-operative beta-blocking therapy is that patients currently on this therapy should continue it during the peri-operative period. Peri-operative initiation of beta-blockers may be considered in patients scheduled for high-risk surgery and those who have at least two clinical risk factors [as assessed by the Revised Cardiac Risk Index (RCRI) score] or ASA status at least 3, and also in patients with known ischaemic heart disease or myocardial ischaemia. When pre-operative oral beta-blockade is started, bisoprolol or atenolol should be considered as first choice. There is currently no evidence to start pre-operative beta-blockade in patients scheduled for low-risk surgery.

The novelties of the 2014 ESC/ESA guidelines were highlighted in an editorial that accompanied their publication.⁶¹ First, the central leading role of the anaesthesiologist in pre-operative assessment is acknowledged. Anaesthesiologists have a leading role in identifying patients who require pre-operative evaluation by a team of integrated multidisciplinary specialists, including anaesthesiologists, cardiologists and surgeons, and when appropriate, an extended team (internists, pulmonologists or geriatricians). Selected patients include those identified by the anaesthesiologist to have the following conditions: suspected or known cardiac disease with sufficient complexity to carry peri-operative risk (congenital heart disease, unstable symptoms or low functional capacity); patients in whom pre-operative medical optimisation is expected to reduce peri-operative risk before low-risk and intermediate-risk surgery; and patients with known or high risk of cardiac disease undergoing high-risk surgery.

For stratification of pre-operative cardiac risk, the RCRI score is not the strongest in terms of discrimination, but alternatives such as the ACS National Surgical Quality Improvement Program index (NSQIP) score require

calculations (<http://www.surgicalriskcalculator.com/mior-cardiacarrest>). Therefore, the consensus view was that the two scores would provide a complementary prognostic perspective that would help the clinician in the decision-making process.

Previous ESC/ESA or AHA/ACC guidelines did not recommend the use of pre-operative and postoperative biomarkers, but the 2014 ESC/ESA guidelines suggest that cardiac troponins in high-risk patients might be assessed both before and 48 to 72 h after major surgery. Similarly, BNP measurements may be considered for obtaining independent prognostic information on peri-operative and late cardiac events in high-risk patients. It must be noted however that routine pre-operative biomarker sampling in all patients for risk stratification and to prevent cardiac events is not recommended. The impact of such biomarker measurement on peri-operative management of noncardiac surgery patients still needs to be determined, but these initial recommendations establish biomarkers as part of peri-operative management.

In addition to peri-operative beta-blockade, recent new evidence has also provided insights into the peri-operative use of aspirin and alpha-2 agonists. Whereas the 2009 guidelines supported the peri-operative use of aspirin and alpha-2 agonists in pharmacological risk reducing strategies, the results of the recent international peri-operative ischaemic evaluation (POISE-2) study indicate the need to revise these recommendations.^{62,63}

The POISE-2 trial randomised 10 010 patients undergoing noncardiac surgery to aspirin or placebo. Aspirin reduced neither the rates of death nor nonfatal myocardial infarction at 30 days [7.0% in the aspirin group versus 7.1% in the placebo group; hazard ratio 0.99, 95% confidence interval (95% CI) 0.86 to 1.15, $P = 0.92$]. Major bleeding was more common in the aspirin group than in the placebo group (4.6 versus 3.8%, respectively; hazard ratio 1.23, 95% CI 1.01 to 1.49, $P = 0.04$). The trial results therefore no longer support routine use of aspirin in patients undergoing noncardiac surgery. Of note, this study did not include patients with a bare metal stent less than 6 weeks or a drug-eluting stent less than 1 year. However, it remains uncertain whether patients with a low peri-operative bleeding risk and a high risk of thrombo-embolic events benefit from low-dose aspirin. Aspirin should therefore be discontinued if the bleeding risk outweighs the potential cardiovascular benefit. For patients undergoing spinal surgery or certain neurosurgical or ophthalmological procedures, stopping aspirin at least 7 days before is recommended. It was therefore concluded that the use of low-dose aspirin in patients undergoing noncardiac surgery should be based on individual assessment of the benefit of preventing a thrombotic complication against the risk of peri-operative bleeding.

The POISE-2 trial also randomised its 10 010 patients to clonidine or placebo. Clonidine reduced neither the rate of death nor that of nonfatal myocardial infarction in

patients undergoing vascular surgery (relative risk 1.08, 95% CI 0.93 to 1.26, $P = 0.29$). On the contrary, clonidine increased the risk of clinically important hypotension (relative risk 1.32, 95% CI 1.24 to 1.40, $P < 0.001$) and nonfatal cardiac arrest (relative risk 3.20, 95% CI 1.17 to 8.73, $P = 0.02$). Therefore, alpha-2 receptor agonists should not be considered as a peri-operative cardiac risk-reducing strategy in noncardiac surgery.

Updated recommendations

- (1) We suggest that selected patients with cardiac disease undergoing low and intermediate-risk noncardiac surgery may be referred by the anaesthesiologist for cardiological evaluation and medical optimisation.⁶ (2C)
- (2) We recommend the NSQIP model or the RCRI for cardiac peri-operative risk stratification.⁶ (1B)
- (3) We suggest considering assessment of cardiac troponins in high-risk patients, both before and 48 to 72 h after major surgery.⁶ (2B)
- (4) We suggest considering BNP measurement for obtaining independent prognostic information on peri-operative and late cardiac events in high-risk patients.⁶ (2B)
- (5) We recommend peri-operative continuation of beta-blockers in patients currently receiving this medication.⁶ (1B)
- (6) We suggest considering pre-operative initiation of beta-blockers in patients scheduled for high-risk surgery and who have at least two clinical risk factors or ASA status at least 3.⁶ (2B)
- (7) We suggest considering pre-operative initiation of beta-blockers in patients who have known ischaemic heart disease or myocardial ischaemia.⁶ (2B)
- (8) We suggest that when oral beta-blockade is initiated in patients who undergo noncardiac surgery, the use of atenolol or bisoprolol as a first choice may be considered.⁶ (2B)
- (9) We suggest that continuation of aspirin, in patients previously thus treated, may be considered in the peri-operative period, and should be based on an individual decision that takes into account the peri-operative bleeding risk weighed against the risk of thrombotic complications.⁶ (2B)
- (10) We suggest discontinuation of aspirin therapy when control of haemostasis is anticipated to be difficult during surgery.⁶ (2B)

Respiratory disease, smoking, obstructive sleep apnea syndrome

Introduction

According to the European Commission, 21% of the EU citizens are smokers, and respiratory diseases are ranked as the third most important cause of mortality within the EU (https://ec.europa.eu/health/sites/health/files/state/docs/health_glance_2016_infograph_en.pdf). Pulmonary

complications, including pneumonia, respiratory failure, exacerbation of chronic lung disease and atelectasis, pose a clinically significant postoperative risk. Established risk factors are summarised in Table 2. The questions that we asked were: faced with respiratory disease, smoking and obstructive sleep apnoea can we predict postoperative pulmonary complications (PPCs); will optimisation and/or treatment alter outcome and if so, what intervention should we make and when should we do it?

Of the 14 635 abstracts screened for the clinical conditions, 129 were identified as relevant for the current topic. Finally, 85 articles were selected for full analysis.

Existing evidence

Predicting postoperative respiratory complications

The incidence of postoperative respiratory complications in noncardiac surgery ranges from 3.1 to 9%.^{64–69} Only in the high-risk procedure of open radical oesophagectomy is a rate of 20% described.⁷⁰ However, the definitions of respiratory complications seem broad (inclusion of atelectasis), and for more severe complications, the reported rate is 1.8% for pneumonia and 0.2% for acute respiratory distress syndrome (ARDS).^{71,72}

Numerous prediction scores for postoperative respiratory failure (PRF) have been developed.^{64–68,72–74} One study analysed a data set of 211 440 patients of whom 6531 suffered from PRF. No significant association between COPD and PRF was found.⁶⁴ In a very small sample of 47 patients undergoing radical nephrectomy, an odds ratio (OR) of 7.11 for PRF was reported.⁷⁴ However, within these scores, pre-existing respiratory disease was not incorporated as its own entity but was included mainly via the ASA status. Other factors (emergency surgery, ongoing sepsis/septic shock, type and duration of surgery) are of at least equal importance in the development of PRF. One study of 405 COPD patients undergoing noncardiac surgery revealed that those suffering from COPD GOLD (Global Initiative for Chronic Obstructive Lung Disease) group C or D have an increased risk for postoperative complications compared with those classified as COPD group A or B.⁷⁵ Of note, the GOLD classification divides in four groups based on spirometry results and the severity of symptoms.

The ability of the 6 Minutes Walking Distance (6MWD) test to predict postoperative pulmonary complications (PPC) was tested by two prospective studies.^{76,77} In 78 patients scheduled for elective noncardiac surgery, a 6MWD of 325 m or less predicted PRC with 77% sensitivity and 100% specificity.⁷⁶ Conversely, in 137 patients undergoing upper gastrointestinal surgery, the 6MWD failed to predict PPC.⁷⁷

How should respiratory disease and obstructive sleep apnoea syndrome be assessed?

Spirometry Although spirometry is of value in diagnosing obstructive lung disease, recent data on risk

prediction for individual patients are contradictory. In a retrospective study of 602 patients undergoing bariatric surgery, pre-operative spirometry predicted postoperative respiratory complications only in patients suffering from OSAS.⁷⁸ Of the 37 patients diagnosed with abnormal spirometry, 31 suffered only from pulmonary restriction.⁷⁸ Conversely, in a second study of 485 patients scheduled for bariatric surgery, an obstructive pattern [forced expired volume (FEV₁)/functional vital capacity (FVC) <70%] and airflow reversibility (Δ FEV₁ >12%) were found in a multivariate analysis to be independently associated with PPCs, with an OR of 3.1 and 2.9, respectively. However, the overall pulmonary complication rate was only 1.6%.⁷⁹ Pre-operative spirometry also failed to predict postoperative FVC in 30 patients undergoing gastric banding whereas duration of pneumoperitoneum significantly contributed to postoperative pulmonary impairment.⁸⁰ A pre-operative pulmonary function test in flaccid neuromuscular scoliosis surgery did not show an increased risk for pulmonary complications in 72 patients with FVC less than 30% or FVC 30 to 50%.⁸¹ Also, in 213 patients more than 60 years old, undergoing laparoscopic assisted gastrectomy, pre-operative spirometry did not independently predict pulmonary complications.⁸² A retrospective study of 2358 surgical patients reported FEV₁ of 85.2% or less and smoking history as independent predictors for the need for peri-operative bronchodilator therapy.⁸³ Finally, a low FEV₁ and FVC were independently associated with increased long-term mortality in 223 consecutive patients receiving endovascular infrarenal aortic aneurysm repair. However, no cut-off values were reported.⁸⁴

Chest radiography No new trials on the value of pre-operative chest radiographs were identified and we refer to the first version of that guideline as well as the recommendations by NICE (HYPERLINK 'http://www.nice.org.uk/guidance/ng45').^{1,190}

Assessment of patients with obstructive sleep apnoea syndrome OSAS is a condition with an increased risk of peri-operative complications⁸⁵ and that risk is greater when the condition is undiagnosed.⁸⁶ Memtsoudis *et al.*⁸⁷ reported pulmonary outcomes in patients undergoing lower extremity orthopaedic surgery or open abdominal surgery. A huge data set with over 2.5 million orthopaedic and 3.4 million abdominal surgery cases was examined. The patients with OSAS were significantly more likely to experience PPCs such as aspiration pneumonia, ARDS and pulmonary embolisation.⁸⁷

As a testament to the importance of OSAS, the ASA has published two practice guidelines, in 2006 and 2014.^{88,89} Interestingly, a majority of patients with OSAS (especially in the bariatric population) were undiagnosed.^{90–93} Diagnosing OSAS is important for planning surgery and deciding whether ambulatory or in-patient is best. As the condition poses special risks to airway management,

there are decisions to be made as to the approach and instrument to be used,⁹⁴ and in the postoperative period, the impact of opioids must be considered, the degree of postoperative monitoring decided and the availability of continuous positive airways pressure (CPAP) devices established.⁹⁵ It is possible that starting treatment for OSAS before surgery could lead to an overall reduction in complications.⁹⁶ Therefore, screening is recommended in order to correctly identify OSAS and avoid complications.

The gold standard for diagnosing sleep-related pathologies is polysomnography and less complex screening tools are required. Although various screening questionnaires for the detection of OSAS patients are available (the Berlin questionnaire),⁹⁷ the STOP-BANG questionnaire is the most sensitive, specific⁹⁸ and best validated score.^{91,99–106}

When planning surgery in the OSAS patient, it is important to ask that whatever home device is used for positive airway pressure therapy [PAP, CPAP, bilevel positive airway pressure (BiPAP)], it is brought to the medical facility. Anxiolytic agents should be administered with caution, as they can lead to airway collapse prior to or during transport to the operating room.

There is no clear evidence for the advantage of regional anaesthesia over general anaesthesia or vice versa.

For the management of the postoperative period, a variety of recommendations exist but with no sound scientific evidence. It seems prudent to conduct close respiratory monitoring in OSAS patients undergoing major surgery that requires parenteral opioids. On the contrary, minor surgery without the need for narcotics can routinely be provided through an ambulatory facility.

Will optimisation and/or treatment alter outcome and if so, which intervention and at what time should it be done in the presence of respiratory disease, smoking and obstructive sleep apnoea?

Incentive spirometry and chest physical therapy A study on the impact of 12-week inspiratory muscle training (IMT) on pulmonary function, PI_{max} and diaphragmatic mobility in the morbidly obese found in seven versus seven patients improved PI_{max} and altered FEV₁, but there was no effect on diaphragmatic mobility.¹⁰⁷ According to a systematic Cochrane review of 12 trials including 695 adults undergoing major abdominal or cardiac surgery, IMT was associated with a reduction in postoperative atelectasis, pneumonia and duration of hospital stay. However, the authors warn of an overestimated treatment effect due to lack of adequate blinding, small-study effects and publication bias.¹⁰⁸

The effect of incentive spirometry was studied in 20 morbidly obese patients scheduled for laparoscopic bariatric surgery.¹⁰⁹ The inspiratory capacity volumes

decreased significantly on postoperative day 1 in both groups and no difference between the study groups was reported. The value of incentive spirometry in preventing respiratory complications in upper abdominal surgery was addressed by an updated Cochrane review.¹¹⁰ It included 12 studies with a total of 1834 participants and concluded that there is low-quality evidence regarding the lack of effectiveness of incentive spirometry for prevention of PPCs.

Nutrition Seventy-two patients undergoing upper abdominal surgery were enrolled in a prospective cohort study on the effect of malnutrition on respiratory muscle strength and PPCs. Malnutrition was defined by using anthropometric data (BMI) and assessment of nutritional status [including haemoglobin (Hb) levels, serum total protein and albumin levels, and weight loss]. Malnutrition was found to be significantly associated with expiratory muscle weakness, decreased chest wall expansion and postoperative respiratory complications.¹¹¹

Smoking cessation Although smokers do know a little about their increased peri-operative risks, their habit is associated with increased postoperative morbidity, including respiratory complications, impaired wound healing, surgical site infections and postoperative mortality.^{68,112–120} Acute toxic effects from inhalation and cumulative chronic effects are probably responsible.¹¹⁴

Twenty studies addressed the issue of smoking cessation. It still remains valid that stopping less than 4 weeks before surgery neither increases nor decreases the peri-operative complication rate. Myers *et al.*¹²¹ in a systematic review and meta-analysis of nine studies reported that quitting smoking within 8 weeks prior to surgery did not influence clinical outcome. However, two other systematic reviews and meta-analyses of 21 and 25 studies found that trials of at least 4 weeks' cessation had a significantly larger treatment effect than with those with shorter duration.^{122,123} In a small RCT with 130 patients with breast cancer, stopping smoking 3 to 7 days before surgery had no influence on postoperative complications.¹²⁴ A large cohort study of 607 558 patients undergoing major surgery showed that cessation for at least 1 year abolished the increased risk of postoperative mortality and reduced the risk of arterial or respiratory events.¹²⁵ However, the optimal moment to stop smoking prior to surgery, in the context of cessation more than 4 weeks before, still needs to be established.¹²⁶

A systematic Cochrane review of 13 trials enrolling in total 2010 participants found that encouragement to stop smoking with behavioural support and the offer of nicotine replacement therapy increased short-term smoking cessation rates and may reduce postoperative morbidity.¹¹⁹ A more intensive approach to smoking cessation seems more beneficial in achieving long-term abstinence.^{124,127,128} Furthermore, the evaluation of smoking

cessation by interview only provided false-positive results compared with biochemical testing (negative carbon monoxide and urine cotinine levels) in a small pilot study.¹²⁹

Updated recommendations

- (1) We do not recommend pre-operative diagnostic spirometry as a general measure to predict the risk of postoperative complications in noncardiothoracic patients.^{80–82} **(1C)**
- (2) We do not recommend routine pre-operative chest radiographs because they rarely alter peri-operative management.^{78,79,81,82} **(1C)**
- (3) We recommend that patients with obstructive sleep apnoea syndrome should be evaluated carefully for a potentially difficult airway and that special vigilance is required in the immediate postoperative period.^{94,95} **(1B)**
- (4) We recommend the use of specific questionnaires to screen for obstructive sleep apnoea syndrome when polysomnography is not available (gold standard). The STOP-BANG questionnaire is the most sensitive, specific and best validated score.^{91,99–106} **(1B)**
- (5) We suggest use of peri-operative CPAP in patients with obstructive sleep apnoea syndrome to reduce hypoxic events.^{95,96} **(2B)**
- (6) We suggest that pre-operative IMT reduces postoperative atelectasis, pneumonia and length of hospital stay.¹⁰⁸ **(2A)**
- (7) We do not suggest that pre-operative incentive spirometry helps prevent PPCs.¹¹⁰ **(2A)**
- (8) We suggest correction of malnutrition.¹¹¹ **(2C)**
- (9) We suggest that smoking cessation of at least 4 weeks prior to surgery reduces postoperative complications.^{122,123} **(2A)**
- (10) We suggest that there is insufficient evidence to indicate that short-term cessation (<4 weeks) of smoking decreases the rate of postoperative complications.¹²¹ **(2A)**

Renal disease

Introduction

Postoperative acute kidney injury (AKI) is a known complication both after cardiac and noncardiac operations.¹³⁰ and is associated with poor outcomes¹³¹ and high healthcare costs.^{132,133} Therefore, it is crucial to recognise early warning signs, predisposing factors and take timely measures. Numerous predictors of AKI such as age, emergency surgery, obesity, smoking, alcohol abuse, diabetes mellitus, hypertension and so on have been reported and should be taken into consideration before taking the patient to the operating theatre.^{134–138}

Many peri-operative measures to preserve kidney function have been proposed, including N-acetylcystein,¹³⁹ steroids¹⁴⁰ and even prophylactic postoperative renal

replacement therapy (RRT). However, no definitive benefit of these preventive measures has been shown to date.¹⁴¹

During the final stage of our guideline development process, 65 articles, dated from 2011 to 2016, were reviewed for renal disease topics and 15 of them were selected. Some large meta-analyses have been excluded because cardiac procedures were included in the analysis. The majority of studies included in our review were retrospective observational studies and this has influenced the recommendations because of lack of high-quality evidence.

It is important to note that previous recommendations from the first edition of our guideline are also valid and should be used in conjunction with our latest recommendations.¹

Existing evidence

How should the patient with impaired renal function or at risk of postoperative acute kidney injury be assessed pre-operatively?

Multiple studies have confirmed that elevated BMI, older age, low pre-operative serum albumin, pre-operative treatment with ACE inhibitors or angiotensin receptor blocker (ARB), and large intra-operative colloid infusion are all predictors of postoperative AKI.^{142,143}

CKD can be associated with a higher risk of wound infection, urinary tract infection, pneumonia and an 18% increased risk of developing acute renal failure.¹⁴⁴

Dehydration [blood urea nitrogen (BUN)/Cr >20],¹⁴⁵ low pre-operative and even slightly decreased postoperative Hb¹⁴⁶ were associated with a higher risk of postoperative AKI and longer hospital stay. Several previous studies have suggested that the BUN/Cr ratio is a sensitive marker for the detect of dehydration.^{147,148} Still, it remains unclear to what extent clinicians should react. Red blood cell (RBC) transfusion to correct pre-operative Hb could be related to additional adverse reactions and increased risk of AKI.¹⁴⁶ These extra measures could help to identify patients at risk of postoperative AKI.

In terms of renal function assessment before surgery, several studies have indicated glomerular filtration rate (GFR) to be a sensitive and more reliable predictor than serum creatinine of in-hospital mortality, 30-day postoperative mortality and development of chronic renal insufficiency.^{149–151} On the basis of these findings, we suggest using calculated GFR for renal function evaluation and prediction of postoperative morbidity and mortality in patients undergoing noncardiac procedures.

To what extent does prescribed medication influence renal function and the development of postoperative acute kidney injury?

Recent studies have confirmed that pre-operative statin therapy does not have any impact on GFR¹⁵² and that it

was not associated with improved renal function either in the long or short-term perspective.¹⁵³ More high-quality evidence is needed before a possible renoprotective effect for statins can be defined.

Evidence with regard to ACEI/ARB administration is contradictory. For years, clinicians have considered them to be nephrotoxic. Recent data, though, have demonstrated that it is diuretics rather than ACE-I/ARB that are associated with the development of postoperative AKI.¹⁵⁴ Moreover, it seems that pre-operative ACEI/ARB use is associated with a 17% lower risk of AKI and a 9% lower risk of all-cause mortality, especially in CKD patients.¹⁵⁵ Interestingly, among the different classes of diuretics, only loop diuretics were significantly associated with postoperative AKI.¹⁵⁴

Studies on other medications have revealed that antibiotic prophylaxis with gentamycin or amikacin for peri-operative infection¹⁵⁶ and intra-operative hydroxyethyl starch (HES) administration¹⁵⁷ may be associated with postoperative AKI development.

Both aspirin and clonidine given pre-operatively failed to reduce the risk of postoperative AKI development in patients undergoing noncardiac surgery.¹⁵⁸ Of note, major bleeding due to aspirin or clinically important hypotension due to clonidine were both associated with an increased risk of postoperative AKI. Peri-operative administration of aspirin and clonidine should therefore be guided by other considerations (bleeding versus thromboembolic risk) rather than renal function.¹⁵⁸

Interestingly, intra-operative remifentanyl administration resulted in a transient renoprotective effect lasting for at least 2 weeks and improved renal function in adult CKD patients undergoing orthopaedic surgery.¹⁵⁹ This was due to a direct organ-protective effect, the ability to suppress surgical stress or maintenance of haemodynamic stability during the surgery.^{160,161}

Updated recommendations

- (1) We suggest taking known risk factors (older age, obesity) into consideration while identifying patients at risk of postoperative AKI. Additional caution is warranted when administering potentially nephrotoxic medication, adjusting the volume status and controlling blood pressure in this subgroup.^{142–144} (2C)
- (2) We suggest taking into consideration test results (BUN/Cr ratio, pre-operative Hb and peri-operative Hb decrease) in order to identify patients at risk of postoperative AKI.^{145,146,148} (2B)
- (3) We suggest using calculated GFR instead of serum creatinine for renal function evaluation and prediction of postoperative morbidity and mortality in patients with impaired renal function undergoing noncardiac procedures.^{149–151} (2B)

- (4) We suggest that adding pre-operative statin therapy is of no benefit in the preservation of renal function in patients undergoing noncardiac procedures.^{152,153}
(2B)

Diabetes

Introduction

Diabetic individuals scheduled for in-patient surgery have a 1.5% risk of death after 30 days and a risk-adjusted 90-day mortality of 2.2%.^{162–164} Diabetes mellitus represents a risk factor for 90-day mortality,¹⁶⁴ and diabetic individuals have a postoperative in-hospital mortality of 3.5% compared with 0.0% in a nondiabetic control group matched for surgical procedure. They also have a significantly higher long-term mortality and incidence of infectious and cardiac complications.^{165,166}

Peri-operative hyperglycaemia is associated with an increased risk of pneumonia, bacteraemia, urinary tract infection, acute renal failure and acute myocardial infarction.¹⁶⁶ Undiagnosed diabetic individuals have a higher risk of death if they present with pre-operative hyperglycaemia.¹⁶⁶ Diabetic individuals are more likely to undergo surgery than controls.^{167,168} As the prevalence of diabetes mellitus is expected to rise, approaching 4.4% by 2030,¹⁶⁹ an increasing number will present for surgery. This is expected to result in an important additional economic burden for healthcare systems.¹⁷⁰

We therefore addressed the following questions:

- Should pre-operative assessment be used for unselective or targeted screening for the presence of diabetes mellitus/impaired glucose tolerance?
- Is there a need for pre-operative assessment of glycaemic control in patients with known diabetes mellitus/impaired glucose tolerance?
- Are there any pre-operative tests, which should be performed purely on the basis of diabetes mellitus / impaired glucose tolerance?

We screened 73 abstracts obtained from a literature search for eligibility, of which 23 remained for full-text analysis. We excluded 11 articles and added two articles retrieved by hand search,^{171,172} resulting in 14 studies fulfilling the inclusion criteria. Three of them were systematic reviews.^{173–175} The other trials were cohort analyses: three had a prospective design, while eight were retrospective analyses. We did not find any RCT. Thus, the level of evidence was rather poor. Especially lacking were randomised controlled studies comparing pre-operative blood glucose or HbA1c testing with untested controls.

Existing evidence

How should the condition be assessed?

Physicians involved in peri-operative care should base screening for diabetes mellitus /risk of hyperglycaemia on

patient history and examination or investigation of glycaemic control.

Patient history Undiagnosed diabetic individuals in particular have an elevated risk of death after surgery if presenting with pre-operative hyperglycaemia.¹⁶⁶ Euglycaemic patients suffering from diabetes mellitus had a higher 1-year mortality than those without diabetes mellitus at the same blood glucose level. Diabetic individuals with elevated blood glucose levels, however, showed a significantly lower risk of death after 1 year than hyperglycaemic patients without diagnosed diabetes mellitus.¹⁷⁶

Around 20% of patients presenting for vascular surgery will have known diabetes mellitus, 10% will have undiagnosed diabetes mellitus and 20 to 25% will have impaired glucose homeostasis when assessed with oral glucose tolerance tests.

History-based screening tools have been developed that predict the risk of diabetes mellitus or prediabetes,¹⁷⁷ and these have been developed into online risk calculators, which clinicians can use for peri-operative risk stratification. Risk factors included in this system include age, sex, family history of diabetes, exercise level and obesity.

Pre-operative blood glucose testing An oral glucose tolerance test was abnormal in 36.3% of vascular surgery patients with no known impaired glucose tolerance or diabetes mellitus.¹⁷⁸ The pre-operative glucose levels significantly predicted the risk of myocardial ischaemia within an observation period of up to 2 days after surgery. Even with a long-term follow-up, these patients had an increased incidence of cardiovascular events and a higher mortality.¹⁷⁹ Amongst patients undergoing orthopaedic surgery, pre-operative hyperglycaemia was also associated with higher mortality and an increased risk of cardiovascular or infectious complications.¹⁷³ Pre-operative hyperglycaemia more than 11.1 mmol l⁻¹ was a risk factor for surgical site infection in orthopaedic trauma patients.¹⁸⁰ Pre-operative hyperglycaemia was also associated with an elevated risk of miscellaneous postoperative complications and prolonged hospital and ICU stay in patients undergoing neurosurgery.¹⁸¹

Apart from these risk-groups, there is, however, no evidence for routine testing of blood glucose among otherwise healthy patients undergoing elective surgery.

Pre-operative HbA1c testing A systematic review analysed the evidence for pre-operative HbA1c testing on postoperative outcome among adult diabetics undergoing all kinds of surgery,¹⁷⁵ and another examined unselected adults scheduled for elective noncardiac surgery.¹⁷³ The latter also investigated the impact of pre-operative blood glucose testing. Both concluded that the level of evidence was low, due to a lack of high-quality studies. No

firm indication for pre-operative HbA1c screening in unselected patients undergoing elective surgery was found.¹⁸²

Patients undergoing arthroplasty and spine surgery represent a specific risk group in which elevated glycated Hb was associated with impaired postoperative outcome.^{173,183,184} Other smaller studies report contradictory results on the impact of pre-operative HbA1c testing. Whilst one reported an association between elevated HbA1c and postoperative wound dehiscence after plastic surgery¹⁸⁵ and major complications after abdominal surgery,¹⁸⁶ the other found that pre-operative HbA1c did not predict complications after gastric bypass surgery¹⁸⁷ or pancreaticoduodenectomy.¹⁸⁸

Pre-operative HbA1c values not only more than 8.0% but also less than 6.5% were associated with an increased length of stay in hospital.¹⁷² Another retrospective analysis of 21 541 patients scheduled for gastrointestinal surgery found an association between pre-operative HbA1c values more than 6.5% and a lower 30-day readmission rate and rate of postoperative complications.¹⁷¹ With increasing pre-operative HbA1c levels, the frequency of 48-h postoperative glucose checks increased, which might explain the improvement in postoperative outcome. In fact, peak postoperative glucose levels of more than 13.9 mmol l^{-1} were associated with increased 30-day readmission rates. The authors therefore advocate the intensive control of postoperative glucose.

The ASA recommends taking the clinical characteristics into account before ordering blood tests for glucose during preanaesthesia evaluation.¹⁸⁹ NICE guidelines do not consider routine testing for pre-operative HbA1c before surgery.¹⁹⁰

Assessment of glycaemic control in patients with known diabetes mellitus/impaired glucose tolerance

There is no evidence that routine blood glucose testing (fasting or random) during pre-operative assessment of patients with known diabetes mellitus/impaired glucose tolerance improves outcome. Accurate history remains the cornerstone of pre-operative assessment. Many patients will be under review by a diabetic service and will be monitoring their own blood glucose levels. The same holds true for HbA1c or other markers of long-term control. The 2016 NICE guideline recommend pre-operative HbA1c if the patients have not been tested within the last 3 months.¹⁹⁰

A systematic review of diabetic individuals scheduled for ambulatory surgery proposed pre-operative testing of blood glucose or HbA1c, but there are no data to indicate a threshold that decides whether surgery proceeds or is postponed.¹⁷⁴

Peri-operative treatment plans for diabetic individuals should consider glucose treatment protocols. Notably,

protocols aiming at intensive glycaemic control constitute a risk for hypoglycaemic episodes.¹⁹¹

Pre-operative assessment instituted purely on the basis of diabetes mellitus/impaired glucose tolerance

Diabetic individuals are known to be at risk of cardiovascular and renal disease. Both of these conditions may be unknown to the patient. Again, without direct evidence of benefit, consensus guidelines such as the NICE guidance¹⁹² and ACC/AHA practice guidelines,^{7,193} suggest that diabetes mellitus, particularly in higher risk surgery or in patients with identified comorbidities, should prompt some degree of cardiovascular investigation. Therefore, diabetic individuals should be assessed in accordance with the guidelines for patients at a high risk of cardiovascular or renal disease. Diabetic individuals are also at a higher risk of difficult laryngoscopy,¹⁹⁴ so although there is no direct evidence of improved outcome, careful airway assessment in diabetic patients would seem prudent.

Updated recommendations

- (1) We suggest that known diabetic individuals should be managed in accordance with guidelines on the management of patients with known or suspected cardiovascular disease.^{7,176,192,193} (2A)
- (2) We suggest that blood sugar is not routinely measured at pre-operative assessment in otherwise healthy individuals scheduled for elective noncardiac surgery, except for major orthopaedic or vascular surgery.^{173,178} (2A)
- (3) We recommend that patients at a high risk of disordered glucose homeostasis should be identified as needing specific attention to peri-operative glucose control.^{166,173} (1C)
- (4) We suggest blood glucose testing and testing for HbA1c in patients with known diabetes mellitus and patients scheduled for major orthopaedic and vascular surgery.^{166,175,190} (2A)
- (5) We suggest that patients with long-standing diabetes should undergo careful airway assessment.¹⁹⁴ (2C)

Obesity

Introduction

The prevalence of obesity in developed countries has increased significantly in recent decades. It is defined as a BMI of 30 kg m^{-2} or greater and morbid obesity as a BMI more than 35 kg m^{-2} . Supermorbid obesity is often categorised as BMI more than 50 kg m^{-2} .

Obesity has major implications for the anaesthesiologist due to the associated changes in cardiovascular, pulmonary and gastro-intestinal physiology.^{195,196} The obese are at an increased risk from procedures such as endotracheal intubation and positioning.^{197,198} Strategies are needed to reduce peri-operative risks and to enable well tolerated anaesthesia.

We screened 1576 abstracts on the topic. All comparative studies investigating an assessment or intervention with regard to pre-operative optimisation of the obese were selected. From 138 studies, we selected 75 for inclusion. We excluded the remainder due to low relevance. Unfortunately, most of the selected publications dealt with bariatric surgery, leading to a bias with respect to the type of the studies.

Existing evidence

How should the condition be assessed?

Obesity is accompanied by numerous comorbidities such as coronary artery disease, hypertension, obstructive sleep apnoea and/or metabolic syndrome. Peri-operative risk stratification should therefore concentrate on cardiac and pulmonary dysfunction and nutritional deficiencies.

Cardiovascular system Obesity is associated with several risk factors for cardiovascular diseases such as hypertension, diabetes and smoking.^{199–201} Pre-operative ECG studies showed conduction or ST-T wave abnormalities in 62% and a prolongation of the QT interval in 17% of the patients.²⁰² Doppler-echocardiography detected hypertrophy of the left ventricular posterior wall in 61% of the obese, however, without any consequences in peri-operative management.²⁰² In this investigation, stress testing using a treadmill was negative in 73% of all patients and in the remaining 27% not interpretable. Furthermore, during stress testing, a complex arrhythmia was observed in some morbidly obese patients.²⁰³ Measurement of cardiorespiratory fitness in 109 obese patients revealed a lower peak VO_2 in those with a BMI less than 45 kg m^{-2} compared with patients with higher BMI values.²⁰⁴ Using dobutamine stress echocardiography, cardiac evaluation showed normal results in 92.4% of the cases.²⁰⁵ Thus, the authors questioned the need for routine pre-operative stress testing.

Pulmonary function and obstructive sleep apnoea syndrome Pulmonary function testing showed mild restrictive pulmonary insufficiency in 20.9% of morbidly obese patients.²⁰⁶ Patients with a BMI more than 49 kg m^{-2} showed a higher incidence of dyspnoea, significantly higher PaCO_2 levels and a significantly lower vital capacity than patients with a BMI less than 49 kg m^{-2} .²⁰⁷ Furthermore, obese patients have high incidences of obstructive and restrictive pulmonary conditions and hypoxaemia.²⁰²

OSAS is apparent in up to 77% of the obese,^{208–212} whereas in the superobese (BMI $>50 \text{ kg m}^{-2}$), the incidence rises to 95%.²⁰⁸ Predictors for OSAS in the severely obese were observed sleep apnoea, male sex, higher BMI, age, fasting insulin and glycosylated HbA1c.²¹³

Endotracheal intubation In a prospective study, a BMI more than 30 kg m^{-2} and a Mallampati score of at least 2

were associated with an increased risk for difficult laryngoscopy in microscopic endolaryngeal procedures.²¹⁴ In contrast, in a prospective study in 100 morbidly obese patients (BMI $>40 \text{ kg m}^{-2}$), obesity itself was no predictor for intubation difficulties.¹⁹⁷ However, Mallampati scores at least 3, a higher Wilson score and a large neck circumference were risk factors for problematic intubation.²¹⁵

Renal system Obesity is an independent risk factor for AKI in patients older than 65 years. In a matched case-control study, it was shown that in patients undergoing colonic, orthopaedic and thoracic surgery, the odds of postoperative AKI in elderly obese patients was 1.68, indicating an increased risk compared with controls.¹⁴³ Also, in younger obese patients, morbid obesity is an independent risk factor (18 to 35 years) for renal complications.²¹⁶

Nutritional deficiencies In obese patients, the prevalence of nutritional deficiencies was calculated at up to 79.2%.²¹⁷ The prevalence of pre-operative iron deficiency was 35%, and 24% for folic acid and ferritin, resulting in a significantly higher prevalence of anaemia (35.5 versus 12%) in obese patients undergoing bariatric surgery.²¹⁸ This was supported in a recent study investigating 400 obese patients undergoing elective laparoscopic bariatric surgery.²¹⁹ In a retrospective study in patients planned for laparoscopic bariatric surgery, the prevalence of anaemia was also significantly increased in the obese, however, to a much lesser extent.²²⁰ Furthermore, numerous morbidly obese patients suffer from deficiencies in micronutrients, such as vitamin D, ascorbic acid, tocopherol and β -carotene.²²¹

Endocrine diseases Diabetes is a common comorbidity in the obese with a significantly higher prevalence than the nonobese.^{203,222} Unrecognised glucose intolerance is a common feature in the obese with a prevalence of increased HbA1c concentrations between 11.4 and 20.8%.²²³

The overall prevalence of endocrine disorders in the morbidly obese is calculated to be 47.4%.²²⁴ Interestingly, the prevalence of newly diagnosed endocrine diseases in this group prior to bariatric surgery was 16.3%, indicating the need for pre-operative detection of disorders of this nature.

Intra-operative bleeding In obese patients undergoing pancreaticoduodenectomy,²²⁵ nephrectomy²²⁶ and colorectal surgery,²²⁷ intra-operative blood loss was greater than normal-weight controls, which might be explained by the fact that surgical preparation in obese patients is more difficult.

Predictors for peri-operative complications and adverse outcome A number of predictors for adverse outcome

in the obese have been proposed. Increasing BMI correlates closely with an increasing incidence of peri-operative complications and longer hospital stay in patients undergoing spinal surgery.^{200,228,229} Peri-operative morbidity is increased in obese patients undergoing breast reconstruction,²³⁰ proctectomy,²³¹ cancer surgery²³² and oesophagectomy.²³³ In particular, superobesity (weight >150 kg)²³⁴ or a BMI more than 50 kg m⁻²^{199,200,235,236} are predictors of adverse outcomes. In obese sufferers of metabolic syndrome²³⁷ and those with elevated MELD scores,²³⁸ the risk for peri-operative morbidity seems to be further increased. In contrast, there are some studies in which no association between obesity and peri-operative outcome and/or complications has been detected.^{239,240}

Reduced cardiorespiratory fitness indicated by low VO₂ levels was associated with increased short-term complications (renal failure, unstable angina) after bariatric surgery.²⁰⁴ Abnormalities in ECG, FEV₁ less than 80%¹⁹⁹ and reduced vital capacity are all predictors of post-operative complications.²⁴¹

An increased neck circumference (> 43 cm) is an independent predictor for an increased apnoea-hypopnoea index,²⁰⁹ or for OSAS.²⁴² (2B) Additional risk factors associated with postoperative complications were smoking²³⁴ and increased age.²⁰⁰

The mortality risk in bariatric surgery can be assessed by the so-called OS-MRS, which uses five pre-operative variables, including BMI at least 50 kg m⁻², male sex, hypertension, known risk factors for pulmonary embolism and age at least 45 years. The score has been validated in 4431 consecutive patients.^{243,244}

Will optimisation and/or treatment improve outcome?

There are no studies available to answer the question whether specific optimisation and/or treatment strategies might have a positive impact on the outcome in the obese undergoing surgery.

Some authors have proposed a pre-operative reduction of body weight in order to reduce peri-operative complication rates.²⁴⁵ However, results of these studies are inconsistent. Two studies found no effects of weight loss on the frequency of complications,^{246,247} whereas in a large number of patients undergoing gastric bypass surgery, reduced complication rates were observed.²⁴⁸

It has been suggested that pre-operative weight loss leads to reduced blood loss peri-operatively,²⁴⁹ but substantially increased blood loss was detected in patients undergoing pancreaticoduodenectomy.²⁵⁰

It has been suggested that pre-operative weight loss can shorten operation times. However, results were inconsistent with not only shorter, unchanged but also prolonged operation times, which were obviously dependent on the type of surgery, whether open or laparoscopic gastric banding, or oesophagectomy.^{222,250–252}

The obese may have a higher probability of a shorter length of stay in hospital after weight reduction.²⁵³ Finally, a retrospective analysis found no differences between the morbidly obese (BMI ≥40 to 49.9 kg m⁻²) and the superobese (BMI ≥50 kg m⁻²) with regard to outcome.²⁵⁴

Because poor cardiorespiratory fitness was associated with increased short-term complication rates, improving fitness prior to bariatric surgery has been proposed.²⁰⁴ Pre-operative polysomnography also seems to be indicated regardless of symptoms due to a high incidence of sleep-related breathing disorders.²⁵⁵ Pre-operative CPAP treatment was proposed, but whether this prevents hypoxic complications remains unproven.

What intervention should the anaesthesiologist make and when should it be done?

Pre-operative assessment of risk factors, clinical evaluation^{256,257} and ECG is essential in the obese.^{202,258}

Because the prevalence of OSAS is high in the obese,^{208,242} polysomnography^{202,209,259} and/or oximetry²⁶⁰ together with the STOP-BANG questionnaire are recommended for the detection of severe OSAS.^{103,261,262} Neck circumference was an independent predictor (> 43 cm) for an apnoea-hypopnoea index at least 15, and it should be measured.²⁰⁹ In order to improve pulmonary function, pre-operative IMT²⁶³ and CPAP^{255,264} have been proposed. Patients using CPAP had a significantly lower postoperative apnoea-hypopnoea-index and a trend towards a shorter length of stay in the hospital than patients without CPAP treatment.²⁶⁴

Pre-operative pulmonary function testing is recommended, as it has been shown that patients with abnormal spirometry test results have up to three times the risk for complications after laparoscopic bariatric surgery.^{265,266} In addition, abnormal spirometry results are predictive for postoperative complications in patients with OSAS and testing should be considered in this group.²⁶⁶

Large neck circumferences and a high Mallampati score are predictors for difficult intubation in the obese; both should be measured prior to anaesthesia.^{197,214,215} In a study of 60 patients with BMI more than 30 kg m⁻², it has been shown that indirect mirror laryngoscopy might help to predict difficult intubation.²⁶⁷

Obesity reduces exercise tolerance so improving pre-operative cardiorespiratory fitness has been proposed.^{204,206,257}

Due to nutritional deficiencies in the obese, Hb levels might be reduced.^{218,220} Glucose intolerance is common in the obese and the prevalence of pathological HbA1c concentrations is increased.²²³ Thus, nutrition deficiencies should be detected and corrected prior to anaesthesia.^{217,219,221}

Updated recommendations

- (1) We suggest that pre-operative assessment of the obese includes at least the STOP-BANG questionnaire, clinical evaluation, ECG, oximetry and/or polysomnography.^{103,202,209,255–262} (2B)
- (2) We suggest laboratory tests to detect pathological glucose/HbA1c concentrations and anaemia in the obese.^{218,220,223} (2C)
- (3) We suggest that neck circumferences at least 43 cm as well as a high Mallampati score are predictors for a difficult intubation in the obese.²⁰⁹ (2C)
- (4) We suggest that the use of CPAP/PSV/BiPAP peri-operatively might reduce hypoxic events in the obese.^{255,264} (2C)

Coagulation disorders

Introduction

This section of the guideline addresses the problem of potential coagulation disorder and does not include screening for coagulation disorders. Assessment of the bleeding history, together with physical examination, is still considered the best way to identify patients with impaired haemostasis and/or an increased risk of bleeding complications during and after surgery. Platelet dysfunction is the most common defect of haemostasis, occurring in up to 5% of patients undergoing surgery. When a coagulation disorder is suspected, based on the patient's history and/or clinical examination, further haematological assessment of the condition is warranted.

Abstracts from 102 references in MEDLINE and Embase were reviewed. All comparative studies investigating an intervention or assessment with regard to pre-operative assessment and treatment of coagulation disorders were analysed and finally 11 articles were included to inform the current recommendations.

Existing evidence

How should we identify and assess patients with impaired haemostasis?

Assessment of the detailed bleeding history, including a physical examination, is still considered the best way to identify patients with impaired haemostasis and/or an increased risk of bleeding. Some studies reported an association between history and abnormal laboratory tests, but the correlation was poor.²⁶⁸ It remains still unclear whether laboratory tests for platelet dysfunction (PFA-100) provide an additional safeguard to detailed history taking, as there was no significant correlation between platelet function or treatment with platelet inhibitors and major blood loss, red cell transfusions, postoperative drainage blood loss and mortality.^{269,270} These data are in agreement with the results of another study²⁷¹ that analysed aspirin-induced platelet-inhibition. There was no correlation between aspirin intake, test results and actual intra-operative or postoperative

bleeding. However, scientific quality was low and there was no adjustment for underlying diseases. Simple laboratory tests such as platelet count do have prognostic value and should be considered in any assessment. The association between thrombocytopenia and several adverse outcomes, including the need for blood transfusion, was examined in 2097 patients scheduled for hepatic resection for hepatocellular carcinoma.²⁷² In the multivariate analysis, 340 patients with mild thrombocytopenia (100 to $149 \times 10^9 \text{ l}^{-1}$) had an OR of 1.35 (95% CI 1.01 to 1.83) and 125 patients with severe thrombocytopenia ($<100 \times 10^9 \text{ l}^{-1}$) had an OR of 1.60 (95% CI 1.02 to 2.60) for postoperative blood transfusion. The risk for other adverse outcomes was also increased. A meta-analysis on the effect of SSRI showed an elevated risk of transfusion in SSRI users in studies from orthopaedic surgery and 'any major surgery', but not in cardiac surgery (CABG). An increased risk of re-operation for bleeding complications in SSRI users was reported in breast surgery, but not in cardiac surgery. No statistically significant association between SSRI use and mortality could be identified.²⁷³

Platelets, anticoagulants and surgery; what matters?

Many patients scheduled for surgery suffer from various chronic diseases that often are treated by the use of anticoagulant medication. Moreover, vitamin K antagonists (VKAs), aspirin, and a variety of anticoagulants such as direct factor X antagonists are in use. The key question in the peri-operative setting is whether continuation or discontinuation is of benefit for patients undergoing elective surgery.

In a systematic review, Grzybowski *et al.*²⁷⁴ tried to answer this question for elderly patients undergoing cataract surgery. They searched 7 years of publications. A total of five studies, including 18 066 patients who continued their anticoagulants and 32 083 who did not, were identified. A meta-analysis was not performed by the authors, as the retrieved studies showed a high grade of heterogeneity. The results showed that there was a tendency to postoperative bleeding in the continuation groups but only minor bleeding. Their conclusion was that cataract surgery can be performed safely provided topical anaesthesia is used and a clear corneal incision is made by a skilled surgeon. The authors did not answer the question of differences in rates of complications such as cardiovascular events between groups.

In 2015, a consortium of six medical societies released an evidence-based guideline for interventional spinal and pain procedures in patients on antiplatelet and anticoagulant therapy.²⁷⁵ The guideline gives advice on the discontinuation times of the following medication: NSAIDs, antiplatelet drugs, heparin, fibrinolytic medication, new anticoagulants (Dabigatran, Rivaroxaban, Apixaban), Glycoprotein IIb/IIIa inhibitors, antidepressants and herbal medication. Relying on evidence and expert

opinion the guideline gives recommendations for when the drugs and medications mentioned above should be discontinued. These times should take into account procedural and patient characteristics in addition to pharmacokinetic properties.

In a prospective study, Akhavan-Sigari *et al.*²⁷⁶ investigated the incidence of postoperative spinal haematoma in patients undergoing spinal surgery who continued taking platelet inhibitors. Sixty-three patients out of 100 were on dual therapy using clopidogrel and aspirin and 37 patients were only taking aspirin. In their case-series, no serious bleeding complication occurred. Three patients suffered from wound dehiscence and there was one case of post-operative wound-infection. The incidence of cardiovascular complications was not investigated.

Patients after percutaneous coronary intervention who had to undergo noncardiac surgery were investigated by Yamamoto *et al.*²⁷⁷ They found that double platelet inhibition therapy was associated with significantly higher peri-operative bleeding rates than patients with single platelet inhibition (9.5 versus 2.3%, $P = 0.049$). None of the 198 patients included suffered from major cardiac events in the peri-operative period. They concluded that noncardiac surgery may be well tolerated in patients on single antiplatelet therapy after coronary stent implantation.

How platelet aggregation inhibitors influence platelet function and bleeding in the peri-operative period was examined by Thaler *et al.*²⁶⁹ in a prospective study. In a sample of 462 patients, 98 were on aspirin and 22 on clopidogrel therapy. In 101 patients (29%) not on antiplatelet medication, platelet function was abnormal on testing. Patients on aspirin ($n=98$) had abnormal findings in 65% ($n=64$) of cases and clopidogrel use correlated with pathological findings in 68% of cases ($n=15$). Bleeding and in-hospital mortality did not differ between groups. The authors concluded that neither the history of platelet inhibitors nor findings from the PFA-100 could predict peri-operative bleeding. In addition, they stated that surgery in patients taking aspirin is well tolerated and stopping clopidogrel 3 days before surgery is sufficient to prevent major bleeding.

Another retrospective study investigated a correlation between discontinuation of clopidogrel, bleeding and acute coronary syndrome. Collyer *et al.*²⁷⁸ screened a total of 1381 patients who were scheduled to undergo hip fracture surgery. Of these, 114 were on clopidogrel therapy and three were operated without stopping clopidogrel. Twenty-three patients suffered from acute coronary syndrome. The peak timing of cardiac events was between 4 and 8 days after withdrawal, whereas bleeding that needed transfusion peaked at day 1. The authors concluded that the discontinuation of clopidogrel in patients undergoing hip fracture surgery does increase the risk of coronary events. Apart from this, transfusion

rates were low in this investigation with a median transfusion of one red cell pack per patient.²⁷⁸

In a systematic review, Soo *et al.*²⁷⁹ asked whether hip fracture surgery can safely be performed while taking clopidogrel. In their literature search, 14 studies were identified and analysed. Taken together, these studies represented data from 2473 patients. Clopidogrel therapy was associated with transfusion with an OR 1.24 (95% CI 0.91 to 1.71). The number of red cell packs given, Hb levels and falls in Hb levels were not significantly different between the groups. In conclusion, hip fracture surgery can be performed on patients taking clopidogrel provided a slightly higher risk of peri-operative bleeding is accepted.

In a prospective randomised trial, Chu *et al.*²⁸⁰ compared general surgical patients who had stopped clopidogrel with patients who had not. A total of 39 patients were analysed. In both groups, there was one bleeding event that needed re-admission. No other complications were reported. There were no fatalities during the 90-day postoperative period. The conclusion was that surgery can safely be performed without discontinuing clopidogrel peri-operatively.

For patients undergoing Roux-en-Y bypass surgery, Gribsholt *et al.*²⁸¹ investigated whether therapy with glucocorticoids was associated with a higher incidence of postoperative bleeding. In a cohort of 13 195 patients, the authors found 325 patients on current glucocorticoid use and 365 on recent glucocorticoid use. The analysis showed an OR 1.2 (95% CI: 0.5 to 2.5).

Venkat *et al.*²⁷² published a retrospective analysis of risks in hepatectomy patients who suffered from thrombocytopenia. A sample of 2097 patients was analysed and the authors found thrombocytopenia to be independently associated with adverse outcomes. For a platelet count less than $100 \times 10^9 \text{ l}^{-1}$ mortality, septic complications, renal failure and septic shock had a significantly higher incidence in comparison to a platelet count above $100 \times 10^9 \text{ l}^{-1}$.

Does pre-operative or intra-operative correction of haemostasis decrease peri-operative bleeding?

There is some information relevant to pre-operative evaluation on the benefits of prophylactic pre-operative correction of acquired and congenital platelet dysfunction that has the potential to cause significant peri-operative bleeding in noncardiac surgery. There is evidence from several patient groups on the risks and benefits of this approach.

PCC are recommended as the treatment of choice in warfarin-related coagulopathy. There is a low risk of thromboembolism in patients treated with VKAs receiving PCC to reverse anticoagulation.²⁸² This was confirmed by another study showing that pharmacological

reversal of warfarin-associated coagulopathy with a combination of vitamin K and FFP appears to be a well tolerated way to optimise patients for operative fixation of hip fractures. It was associated with a shorter surgical delay in patients with elevated pre-operative INR.²⁸³ In trauma patients with hip fractures, Collyer *et al.*²⁷⁸ demonstrated that the cardiovascular risk of routinely interrupting clopidogrel therapy required a considered, individualised and evidenced-based approach. There are also studies that show that clopidogrel can be continued without increased bleeding.²⁸⁰ Thirty-nine patients were enrolled and underwent 43 general surgical operations. No peri-operative deaths, bleeding requiring blood transfusion or re-operations occurred.

A systematic review and meta-analysis by Soo *et al.*²⁷⁹ showed that hip fracture patients can be managed by normal protocols with early surgery. Operating early on patients taking clopidogrel was well tolerated and did not appear to confer any clinically significant bleeding risk. Clopidogrel should not be withheld throughout the peri-operative period due to the increased risk of cardiovascular events associated with stopping it. Greater intra-operative care should be taken to minimise blood loss due to the increased potential for bleeding.²⁷⁹

Updated recommendations

- (1) We recommend assessment of the bleeding history, including a physical examination, as the best way to identify patients with impaired haemostasis and/or an increased risk of bleeding complications during and after surgery.²⁶⁸ (1B)
- (2) We suggest that, in addition to detailed history taking, laboratory tests can be used to improve identification of coagulation disorders.^{269,270} (2C)
- (3) We suggest that simple laboratory tests like platelet count may have a prognostic value and can be used in the evaluation.^{272,273} (2A)
- (4) We suggest that cataract surgery with continued anticoagulant medication can be performed safely provided that topical anaesthesia is used and a clear corneal incision is made by a skilled surgeon.²⁷⁴ (2B)
- (5) We suggest that noncardiac surgery may be safely performed in patients on single antiplatelet therapy after coronary stent implantation.²⁷⁷ (2B)
- (6) We suggest that neither a history of platelet inhibitors nor findings from the PFA-100 can predict peri-operative bleeding. Surgery for hip fracture in patients taking aspirin is considered well tolerated and stopping clopidogrel for 3 days is sufficient to prevent major bleeding.^{269–271} (2B)
- (7) We recommend that hip fracture surgery can be safely performed without stopping clopidogrel peri-operatively.^{278,279} (1B)
- (8) We suggest that if reversal of warfarin-associated coagulopathy is necessary, primarily PCC are to be

used. In the absence of PCC, the combination of FFP and vitamin K is a possibility.^{282,283} (2C)

- (9) We recommend an evidence-based approach in the decision to withdraw clopidogrel in specific patient groups because of the potential risks.²⁷⁸ (1C)
- (10) We suggest that elective surgical procedures can be safely performed while on clopidogrel without increased peri-operative bleeding risk.²⁸⁰ (2C)

Anaemia and pre-operative blood conservation strategies

Introduction

It is widely known that low pre-operative Hb levels are associated with increased morbidity and mortality, longer hospital stay²⁸⁴ and a higher rate of allogeneic blood transfusion, which is itself associated with an increased risk of various adverse effects.²⁸⁵ In order to update the anaemia topic from the previous pre-operative assessment guideline,¹ we have analysed recent studies of those at risk of postoperative anaemia undergoing major orthopaedic or colorectal cancer operations. The majority of these included slightly anaemic patients.

In all studies, anaemia was defined according to the WHO definition ($<12 \text{ g dl}^{-1}$ for women, $<13 \text{ g dl}^{-1}$ for men).²⁸⁶ Autologous blood donation and various blood conservation strategies were popular methods of pre-operative anaemia management, but with time, the use of pre-operative autologous donation has declined due to logistical problems and wastage.²⁸⁷ Other methods and recommendations for treatment have been investigated and will be discussed in this section.

By the end of the guideline process, 105 articles on peri-operative anaemia management were reviewed and 22 large sample size prospective or retrospective observational studies and RCTs were included, all comparative studies with anaemic pre-operative patients or those at risk of postoperative anaemia.

Existing evidence

Do intravenous or oral iron supplements administered with or without erythropoiesis stimulating agents (erythropoietin) have any positive impact on the outcome of pre-operative anaemia or those at risk of postoperative anaemia?

Studies on anaemic orthopaedic and colon cancer surgical patients revealed that pre-operative administration of parenteral iron supplements resulted in significantly higher Hb levels immediately after surgery,²⁸⁸ at hospital discharge²⁸⁹ and at 4-week follow-up.²⁹⁰ Baseline Hb levels were achieved sooner than standard care,²⁹¹ and intravenous iron was more effective than oral.²⁹² However, evidence on transfusion rates are contradictory. Although two studies stated that parenteral iron had no significant impact on the incidences of transfusion, hospital infections, postdischarge morbidity, length of hospital stay or total mortality,^{291,292} Calleja *et al.*²⁸⁹ reported

that a significantly lower percentage of patients required allogeneic blood transfusion.

Three studies analysing benefits of erythropoietin were included in our analysis and all three demonstrated significantly increased mean and discharge Hb levels^{293,294} and fewer autologous blood transfusions.^{293,295} Nevertheless, bearing in mind that erythropoietin may have adverse effects, it should only be used if other causes of anaemia have been excluded or treated, and mostly for renal anaemia or anaemia associated with chronic disease.

Although there may be advantages to iron supplements and erythropoietin when administered separately, two studies confirmed significantly higher Hb levels and fewer transfusions^{296,297} in orthopaedic cohorts when they were combined. This combination also had a positive impact in reducing postoperative nosocomial infection rates, the 30-day mortality rate and shortening length of hospital stay after major orthopaedic procedures.²⁹⁷

Parenteral iron, erythropoietin or combination of the latter could serve as an alternative to blood transfusion and have a positive impact on outcome.

Do blood management decisions influence routine practice and outcome? Does implementation of blood management principles or goal-directed blood transfusion policy make any significant difference?

PBM relies on multimodal and multidisciplinary strategies that allow the detection and treatment of peri-operative anaemia, the reduction of surgical blood loss, less risk of peri-operative coagulopathy and optimisation of haematopoiesis and anaemia tolerance.^{298,299} Several studies analysing the effect of PBM implementation reported significantly increased tranexamic acid administration,³⁰⁰ Hb concentration,^{300,301} fewer allogeneic blood transfusions and fewer PRBC units given^{301,302} compared with standard care.³⁰⁰ Goal-directed transfusion policy was also proven to be an effective management approach with significantly increased RBC, Hb and Hct levels and shorter wound healing time.³⁰³

Do other measures such as tranexamic acid, cell salvage or pre-operative autologous blood donation make any difference to outcome of patients suffering from pre-operative anaemia?

Tranexamic acid administration was shown to reduce transfusion and complication rates. It may prove a beneficial adjunct for anaemic TIA patients.³⁰⁴

Conflicting evidence suggests that patients receiving cell salvaged blood are less likely to require allogeneic RBC transfusion.³⁰⁵

Pre-operative donation of autologous blood is a controversial measure. Using it to treat anaemia has resulted in fewer allogeneic blood transfusions and a higher discharge Hb, even though the overall transfusion rate

was higher.³⁰⁶ Others argue that allogeneic blood donation could induce iron deficiency and anaemia.³⁰⁷ Oral administration of ferrous bisglycinate chelate has been proposed as an effective and well tolerated therapy to support a pre-operative autologous blood donation programme.³⁰⁸

Updated recommendations

- (1) We recommend treating known iron deficiency anaemia with intravenous iron before elective procedures.^{288–292} **(1B)**
- (2) We recommend using parenteral iron rather than oral iron supplements for iron deficiency anaemia before elective procedures.²⁹² **(1C)**
- (3) We suggest using erythropoietin supplements for anaemic patients before elective surgery and those at risk of postoperative anaemia once other causes of anaemia have been excluded or treated.^{293,295} **(2B)**
- (4) For the best results in peri-operative anaemia management, we recommend using intravenous iron together with erythropoiesis-stimulating agents.^{296,297} **(1C)**
- (5) We recommend implementing PBM principles and goal-directed transfusion policy into daily hospital practice.^{298–301,303} **(1C)**
- (6) We recommend using tranexamic acid for known anaemic patients and those at risk of postoperative anaemia undergoing elective joint arthroplasty.³⁰⁴ **(1C)**
- (7) We suggest using cell salvage for all patients having orthopaedic procedures with anticipated high blood loss.^{295,305} **(2B)**
- (8) We suggest that pre-operative donation of autologous blood (or acute normovolaemic haemodilution) should be considered carefully and used according to individual condition and the type of surgery.^{306,308} **(2C)**

The geriatric patient

Introduction

In Europe in 2016, it was estimated that the geriatric population (≥ 65 years) represented 16.8% of the global population and that the subgroup that would grow the fastest (from the actual 5.3 to 9% in 2040) would be that of those more than 80 years old. This suggests dramatic growth in the number of elderly patients undergoing an increasing variety of surgical and nonsurgical interventional procedures. The recently published WHO 'World Report on Ageing and Health' reveals multiple morbidities in 10 to 24% of Europeans older than 80 years. In addition, the prevalence of impairment in daily active life in Europeans older than 75 years ranges from 14 to 50%.³⁰⁹ Little is known about the peri-interventional 30-day mortality rates in the geriatric patient. Compared with younger patients, the elderly are at a greater risk of mortality and morbidity after elective and especially

emergency surgery.³¹⁰ The underlying mechanisms include age-related decline in physiological and cognitive reserve and frequent comorbidities such as impaired renal and hepatic function, diabetes mellitus, dementia, delirium, coronary artery disease, heart failure and polypharmacy.

In the present section, 130 abstracts from Cluster 2 and 30 abstracts from Cluster 1 of potential interest have been identified. After eliminating duplication, 142 abstracts remained and were screened. From these, 83 articles were eliminated for being irrelevant to the topic or for referring to postoperative delirium (POD). Of note, POD was not included because the recently issued 'ESA evidence-based and consensus-based guidelines on postoperative delirium' was considered as the main referral point.³¹¹ Fifty-four relevant articles remained on which to base the recommendations.

In addition, the task force members identified four relevant guidelines, which had been missed in the search process.^{311–314} In total, 58 papers formed the basis for building the following 10 recommendations. Every recommendation includes a pathophysiological/epidemiological comment, an analysis of the risk factor as a premise for the core recommendation and recommended evaluation score/criteria. Recommendations refer to factors that were shown to increase surgical risk in the elderly in the selected studies. Conceptual pillars are both age-related pathophysiological changes and evidence supporting their role as predictors of complications or surgical adverse outcome. The ageing processes that reduce functional reserve in a variable measure, and the associated conditions, the number of which increases with age, are major determinants of this increased risk.

Existing evidence

What factors should be evaluated to assess surgical risk in the geriatric patient?

Functional status and level of independence Functional status is the sum of abilities that are needed to maintain daily activities, including social and cognitive functions.³¹⁵ It determines the patient's ability to autonomously perform basal activities of daily living (BADL) and IADL. With age, these abilities can reduce due to changes in active motion, cognition, affective status and sensorial functions, associated conditions and poor nutritional status. Functional dependence has been shown to predict mortality after surgery in a number of prospective cohort studies^{316–329} and in three guidelines.^{311,312,314} It was also shown to be a risk factor for cognitive and noncognitive postoperative complications.^{311,312}

The level of independence can be quantified by scoring the number of preserved BADL and IADL abilities. Comprehensive Geriatric Assessment (CGA) provides a more inclusive approach; several studies and systematic reviews confirmed its usefulness in predicting outcome in

surgical geriatric patients. CGA is also recommended by the Association of Anaesthetists of Great Britain and Ireland, the American College of Surgeons – National Surgical Quality Improvement Program (ACS-NSQIP) and the American Geriatrics Society guidelines in the risk assessment of the elderly.^{312,314,330–332} TUG testing is another useful score.

Comorbidities Chronic disease is present in more than 50% of patients more than 70 years old; the most common are hypertension, coronary artery disease, diabetes and chronic obstructive pulmonary disease, with respective prevalences of 40 to 50, 35 to 40, 12 to 15 and 7 to 9%. With advancing age, renal function also declines. Thirty percent of those more than 70 years old suffer from multiple comorbidities. Age and disease combine to reduce resistance to stress making older patients more vulnerable to cardiac and respiratory adverse events. Identification of patients at risk is critical to the planning of peri-operative management.^{314,333–337} The presence of associated conditions – mostly cardiac and respiratory – before surgery was shown to be an important risk factor for increased rates of postoperative complications and mortality, and is addressed in the guidelines of the Association of Anaesthetists of Great Britain and Ireland and the American Geriatrics Society.^{312,314}

Polymedication and use of inappropriate medication In comparison to young adults, the elderly are greater consumers of medication due to comorbidity, multiple prescriptions and use of nonprescribed or over-the-counter drugs, which they often fail to report. Age-related changes in drug metabolism increase the risk of overdose and drug accumulation. Polymedication (three or more different drugs per day) and use of inappropriate medication (such as anticholinergics or sedatives) was shown to increase the risk of cognitive and noncognitive complications such as POD and ADE in several studies and three guidelines.^{311,312,314,338}

Cognition The prevalence of cognitive impairment exponentially increases with age. Alzheimer's disease is present in 50 to 80% of all cases. Other types include vascular dementia (20 to 30%), frontotemporal dementia (5 to 10%) and dementia with Lewy bodies (<5%). Advanced Parkinson's disease can be accompanied by cognitive deterioration. Cognitive impairment may compromise comprehension and the ability to make decisions, and is an important risk factor for POD and postoperative cognitive dysfunction (POCD). A result is more cognitive and noncognitive complications, prolonged hospital stay and higher mortality. Cognitive assessment is recommended in patients more than 65 years of age, even without a history of cognitive decline.^{311,312,314,339–341} Basal cognitive assessment, such as Mini-Cog or Clock test, is recommended for screening for cognitive decline. When present, it is an indication for

further investigation designed to quantify the deficit, identify the individual opportunities for possible improvement such as stopping nonessential medication that might affect cognition, provide cognitive prehabilitation and define the ability to make decisions.^{311,312,314,339–341}

Depression Ageing is accompanied by an increased prevalence of depression, mostly with predisposing factors such as female sex, loss of companion, disability and sleep disturbance. The diagnosis of cancer may precipitate emotional imbalance. Depressed patients are less compliant with medical direction and their postoperative pain is more difficult to treat. Depression has been shown to be a risk factor for POD, longer hospital stay and greater mortality, mostly after cardiac surgery. Screening should be performed using validated scales such as the Geriatric Depression Scale, of which different versions exist. Cognitive impairment may affect the score.^{311,314}

Postoperative delirium POD is a serious, preventable postoperative complication frequently occurring in the elderly. Its incidence ranges between 4 and 53.3% and varies with risk factors, surgical procedure and peri-operative management. It causes prolonged hospital stay and increased morbidity and mortality. In the elderly, risk factors for POD may accumulate and overlap. Dementia is the main predisposing factor and long-term cognitive consequences can be extremely serious. Careful risk assessment and appropriate management of risk factors are key issues. According to the European Society of Anaesthesiology evidence-based and consensus-based guidelines, cognitive impairment, comorbidity, frailty, use of inappropriate medication (especially anticholinergics and sedatives), polymedication, impaired functional status, sensorial deficits, malnutrition and alcohol abuse are risk factors for POD. Careful POD risk assessment and appropriate peri-operative management are key to reducing its consequences.³¹¹

Sensory impairment With ageing, visual and hearing deficits become more frequent. Fifty percent of those over 70 years old present with presbycusis. Cataract, macular degeneration and glaucoma affect 50 to 70% of over the over 65s, creating difficulties in reading written instructions. Sensory impairment is a risk factor for depression and POD. Communication can be hampered by visual and hearing deficits. It is important that, when interacting with patients with possible sensorial deficit, they are detected, appropriate allowance is made and a decision is made whether further measures are needed.^{25,312,314}

Nutritional status Poor nutrition is observed in 6% of the over 70s due to drug-induced loss of appetite, difficulty in chewing or swallowing, depression, loneliness or economic restraints. It is more frequent in hospitals (40%) and nursing homes.³⁴² Risk factors for major peri-operative

nutritional problems are reduced BMI, serum albumin less than 30 g l⁻¹ and unintentional weight loss. Obesity is associated with an increased risk of kidney injury. Malnutrition is associated with an increased risk of POD, infectious and noninfectious complications, prolonged hospital stay and wound complications.^{143,312–314,342–344}

Frailty Frailty is an age-dependent multisystem disorder consisting of reduced resistance to causes of stress. It is associated with physiological decline, comorbidity, disability, risk of institutionalisation and death. Its prevalence is high in the surgical population. As early stages of frailty can be reversed, understanding onset points (malnutrition, inappropriate medication, the need for psychological and social support) allows targeted interventions. Frailty can be assessed by single (hand-grip strength, TUG) or multiple (Fried Score, Edmonton Frailty Score) tests. Frail patients are at a major risk of adverse surgical outcome and in-hospital falls. Frailty is independently associated with increased peri-operative risk.^{22,23,311,312,314,337,339,345–360}

Updated recommendations

- (1) Functional status can be impaired among the elderly and predicts functional outcome. We recommend the assessment of functional status, preferably through comprehensive geriatric measures to identify patients at risk and/or to predict complications.^{311,312,314,316–329} **(1B)**
- (2) Level of independence may be impaired that predicts complications. We recommend scoring the level of independence using validated tools such as the Basal and Instrumental Activities of Daily Life.^{312,314,330–332} **(1B)**
- (3) Comorbidity and multiple morbidities become more frequent with ageing and are related to increased morbidity and mortality. We recommend the assessment of comorbidities and multiple morbidities using age-adjusted scores, such as the Charlson Comorbidity Index.^{312,314,333–337} **(1B)**
- (4) Polymedication and inappropriate medication (mostly anticholinergic or sedative-hypnotic drugs) are common and predict complications and mortality. We recommend the consideration of appropriate peri-operative medication adjustments. We recommend the evaluation of medication in a structured way, such as the Beers criteria.^{311,312,314,338} **(1B)**
- (5) Cognitive impairment is frequent and often underevaluated. It may affect comprehension, hampering appropriate informed consent. Cognitive impairment predicts complications and mortality. We recommend the evaluation of cognitive function based on validated tools.^{311,312,314,339–341} **(1B)**
- (6) Depression is frequent in the elderly and is related to increased complication rates. We recommend the assessment of depression by validated tools.^{311,314} **(1B)**

- (7) We recommend the evaluation and management of risk factors for postoperative delirium in accordance with the ESA evidence-based and consensus-based guidelines on postoperative delirium.³¹¹ **(1B)**
- (8) Sensory impairment weakens communication and is associated with postoperative delirium. We recommend the assessment of sensory impairment and to minimise time spent in the peri-operative setting without sensory aids.^{25,312,314} **(1B)**
- (9) Malnutrition is frequent, often underevaluated and predicts complications. Obesity is associated with an increased risk for kidney injury. We recommend the assessment of nutritional status (preferably by Nutritional Risk Screening) before making the appropriate interventions in patients at risk and that pre-operative fasting is minimised.^{143,312–314,343,344} **(1B)**
- (10) Frailty is a state of extreme vulnerability. It predicts morbidity and mortality. We recommend the assessment of frailty in a structured, multimodal way such as the Fried Score or Edmonton Frailty Scale, avoiding surrogate single measures.^{22,23,311,312,314,337,339,345–360} **(1B)**

Alcohol and drug misuse and addiction

Introduction

According to the 'Health at Glance: Europe 2016' report of the European Commission, alcohol-related harm is regarded as the third leading risk factor for disease and mortality (https://ec.europa.eu/health/sites/health/files/state/docs/health_glance_2016_rep_en.pdf). The overall pre-operative prevalence of AUD ranges between 5 and 16%, while the prevalence of severe misuse is reported to be between 2 and 4% in the year preceding a surgical procedure.^{361,362} More than one quarter of adults in the European Union (88 million people) have used illicit drugs, mostly cannabis, at some point in their lives.

Pre-operative AUDs are associated with an increased risk of general postoperative morbidity such as general infections, wound complications, pulmonary complications, prolonged length of stay and admission to the ICU.^{363–365} High alcohol consumption (commonly defined as $>24\text{ g day}^{-1}$ for women and $>36\text{ g day}^{-1}$ for men³⁶⁶) is also associated with an increased risk of postoperative mortality.^{366–368} Data on the risks of drug and illicit substance abuse (ISA) are scarce with one study reporting a prolonged length of stay in patients taking narcotic drugs,³⁶⁹ while in another study, a documented ISA in the previous 12 months was not associated with increased length of PACU and/or hospital stay in a control matched cohort.³⁷⁰

After identification of 659 abstracts for the total number of guideline topics, 26 were allocated to the chapter 'alcohol misuse and addiction'. Two researchers reached a final consensus, choosing 17 for analysis.

Existing evidence

How should addiction and drug abuse be assessed pre-operatively?

The detection of harmful alcohol consumption is regularly assessed with ISA-validated questionnaires. Following the ESA guideline of 2011, no new publications dealing with laboratory tests were found. Nonetheless, they still seem valuable for the identification of AUD. Gamma gluteryl transferase (GGT) and carbohydrate-deficient transferrin (CDT) were reported to be superior to ALT in the detection of high-risk alcohol consumption, with CDT having the highest specificity (92%).³⁷¹

For the detection of AUD, the following questionnaires are used: the CAGE questionnaire; the 10-item AUDIT list; the shorter form asking only three alcohol consumption questions (AUDIT-C); the US National Institute on Alcohol Abuse and Alcoholism two and four questions tests (NIAAA-2Q/4Q).^{372–375} There was no new evidence on the value of combining laboratory tests and questionnaires for detecting AUD. Hence, we refer to the 2011 ESA guideline, which advised that combining the CAGE questionnaire with GGT and CDT showed the highest sensitivity.³⁷⁶

One prospective trial ($n=1556$) tested the ability of the AUDIT-C versus the full AUDIT score to identify AUD in a pre-operative assessment clinic. Both scores were assessed and more than 10% of all female and male patients were either AUDIT-C-positive while AUDIT-negative or vice versa.³⁷⁴ In conclusion, Neumann *et al.*³⁷⁴ were unable to show that the short version of the AUDIT-questionnaire (AUDIT-C) had comparable results to the original AUDIT-tool.

In a prospective study, the National Institute of Alcohol and Alcoholism tools NIAAA-2Q and NIAAA-4Q tool were tested against the AUDIT score during a pre-operative bedside visit to 200 surgical patients to identify unhealthy drinkers. The reported sensitivity and specificity were 0.79 and 0.87, respectively, for NIAAA-4Q and 0.19 and 0.9 for NIAAA-2Q.³⁷⁵

In a sample of 2938 patients, pre-operative computer based self-assessment has proven to be superior to medical history taking during routine anaesthetic evaluation in the detection of ISU.³⁷⁰ The detection rate by anaesthetists was higher in more frequent users.

A retrospective matched cohort study ($n=300$) examined the risk for intra-operative adverse haemodynamic events in patients who tested cocaine positive on a urine drug screen at hospital admission.³⁷⁷ The cocaine-positive cohort did not show more haemodynamic adverse events. This is explained by the fact that the cocaine half-life time is short (1 to 1.5 h) and the urine screening test detects cocaine metabolites up to 14 days after consumption. However, in a survey among anaesthesia departments of the Veterans Affairs health system, two-thirds of respondents cancelled or delayed patients with a positive screen regardless of clinical symptoms.³⁷⁸ Only 11% of the facilities ($n=11$) had a formal policy in place.

Will optimisation and/or treatment alter outcome and what intervention (and at what time) should be made by the anaesthetist in the presence of a specific condition?

According to a Cochrane review composed of two RCTs ($n=69$), alcohol abstinence significantly decreased post-operative complications, but no effect on mortality and length of stay was reported.³⁷⁹ A cohort study of 8811 male Veterans Affairs patients undergoing elective non-cardiac surgery showed that a past year AUDIT-C score more than 4 was only associated with an increased risk of peri-operative complications if more than two drinks per day (28 g ethanol) were consumed in the 2 weeks prior to surgery.³⁸⁰ However, timing, duration and intensity of measures around alcohol cessation need to be subject to further investigation.³⁷⁹

Updated recommendations

- (1) We recommend that for the pre-operative detection of AUD, a combination of the standardised CAGE questionnaires and laboratory tests such as GGT and CDT should be used, as they appear superior to the sole use of laboratory tests or using a questionnaire alone.³⁷⁶ **(1B)**
- (2) We recommend using only the combination of GGT and CDT as biomarkers for the pre-operative identification of AUD, as they provide the highest sensitivity.³⁷¹ **(1C)**
- (3) We recommend the use of a computerised self-assessment questionnaire, as it appears superior to an interview by an anaesthesiologist in the identification of patients with AUD and illicit substance use.^{370,374} **(1C)**
- (4) We recommend attention is drawn to the fact that the AUDIT-C and the AUDIT score are not interchangeable for the detection of AUD in pre-operative assessment.³⁷⁰ **(1C)**
- (5) We suggest that the NIAAA-4Q tool can be used pre-operatively to identify AUD.³⁷⁵ **(2C)**
- (6) We recommend pre-operative alcohol cessation measures, including pharmacological strategies to prevent relapse and withdrawal symptoms, as they may significantly reduce postoperative complication rates.^{379,380} **(1B)**
- (7) We have no suggestions for the timing, duration and intensity of alcohol cessation measures.³⁷⁹ **(2A)**
- (8) A positive pre-operative cocaine screen may not be associated with adverse intra-operative haemodynamic events. When evaluating these patients, we suggest that clinical symptoms of cocaine abuse should be sought.^{377,378} **(2C)**

Neuromuscular disease

Introduction

As the population ages, the prevalence of many neurological diseases is increasing.³⁸¹ At the same time, older patients are undergoing more surgical procedures.³⁸¹

Neuromuscular diseases do have a certain impact on the peri-operative outcome and, therefore, need to be evaluated properly prior to anaesthesia.³⁸² Neuromuscular disorders, myopathic disorders and other neurological diseases should be differentiated.

Existing evidence

How should this condition be assessed?

The pre-anaesthetic assessment aims at the detection of potentially undiagnosed myopathic patients and, in case of known or suspected muscular disease, on the quantification of disease progression. Ancillary testing (echocardiography, ECG, lung function testing) is frequently indicated, even at a young patient age. Early pre-operative consultation is recommended for patients with severe, poorly controlled or decompensated neurological disease, a recent stroke, or those undergoing procedures with a high risk of neurological complications.³⁸¹

We must differentiate between myopathies associated with malignant hyperthermia and those that are not, as this has significant impact on pre-operative preparation of the anaesthesia workstation and pharmacological management.^{383,384} If the myopathic patient is at risk of malignant hyperthermia, all trigger substances (inhalation agents, succinylcholine) must be avoided.

What is the influence of neuromuscular diseases?

The main risks for surgery in patients with any underlying neuromuscular disorder are respiratory and cardiac complications, some of which may be life-threatening.

Because most of these diseases are chronic in nature, identification and risk stratification during the pre-operative period is beneficial to minimise potential complications and improve surgical outcome. Pulmonary and cardiac testing should be recommended on an individual basis.³⁸⁴

There should be an assessment of pulmonary function including vital capacity and FVC and for cardiac assessment an ECG and especially a TTE should be obtained for quantifying the degree of cardiomyopathy. Also, receptor diseases – like myasthenia gravis – are associated with the above-mentioned functional impairments.³⁸⁴

In general, patients with these disorders are more sensitive to respiratory depression from opioids, benzodiazepines and barbiturates. They are also at risk for adverse responses to certain anaesthetic agents and neuromuscular blockers. There is an increased sensitivity to non-depolarising agents and the potential for severe reactions to depolarising agents such as succinylcholine, so these agents should be used with caution or avoided altogether, depending on the disease. Therefore, monitoring neuromuscular function should be obligatory.³⁸⁴

After the procedure, a prolonged stay in the recovery room or an ICU-stay should be included in the plan.

Will optimisation and/or treatment improve outcome?

The neurologist's role includes optimising management of pre-existing diseases, such as epilepsy, neuromuscular disorders, Parkinson's disease, dementia and cerebrovascular disease, in addition to providing guidance for peri-operative management and clarification of risks. In the postoperative period, the neurologist will frequently be consulted to mitigate any negative impact of neurological complications that do occur.³⁸¹

Updated recommendations

- (1) We suggest early pre-operative consultation for patients with severe, poorly controlled or decompensated neurological disease, a recent stroke or those undergoing procedures with a high risk of neurological complications.³⁸¹ (2B)
- (2) We suggest an assessment of pulmonary function including VC and FVC. For assessment of cardiac function, we suggest an ECG and TTE be obtained for quantifying the degree of cardiomyopathy.³⁸⁴ (2B)
- (3) We suggest that pre-operative optimisation and/or treatment may improve the outcome.³⁸¹ (2C)

How to deal with the following concurrent medication?

Herbal medication

Introduction

Herbal over-the-counter drugs as well as dietary supplements pose an increasing risk because of side effects due to the uncontrolled intake of these substances. Various studies have reported a wide range of consumption of remedies containing *Gingko biloba*, *Panax Ginseng*, *Allium sativum* (Garlic), *Zingiber officinale* (Ginger), Green Tea, Vitamin E and Fish oil.^{385–388} A cross-sectional survey of practice and policies within anaesthetic departments in the UK showed that 98.3% of departments did not have a specific section for documenting herbal medicine use. Only 15.7% of the departments that held preassessment clinics asked routinely about herbal medicines and the patients themselves in most of the cases did not inform the anaesthesiologist about the use of herbal substances.^{389,390} Therefore, questionnaires on the chronic use of such substances are available for use in pre-operative evaluation.³⁸⁷

A total of 3661 abstracts were screened under the topic 'concurrent medication'. Fifty-one abstracts were kept for analysis on the topic 'herbal medication'. The final number of articles analysed was 15.

Existing evidence

Garlic, Ginseng, *Gingko*, Ginger, Vitamin E and Green tea can all affect haemostasis. Both garlic and ginseng are known platelet aggregation inhibitors. Garlic acts in a

dose-dependent manner. Ginseng also diminishes the effect of VKA and *Gingko* is a platelet-activating factor antagonist.³⁹¹ A recent narrative review provides an overview of the haemostatic effects of a wide range of herbal products.³⁹² The clinical significance of these effects remains unclear, as most of the reports cited are case reports and small sample case studies.^{393–395} A randomised controlled study in volunteers found no effect of *Gingko biloba* extracts on bleeding time and coagulation.³⁹⁶ The recommendation on stopping these drugs prior to surgery remain controversial, while the ESA guideline on peri-operative management of severe bleeding and a systematic review do not support stopping *Gingko biloba* extracts,^{397,398} others do.³⁹¹ As the effect that these drugs have on haemostasis has been proven in *in vitro* studies, we recommend weighing up carefully whether to stop or continue before 'closed compartment' surgery such as intracranial procedures.

Another herbal drug that is often used is St John's wort (*Hypericum perforatum*). St John's wort interacts with other drugs relevant to anaesthesia such as alfentanil, midazolam, lidocaine, calcium channel blockers and serotonin receptor antagonists. It is recommended that it is stopped at least 5 days prior to surgery.³⁹⁹

Valerian officinalis is used for the treatment of insomnia. Its abrupt discontinuation resembles benzodiazepine withdrawal and can be treated with benzodiazepines should withdrawal symptoms develop during the peri-operative period. It may be prudent to taper the dose of valerian over several weeks before surgery.^{399,400}

Updated recommendations

- (1) We suggest that patients are asked explicitly about their intake of herbal drugs, particularly those that may increase bleeding in the peri-operative period and when there is concomitant use of other drugs that also may influence haemostasis like NSAIDs.³⁹¹ (2B)
- (2) We suggest that herbal medicines are stopped 2 weeks prior to surgery.^{391,399} (2B)
- (3) There is no evidence to support postponement of elective surgery, but for high-risk surgery in 'closed compartments' such as intracranial procedures, we suggest that the possible impairment of haemostasis by these drugs is taken into account.³⁹¹ (2B)

Psychotropic drugs

Introduction

Prescription of psychotropic drugs in the general population has continuously increased in recent years.⁴⁰¹ Epidemiological studies indicate that antidepressants are most commonly used (14.6%) followed by statins (13.9%) and β -receptor-blockers (10.6%).⁴⁰² More recent data have revealed that 20.6% of patients undergoing surgery are taking antidepressants, 15.6% anxiolytics and 6.7% both.⁴⁰³

Antipsychotic medication has several implications for the anaesthesiologist, including drug interaction, the decision whether to continue or to terminate the medication, potential withdrawal problems and acute or long-term relapse of psychiatric morbidity.⁴⁰⁴ Drug treatment of psychoses is a risk factor for postoperative morbidity that is independent of pre-operative comorbidities.^{403,405} Patients receiving selective serotonin reuptake inhibitors have a higher in-hospital mortality and higher re-admission rate than nontakers.⁴⁰⁶ Recommendations for the management of psychotropic drugs during the peri-operative period are therefore desirable.

The initial search revealed a total number of 198 abstracts from Medline and 584 from Embase. All comparative studies investigating an assessment or intervention with regard to pre-operative optimisation of patients using psychotropic medications were selected. A total number of 29 studies were included.

Existing evidence

Psychotropic drugs

There are five relevant groups of psychotropic drugs, which will be considered: tricyclic antidepressants, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, lithium and traditional Chinese herbal medicines.⁴⁰⁷

Tricyclic antidepressants TCAs act by presynaptic inhibition of the uptake of norepinephrine and serotonin and also by blocking postsynaptic cholinergic, histaminergic and α_1 -adrenergic receptors.⁴⁰⁸ All TCAs lower the seizure threshold and exhibit several effects on the cardiac conduction system.

Main side effects of TCA are potentiation of the sympathomimetic effects of adrenaline and noradrenaline, resulting in hypertensive crisis. The effects of norepinephrine can be reduced in patients with chronic TCA treatment. Furthermore, TCAs cause varying degrees of anticholinergic symptoms, cardiac dysrhythmia and sedation; these substances should be avoided in patients with known cardiac conduction abnormalities.

Stopping TCAs can lead to cholinergic symptoms particularly, such as gastrointestinal symptoms, and also movement disorders and cardiac arrhythmia. Increased rates of delirium, confusion and depressive symptoms might occur.⁴⁰⁹ The relapse rate has been estimated to be two to five times higher in the year after discontinuation than those patients who continue treatment.⁴¹⁰

Selective serotonin re-uptake inhibitors SSRIs are increasingly used for antidepressant therapy in industrial countries. They increase extracellular levels of serotonin by inhibiting its re-uptake into the presynaptic cell and potentiate the transmission of impulses along serotonergic central nervous pathways. Relevant side effects are

due to serotonergic potentiation, including gastrointestinal symptoms, headache, agitation, insomnia, alteration of platelet function and others. Overdose of SSRI or a combination with MAOI or serotonergic TCA can lead to a serotonin syndrome, which is characterised by hyperthermia, hypertension, neuromotor and cognitive-behavioural dysfunction. Withdrawal of SSRI may induce a variety of different symptoms such as psychosis, agitation, dizziness, palpitations and much more.

Monoamine oxidase inhibitors MAOIs inhibit the metabolic breakdown of serotonin, dopamine and norepinephrine by the MAO enzyme, leading to an increase of these neurotransmitters at the receptor site. Older substances (tranylcypromine, phenelzine) irreversibly inhibit MAO, whereas the newer preparation moclobemide is a reversible inhibitor with a half-life of 1 to 3 h.

Due to their pharmacological properties, MAOIs have effects on blood pressure and on the central nervous system (CNS). The effects on blood pressure can be enhanced by combination with analgesics such as pethidine, and sympathomimetic agents, especially indirectly acting drugs such as ephedrine and pancuronium resulting in severe hypertensive crisis.

Acute withdrawal of classical MAOIs can induce a severe syndrome, including serious depression, suicidal inclination, paranoid delusions and others. Withdrawal syndromes after stopping reversible MAOIs are in contrast rarely observed and can be reversed with 12 to 18 h.

Lithium Lithium is used as a mood stabiliser in bipolar disorders. It has a narrow therapeutic index and a high side-effect profile, so intoxication is a frequent and life-threatening complication of chronic treatment.⁴⁰⁴ Signs of intoxication are gastrointestinal, CNS symptoms and ECG changes.

There seems to be no withdrawal effect after abrupt discontinuation of lithium administration. However, the risk of recurrence of the depression and total affective relapse is very high, especially in the period immediately after discontinuation.⁴¹¹

How should patients with psychotropic medication be assessed?

The pharmacological properties of TCAs on the cardiac conduction system and also an increased sensitivity to sympathomimetic stimulation leads to increased cardiovascular risk.⁴⁰⁸ Pre-operative evaluation should target the cardiovascular system with an ECG and further cardiological examination if indicated.

SSRIs may increase bleeding^{412–416} and the need for peri-operative blood transfusion,⁴¹⁷ particularly in those patients on antiplatelet therapy.⁴¹⁸ Although definite recommendations for pre-operative evaluation in this situation are not available, platelet count and coagulation

tests should be considered, especially in patients undergoing orthopaedic surgery.^{413,414}

Two relevant interactions have been described when anaesthetising patients on chronic treatment with MAOIs. First, administration of pethidine, pentazocine and dextrometorphan block presynaptic uptake of serotonin and may induce an excitatory reaction due to central serotonergic overactivity.⁴¹⁹ A depressive type of reaction is supposed to be related to an inhibition of hepatic microsomal enzymes, leading to accumulation of anaesthetic agents. Second, use of indirectly acting sympathomimetic drugs induces release of norepinephrine from intracellular stores possibly resulting in a hypertensive crisis. Thus, indirectly acting drugs are contraindicated and, if required, direct acting sympathomimetics should be used.⁴⁰⁸ However, specific recommendations for pre-operative assessment of these patients do not exist.

Ageing leads to a decrease in total body water and an increase in adipose tissue, affecting the volume of distribution of lithium. Therefore, it has been recommended that older adults taking lithium should check their renal function every 3 months.⁴²⁰ Whether laboratory measurement of renal function is beneficial prior to surgery is unclear.

What interactions must be considered in the presence of prescribed psychotropic medication in the peri-operative period?

The risk of an interaction between TCAs and other medications is increased during anaesthesia. Sympathomimetics should be avoided, for example when used as an adjunct to local anaesthetics. Due to metabolism via the CYP P450 system, interactions with a variety of drugs (antibiotics, analgesics) are possible.⁴⁰⁸ Via this pathway, TCAs may also potentiate the effects of hypnotics, opioids and volatile anaesthetics.

SSRIs are metabolised by the CYP P450 system and some of these molecules or their metabolites are potent inhibitors of the same CYP system isoenzymes.⁴⁰⁴ This can lead to increased levels and even toxic effects of SSRI and/or other medications that may be combined with them. The most dangerous combinations are SSRI and MAOI or serotonergic TCA such as clomipramine. Also, the combination of SSRI with pethidine, dextrometorphan, pentazocine and tramadol can result in a serotonergic syndrome.

Indirect acting sympathomimetics can displace endogenous noradrenaline in high concentration causing hypertension, whereas direct acting sympathomimetics may exert an enhanced effect due to receptor hypersensitivity and should be used cautiously in combination with MAOIs. Pancuronium should be avoided, because it releases stored noradrenaline; also, MAOIs decrease the dose requirement of thiopentone.⁴²¹

Lithium interacts with some analgesics and anaesthetics, which must be taken into account. NSAIDs can increase serum levels of lithium to toxic levels by diminishing lithium excretion and/or increased reabsorption in the kidneys.⁴²² ACE-inhibitors, thiazide diuretics and metronidazole can also increase lithium serum levels.⁴⁰⁸ Diuretics should be given with caution because they can reduce lithium clearance. Interactions with both nondepolarising and depolarising muscle relaxants have been described, leading to a prolongation of neuromuscular blockade.⁴⁰⁸

Traditional herbal medicines are increasingly used worldwide because of assumptions that they are effective and have only a few side effects. However, there are considerable risks of adverse events and interactions with other medications. For example, kavalactones are used as sedatives and anxiolytics, and can cause hypotension, prolonged sedation and a decreased renal blood flow. It has been shown that the incidence and risk of adverse events (hypertension, hypotension, delayed emergence) peri-operatively is significantly increased in patients taking herbal medicines.⁴²³ Some substances can affect platelet function resulting in an enhanced bleeding risk.³⁹⁹

Thermoregulation is often impaired in patients with psychiatric disorders receiving antipsychotic drugs. Compared with unmedicated controls, those chronically treated with antipsychotic agents have a significantly lower core temperature during anaesthesia, but the incidence of postanaesthetic shivering was not increased.⁴²⁴

Will outcome be affected by stopping psychotropic drugs in good time before or immediately before anaesthesia?

Whether TCAs should be discontinued prior to anaesthesia is matter of debate. Two studies investigated whether antipsychotic medication should be continued or not. In the first trial, it was shown that stopping resulted in higher rates of postoperative confusion.⁴²⁵ The authors recommended continuation of medication in order to prevent postoperative complications. A second randomised study showed that stopping antidepressants did not increase the incidences of hypotension and cardiac arrhythmia during anaesthesia, but did cause symptoms of depression and confusion.⁴²⁶ Patients taking TCAs and scheduled for surgery should continue until the day of the surgical procedure.⁴⁰⁹

In most publications, the continuation of SSRIs is recommended in order to prevent a withdrawal syndrome,^{409,420,421} but where there is a high risk of bleeding discontinuation 2 weeks before the operation should be considered.⁴²⁷

First-generation MAOIs are nonselective and block MAO-A and MAO-B irreversibly. The second generation not only acts selectively but also irreversibly. The latest generation, in contrast, are both selective and reversible.

Generation one and two MAOIs should be discontinued, if possible, and switched to a third-generation drug in order to avoid a psychiatric relapse. However, this is still matter of debate given that the results are from a small retrospective study.⁴²⁸ In patients taking a third-generation MAOI surgery can be performed.

Termination of lithium administration is not required prior to minor surgical procedures, whereas discontinuation 72 h before surgery has been proposed.⁴⁰⁸ However, the latter is a matter of debate. Lithium may increase the risk of cardiovascular instability and the risk of withdrawal is small, but there are no studies to support better outcome after lithium has been stopped.

Numerous herbal medications are associated with an increased risk of bleeding and may interact with anaesthetic agents. It is recommended that they are stopped at least 1 week prior to anaesthesia and surgery.

In adults undergoing elective noncardiac surgery on medication with psychotropic drugs, does pre-operative optimisation influence outcomes?

Outcome studies for this question are not available.

Updated recommendations

- (1) We suggest that patients chronically treated with TCAs should undergo comprehensive cardiac evaluation prior to anaesthesia.^{404,408} (2B)
- (2) We recommend that antidepressant treatment for chronically depressed patients should not be discontinued prior to anaesthesia.⁴²⁴ (1B)
- (3) We suggest that there is insufficient evidence for discontinuation of SSRI treatment peri-operatively.^{409,420,421} (2B)
- (4) We recommend stopping irreversible MAOIs at least 2 weeks prior to anaesthesia. In order to avoid relapse of underlying disease, medication should be changed to a reversible MAOI.⁴⁰⁹ (1C)
- (5) We suggest continuing antipsychotic medication in patients with chronic schizophrenia peri-operatively.⁴⁰⁸ (2B)
- (6) We suggest stopping lithium administration 72 h prior to surgery. It can be restarted if electrolytes are in the normal range, there is cardiovascular stability and the patient is eating and drinking. We suggest that blood levels of lithium are brought under control within 1 week.⁴⁰⁸ (2B)
- (7) We suggest continuing lithium therapy in patients undergoing minor surgery under local anaesthesia.⁴⁰⁸ (2C)
- (8) We suggest stopping herbal medicine 2 weeks prior to surgery.³⁹⁹ (2B)

Peri-operative bridging of anticoagulation therapy

Introduction

Management of anticoagulation during invasive procedures varies widely and remains challenging and

controversial. ‘Bridging anticoagulation’, based on the use of therapeutic doses of LMWH or UFH, aims to limit the period during which patients are subtherapeutically anticoagulated to minimise the risk of peri-operative thromboembolism, particularly embolic stroke.

The 2012 Antithrombotic Practice Guidelines of the ACCP and the 2016 Guidelines of the ESA for Management of Severe Preoperative Bleeding recommend an individualised approach to determining the need for ‘bridging anticoagulation’ based on the patient’s estimated thromboembolic risk and peri-procedural bleeding risk.^{397,429} Yet, evidence continues to be generally weak and primarily deals with VKAs, mostly warfarin, despite it being not commonly used in many European countries. The 2016 ESA Guidelines recommend bridging therapy for high thrombotic risk patients (atrial fibrillation patients with a CHADS₂ score >4, recurrent VTE treated for <3 months or patients with a prosthetic cardiac valve) taking VKA.³⁹⁷ For warfarin, the last dose should be given 5 days before surgery, and bridging therapy with LMWH should be started on day 3 before surgery and continued until 24 h before surgery. Alternatively, subcutaneous UHF could be given starting on day 3 before surgery. For Acenocoumarol, the last dose should be on day 3 before surgery followed by bridging therapy on days 2 and 1 prior to surgery (the last therapeutic dose of LMWH 24 h before surgery). The 2016 ESA Guidelines recommend that for low to moderate thrombotic risk patients (atrial fibrillation patients with CHADS₂ score ≤4, patients treated for >3 months for a nonrecurrent VTE) taking VKA, treatment (acenocoumarol, warfarin) should be stopped 3 or 5 days before surgery and bridging therapy is not needed.³⁹⁷

In recent years, several direct oral anticoagulants (DOACs) such as apixaban, dabigatran, edoxaban and rivaroxaban have been approved for long-term anticoagulation. On the basis of the pharmacological profile of DOACs, with shorter half-lives and faster onset of action than VKA, some have raised concerns about the routine use of ‘bridging’ therapy for DOAC treatment, while others have argued that ‘bridging’ should still be considered for high-risk patients.

The systematic literature search was to answer the following important clinical questions about the management of anticoagulation during invasive procedures or surgery; to a large extent, they remain unanswered. A total of 229 references were reviewed, from which 27 were selected.

Existing evidence

What is the adherence to (compliance with) the guidelines on ‘bridging’?

Only a few relevant studies have addressed this important question. A retrospective chart review was conducted in Canada by Perrin *et al.*⁴³⁰ in patients on chronic anticoagulation who underwent cardiac rhythm device surgery

over a period of 14 months in 2008 to 9. This study identified significant underutilisation of ‘bridging’ among patients with moderate to high thromboembolic risk, particularly during the postoperative period. Conversely, ‘bridging’ was overused among low-risk patients, which resulted in increased bleeding complications.

More recently, Steib *et al.*⁴³¹ assessed, through a national prospective registry in France, practitioner compliance with the guidelines on peri-operative VKA management issued by the French National Health Authority. Overall, 932 patients who underwent surgery between October 2009 and December 2010 were reviewed. ‘Bridging’ was not used in 13% of patients with high thromboembolic risk nor in 60% of those with low thromboembolic risk. Of note, only 18% of high-risk patients received a therapeutic dose of LMWH. On the basis of these findings, the authors of the study concluded that ‘bridging’ was overused and pointed to an inadequate knowledge-to-action transfer plan resulting into poor compliance rates.

Eijgenraam *et al.*⁴³² conducted a retrospective cohort study in the Netherlands where 181 chronically anticoagulated patients undergoing 222 surgical procedures were ‘bridged’ with LMWH. Most patients either had a low thromboembolic risk or underwent low-risk surgical procedures. Yet, the majority of patients were given therapeutic doses of LMWH, including 84.3% of 102 patients considered to be at a low risk for VTE. The median duration of postprocedural LMWH administration was 8 days. The 30-day incidence of major bleeding was 11.3% in the entire group. The authors concluded that adherence to the 2008 ACCP guidelines for peri-operative management of antithrombotic therapy was low, leading to prolonged and/or excessive ‘bridging’ treatment in association with high bleeding rates.

The BORDER (BNK Online bRiDging REgistRy) multicentre registry included an analysis of 1000 invasive procedures in the years 2009 and 2010. It was designed to evaluate current practice of peri-operative management of patients who receive long-term oral anticoagulant (OAC) therapy. In a large outpatient cohort treated by German cardiologists, it showed that 94% of patients who required interruption of OAC before invasive procedures received LMWH as a ‘bridging’ therapy, of whom 73% were treated with halved therapeutic doses of LMWH.⁴³³ Guideline recommendations were followed in only 31% of cases. Importantly, 69% of patients with atrial fibrillation were overtreated, while 51% of patients with heart valve replacement were undertreated with LMWH.⁴³³

Is there harm associated with the use of ‘bridging’ anticoagulation?

Different retrospective cohort studies have shown increased complications associated with ‘bridging’ therapy. One such study recently conducted evaluated a total of 1812 procedures between 2006 and 2012 in 1178

patients in whom long-term warfarin therapy for a history of VTE had been interrupted for invasive procedures. It compared the rates of bleeding and recurrent VTE in patients who did and did not receive ‘bridge’ therapy.⁴³⁴ ‘Bridging’ was associated with an increased risk of bleeding either directly attributed to the administration of the ‘bridging’ agent or a complication of the procedure (hazard ratio, 17.2; 95% CI, 3.9 to 75.1) without a significant difference in the rate of recurrent VTE. Of note, bleeding rates did not differ significantly between patients receiving therapeutic and prophylactic doses of the ‘bridge’ therapy agent. Another retrospective cohort study in more than 1400 patients undergoing radical prostatectomy showed an increased probability of blood transfusion and longer duration of in situ drains in patients receiving ‘bridging’ therapy with LMWH versus those receiving prophylactic LMWH only.⁴³⁵ However, in a more recent retrospective cohort study conducted in 117 patients with mechanical heart valves who underwent 185 invasive procedures requiring VKA interruption and LMWH ‘bridging’, the bleeding risk of the surgery was the only significant predictor of major bleeding during peri-operative ‘bridging’ with LMWH (OR 12.0, 95% CI 1.4 to 108.8).⁴³⁶

Some prospective registry data also suggest that there may be increased risks associated with ‘bridging’ therapy. Hammersting and Omran have reported the results of ‘bridging’ therapy in patients undergoing pacemaker implantations.^{435,437} The data were collected from the BRAVE registry (Bonn Registry for Alternative Peri-Operational Anticoagulation to Prevent Vascular Events), which prospectively documents the risk of bleeding and thromboembolism in patients under such therapy who require surgery or an invasive procedure with need for interruption of OAC. The following independent predictors of bleeding were identified in a multivariate regression analysis: development of thrombocytopenia (hazard ratio 6.0, 95% CI 0.3 to 139.8), prevalence of congestive heart failure (hazard ratio 4.5, 95% CI 0.9 to 22.2), high thromboembolic risk (hazard ratio 6.9, 95% CI 1.9 to 25.6) and an increasing CHADS₂ score (hazard ratio 2.3, 95% CI 1.0 to 5.4). Similarly, in a recent analysis of the prospective Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) including data from 7372 patients on OAC and 2803 interruptions, of which 24% were managed with ‘bridging’ therapy, ‘bridged’ patients were more likely to have bleeding events. Also, the incidences of myocardial infarction, stroke, embolism and death were significantly higher in patients receiving ‘bridging’.⁴³⁸

Lastly, in a systematic review and meta-analysis evaluating the safety and efficacy of peri-procedural anticoagulation ‘bridging’,⁴³⁹ 34 studies were reviewed that assessed peri-operative thromboembolism and bleeding events in patients undergoing elective surgical or invasive procedures. The dataset used involved around 12 000 patients

and low thromboembolic risk and/or non-VKA patient groups were used for comparison. 'Bridging' was associated with an increased risk of overall bleeding in 13 studies (OR, 5.40; 95% CI, 3.00 to 9.74) and major bleeding in five studies (OR, 3.60; 95% CI, 1.52 to 8.50) versus non-'bridged' patients. Also, there was an increased risk of overall bleeding (OR, 2.28; 95% CI, 1.27 to 4.08) with full versus prophylactic/intermediate-dose LMWH 'bridging'. Yet, there was no difference in thromboembolic events (OR, 0.30; 95% CI, 0.04 to 2.09).⁴³⁹

Is bridging redundant for patients who require direct oral anticoagulant interruption given the rapid action of these agents?

DOACs have short half-lives and rapid onset of action, which should allow for short periods of interruption without heparin 'bridging'. Although no prospective studies have so far evaluated this approach, some experts still warn against 'bridging' therapy for DOAC patients in daily care. Their concerns are based on pharmacological considerations together with some post hoc analyses from Phase III trials.^{440,441}

Beyer-Westendorf *et al.*⁴⁴² analysed data from a registry of 2179 patients on DOAC therapy. DOAC therapy was continued during 863 procedures in 187 (21.7%) cases, interrupted temporarily without heparin 'bridging' in 419 (48.6%) or interrupted with heparin 'bridging' using prophylactic or therapeutic doses in 63 (7.3%) and 194 (22.5%) cases, respectively. The use of heparin 'bridging' significantly increased with the severity of the surgical procedure. Rates of major cardiovascular events were similar for patients without heparin 'bridging' (DOAC was continued or interrupted without heparin bridging; event rate 0.8%; 95% CI 0.3 to 1.9%) and for those with heparin 'bridging' (1.6%; 95% CI 0.4 to 3.9%). Heparin 'bridging' was not an independent risk factor for cardiovascular events in the multivariate analysis (OR 1.9; 95% CI 0.5 to 7.1). For major bleeding, major procedures (OR 16.8; 95% CI 3.8 to 78.9) and heparin 'bridging' (OR 5.0; 95% CI 1.2 to 20.4) were the only independent risk factors.

However, there are small groups of patients at a higher risk of thrombosis (CHADS₂ >5, recent TIA or stroke) wherein an individualised approach is required to minimise the period of subtherapeutic anticoagulation. Also, longer periods of pre-operative DOAC discontinuation, up to 5 days, may be considered for patients with renal or hepatic impairment or other conditions associated with decreased drug clearance. In this setting, 'bridging' with LMWH has been proposed for patients with a high risk of thrombosis.⁴⁴³

Can 'bridging' be avoided in selected surgical procedures?

Most studies addressing this question were conducted in low-risk surgery settings or minor soft tissue procedures. Two meta-analyses have assessed the safety and efficacy

of 'bridging' therapy versus uninterrupted warfarin therapy in patients undergoing pacemaker or cardioverter-defibrillator implantation.^{444,445} Both concluded that a strategy of uninterrupted warfarin therapy was associated with a decreased risk of bleeding without increasing the risk of thromboembolic events. Hence, a strategy of uninterrupted VKA may be a viable alternative to heparin-based 'bridging' therapy and could be considered the approach of choice in patients at moderate to high risk of thromboembolic events.^{444,445}

On a similar note, a prospective, open-label, randomised, parallel-group, multicentre study enrolling 1584 patients showed that performing catheter ablation of atrial fibrillation without warfarin discontinuation reduced the occurrence of peri-procedural stroke and minor bleeding complications compared with 'bridging' with LMWH.⁴⁴⁶

Additional retrospective studies have suggested that oral surgical procedures,⁴⁴⁷ atrial fibrillation ablation,⁴⁴⁸ carotid artery stenting,⁴⁴⁹ facial plastic and reconstructive surgery, cataract surgery⁴⁵⁰ and total knee replacement^{451,452} may be performed safely with minimal serious complications without alteration of OAC treatment with VKA.

The German S3 guidelines for the management of anticoagulation in cutaneous surgery recommend that bridging from VKA to heparin should not be performed in surgery of the skin.⁴⁵³

Of note, the safety and efficacy of uninterrupted DOAC therapy during surgical or other invasive procedures has not been assessed in a controlled clinical study setting yet. However, a RCT, the BRUISE CONTROL-2 trial, is currently underway to investigate whether a strategy of continued versus interrupted DOAC (dabigatran, rivaroxaban or apixaban) at the time of cardiac device surgery, in patients with moderate to high risk of arterial thromboembolic events, reduces the incidence of clinically significant haematoma.⁴⁵⁴

The 2016 ESA Guidelines recommend that VKA should not be interrupted in patients undergoing procedures with a low risk of bleeding such as skin surgery, dental surgery, gastric and colonic endoscopies (including biopsies but not polypectomies) and cataract surgery.³⁹⁷

Updated recommendations

- (1) In high-risk patients under VKA, we recommend a 'bridging' strategy for the peri-operative period in accordance with existing ESA clinical guidelines. However, we suggest an individualised approach in determining the need for 'bridging anticoagulation' based on the patient's estimated thromboembolic risk and peri-procedural bleeding risk.³⁹⁷ **(2C)**
- (2) In minor surgical procedures, such as cataract or minor soft tissue surgery, we recommend continuation of VKA instead of instituting 'bridging' therapy.³⁹⁷ **(1B)**

- (3) In implantation of pacemaker and defibrillator devices, we recommend that VKA therapy is continued in preference to ‘bridging’ therapy with LMWH.^{444,445} **(1B)**
- (4) We do not recommend ‘bridging’ with LMWH for short interruptions in patients receiving a DOAC agent.³⁹⁷ **(1C)**

Which pre-operative tests should be ordered?

Historically, testing before noncardiac surgery involved a series of standard tests applied to all patients (chest radiography, electrocardiography, laboratory testing, urinalysis). However, these tests often do not change peri-operative management, may lead to follow-up testing and surgical delay for results that are often normal and which increase the cost of care. An extensive systematic review concluded that there was no evidence to support routine pre-operative testing.^{455,456}

More recent practice guidelines now recommend specific testing in selected patients guided by a peri-operative risk assessment based on clinical history and examination, although this recommendation is based primarily on expert opinion or low-level evidence.

NICE regularly updates its recommendations on pre-operative testing for elective noncardiac surgery. Our previous guidelines referred to the 2003 version of the NICE recommendations on pre-operative testing (<http://www.nice.org.uk/Guidance/CG3>). These recommendations were updated in 2016 and we refer to these guidelines to decide which pre-operative tests to order for each individual (<http://www.nice.org.uk/guidance/ng45>).¹⁹⁰

The tests covered by these guidelines are chest radiograph, resting echocardiography, full blood count (Hb, white blood cell count and platelet count), glycated Hb (HbA1c), haemostasis tests, kidney function (estimated GFR, electrolytes, creatinine, urea levels), lung function tests (spirometry), arterial blood gas analysis, polysomnography, pregnancy testing, sickle cell disease/trait tests and urine tests. The recommendations are developed in relation to the following comorbidities: cardiovascular, diabetes, obesity, renal and respiratory.

As discussed before, peri-operative risk depends on a combination of specific patient-related risk factors and the severity of the surgical intervention. The NICE guidelines on pre-operative testing are designed in such a way that they provide recommendations specific to the grade of severity of surgery (minor, intermediate and major or complex) combined with the patient’s ASA class. As a consequence, the NICE recommendations help the practitioner in selecting the appropriate pre-operative tests for the individual surgical patient undergoing all types of surgery.

How should the airway be evaluated?

Introduction

Pre-operative evaluation of the airway aims at predicting the risk of difficult or failed airway management. This

includes not only difficult conventional laryngoscopy and intubation, including difficult videolaryngoscopy, but also difficult face mask ventilation, difficult insertion of extraglottic airway devices or difficult cricothyrotomy/FONA. As these alternative techniques are often chosen following failed intubation, pre-operative detection of patients in whom alternative means of ventilation/oxygenation are also likely to fail is important to minimise the risk of potential ‘cannot ventilate, cannot oxygenate’ situations.

Pre-operative airway evaluation also guides the decision on whether to employ conventional induction of anaesthesia and airway management or to secure the airway before inducing anaesthesia and apnoea, for example by awake intubation with bronchoscopy or, more recently, videolaryngoscopy. Traditionally, several clinical tests are used, together with patient history and the clinical intuition of an experienced anaesthetist. However, these clinical tests, and in particular *one* clinical test standing alone, does not provide sufficient sensitivity and specificity to reliably predict or rule out difficult airway management.

The primary title search included 164 titles. After screening titles and abstracts, 41 papers remained for full-text-analysis. It is remarkable that the majority of studies originate from India. Therefore, scepticism as to the transferability and application of the results to a European population might be reasonable.

Identification of the difficult airway

The search for signs to predict difficult airway management is intended to prevent the unanticipated unexpected difficulty and eventually the death of patients found to be impossible to intubate and impossible to oxygenate. Failed or difficult intubation causes 2.3% of anaesthesia-related deaths in the USA.⁴⁵⁷

The entire scope of this topic including the definition of what is a difficult intubation has undergone profound modification, partly related to the general acceptance of the supraglottic airway devices and the widespread introduction of videolaryngoscopes. In this context, the usual predictive signs for difficult intubation now appear old fashioned. These clinical predictors are almost all predictors for difficult laryngoscopy and not for difficult intubation. Direct laryngoscopy is still the gold standard for endotracheal intubation, and difficult laryngoscopy is an acceptable surrogate for difficult intubation (except in the presence of an undiagnosed subglottic obstruction), but the real goal is the prediction of ability to oxygenate effectively. There is not strong evidence identifying significant predictors of difficult videolaryngoscopy or difficult supraglottic airway devices insertion and ventilation, and finally of difficult FONA. Nevertheless, recent studies suggest that there are specific predictive criteria that should be considered during airway

Table 3 Independent predictors for difficult mask ventilation

| Predictors for grade 3 mask ventilation | Predictors for grade 4 mask ventilation | Predictors for grade 3 or 4 mask ventilation combined with difficult intubation |
|---|---|---|
| BMI >30 kg m ⁻² | Snoring | BMI >30 kg m ⁻² |
| Jaw protrusion severely limited | Thyromental distance < 6 cm | Jaw protrusion severely limited |
| Snoring | | Snoring |
| Beard | | Thick/obese neck anatomy |
| Mallampati classification 3 or 4 | | Sleep apnoea |
| Age >75 years | | |

Modified from Greib *et al.*⁴⁵⁸

evaluation, but validated predictive signs specific for difficult videolaryngoscopy and difficult laryngeal mask placement are lacking.

Difficult and impossible facemask ventilation

Prediction of difficult mask ventilation (DMV) was largely ignored until this century but is of utmost importance, as facemask ventilation represents a crucial step in the maintenance of proper oxygenation of the anaesthetised patient when attempts at instrumental airway control have failed, before and while performing a FONA procedure. Screening for high-risk situations using simple clinical signs, while insufficient on its own, is crucial if the stress and risk of an unanticipated situation is to be avoided. Forewarned is forearmed with the best equipment and the best personnel.⁴⁵⁸

The reported incidence of DMV varies widely (from 0.08 to 15%) depending on the criteria used for its definition. The very first figure given for prevalence of DMV was approximately 5%.⁴⁵⁹ Analysis showed five criteria to be independent factors for a DMV in adults undergoing scheduled general surgery: age older than 55 years; BMI more than 26 kg m⁻²; presence of a beard; lack of teeth; and history of snoring. The presence of two of these factors predicts DMV with a sensitivity of 72% and a specificity of 73%. In the absence of these factors, the patient is very likely to be easy to ventilate (negative predictive value: 98%). The risk for difficult intubation is four times higher in the presence of risk for DMV. In another study, several independent predictors for DMV were identified.⁴⁵⁸ In that study, the importance of the mandibular protrusion test in predicting DMV and DMV combined with difficult intubation was stressed (Table 3).

A beard is the only easily modifiable risk factor for DMV. Patients should be informed of this risk, especially when other risk factors for DMV are present and shaving may be recommended before the procedure.

A study devoted to impossible mask ventilation confirmed the incidence of grade 4 MV to be 0.15% in a series of 53041 patients.⁴⁶⁰ The five independent predictors of impossible mask ventilation were neck radiation changes; male sex; sleep apnoea; Mallampati class 3 or 4; and presence of a beard; the relative weights of these

predictors being 6, 4, 3, 2 and 2, respectively. Patients with three or four risk factors demonstrated OR of 8.9 and 25.9, respectively, for impossible mask ventilation when compared with patients with no risk factors.

Criteria for difficult intubation

Research regarding the incidence of combined DMV and difficult laryngoscopy is extremely limited,⁴⁵⁸ unsurprising given that it appears to be a rare though critical scenario. Most patients can be managed with the use of direct or videolaryngoscopy,⁴⁵⁸ but a low percentage can be safely managed with only fiberoptic intubation, or for all, with an awake intubation technique.⁴⁶¹

No single test is able to predict effectively and reliably difficulties in airway management and evidence shows that combining multiple tests is more reliable. The combination of predictive criteria for difficult intubation is 100% sensitive and specific, with good positive and negative predictive values. As difficult airway management results from a combination of many different anatomical, functional, environmental and human factors, airway assessment should concentrate on oxygenation rather than on intubation, it should be multifactorial (with some critical single factors), with a range of strategies (ventilation, intubation, supraglottic device positioning, fiberoptic intubation and cricothyrotomy/FONA). It should always be documented in the patient chart to ensure that the information is passed on.

The association between ultrasonic thyroid volume and traditional tests and difficult intubation (Intubation Difficulty Scale >0) in 50 patients with goitre was assessed by Meco *et al.*⁴⁶² Thyroid volumes did not significantly differ between the difficult and nondifficult intubation groups. An association between clinical characteristics and difficult intubation in 109 patients for benign goitre surgery was investigated by Loftus *et al.*⁴⁶³ In 58 patients, conventional laryngoscopy was used, and intubation was difficult (>1 attempt) in two patients but eventually successful in all. The other patients with a higher share of airway difficulties were scheduled for intubation via a fiberoptic approach or videolaryngoscopy. There was no significant association between difficult intubation and goitre size, tracheal deviation/compression, retrosternal thyroid, peri-operative hoarseness, dyspnoea or

dysphagia. Patients with airway difficulties tended to be older than those without airway difficulties.

Screening tests

Mallampati classification

The Mallampati class can be established when the patient is awake, lying, sitting or standing; it has been validated in the supine position.^{464,465} Correlation with Cormack and Lehane grades is poor for Mallampati classifications 2 and 3, but there is a good correlation between class 1 and a grade I laryngoscopy.

The inadequacy of the Mallampati classification has been specifically shown for the obese. It remains useful in this group (BMI 40 kg m⁻²) only if it is performed with craniocervical junction extended rather than neutral and if the patient is diabetic.⁴⁶⁶ This demonstrates that Mallampati should no longer be considered capable of predicting the laryngoscopic view with precision.⁴⁶⁷

In 1987, Samsoun and Young⁴⁶⁸ described the modified Mallampati test with the patient sitting upright. A recent article has analysed predictive values of the modified Mallampati test in the supine or upright position and with or without phonation during the examination. Examining 651 patients to predict difficult laryngoscopy, sensitivity was found to be higher during phonation, whereas specificity was higher when the test was performed without phonation.⁴⁶⁹ For sensitivity without phonation, there was no difference between the supine or upright position.

El-Ganzouri score

The El-Ganzouri score takes into account body weight, head and neck mobility, mouth opening, possibility of subluxation of the jaw, the thyromental distance, Mallampati classification and history of difficult intubation. A value of 4 or more has a better predictive value for difficult laryngoscopy than a Mallampati classification higher than 2.⁴⁷⁰ It was derived from a study of 10 507 patients of whom 5.1% were grade III and 1% were grade IV according to Cormack and Lehane.

There has been renewed interest in the El-Ganzouri score when laryngoscopy is performed with the GlideScope videolaryngoscope rather than with a conventional direct Macintosh laryngoscope (Table 4). In this setting, the score was considered as a decisional tool by the authors.⁴⁷¹ It does, however, have some intrinsic limitations.

Table 4 El-Ganzouri score

| Criterion | Score 0 | Score 1 | Score 2 |
|---------------------------------|----------|--------------|-------------|
| Weight (kg) | < 90 | 90 to 110 | > 110 |
| Head and neck mobility (°) | < 90 | 90 ± 10 | < 80 |
| Mouth opening (cm) | ≥ 4 | < 4 | |
| Subluxation > 0 | Possible | Not possible | |
| Thyromental distance (cm) | > 6.5 | 6 to 6.5 | < 6 |
| Mallampati classification | 1 | 2 | 3 |
| History of difficult intubation | no | possible | established |

Modified from El-Ganzouri *et al.*⁴⁷⁰

It is based on body weight rather than BMI and does not take into account the environment, experience and human factors.

Upper lip bite test

The ULBT consists of three classes: class I, the lower incisors can bite the upper lip, making the mucosa of the upper lip totally invisible; class II, the same biting manoeuvre reveals a partially visible upper lip mucosa; and class III, the lower incisors fail to bite the upper lip. In the initial series, the ULBT class III is a better predictor for difficult intubation than a Mallampati classification of at least 2.⁴⁷²

Like the Mallampati classification, it should be used as a part of a multimodal evaluation for difficult intubation and not as a single test. The combination of the ULBT with the thyromental distance (threshold: 6.5 cm) and interincisor distance (mouth opening; threshold: 4.5 cm) is easy to perform and more reliable as a predictor for difficult intubation.⁴⁷³ Of particular interest, the ULBT seems to be of value as a predictor for difficult intubation with GlideScope videolaryngoscopy.⁴⁷⁴

Practical evaluation

Benumof⁴⁷⁵ found 11 main elements of the physical examination which indicate that intubation will not be difficult. This evaluation uses the most relevant elements of the main tests or scores proposed at the time the list was set up (Table 5). It is carried out easily and quickly and requires no specific equipment. Additional elements are obtained by questioning the patient and studying previous anaesthesia reports, keeping in mind that a previously easy intubation does not necessarily exclude a difficult intubation and that intubation difficulty can vary in the same patient from one procedure to another, during labour⁴⁷⁶ and even only a few hours apart, especially after extubation, and depending on the type of surgery.⁴⁷⁶

It has been proposed that the ideal combination includes three airway tests: mouth opening, chin protrusion and atlanto-occipital extension. This preference is based on a multivariable analysis of predictive criteria, in an observational study of 461 patients of whom 38 had a difficult intubation.⁴⁷⁷ Airway evaluation should, therefore, be multifactorial and based on multiple tests to improve the predictive value.

Para-clinical examination for systematic detection of difficult intubation

No para-clinical tests can be advocated in the routine preanaesthesia airway evaluation. Indirect laryngoscopy is predictive of a similar direct laryngoscopy view.⁴⁷⁸ This examination may not be possible to perform in certain patients, including 15% who have a strong gag reflex, and others who cannot sit up or who refuse it.

Table 5 The 11 items are presented in an anatomical order from the teeth followed by mouth and then the neck

| 11 items for examination | Criteria in favour of easy intubation |
|--|--|
| Length of the upper incisors | Short incisors (qualitative evaluation) |
| Retrognathism (involuntary anterior overriding of the maxillary teeth on the mandibular teeth) | No overriding of the maxillary teeth on the mandibular teeth |
| Voluntary protrusion of the mandibular teeth anterior to the maxillary teeth | Anterior protrusion of the mandibular teeth relative to the maxillary teeth (subluxation of the temporomandibular joint) |
| Intercisor distance (mouth opening) | > 3 cm |
| Mallampati classification (sitting position) | 1 or 2 |
| Configuration of the palate | Should not appear very narrow or highly arched |
| Thyromental distance (mandibular space) | 5 or 3 cm finger breaths |
| mandibular space compliance | Qualitative palpation of normal resilience/softness |
| Length of neck | Not a short neck (qualitative evaluation) |
| Thickness of neck | Not a thick neck (qualitative evaluation) |
| Range of motion of head and neck | Neck flexed 35° on chest and head extended 80° on the neck (= sniffing position) |

No element is sufficient on its own. Modified from Khan *et al.*⁴⁶⁹

High-risk groups

Intubation is generally considered more difficult in pregnant women and in otolaryngology and trauma patients.⁴⁶¹

Certain diseases are associated with an increased risk of airway difficulty. Among the most common of these is diabetes. The positive 'prayer sign' is patients' inability to press their palms together completely without a gap remaining between opposed palms and fingers is a marker for probable general ligament rigidity (stiff joint or stiff man syndrome). When present, difficult intubation should be anticipated. A variant of the prayer sign test is a palm print study of the patient's dominant hand.⁴⁷⁹

In 657 women undergoing elective caesarean section, 53 (8.06%) difficult laryngoscopies occurred.⁴⁸⁰ The area under the ROC curve was very low for Mallampati (0.497) and upper lip bite test (0.5), and slightly better for the ratio of height to thyromental distance (0.627), neck circumference (0.691), thyromental distance (0.606) and neck circumference to thyromental distance ratio (0.689).

Among 2158 women who received general anaesthesia for caesarean section, 12 (0.56%) were difficult to intubate.⁴⁸¹ The distribution of Mallampati classes I-IV in these cases was I: 25%, II: 58%, III: 17%, IV: 0%, whereas in those without a difficult airway it was I: 27.6%, II: 63.5%, III: 8.6%, IV: 0.3%. There were no significant differences in sternomental distance, thyromental distance, mandible-hyoid distance and mandible length or width between the groups that were easy or difficult to intubate.

Acromegaly is also considered a risk factor. Difficult intubation occurs in about 10% of patients with this disease.⁴⁸² Difficult intubation is more common in obese than in lean patients, with a difficult intubation rate of 15.5% in the obese (BMI >35 kg m⁻²) compared with 2.2% in lean patients (BMI <30 kg m⁻²).⁴⁸³

In a small sample of 39 acromegalic patients,⁴⁶⁵ the Mallampati test scored lower in acromegalic patients than

in the control group (sensitivity 13% versus 50%, specificity 81% versus 94%, positive predictive value 14% versus 60%, negative predictive value 78% versus 91%).

In general, problems linked to tongue piercing, congenital disease, rheumatic conditions, local pathology and history of trauma are easily identified during physical examination or by questioning the patient. Cowden syndrome, lingual papillomatosis and angioedemas can be formidable pitfalls.⁴⁸⁴

In conclusion, despite many predictive tests for difficult airway management, none is perfect, and better performance can be achieved only by a combination of tests and prioritising oxygenation over intubation. The reproducibility of the tests from one observer to another remains poor because difficult airway management comes from a continuum of possible differences between individuals, so evaluation must take the individual circumstances into account. Avoidance of death or brain damage from difficult or impossible oxygenation remains of paramount importance in anaesthesia. Every effort must be made to predict a problem airway and plan an airway strategy before induction of anaesthesia. We should direct our efforts towards the management of difficult intubation as much as towards detecting it. This must be underpinned by good team communication and education in airway management.^{485,486}

Updated recommendations

- (1) We recommend that screening for DMV and difficult intubation should be carried out, whenever feasible, in all patients potentially requiring airway management for anaesthesia or in the ICU. This screening includes taking a medical history, surgical history, history of difficult airway management and, if available, examination of previous anaesthetic records. A record of screening should be made in the patient chart.⁴⁵⁸ (1A)
- (2) We recommend that no single predictive sign for difficult airway management is sufficient by itself

and the preanaesthesia assessment needs the combination of different validated evaluation criteria.^{467,470,475} (1A)

- (3) We suggest that although the Mallampati test has been validated in awake patients, lying, sitting or standing, there is little correlation with glottic view by direct laryngoscopy.^{464,465} (2B)
- (4) We recommend that the Mallampati classification alone should no longer be considered capable of predicting the laryngoscopic view with precision.^{461,464–467} (1B)
- (5) We recommend that the potential for DMV should be evaluated and relies on the presence of two or more of the following factors: BMI of at least 30 kg m⁻²; severely limited jaw protrusion; snoring; beard; Mallampati classification 3 or 4; and age at least 57 years.^{458–460} (1C)
- (6) We suggest that the potential for impossible mask ventilation should be evaluated and relies on the presence of three or more of the following factors: neck radiation changes, male sex, presence of OSAS, Mallampati class 3 or 4 and presence of a beard.⁴⁶⁰ (2B)
- (7) We suggest that the combination of the ULBT with the thyromental distance (threshold: 6.5 cm) and interincisor distance (mouth opening; threshold: 4.5 cm) is easy to perform and reliable as a predictor for difficult intubation.^{473,474} (2A)
- (8) We suggest that particular attention is given to evaluating for possible difficult intubation in medical conditions such as obesity, OSAS, diabetes, fixed cervical spine, ENT pathologies and pre-eclampsia. Neck circumference of more than 45 cm is another warning sign.⁴⁸⁰ (2C)
- (9) We suggest that difficult videolaryngoscopy is hard to predict, as only a few studies have addressed this question so far.^{461,463,471} (2C)
- (10) We recommend the use of ULBT as a predictor for difficult intubation with GlideScope videolaryngoscopy.⁴⁷⁴ (1B)

The place of risk indices and biomarkers

The search for the combined topics of ‘biomarkers’ and ‘risk indices’ resulted in 5150 papers. We excluded papers that dealt exclusively with the elderly or frail (covered elsewhere in this guideline), specific types of surgery such as liver resections only, but were inclusive of groups of procedures such as hip fracture surgery and colorectal surgery. We also excluded narrative reviews and papers that evaluated risk scores and biomarkers where intra-operative or postoperative variables were required to assess risk. Only elective surgical procedures were considered. For risk indices, a hand search identified a further 34 papers. For biomarkers, a hand search identified a further four papers on cardiac Troponins, seven on natriuretic peptides and one on other novel biomarkers.

For risk indices, we screened all abstracts with a pre-defined aim of identifying any risk score designed to predict the risk of poor peri-operative outcome. The latter was defined as any mortality (any length of follow up), cardiovascular mortality and morbidity as defined by the original papers and any postoperative complication.

For biomarkers, we screened all abstracts for pre-operative measurements of cardiac biomarkers only. The pre-defined outcomes were any mortality (at any length of follow-up), cardiovascular mortality and morbidity as defined by the original papers and any postoperative complication.

Do risk indices predict outcome?

Introduction

Accurate pre-operative prediction of risk may be aided by the use of risk scores and risk prediction models. Risk scores for the prediction of adverse outcomes are widely used, and a multitude of scores are available. Some of these are surgery-specific, whilst others include intra-operative and postoperative components. Risk prediction models are usually more sophisticated, and require entering data into a statistical model in order to calculate an individual’s risk of poor outcome. Both may be used to make an adequate pre-operative assessment and to inform patients of risk.

The different types of risk scores/prediction models and the outcomes that they are designed to predict vary. Two different questions arise: first, which *pre-operative* risk scores/models are available and which outcomes do they predict; second, which *pre-operative* risk scores/models are validated?

Existing evidence

A total of 32 risk scores or prediction models that were based exclusively on pre-operative variables were identified. The majority were conducted in single centres and poorly validated. Quality of evidence varied widely.

In a systematic review that included all scores, including those with intra-operative and postoperative components, Moonesinghe *et al.*⁴⁸⁷ identified 18 exclusively pre-operative scores, of which only four have been validated in multiple studies: ASA-PS, Surgical Risk Scale, Surgical Risk Score and Charlson Comorbidity Index. The discriminant ability for these four scores varied widely but was generally acceptable with most area under ROC curve values (AUROC) more than 0.7, depending on the score or outcomes studied.

The following risk indices were identified by our search.

ASA-PS

Ten articles including three systematic reviews/meta-analyses were identified.^{487–496} For the prediction of mortality, the AUROC ranged from 0.73 to 0.93 with validation across various surgical groups. Although not

designed to predict mortality, and despite its known inter-rater variation, the ASA-PS score has at least a moderate predictive ability for mortality in multiple surgical settings.

Revised Cardiac Risk Index

Eighteen articles were identified.^{64,487,490,497–511} For the prediction of adverse cardiovascular outcomes in nonvascular surgical patients, the RCRI performs acceptably with AUROCs ranging from 0.65 to 0.79, in line with the original study by Lee *et al.*^{498–502,505,511} The RCRI performs less well in vascular surgical patients with AUROCs of 0.54 to 0.68.^{490,501,503,504,510}

The CHADS-VASC scores may be superior to RCRI in predicting mortality and adverse cardiovascular outcomes in patients with atrial fibrillation.^{502,505}

Incorporating additional variables such as eGFR, ECG changes and cardiac biomarkers may improve the predictive ability of the RCRI.^{497–499,506,507}

In general, the RCRI may be used to assess peri-operative cardiovascular risk with moderate predictive accuracy. However, its value is limited in vascular surgery.

Charlson morbidity index and Elixhauser Comorbidity method

Although the Charlson and Elixhauser Comorbidity indices were not developed to evaluate risk in surgical patients, they have been used for this purpose. Three articles reported good predictive accuracy.^{493,512,513} In the systematic review by Moonesinghe *et al.*,⁴⁸⁷ three further studies investigating these indices were identified with a large variation in their predictive value.^{514–516}

The use of the Charlson and Elixhauser Comorbidity indices can therefore not be recommended for pre-operative risk stratification; however, they remain an important variable for the purposes of risk adjustment within research into perioperative outcomes.

National Surgical Quality Improvement Program index Myocardial Infarction and Cardiac Arrest index

This is a risk prediction model derived from data from the National Surgical Quality Improvement Program and includes five predictor variables. It is designed to predict peri-operative myocardial infarction and cardiac arrest, with the original validation study reporting excellent discriminant ability. Two articles were identified.^{64,509}

The discriminant ability was good with AUROCs ranging from 0.85 to 0.88. NSQIP Myocardial Infarction and Cardiac Arrest index (MICA) has only been validated in North American populations.

The Nottingham Hip Fracture Score

The NHFS is a seven-item scoring system designed to predict the risk of 30-day mortality in patients with hip fractures. It has been validated externally, in mostly

British populations, with moderate to good predictive accuracy.^{517–522}

Risk scores for vascular surgery

Six articles dealt with pre-operative risk scores for vascular surgical patients. The risk scores were Eagle criteria, VSG-CRI and SAVS-CRI. None of these risk scores have been adequately validated and none can be recommended for the pre-operative evaluation of the vascular surgical patient.

The Eagle criteria predict nonfatal or fatal myocardial infarction or cardiac death in elective vascular surgery. Two studies were identified in our search, showing acceptable discrimination for the prediction of fatal myocardial infarction or cardiac death (AUROC 0.73–0.76).^{490,523}

The VSG-CRI is a risk score predicting MACE in vascular surgery. Three studies, including the original study, were included.^{503,510,524} For the prediction of MACE, the AUROCs in the original study ranged from 0.68 to 0.74 depending on type of vascular surgical procedure. VSG-CRI has been externally validated in one small study that showed poor discriminative ability for cardiovascular complications.⁵¹⁰

The SAVS-CRI is a risk score for predicting 30-day MACE in elective vascular surgery.⁵⁰⁴ This risk score has, to our knowledge, never been externally validated.

Other pre-operative risk scores and risk prediction models

A number of other risk prediction scores were identified by our search. These include the Surgical Risk Scale,^{495,525} the Surgical Risk Score^{494,526} and the Surgical Outcome Risk Tool^{492,527,528} that seem to predict mortality with moderate to good discrimination. However, these risk scores are still poorly validated.

Several studies have evaluated the value of more bespoke risk prediction models. Many of these have been conducted using data within existing databases and have been limited to individual studies without external validation. Thus, their generalisability is unknown. The quality of these studies also varies widely, from those involving more than 100 000 participants and internal validation to smaller studies without validation (IIC).^{493,529,530}

Risk scores associated with specific pathological conditions

STOP-BANG

The STOP-BANG score is a validated questionnaire that is used to screen for obstructive sleep apnoea (OSA). Our search identified one large, retrospective study showing an association between a high STOP-BANG score and unexpected intra-operative and early postoperative adverse events, corroborating the results of two smaller

studies.^{103–105} In a recent meta-analysis of 10 studies involving 23 609 patients, high risk-OSA patients screened using the STOP-BANG questionnaire had increased risk of postoperative adverse events and longer length of hospital stay when compared with low risk-OSA patients.¹⁰⁶

Nutritional risk scores

Six studies investigating nutritional risk scores in predicting mortality and postoperative complications were identified.^{531–536} Most studies were conducted in small populations and were assessed to have a medium to high risk of bias. The studies report divergent findings regarding the association between nutritional risk scores and postoperative outcomes. The value of nutritional risk scores for the prediction of postoperative complications and mortality is therefore inconclusive.

Postoperative pulmonary complications score

The 'Assess Respiratory Risk in Surgical Patients in Catalonia' (ARISCAT) score was developed to predict patients at risk of PPCs and is the only score that has been externally validated.^{66,73,537} The score has good discriminative ability; however, it has only been evaluated in a single study in a European population.⁷³

Risk prediction models with intra-operative or postoperative variables

Although we did not include risk scores that included intra-operative or postoperative components, it is worth mentioning some of these. The POSSUM score and its updated version the Portsmouth-POSSUM score have been validated in a large number of studies.^{487,525,538–541}

The National Surgical Quality Improvement Program Surgical Risk Calculator (NSQIP-SRC) uses 22 pre-operative and surgery-related variables in a complex risk estimation method to predict the occurrence of postoperative complications.⁵⁴² The NSQIP SRC is well validated for the North American population across a large number of patients and surgical procedures.^{543–545} The use of only pre-operative variables in NSQIP-SRC also yields good predictive accuracy, although it is inferior to the original model.⁵³⁰

Updated recommendations

- (1) We recommend using ASA-PS to stratify mortality risk in patients undergoing noncardiac surgery.^{487,488,491–496} (1B)
- (2) We recommend using RCRI for assessing peri-operative cardiovascular risk in patients undergoing noncardiac, nonvascular surgery.^{64,487,498–502,505,506,509,511} (1B)
- (3) We recommend using ASA-PS, RCRI, NSQIP MICA to assess peri-operative morbidity risk.^{64,489–491,496,498–502,505,506,509,511} (1C)

(4) We suggest using the Nottingham Hip Fracture Score to stratify peri-operative mortality risk in patients undergoing surgery for hip fractures.^{517–522} (2C)

(5) We recommend using the STOP BANG questionnaire to assess the risk of OSAS and postoperative complications.^{103–106} (1C)

Do measurements of pre-operative biomarkers help predict the risk of adverse cardiac outcomes in noncardiac surgery?

Introduction

Pre-operative biomarkers may improve risk stratification beyond that provided by risk scores only. For example, current ESC/ESA Guidelines on *noncardiac surgery: cardiovascular assessment and management* states that the addition of pre-operative natriuretic peptides may be considered for the stratification of high-risk patients for predicting cardiac complications.⁶ Less is known about the utility of cardiac troponins and novel biomarkers such as CoPeptin.

Existing evidence

Pre-operative natriuretic peptides

Serum levels of natriuretic peptides increase in response to stress in the myocardial wall. The value of pre-operative NP measurements has been best demonstrated for patients undergoing noncardiac vascular surgery. A meta-analysis with individual patient data has demonstrated the usefulness of pre-operative natriuretic peptides with improvements in the net reclassification index for prediction of mortality and adverse cardiovascular outcomes in comparison with the RCRI alone.^{546,547} An elevated pre-operative natriuretic peptides measurement in patients undergoing thoracic surgery may indicate an increased risk of postoperative atrial fibrillation.⁵⁴⁸ In general or orthopaedic surgical groups, it has also been shown that increased pre-operative plasma levels of NP are associated with adverse postoperative outcome.^{549–550} However, studies showing further improvement on clinical risk scores for the prediction of mortality or cardiovascular outcomes by NP in general surgical or orthopaedic patients are only indicative.^{550,551}

Publications showing that modification of clinical management based on the pre-operative measurement of natriuretic peptides could reduce postoperative complications are still lacking. However, in patients with an intermediate risk undergoing vascular surgery or high-risk patients, natriuretic peptides may be determined pre-operatively to adjust postoperative management by risk stratification.

Pre-operative troponins

The development of high-sensitivity assays for cardiac troponin has enhanced the pre-operative assessment of postoperative myocardial injury, major adverse cardiovascular events and death. Although few studies of high

quality were identified, the available evidence suggests that pre-operative troponin measurement, in particular hsTnT, predicts adverse outcomes even after adjustment for other risk factors including the RCRI.^{507,552–557} Many studies note increased levels of cardiac troponins prior to surgery, although a large variation exists, depending on the groups studied.^{507,551,553,556–559} Absolute changes in hsTnT are independently predictive of adverse outcomes, best demonstrated by the VISION study, arguing for the need for pre-operative measurements.⁵⁵⁷ Most studies have been conducted in vascular surgical patients, or in groups either with, or at high risk of coronary vascular disease.^{507,551–554,557–559} Only a few studies have calculated their utility using the Net Reclassification Index, and few adequately powered studies have been explicitly designed with the specific goal of investigating the independent predictive value of pre-operative troponin measurement in predicting death, adverse cardiovascular outcomes and other complications. Taken together, the data suggest that pre-operative hsTroponin measurement is useful for predicting adverse outcomes and should be measured in patients in whom follow-up with postoperative measurement is planned.

Pre-operative copeptin

Copeptin is a glycosylated peptide that is released from the same precursor (prepro-vasopressin) as arginine-vasopressin or antidiuretic hormone. It is elevated in response to osmotic stimuli or by stress, hypotension and hypoxaemia. The potential in combining measurements of copeptin and troponin has been established in patients presenting to the emergency room with acute chest pain. However, little is known about its utility in the peri-operative setting. Our search identified three articles attesting the usefulness of pre-operative copeptin measurement in the vascular surgical setting and in high-risk patients undergoing noncardiac surgery.^{560–562} Pre-operative copeptin was independently predictive of poor cardiovascular outcomes even after adjustment for other risk factors such as pre-operative risk scores, pre-operative natriuretic peptides and troponin levels.^{560–562} Current data are however sparse and no recommendation can be made for the measurement of this biomarker until these results have been confirmed by further prospective studies, and in other groups.

Updated recommendations

- (1) We suggest using pre-operative hsTnT measurement to aid risk assessment in patients at risk of coronary artery disease and in patients undergoing major surgery.^{507,552–559} (2C)
- (2) We recommend that pre-operative measurements of natriuretic peptides be used for risk stratification in intermediate or high-risk patients undergoing vascular or major thoracic surgery.^{546–551} (1C)

- (3) We suggest pre-operative measurement of natriuretic peptides for risk stratification in high-risk patients undergoing major general or orthopaedic surgery.^{549–551} (2C)

Postoperative nausea and vomiting Introduction

Although there are several guidelines on the treatment of PONV, we include this chapter in our guideline in order to provide a concise clinical overview of current strategies for the prevention of PONV.^{563–565} This should also update an excellent guideline published by the Society for Ambulatory Anesthesiology in 2014 by including new studies from our search strategy (1770 abstracts screened, 98 included).⁵⁶³

Existing evidence

There are some new studies confirming that using total intravenous anaesthesia (TIVA)⁵⁶⁶ or avoiding nitrous oxide reduces PONV, especially in procedures lasting more than 1 h.⁵⁶⁷ The combination of regional or neuroaxial anaesthesia with general anaesthesia and opioid sparing also reduces the incidence of PONV.⁵⁶⁸

There are several studies of drugs of the same subgroup, 5-HT₃ antagonists, NK-1 receptor antagonists, corticosteroids, butyrophenones, given in a wide range of doses to different groups of patients undergoing a variety of procedures. These trials differ with regard to the time the drugs were given during the peri-operative period. There is good evidence that drug combinations of different subgroups increase effectiveness.

Improving the clinical setting

Most of the newly published studies emphasise implementation of clinical pathways to improve prophylaxis and treatment of PONV. There is evidence that the rate of PONV can be reduced if patients are scored in advance with a reliable scoring device, and a treatment algorithm based on the score that details the antiemetics to be given, is employed.^{563–565,569–571} The implementation of an algorithm to the whole clinical setting will also reduce the number of patients with PONV (Table 6) and the effectiveness of the treatment should be measured to improve the system.⁵⁷² Another approach is to provide liberal antiemetic prophylaxis since most antiemetics are well tolerated and acquisition costs are low.

Table 6 Actions to reduce the rate of postoperative nausea and vomiting

| Action | Level of evidence |
|--|-------------------|
| Introducing a PONV risk score | 1A |
| Developing a treatment algorithm based on the score results | 2A |
| Treatment with antiemetic drugs according to the algorithm | 1A |
| Implementing the whole scoring and algorithm to the local clinical setting | 1A |

Drug treatment of postoperative nausea and vomiting

A reasonable number of drugs are available to treat PONV. HT₃-antagonists are effective^{573–575} and should be administered at the end of surgery in order to increase duration into the postoperative period. This approach might be less important for long-acting substances such as palonosetron.⁵⁶⁵ NK1-antagonists usually have a longer half-time than HT₃-antagonists and also reduce the rate of PONV significantly.⁵⁷⁶ There is some evidence of a slightly greater effect of aprepitant in reducing the PONV rate than ondansetron.⁵⁷⁴ However, aprepitant is not yet available for use.

Corticosteroids are also effective in reducing PONV.^{577,578} There is neither evidence for an increased risk of wound infection using dexamethasone for PONV prophylaxis nor hints of negative effects on tumour recurrence after surgery.⁵⁷⁹ Many antiemetics (butyrophenones, 5-HT₃ antagonists) cause prolongation of the QT-interval. However, there is no evidence for an increased incidence of arrhythmia in the peri-operative period with their use.⁵⁶⁵

Avoiding N₂O and using TIVA instead of balanced anaesthesia together with postoperative opioid sparing also reduces PONV.⁵⁶⁵ Other drugs such as α_2 -agonists, mirtazapine, gabapentin and midazolam seem to have only indirect effects on reducing the incidence of PONV.^{565,580–584}

A multimodal approach based on a PONV scoring system with different antiemetics is recommended especially in patients at a high risk.^{570,572} Nearly all studies used combinations of different subgroups of antiemetic drugs; combinations from the same subgroup with the same mode of action are not advisable.^{563,565,585} The results of studies investigating nonpharmacological approaches such as acupuncture, acupressure and electrical stimulation are contradictory, although several studies have shown effectiveness.^{565,574,586–594} The stimulation point is mostly P6, but the right time for the stimulation remains still unclear.⁵⁸⁷ When incorporated into a multimodal approach and/or a PONV algorithm, there may be a small positive effect.^{595,596}

Genome assays will be able to predict the risk of PONV, but this remains in the future.⁵⁹⁷

Updated recommendations

- (1) We recommend implementing a PONV guideline according to the local clinical setting.^{569–571} **(1B)**
- (2) We recommend the inclusion of a pre-operative PONV score taken during the preanaesthetic evaluation.⁵⁶⁹ **(2B)**
- (3) According to the score, we recommend adoption of a risk-adapted multimodal approach to reduce the PONV rate.^{563–565,570,572,595,596} **(1B)**
- (4) We recommend monitoring the incidence of PONV with feedback to improve the guideline and encourage staff.^{570,572} **(1C)**

Final remarks

This guideline that updates the previous 2011 ESA guidelines on the pre-operative evaluation of the adult patient undergoing noncardiac surgery¹ makes recommendations that address two main clinical questions: how should a pre-operative consultation clinic be organised and how should pre-operative assessment of a patient be performed? In addressing these questions, new evidence published after 2011 was screened and evaluated in accordance with GRADE in order to provide a hierarchy of recommendations on different topics. We took a systematic approach to searching for all available relevant evidence and this information was interpreted by experts in the field in order to provide a comprehensive and useful guideline that clinicians across Europe easily can implement in their various clinical settings.

A systematic review with a predefined protocol and transparent methodology systematically gathers evidence to answer a specific clinical question, and is combined with data-synthesis (meta-analysis) that is dependent on availability of data and the level of heterogeneity. Our approach differs from this, as a systematic review does not make recommendations. Due to the magnitude of the topics covered in the preparation of the guideline, containing several hundred specific PICO questions, and the overall quality of evidence, there was little scope for appropriate data-synthesis.

We acknowledge that the present list of recommendations covers only a fraction of the questions relevant to pre-operative evaluation and that there is a large number of groups and subgroups encountered in the clinical setting. Uncommon diseases, specific medications and treatment strategies have deliberately been omitted for two reasons. First, there is even less available scientific evidence upon which to base possible recommendations than there is for the more common issues. Second, to attempt to produce a comprehensive document would have resulted in something too large to be of help in daily clinical practice. For less common situations, the global recommendation is to rely on specialist advice and screen the literature for case reports and/or case series providing information on how to best deal with specific rare clinical cases.

Accordingly, the recommendations given deal with some of the most frequently encountered questions in an adult pre-operative evaluation clinic. They are based on a summary and grading of the most recent evidence on the different topics addressed, which should allow the readers to interpret this evidence and if they choose, make their own 'expert opinion'.

The task force is aware that there will inevitably be certain, mostly minor differences compared with available national guidelines. Differences may be related to the sometimes low grade of evidence, which gives room for expert opinion and as a consequence may be subject

Table 7 Drugs reducing the rate of postoperative nausea and vomiting

| Drugs | Level of evidence | References |
|--|-------------------|-------------|
| 5-HT ₃ receptor antagonists | 1A | 579 to 581 |
| NK-1 receptor antagonists | 1A | 582 |
| Corticosteroids | 1A | 583,584,587 |
| Butyrophenones | 1A | 600 |
| Antihistamines | 1A | 571 |
| Anticholinergics | 1A | 589 |
| Phenothiazines | 1A | 589 |

to different interpretations. Therefore, the present guideline is not intended to replace possible national guidelines, although we hope that they may help to develop a unified approach among the different European countries. The task force aimed to summarise the recent scientific background in addressing a variety of important clinical issues in pre-operative evaluation in the hope that they might help each European anaesthetologist in their daily practice.

Because well designed and sufficiently powered RCTs on the many issues around pre-operative evaluation are scarce prompts us to plead for more initiatives on this subject. For some of the topics addressed in the present guideline, there are no RCTs at all. One area wherein evidence is particularly poor is the geriatric patient. In a majority of studies, the ageing population is excluded a priori and it becomes very difficult to base recommendations on hard evidence. Nevertheless, various societies seem to provide strong recommendations on different aspects in the elderly, based mainly on expert opinions. Similarly, studies on prognostic or diagnostics tests and scoring of severity of illness cannot have a randomised and controlled design. As a consequence, from a methodological standpoint, evidence upon which to make the recommendation is downgraded to low grade. Yet, scores such as ASA-PS, RCRI, NSQIP-MICA, POSSUM and others have been externally validated in thousands of patients. Thus, assessment of the evidence and formulation of recommendations when relying on the GRADE methodology is often difficult for such topics and great care is needed lest valuable information is overlooked.

The main purpose of this guideline is to address the topics pertinent for pre-operative *evaluation*. This implies that another important aspect of the pre-operative process, *pre-operative optimisation*, is not addressed (except partially for the anaemia and PONV section). Whilst this might be seen as a shortcoming of our scientific approach, our opinion is that optimisation differs sufficiently from evaluation to merit a separate literature search and assessment of evidence.

Finally, these guidelines should be regarded as an add-on and not necessarily a replacement of the 2011 ESA recommendations. Guidelines are often perceived as a steering tool, but we appreciate the fact that our

recommendations should be evaluated and sometimes adapted prior to implementation locally. Some countries and national societies may decide to assess the evidence and recommendations differently. We emphasise that our recommendations can be adopted, modified or even not implemented, depending on institutional or national requirements and legislation and local availability of devices, drugs and resources (Table 7).

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References

- De Hert S, Imberger G, Carlisle J, *et al.* Preoperative evaluation of the adult patient undergoing noncardiac surgery: guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol* 2011; **28**:684–722.
- Van Klei W, Hennis P, Moen J, *et al.* The accuracy of trained nurses in preoperative health assessment: results of the OPEN study. *Anaesthesia* 2004; **59**:971–978.
- Schwartz PJ, Breithardt G, Howard A, *et al.* Task Force Report: the legal implications of medical guidelines—a Task Force of the European Society of Cardiology. *Eur Heart J* 1999; **20**:1152–1157.
- Neary W, Heather B, Earnshaw J. The Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM). *Br J Surg* 2003; **90**:157–165.
- Kheterpal S, O'Reilly M, Englesbe MJ, *et al.* Preoperative and intraoperative predictors of cardiac adverse events after general, vascular, and urological surgery. *Anesthesiology* 2009; **110**:58–66.
- Kristensen S, Knuuti J, Saraste A. European Society of Anaesthesiology guidelines on noncardiac surgery: cardiovascular assessment and management. The Joint Task Force on noncardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur J Anaesthesiol* 2014; **31**:517–573.
- Fleisher LA, Fleischmann KE, Auerbach AD, *et al.* 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation* 2014.
- Kolh P, De Hert S, De Rango P. The concept of risk assessment and being unfit for surgery. *Eur J Vasc Endovasc Surg* 2016; **51**:857–866.
- Jamjoom AA, White S, Walton SM, *et al.* Anaesthetists' and surgeons' attitudes towards informed consent in the UK: an observational study. *BMC Med Ethics* 2010; **11**:2.
- Gogarten W, Vandermeulen E, Van Aken H, *et al.* Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. *Eur J Anaesthesiol* 2010; **27**:999–1015.

- 11 Slater L. Product Review: PubMed PubReMiner. *JCHLA* 2012; **33**: 106–107.
- 12 Frantzi K, Ananiadou S, Mima H. Automatic recognition of multiword terms: the c-value/nc-value method. *Int J Digital Libr* 2000; **3**:115–130.
- 13 Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from <http://handbook.cochrane.org>.
- 14 Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. *J Clin Epidemiol* 2011; **64**:395–400.
- 15 De Robertis E, Longrois D. To streamline the guideline challenge: the European Society of Anaesthesiology policy on guidelines development. *Eur J Anaesthesiol* 2016; **33**:794–799.
- 16 Grant C, Ludbrook G, O'Loughlin E, Corcoran T. An analysis of computer-assisted prescreening prior to elective surgery. *Anaesth Intensive Care* 2012; **40**:297.
- 17 Ireland S, Kent B. Telephone preoperative assessment for adults: a comprehensive systematic review. *JBI Libr Syst Rev* 2012; **10**:1452–1503.
- 18 Edward G, Naald NV, Oort F, et al. Information gain in patients using a multimedia website with tailored information on anaesthesia. *Br J Anaesth* 2010; **106**:319–324.
- 19 Jastrzebski A, Villafranca A, Sethi S, Bellan L, Group MHCCSW. Safety and comparative costs of preoperative assessments for cataract surgery: traditional mandatory assessment versus a novel graded assessment system. *Can J Anesth* 2016; **63**:842–850.
- 20 Flamm M, Fritsch G, Hysek M, et al. Quality improvement in preoperative assessment by implementation of an electronic decision support tool. *J Am Med Inform Assoc* 2013; **20**:e91–e96.
- 21 Dronkers J, Chorus A, Meeteren N, Hopman-Rock M. The association of preoperative physical fitness and physical activity with outcome after scheduled major abdominal surgery. *Anaesthesia* 2013; **68**:67–73.
- 22 Dunne MJ, Abah U, Scarci M. Frailty assessment in thoracic surgery. *Interact Cardiovasc Thorac Surg* 2014; **18**:667–670.
- 23 Revenig LM, Canter DJ, Taylor MD, et al. Too frail for surgery? Initial results of a large multidisciplinary prospective study examining preoperative variables predictive of poor surgical outcomes. *J Am Coll Surg* 2013; **217**:665–670; e1.
- 24 Trufă D, Arhire LI, Niță O, et al. The evaluation of preoperative nutritional status in patients undergoing thoracic surgery. *Rev Med Chir Soc Med Nat Iasi* 2014; **118**:514–519.
- 25 Gajdos C, Kile D, Hawn MT, et al. The significance of preoperative impaired sensorium on surgical outcomes in nonemergent general surgical operations. *JAMA Surg* 2015; **150**:30–36.
- 26 Robinson TN, Wu DS, Sauaia A, et al. Slower walking speed forecasts increased postoperative morbidity and one-year mortality across surgical specialties. *Ann Surg* 2013; **258**:582.
- 27 Huisman MG, Van Leeuwen BL, Ugolini G, et al. Timed up & go': a screening tool for predicting 30-day morbidity in onco-geriatric surgical patients? A multicenter cohort study. *PLoS One* 2014; **9**:e0086863.
- 28 Katsanos S, Babalis D, Kafkas N, et al. B-type natriuretic peptide vs. cardiac risk scores for prediction of outcome following major orthopedic surgery. *J Cardiovasc Med* 2015; **16**:465–471.
- 29 Nojiri T, Inoue M, Shintani Y, et al. B-type natriuretic peptide-guided risk assessment for postoperative complications in lung cancer surgery. *World J Surg* 2015; **39**:1092–1098.
- 30 Bryce GJ, Payne CJ, Gibson SC, et al. B-type natriuretic peptide predicts postoperative cardiac events and mortality after elective open abdominal aortic aneurysm repair. *J Vasc Surg* 2013; **57**:345–353.
- 31 Laufenberg-Feldmann R, Kappis B. Assessing preoperative anxiety using a questionnaire and clinical rating: a prospective observational study. *Eur J Anaesthesiol* 2013; **30**:758–763.
- 32 Schiff J, Frankenhauser S, Pritsch M, et al. The Anesthesia Preoperative Evaluation Clinic (APEC): a prospective randomized controlled trial assessing impact on consultation time, direct costs, patient education and satisfaction with anesthesia care. *Minerva Anestesiol* 2010; **76**:491–499.
- 33 Nicholson A, Coldwell C, Lewis S, Smith A. Nurse-led versus doctor-led preoperative assessment for elective surgical patients requiring regional of general anaesthesia. *Cochrane Database Syst Rev* 2013;CD010160.
- 34 Hines S, Munday J, Kynoch K. Effectiveness of nurse-led preoperative assessment services for elective surgery: a systematic review update. *JBI Database System Rev Implement Rep* 13 2015;279–317.
- 35 Kinnersley P, Phillips K, Savage K, et al. Interventions to promote informed consent for patients undergoing surgical and other invasive healthcare procedures. *Cochrane Database Syst Rev* 2013;CD009445.
- 36 McDonald S, Page MJ, Beringer K, et al. Preoperative education for hip or knee replacement. *Cochrane Database Syst Rev* 2014;CD003526.
- 37 Eley V, Searles T, Donovan K, Walters E. Effect of an anaesthesia information video on preoperative maternal anxiety and postoperative satisfaction in elective caesarean section: a prospective randomised trial. *Anaesth Intensive Care* 2013; **41**:774–781.
- 38 Fraval A, Chandrananth J, Coventry LS, et al. Internet based patient education improves informed consent for elective orthopaedic surgery: a randomized controlled trial. *BMC Musculoskelet Disord* 2015; **16**:14.
- 39 Yin B, Goldsmith L, Gambardella R. Web-based education prior to knee arthroscopy enhances informed consent and patient knowledge recall: a prospective, randomized controlled study. *J Bone Joint Surg Am* 2015; **97**:964–971.
- 40 Alanazi AA. Reducing anxiety in preoperative patients: a systematic review. *Br J Nurs* 2014; **23**:387–393.
- 41 de Aguiar-Nascimento JE, Leal FS, Dantas DC, et al. Preoperative education in cholecystectomy in the context of a multimodal protocol of perioperative care: a randomized, controlled trial. *World J Surg* 2014; **38**:357–362.
- 42 Kekecs Z, Jakubovits E, Varga K, Gombos K. Effects of patient education and therapeutic suggestions on cataract surgery patients: A randomized controlled clinical trial. *Patient Educ Couns* 2014; **94**: 116–122.
- 43 Uldry E, Schäfer M, Saadi A, et al. Patients' preferences on information and involvement in decision making for gastrointestinal surgery. *World J Surg* 2013; **37**:2162–2171.
- 44 Nehme J, El-Khani U, Chow A, et al. The use of multimedia consent programs for surgical procedures: a systematic review. *Surg Innov* 2013; **20**:13–23.
- 45 Huber J, Ihrig A, Yass M, et al. Multimedia support for improving preoperative patient education: a randomized controlled trial using the example of radical prostatectomy. *Ann Surg Oncol* 2013; **20**:15–23.
- 46 Straessle R, Gilliard N, Frascarolo P, et al. Is a preanaesthetic information form really useful? *Acta Anaesthesiol Scand* 2011; **55**:517–523.
- 47 Kakinuma A, Nagatani H, Otake H, et al. The effects of short interactive animation video information on preanesthetic anxiety, knowledge, and interview time: a randomized controlled trial. *Anesth Analg* 2011; **112**:1314–1318.
- 48 Gautschi OP, Stienen MN, Hermann C, et al. Web-based audiovisual patient information system: a study of preoperative patient information in a neurosurgical department. *Acta Neurochir* 2010; **152**:1337–1341.
- 49 Jjala H, French J, Foxall G, et al. Effect of preoperative multimedia information on perioperative anxiety in patients undergoing procedures under regional anaesthesia. *Br J Anaesth* 2010; **104**:369–374.
- 50 Renouf T, Leary A, Wiseman T. Do psychological interventions reduce preoperative anxiety? *Br J Nurs* 2014; **23**:1208–1212.
- 51 Granziera E, Guglieri I, Del Bianco P, et al. A multidisciplinary approach to improve preoperative understanding and reduce anxiety: a randomised study. *Eur J Anaesthesiol* 2013; **30**:734–742.
- 52 Sadati L, Pazouki A, Mehdizadeh A, et al. Effect of preoperative nursing visit on preoperative anxiety and postoperative complications in candidates for laparoscopic cholecystectomy: a randomized clinical trial. *Scand J Caring Sci* 2013; **27**:994–998.
- 53 Tou S, Tou W, Mah D, et al. Effect of preoperative two-dimensional animation information on perioperative anxiety and knowledge retention in patients undergoing bowel surgery: a randomized pilot study. *Colorect Dis* 2013; **15**:e256–e265.
- 54 Lin S-Y, Huang H-A, Lin S-C, et al. The effect of an anaesthetic patient information video on perioperative anxiety: a randomised study. *Eur J Anaesthesiol* 2016; **33**:134–139.
- 55 Lim L, Chow P, Wong C-Y, et al. Doctor–patient communication, knowledge, and question prompt lists in reducing preoperative anxiety: a randomized control study. *Asian J Surg* 2011; **34**:175–180.
- 56 Angioli R, Plotti F, Capriglione S, et al. The effects of giving patients verbal or written preoperative information in gynecologic oncology surgery: a randomized study and the medical-legal point of view. *Eur J Obstet Gynecol Reprod Biol* 2014; **177**:67–71.
- 57 Crabtree TD, Puri V, Bell JM, et al. Outcomes and perception of lung surgery with implementation of a patient video education module: a prospective cohort study. *J Am Coll Surg* 2012; **214**:816–821; e2.
- 58 De Hert S, Moerman A, De Baerdenaer L. Postoperative complications in cardiac patients undergoing noncardiac surgery. *Curr Opin Crit Care* 2016; **22**:357–364.
- 59 Poldermans D, Bax JJ, Boersma E, et al. Guidelines for preoperative cardiac risk assessment and perioperative cardiac management in noncardiac surgery: the Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Noncardiac Surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anaesthesiology (ESA). *Eur J Anaesthesiol* 2010; **27**:92–137.

- 60 Bouri S, Shun-Shin MJ, Cole GD, *et al.* Meta-analysis of secure randomised controlled trials of β -blockade to prevent perioperative death in noncardiac surgery. *Heart* 2014; **100**:456–464.
- 61 Longrois D, Hoefst A, De Hert S. 2014 European Society of Cardiology/ European Society of Anaesthesiology guidelines on noncardiac surgery: cardiovascular assessment and management: A short explanatory statement from the European Society of Anaesthesiology members who participated in the European Task Force. *Eur J Anaesthesiol* 2014; **31**:513–516.
- 62 Devereaux P, Mrkobrada M, Sessler DI, *et al.* Aspirin in patients undergoing noncardiac surgery. *N Engl J Med* 2014; **370**:1494–1503.
- 63 Devereaux P, Sessler DI, Leslie K, *et al.* Clonidine in patients undergoing noncardiac surgery. *N Engl J Med* 2014; **370**:1504–1513.
- 64 Gupta HG, Gupta PK, Fang X, *et al.* Development and validation of a risk calculator predicting postoperative respiratory failure. *Chest* 2011; **140**:1207–1215.
- 65 Imposti FC, Cizik A, Bransford R, *et al.* Risk factors for pulmonary complications after spine surgery. *Evid Based Spine Care J* 2010; **1**: 26–33.
- 66 Canet J, Sabaté S, Mazo V, *et al.* Development and validation of a score to predict postoperative respiratory failure in a multicentre European cohort: a prospective, observational study. *Eur J Anaesthesiol* 2015; **32**:458–470.
- 67 Fischer JPS, Shang EK, Butler CE, *et al.* Validated model for predicting postoperative respiratory failure: analysis of 1706 abdominal wall reconstructions. *Plast Reconstr Surg* 2013; **132**:826e–835e.
- 68 Jeong BHS, Shin B, Eom JS, *et al.* Development of a prediction rule for estimating postoperative pulmonary complications. *PLoS One [Electronic Resource]* 2014; **9**:e113656.
- 69 Mazo V, Sabaté S, Canet J, *et al.* Prospective external validation of a predictive score for postoperative pulmonary complications. *Anesthesiology* 2014; **121**:219–231.
- 70 Shiozaki AF, Fujiwara H, Okamura H, *et al.* Risk factors for postoperative respiratory complications following esophageal cancer resection. *Oncol Lett* 2012; **3**:907–912.
- 71 Gupta HG, Gupta PK, Schuller D, *et al.* Development and validation of a risk calculator for predicting postoperative pneumonia. *Mayo Clin Proc* 2013; **88**:1241–1249.
- 72 Blum JMS, Stentz MJ, Dechert R, *et al.* Preoperative and intraoperative predictors of postoperative acute respiratory distress syndrome in a general surgical population. *Anesthesiology* 2013; **118**:19–29.
- 73 Mazo VS, Sabaté S, Canet J, *et al.* Prospective external validation of a predictive score for postoperative pulmonary complications. *Anesthesiology* 2014; **121**:219–231.
- 74 Tokgoz HA, Akduman B, Unal I, *et al.* Chronic pulmonary diseases are independent risk factors for complications after radical nephrectomy. *Int Urol Nephrol* 2011; **43**:1025–1031.
- 75 Kim HJL, Lee J, Park YS, *et al.* Impact of GOLD groups of chronic pulmonary obstructive disease on surgical complications. *Int J COPD* 2016; **11**:281–287.
- 76 Keeratchananont WT, Thanadetsuntorn C, Keeratchananont S. Value of preoperative 6-minute walk test for predicting postoperative pulmonary complications. *Ther Adv Respir Dis* 2016; **10**:18–25.
- 77 Paisani DMF, Fiore JF Jr, Lunardi AC, *et al.* Preoperative 6-min walking distance does not predict pulmonary complications in upper abdominal surgery. *Respirology* 2012; **17**:1013–1017.
- 78 Clavellina-Gaytan DV, Velázquez-Fernández D, Del-Villar E, *et al.* Evaluation of spirometric testing as a routine preoperative assessment in patients undergoing bariatric surgery. *Obesity Surg* 2015; **25**:530–536.
- 79 van Huisstede AB, Biter LU, Luitwieler R, *et al.* Pulmonary function testing and complications of laparoscopic bariatric surgery. *Obesity Surg* 2013; **23**:1596–1603.
- 80 Valenza FF, Froio S, Coppola S, *et al.* Preoperative changes of forced vital capacity due to body position do not correlate with postoperative respiratory function in obese subjects. *Minerva Anesthesiol* 2013; **79**: 342–348.
- 81 Chong HSM, Moon ES, Park JO, *et al.* Value of preoperative pulmonary function test in flaccid neuromuscular scoliosis surgery. *Spine (Phila Pa 1976)* 2011; **36**:E1391–E1394.
- 82 Huh JS, Sohn TS, Kim JK, *et al.* Is routine preoperative spirometry necessary in elderly patients undergoing laparoscopy-assisted gastrectomy? *J Int Med Res* 2013; **41**:1301–1309.
- 83 Takiguchi HN, Niimi K, Tomomatsu H, *et al.* Preoperative spirometry and perioperative drug therapy in patients with obstructive pulmonary dysfunction. *Tokai J Exp Clin Med* 2014; **39**:151–157.
- 84 Ohrlander TD, Dencker M, Acosta S. Preoperative spirometry results as a determinant for long-term mortality after EVAR for AAA. *Eur J Vasc Endovasc Surg* 2012; **43**:43–47.
- 85 Kaw RP, Pasupuleti V, Walker E, *et al.* Postoperative complications in patients with obstructive sleep apnea. *Chest* 2012; **141**:436–441.
- 86 Abdelsattar ZMH, Hendren S, Wong SL, *et al.* The impact of untreated obstructive sleep apnea on cardiopulmonary complications in general and vascular surgery: a cohort study. *Sleep* 2015; **38**:1205–1210.
- 87 Memtsoudis S, Liu SS, Ma Y, *et al.* Perioperative pulmonary outcomes in patients with sleep apnea after noncardiac surgery. *Anesth Analg* 2011; **112**:113–121.
- 88 Gross JB, Bachenberg KL, Benumof JL, *et al.* Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. *Anesthesiology* 2006; **104**:1081–1093.
- 89 American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep a. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. *Anesthesiology* 2014; **120**:268–286.
- 90 Chong CTT, Tey J, Leow SL, *et al.* Management plan to reduce risks in perioperative care of patients with obstructive sleep apnoea averts the need for presurgical polysomnography. *Ann Acad Med Singapore* 2013; **42**:110–119.
- 91 Lockhart EMW, Willingham MD, Abdallah AB, *et al.* Obstructive sleep apnea screening and postoperative mortality in a large surgical cohort. *Sleep Med* 2013; **14**:407–415.
- 92 Rasmussen JJF, Fuller WD, Ali MR. Sleep apnea syndrome is significantly underdiagnosed in bariatric surgical patients. *Surg Obes Relat Dis* 2012; **8**:569–573.
- 93 Singh ML, Liao P, Kobah S, *et al.* Proportion of surgical patients with undiagnosed obstructive sleep apnoea. *Br J Anaesth* 2013; **110**:629–636.
- 94 Siyam MA, Benhamou D. Difficult endotracheal intubation in patients with sleep apnea syndrome. *Anesth Analg* 2002; **95**:1098–1102.
- 95 Chung FL, Liao P, Elsaid H, *et al.* Factors associated with postoperative exacerbation of sleep-disordered breathing. *Anesthesiology* 2014; **120**:299–311.
- 96 Mutter TCC, Chateau D, Moffatt M, *et al.* A matched cohort study of postoperative outcomes in obstructive sleep apnea: could preoperative diagnosis and treatment prevent complications? *Anesthesiology* 2014; **121**:707–718.
- 97 Chung F, Ward B, Ho J, *et al.* Preoperative identification of sleep apnea risk in elective surgical patients, using the Berlin questionnaire. *J Clin Anesth* 2007; **19**:130–134.
- 98 Chung F, Yegneswaran B, Liao P, *et al.* Stop questionnaire tool to screen patients for obstructive sleep apnea. *Anesthesiology* 2008; **108**:812–821.
- 99 Khanna AKS, Sessler DI, Sun Z, *et al.* Using the STOP-BANG questionnaire to predict hypoxaemia in patients recovering from noncardiac surgery: a prospective cohort analysis. *Br J Anaesth* 2016; **116**:632–640.
- 100 Farney RJ, Walker BS, Farney RM, *et al.* The STOP-Bang equivalent model and prediction of severity of obstructive sleep apnea: relation to polysomnographic measurements of the apnea/hypopnea index. *J Clin Sleep Med* 2011; **7**:459–465B.
- 101 Chung FS, Subramanyam R, Liao P, *et al.* High STOP-Bang score indicates a high probability of obstructive sleep apnoea. *Br J Anaesth* 2012; **108**:768–775.
- 102 Chung FY, Yang Y, Liao P. Predictive performance of the stop-bang score for identifying obstructive sleep apnea in obese patients. *Obes Surg* 2013; **23**:2050–2057.
- 103 Seet E, Chua M, Liaw CM. High STOP-BANG questionnaire scores predict intraoperative and early postoperative adverse events. *Singapore Med J* 2015; **56**:212.
- 104 Vasu TS, Doghranji K, Cavallazzi R, *et al.* Obstructive sleep apnea syndrome and postoperative complications: clinical use of the STOP-BANG questionnaire. *Arch Otolaryngol Head Neck Surg* 2010; **136**:1020–1024.
- 105 Chia P, Seet E, Macachor J, *et al.* The association of preoperative STOP-BANG scores with postoperative critical care admission. *Anaesthesia* 2013; **68**:950–952.
- 106 Nagappa M, Patra J, Wong J, *et al.* Association of STOP-Bang questionnaire as a screening tool for sleep apnea and postoperative complications: a systematic review and bayesian meta-analysis of prospective and retrospective cohort studies. *Anesth Analg* 2017; **125**:1301–1308.
- 107 Tenorio LHS, Santos AC, Camara Neto JB, *et al.* The influence of inspiratory muscle training on diaphragmatic mobility, pulmonary function and maximum respiratory pressures in morbidly obese individuals: a pilot study. *Disabil Rehabil* 2013; **35**:1915–1920.

- 108 Katsura M, Kuriyama A, Takeshima T, *et al.* Preoperative inspiratory muscle training for postoperative pulmonary complications in adults undergoing cardiac and major abdominal surgery. *Cochrane Database Syst Rev* 2015;CD010356.
- 109 Cattano DA, Altamirano A, Vannucci A, *et al.* Preoperative use of incentive spirometry does not affect postoperative lung function in bariatric surgery. *Transl Res* 2010; **156**:265–272.
- 110 do Nascimento Junior P, Modolo NS, Andrade S, *et al.* Incentive spirometry for prevention of postoperative pulmonary complications in upper abdominal surgery. *Cochrane Database Syst Rev* 2014;CD006058.
- 111 Lunardi ACM, Miranda CS, Silva KM, *et al.* Weakness of expiratory muscles and pulmonary complications in malnourished patients undergoing upper abdominal surgery. *Respirology* 2012; **17**:108–113.
- 112 Webb ARR, Robertson N, Sparrow M. Smokers know little of their increased surgical risks and may quit on surgical advice. *ANZ J Surg* 2013; **83**:753–757.
- 113 Bettin CCG, Gower K, McCormick K, *et al.* Cigarette smoking increases complication rate in forefoot surgery. *Foot Ankle Int* 2015; **36**:488–493.
- 114 Hawn MTH, Houston TK, Campagna EJ, *et al.* The attributable risk of smoking on surgical complications. *Ann Surg* 2011; **254**:914–920.
- 115 McCunniff PTY, Young ES, Ahmadinia K, *et al.* Smoking is associated with increased blood loss and transfusion use after lumbar spinal surgery. *Clin Orthop Relat Res* 2016; **474**:1019–1025.
- 116 Sharma AD, Deeb AP, Iannuzzi JC, *et al.* Tobacco smoking and postoperative outcomes after colorectal surgery. *Ann Surg* 2013; **258**:296–300.
- 117 Singh JA. Smoking and outcomes after knee and hip arthroplasty: a systematic review. *J Rheumatol* 2011; **38**:1824–1834.
- 118 Turan AM, Mascha EJ, Roberman D, *et al.* Smoking and perioperative outcomes. *Anesthesiology* 2011; **114**:837–846.
- 119 Thomsen TV, Villebro N, Moller AM. Interventions for preoperative smoking cessation. *Cochrane Database Syst Rev* 2014; **3**:CD002294.
- 120 Gajdos CH, Hawn MT, Campagna EJ, *et al.* Adverse effects of smoking on postoperative outcomes in cancer patients. *Ann Surg Oncol* 2012; **19**:1430–1438.
- 121 Myers KH, Hajek P, Hinds C, McRobbie H. Stopping smoking shortly before surgery and postoperative complications: a systematic review and meta-analysis. *Arch Intern Med* 2011; **171**:983–989.
- 122 Mills EE, Eyawo O, Lockhart I, *et al.* Smoking cessation reduces postoperative complications: a systematic review and meta-analysis. *Am J Med* 2011; **124**:144–154; e8.
- 123 Wong JL, Lam DP, Abrishami A, *et al.* Short-term preoperative smoking cessation and postoperative complications: a systematic review and meta-analysis. *Can J Anaesth* 2012; **59**:268–279.
- 124 Thomsen TT, Tønnesen H, Okholm M, *et al.* Brief smoking cessation intervention in relation to breast cancer surgery: a randomized controlled trial. *Nicotine Tob Res* 2010; **12**:1118–1124.
- 125 Musallam KMR, Rosendaal FR, Zaatari G, *et al.* Smoking and the risk of mortality and vascular and respiratory events in patients undergoing major surgery. *JAMA Surg* 2013; **148**:755–762.
- 126 Song FB, Brown TJ, Blyth A, *et al.* Identifying and recruiting smokers for preoperative smoking cessation: a systematic review of methods reported in published studies. *Syst Rev* 2015; **4**:157.
- 127 Berlin NLC, Cutter C, Battaglia C. Will preoperative smoking cessation programs generate long-term cessation? A systematic review and meta-analysis. *Am J Manag Care* 2015; **21**:e623–e631.
- 128 Wong JA, Abrishami A, Yang Y, *et al.* A perioperative smoking cessation intervention with varenicline: a double-blind, randomized, placebo-controlled trial. *Anesthesiology* 2012; **117**:755–764.
- 129 Kunzel BC, Cabalza J, Faurot M, *et al.* Prospective pilot study of smoking cessation in patients undergoing urologic surgery. *Urology* 2012; **80**:104–109.
- 130 Khetarpal S, Tremper KK, Englesbe MJ, *et al.* Predictors of postoperative acute renal failure after noncardiac surgery in patients with previously normal renal function. *Anesthesiology* 2007; **107**:892–902.
- 131 van Kuijk J-P, Flu W-J, Chonchol M, *et al.* Temporary perioperative decline of renal function is an independent predictor for chronic kidney disease. *Clin J Am Soc Nephrol* 2010; **5**:1198–1204.
- 132 Chertow GM, Burdick E, Honour M, *et al.* Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol* 2005; **16**:3365–3370.
- 133 Coca SG, Yusuf B, Shlipak MG, *et al.* Long-term risk of mortality and other adverse outcomes after acute kidney injury: a systematic review and meta-analysis. *Am J Kidney Dis* 2009; **53**:961–973.
- 134 Nielson E, Hennrikus E, Lehman E, Mets B. Angiotensin axis blockade, hypotension, and acute kidney injury in elective major orthopedic surgery. *J Hosp Med* 2014; **9**:283–288.
- 135 Teixeira C, Rosa R, Rodrigues N, *et al.* Acute kidney injury after major abdominal surgery: a retrospective cohort analysis. *Crit Care Res Pract* 2014; **2014**:132175.
- 136 Wiener S, Kiziloz H, Dorin RP, *et al.* Predictors of postoperative decline in estimated glomerular filtration rate in patients undergoing robotic partial nephrectomy. *J Endourol* 2014; **28**:807–813.
- 137 Warth LC, Noiseux NO, Hogue MH, *et al.* Risk of acute kidney injury after primary and revision total hip arthroplasty and total knee arthroplasty using a multimodal approach to perioperative pain control including ketorolac and celecoxib. *J Arthroplasty* 2016; **31**:253–255.
- 138 Masoomi H, Carmichael JC, Dolich M, *et al.* Predictive factors of acute renal failure in colon and rectal surgery. *Am Surg* 2012; **78**:1019–1023.
- 139 Burns KE, Chu MW, Novick RJ, *et al.* Perioperative N-acetylcysteine to prevent renal dysfunction in high-risk patients undergoing CABG surgery: a randomized controlled trial. *JAMA* 2005; **294**:342–350.
- 140 McBride WT, Allen S, Gormley SM, *et al.* Methylprednisolone favourably alters plasma and urinary cytokine homeostasis and subclinical renal injury at cardiac surgery. *Cytokine* 2004; **27**:81–89.
- 141 Zacharias M, Conlon NP, Herbison GP, *et al.* Interventions for protecting renal function in the perioperative period. *Cochrane Database Syst Rev* 2008; **4**:CD003590.
- 142 Lee E-H, Kim HR, Baek S-H, *et al.* Risk factors of postoperative acute kidney injury in patients undergoing esophageal cancer surgery. *J Cardiothorac Vasc Anesth* 2014; **28**:936–942.
- 143 Kelz RR, Reinke CE, Zubizarreta JR, *et al.* Acute kidney injury, renal function, and the elderly obese surgical patient: a matched case-control study. *Ann Surg* 2013; **258**:359–363.
- 144 Canedo J, Ricciardi K, DaSilva G, *et al.* Are postoperative complications more common following colon and rectal surgery in patients with chronic kidney disease? *Colorectal Dis* 2013; **15**:85–90.
- 145 Moghadamyeghaneh Z, Phelan MJ, Carmichael JC, *et al.* Preoperative dehydration increases risk of postoperative acute renal failure in colon and rectal surgery. *J Gastrointest Surg* 2014; **18**:2178–2185.
- 146 Walsh M, Garg AX, Devereaux P, *et al.* The association between perioperative hemoglobin and acute kidney injury in patients having noncardiac surgery. *Anesth Analg* 2013; **117**:924–931.
- 147 Robinson BE, Weber H. Dehydration despite drinking: beyond the BUN/Creatinine ratio. *J Am Med Dir Assoc* 2002; **3**:386–389.
- 148 Riccardi A, Chiarbonello B, Minuto P, *et al.* Identification of the hydration state in emergency patients: correlation between caval index and BUN/creatinine ratio. *Eur Rev Med Pharmacol Sci* 2013; **17**:1800–1803.
- 149 Cywinski JB, Mascha EJ, Kurz A, Sessler DI. Estimated glomerular filtration rate better predicts 30-day mortality after noncardiac surgery than serum creatinine: a retrospective analysis of 92,888 patients. *Can J Anesth* 2015; **62**:745–752.
- 150 AbuRahma AF, Srivastava M, Chong B, *et al.* Impact of chronic renal insufficiency using serum creatinine vs glomerular filtration rate on perioperative clinical outcomes of carotid endarterectomy. *J Am Coll Surg* 2013; **216**:525–532.
- 151 AbuRahma AF, Alhalbouni S, Abu-Halimah S, *et al.* Impact of chronic renal insufficiency on the early and late clinical outcomes of carotid artery stenting using serum creatinine vs glomerular filtration rate. *J Am Coll Surg* 2014; **218**:797–805.
- 152 Argalious M, Dalton J, Cywinski J, *et al.* Association between preoperative statin therapy and postoperative change in glomerular filtration rate in endovascular aortic surgery. *Br J Anaesth* 2012; **109**:161–167.
- 153 Krane LS, Sandberg JM, Rague JT, Hemal AK. Do statin medications impact renal functional or oncologic outcomes for robot-assisted partial nephrectomy? *J Endourol* 2014; **28**:1308–1312.
- 154 Tagawa M, Ogata A, Hamano T. Preand/or intra-operative prescription of diuretics, but not renin-angiotensin-system inhibitors, is significantly associated with acute kidney injury after noncardiac surgery: a retrospective cohort study. *PLoS One* 2015; **10**:e0132507.
- 155 Shah M, Jain AK, Brunelli SM, *et al.* Association between angiotensin converting enzyme inhibitor or angiotensin receptor blocker use prior to major elective surgery and the risk of acute dialysis. *BMC Nephrol* 2014; **15**:53.
- 156 Giri VP, Giri OP, Bajracharya S, *et al.* Risk of acute kidney injury with amikacin versus gentamycin both in combination with metronidazole for surgical prophylaxis. *J Clin Diagn Res* 2016; **10**:FC09–FC12.
- 157 Ishikawa S, Griesdale DE, Lohser J. Acute kidney injury after lung resection surgery: incidence and perioperative risk factors. *Anesth Analg* 2012; **114**:1256–1262.
- 158 Garg AX, Kurz A, Sessler DI, *et al.* Perioperative aspirin and clonidine and risk of acute kidney injury: a randomized clinical trial. *JAMA* 2014; **312**:2254–2264.
- 159 Terashi T, Takehara A, Kuniyoshi T, *et al.* Remifentanyl temporarily improves renal function in adult patients with chronic kidney disease undergoing orthopedic surgery. *J Anesth* 2013; **27**:340–345.

- 160 Winterhalter M, Brandl K, Rahe-Meyer N, *et al.* Endocrine stress response and inflammatory activation during CABG surgery. A randomized trial comparing remifentanyl infusion to intermittent fentanyl. *Eur J Anaesthesiol* 2008; **25**:326–335.
- 161 Wong GT, Huang Z, Ji S, Irwin MG. Remifentanyl reduces the release of biochemical markers of myocardial damage after coronary artery bypass surgery: a randomized trial. *J Cardiothorac Vasc Anesth* 2010; **24**:790–796.
- 162 Noordzij PG, Poldermans D, Schouten O, *et al.* Postoperative mortality in the Netherlands: a population-based analysis of surgery-specific risk in adults. *Anesthesiology* 2010; **112**:1105–1115.
- 163 Haynes AB, Weiser TG, Berry WR, *et al.* A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med* 2009; **360**:491–499.
- 164 Bock M, Fanolla A, Segur-Cabanac I, *et al.* A comparative effectiveness analysis of the implementation of surgical safety checklists in a tertiary care hospital. *JAMA Surg* 2016; **151**:639–646.
- 165 Krolikowska M, Kataja M, Pöyhä R, *et al.* Mortality in diabetic patients undergoing noncardiac surgery: a 7-year follow-up study. *Acta Anaesthesiol Scand* 2009; **53**:749–758.
- 166 Frisch A, Chandra P, Smiley D, *et al.* Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. *Diabetes Care* 2010; **33**:1783–1788.
- 167 Sebranek J, Lugli AK, Coursin D. Glycaemic control in the perioperative period. *Br J Anaesth* 2013; **111**:i18–i34.
- 168 Clement S, Braithwaite SS, Magee MF, *et al.* Management of diabetes and hyperglycemia in hospitals. *Diabetes Care* 2004; **27**:553–591.
- 169 Wild SH, Roglic G, Green A, *et al.* Global prevalence of diabetes: estimates for the year 2000 and projections for 2030: response to Rathman and Giani. *Diabetes Care* 2004; **27**:2568–2569.
- 170 Dimick JB, Chen SL, Taheri PA, *et al.* Hospital costs associated with surgical complications: a report from the private-sector National Surgical Quality Improvement Program. *J Am Coll Surg* 2004; **199**:531–537.
- 171 Jones CE, Graham LA, Morris MS, *et al.* Association between preoperative hemoglobin A1c levels, postoperative hyperglycemia, and readmissions following gastrointestinal surgery. *JAMA Surg* 2017; **152**:1031–1038.
- 172 Underwood P, Askari R, Hurwitz S, *et al.* Preoperative A1C and clinical outcomes in patients with diabetes undergoing major noncardiac surgical procedures. *Diabetes Care* 2014; **37**:611–616.
- 173 Bock M, Johansson T, Fritsch G, *et al.* The impact of preoperative testing for blood glucose concentration and haemoglobin A1c on mortality, changes in management and complications in noncardiac elective surgery: a systematic review. *Eur J Anaesthesiol* 2015; **32**:152–159.
- 174 Joshi GP, Chung F, Vann MA, *et al.* Society for Ambulatory Anesthesia consensus statement on perioperative blood glucose management in diabetic patients undergoing ambulatory surgery. *Anesth Analg* 2010; **111**:1378–1387.
- 175 Rollins KE, Varadhan KK, Dhatriya K, Lobo DN. Systematic review of the impact of HbA1c on outcomes following surgery in patients with diabetes mellitus. *Clin Nutr* 2016; **35**:308–316.
- 176 Abdelmalak B, Knittel J, Abdelmalak J, *et al.* Preoperative blood glucose concentrations and postoperative outcomes after elective noncardiac surgery: an observational study. *Br J Anaesth* 2013; **112**:79–88.
- 177 Heikes KE, Eddy DM, Arondekar B, Schlessinger L. Diabetes risk calculator. *Diabetes Care* 2008; **31**:1040–1045.
- 178 Dunkelgrun M, Schreiner F, Schockman DB, *et al.* Usefulness of preoperative oral glucose tolerance testing for perioperative risk stratification in patients scheduled for elective vascular surgery. *Am J Cardiol* 2008; **101**:526–529.
- 179 van Kuijk J-P, Dunkelgrun M, Schreiner F, *et al.* Preoperative oral glucose tolerance testing in vascular surgery patients: long-term cardiovascular outcome. *Am Heart J* 2009; **157**:919–925.
- 180 Richards JE, Kauffmann RM, Zuckerman SL, *et al.* Relationship of hyperglycemia and surgical-site infection in orthopaedic surgery. *J Bone Joint Surg Am* 2012; **94**:1181–1186.
- 181 Davis MC, Ziewacz JE, Sullivan SE, El-Sayed AM. Preoperative hyperglycemia and complication risk following neurosurgical intervention: a study of 918 consecutive cases. *Surg Neurol Int* 2012; **3**:49.
- 182 Van den Boom W, Schroeder RA, Manning MW, *et al.* Effect of A1C and glucose on postoperative mortality in noncardiac and cardiac surgeries. *Diabetes Care* 2018; **41**:782–788.
- 183 Harris AH, Bowe TR, Gupta S, *et al.* Hemoglobin A1C as a marker for surgical risk in diabetic patients undergoing total joint arthroplasty. *J Arthroplasty* 2013; **28**:25–29.
- 184 Stryker LS, Abdel MP, Morrey ME, *et al.* Elevated postoperative blood glucose and preoperative hemoglobin A1C are associated with increased wound complications following total joint arthroplasty. *J Bone Joint Surg Am* 2013; **95**:808–814.
- 185 Endara M, Masden D, Goldstein J, *et al.* The role of chronic and perioperative glucose management in high-risk surgical closures: a case for tighter glycemic control. *Plast Reconstr Surg* 2013; **132**:996–1004.
- 186 Goodenough CJ, Liang MK, Nguyen MT, *et al.* Preoperative glycosylated hemoglobin and postoperative glucose together predict major complications after abdominal surgery. *J Am Coll Surg* 2015; **221**:854–861; e1.
- 187 Rawlins L, Rawlins MP, Brown CC, Schumacher DL. Effect of elevated hemoglobin A1c in diabetic patients on complication rates after Roux-en-Y gastric bypass. *Surg Obes Relat Dis* 2013; **9**:749–752.
- 188 Kunstman JW, Healy JM, Araya DA, Salem RR. Effects of preoperative long-term glycemic control on operative outcomes following pancreaticoduodenectomy. *Am J Surg* 2015; **209**:1053–1062.
- 189 Apfelbaum JL, Connis RT, Nickinovich DG, *et al.* Practice advisory for preanesthesia evaluation: an updated report by the American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. *Anesthesiology* 2012; **116**:522–538.
- 190 O'Neill F, Carter E, Pink N, Smith I. Routine preoperative tests for elective surgery: summary of updated NICE guidance. *BMJ* 2016; **354**:i3292.
- 191 Buchleitner AM, Martínez-Alonso M, Hernández M, *et al.* Perioperative glycaemic control for diabetic patients undergoing surgery. *Cochrane Database Syst Rev* 2012;CD007315.
- 192 McGuire H, Longson D, Adler A, *et al.* Management of type 2 diabetes in adults: summary of updated NICE guidance. *BMJ* 2016; **353**:i1575.
- 193 Rooke TW, Hirsch AT, Misra S, *et al.* 2011 ACCF/AHA Focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Developed in Collaboration With the Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society for Vascular Medicine, and Society for Vascular Surgery. *J Vasc Surg* 2011; **54**:e32–e58.
- 194 Erden V, Basaranoglu G, Delatioglu H, Hamzaoglu N. Relationship of difficult laryngoscopy to long-term noninsulin-dependent diabetes and hand abnormality detected using the 'prayer sign'. *Br J Anaesth* 2003; **91**:159–160.
- 195 Coe A, Saleh T, Samuel T, Edwards R. The management of patients with morbid obesity in the anaesthetic assessment clinic. *Anaesthesia* 2004; **59**:570–573.
- 196 Tsai A, Schumann R. Morbid obesity and perioperative complications. *Curr Opin Anesthesiol* 2016; **29**:103–108.
- 197 Brodsky JB, Lemmens HJ, Brock-Utne JG, *et al.* Morbid obesity and tracheal intubation. *Anesth Analg* 2002; **94**:732–736.
- 198 Collier B, Goreja MA, Duke BE. Postoperative rhabdomyolysis with bariatric surgery. *Obes Surg* 2003; **13**:941–943.
- 199 Gonzalez R, Bowers S, Venkatesh K, *et al.* Preoperative factors predictive of complicated postoperative management after Roux-en-Y gastric bypass for morbid obesity. *Surg Endosc* 2003; **17**:1900–1904.
- 200 Patel N, Bagan B, Vadera S, *et al.* Obesity and spine surgery: relation to perioperative complications. *J Neurosurg Spine* 2007; **6**:291–297.
- 201 Nwachukwu BU, Nelson EP, Collins JE, *et al.* Obesity & hypertension are determinants of poor hemodynamic control during total joint arthroplasty: a retrospective review. *BMC Musculoskelet Disord* 2013; **14**:20.
- 202 Catheline J-M, Bihan H, Le Quang T, *et al.* Preoperative cardiac and pulmonary assessment in bariatric surgery. *Obes Surg* 2008; **18**:271–277.
- 203 Fornitano LD, Godoy MF. Exercise testing in individuals with morbid obesity. *Obes Surg* 2010; **20**:583–588.
- 204 McCullough PA, Gallagher MJ, Sandberg KR, *et al.* Cardiorespiratory fitness and short-term complications after bariatric surgery. *Chest* 2006; **130**:517–525.
- 205 Lerakis S, Kalogeropoulos AP, El-Chami MF, *et al.* Transthoracic dobutamine stress echocardiography in patients undergoing bariatric surgery. *Obes Surg* 2007; **17**:1475–1481.
- 206 Faintuch J, Souza SA, Valezi AC, *et al.* Pulmonary function and aerobic capacity in asymptomatic bariatric candidates with very severe morbid obesity. *Rev Hosp Clin Fac Med Sao Paulo* 2004; **59**:181–186.
- 207 Collet F, Mallart A, Bervar J, *et al.* Physiologic correlates of dyspnea in patients with morbid obesity. *Int J Obes* 2007; **31**:700–706.
- 208 Lopez PP, Stefan B, Schulman CI, Byers PM. Prevalence of sleep apnea in morbidly obese patients who presented for weight loss surgery evaluation: more evidence for routine screening for obstructive sleep apnea before weight loss surgery. *Am Surg* 2008; **74**:834–838.
- 209 Lee YH, Johan A, Wong KKH, *et al.* Prevalence and risk factors for obstructive sleep apnea in a multiethnic population of patients presenting for bariatric surgery in Singapore. *Sleep Med* 2009; **10**:226–232.
- 210 Sareli AE, Cantor CR, Williams NN, *et al.* Obstructive sleep apnea in patients undergoing bariatric surgery: a tertiary center experience. *Obes Surg* 2011; **21**:316–327.

- 211 Carneiro G, Flório RT, Zanella MT, *et al.* Is mandatory screening for obstructive sleep apnea with polysomnography in all severely obese patients indicated? *Sleep Breath* 2012; **16**:163–168.
- 212 Rasmussen JJ, Fuller WD, Ali MR. Sleep apnea syndrome is significantly underdiagnosed in bariatric surgical patients. *Surg Obes Relat Dis* 2012; **8**:569–573.
- 213 Dixon JB, Schachter LM, O'Brien PE. Predicting sleep apnea and excessive day sleepiness in the severely obese: indicators for polysomnography. *Chest* 2003; **123**:1134–1141.
- 214 Hekiart AM, Mick R, Mirza N. Prediction of difficult laryngoscopy: does obesity play a role? *Ann Otol Rhinol Laryngol* 2007; **116**:799–804.
- 215 Kim W, Ahn H, Lee C, *et al.* Neck circumference to thyromental distance ratio: a new predictor of difficult intubation in obese patients. *Br J Anaesth* 2011; **106**:743–748.
- 216 Calder CL, Ortega G, Vij A, *et al.* Morbid obesity is an independent risk factor for postoperative renal dysfunction in young adults: a review of the American College of Surgeons National Surgical Quality Improvement Program database. *Am J Surg* 2016; **211**:772–777.
- 217 Flancbaum L, Belsley S, Drake V, *et al.* Preoperative nutritional status of patients undergoing Roux-en-Y gastric bypass for morbid obesity. *J Gastrointest Surg* 2006; **10**:1033–1037.
- 218 Schweiger C, Weiss R, Berry E, Keidar A. Nutritional deficiencies in bariatric surgery candidates. *Obes Surg* 2010; **20**:193–197.
- 219 Khanbhai M, Dubb S, Patel K, *et al.* The prevalence of iron deficiency anaemia in patients undergoing bariatric surgery. *Obes Res Clin Pract* 2015; **9**:45–49.
- 220 Toh SY, Zarshenas N, Jorgensen J. Prevalence of nutrient deficiencies in bariatric patients. *Nutrition* 2009; **25**:1150–1156.
- 221 Wolf E, Utech M, Stehle P, *et al.* Preoperative micronutrient status in morbidly obese patients before undergoing bariatric surgery: results of a cross-sectional study. *Surg Obes Relat Dis* 2015; **11**:1157–1163.
- 222 Kilic A, Schuchert MJ, Pennathur A, *et al.* Impact of obesity on perioperative outcomes of minimally invasive esophagectomy. *Ann Thorac Surg* 2009; **87**:412–415.
- 223 Pratap J, Clements E, Levy D. Prevalence of obesity and unrecognised glucose intolerance in a UK day-case surgery unit: observational study. *Pract Diabetes* 2006; **23**:408–412.
- 224 Fierabracci P, Pinchera A, Martinelli S, *et al.* Prevalence of endocrine diseases in morbidly obese patients scheduled for bariatric surgery: beyond diabetes. *Obes Surg* 2011; **21**:54–60.
- 225 Del Chiaro M, Rangelova E, Ansoorge C, *et al.* Impact of body mass index for patients undergoing pancreaticoduodenectomy. *World J Gastrointest Pathophysiol* 2013; **4**:37–42.
- 226 Isac WE, Autorino R, Hillyer SP, *et al.* The impact of body mass index on surgical outcomes of robotic partial nephrectomy. *BJU Int* 2012; **110**:E997–E1002.
- 227 Ballian N, Yamane B, Levenson G, *et al.* Body mass index does not affect postoperative morbidity and oncologic outcomes of total mesorectal excision for rectal adenocarcinoma. *Ann Surg Oncol* 2010; **17**:1606–1613.
- 228 Basques BA, Fu MC, Buerba RA, *et al.* Using the ACS-NSQIP to identify factors affecting hospital length of stay after elective posterior lumbar fusion. *Spine (Phila Pa 1976)* 2014; **39**:497–502.
- 229 Seicean A, Alan N, Seicean S, *et al.* Impact of increased body mass index on outcomes of elective spinal surgery. *Spine (Phila Pa 1976)* 2014; **39**:1520–1530.
- 230 Fischer JP, Nelson JA, Kovach SJ, *et al.* Impact of obesity on outcomes in breast reconstruction: analysis of 15,937 patients from the ACS-NSQIP datasets. *J Am Coll Surg* 2013; **217**:656–664.
- 231 Hrabec JE, Sherman SK, Charlton ME, *et al.* The effect of BMI on outcomes in proctectomy. *Dis Colon Rectum* 2014; **57**:608–615.
- 232 Al-Refaie WB, Parsons HM, Henderson WG, *et al.* Body mass index and major cancer surgery outcomes: lack of association or need for alternative measurements of obesity? *Ann Surg Oncol* 2010; **17**:2264–2273.
- 233 Zhang S, Yang H, Luo K, *et al.* The impact of body mass index on complication and survival in resected oesophageal cancer: a clinical-based cohort and meta-analysis. *Br J Cancer* 2013; **109**:2894–2903.
- 234 Livingston EH, Arterburn D, Schifftner TL, *et al.* National Surgical Quality Improvement Program analysis of bariatric operations: modifiable risk factors contribute to bariatric surgical adverse outcomes. *J Am Coll Surg* 2006; **203**:625–633.
- 235 Joshi GP, Ahmad S, Riad W, *et al.* Selection of obese patients undergoing ambulatory surgery: a systematic review of the literature. *Anesth Analg* 2013; **117**:1082–1091.
- 236 Khan MA, Grinberg R, Johnson S, *et al.* Perioperative risk factors for 30-day mortality after bariatric surgery: is functional status important? *Surg Endosc* 2013; **27**:1772–1777.
- 237 Bhayani NH, Hyder O, Frederick W, *et al.* Effect of metabolic syndrome on perioperative outcomes after liver surgery: a National Surgical Quality Improvement Program (NSQIP) analysis. *Surgery* 2012; **152**:218–226.
- 238 Elnahas A, Nguyen GC, Okrainec A, *et al.* The effect of underlying liver disease on short-term outcomes following bariatric surgery. *Surg Endosc* 2014; **28**:2708–2712.
- 239 Ejaz A, Spolverato G, Kim Y, *et al.* Impact of body mass index on perioperative outcomes and survival after resection for gastric cancer. *J Surg Res* 2015; **195**:74–82.
- 240 de la Garza G, Militsakh O, Panwar A, *et al.* Obesity and perioperative complications in head and neck free tissue reconstruction. *Head Neck* 2016; **38** (Suppl 1):E1188–E1191.
- 241 Hamoui N, Anthonie G, Crookes PF. The value of pulmonary function testing prior to bariatric surgery. *Obes Surg* 2006; **16**:1570–1573.
- 242 Yeh P-S, Lee Y-C, Lee W-J, *et al.* Clinical predictors of obstructive sleep apnea in Asian bariatric patients. *Obes Surg* 2010; **20**:30–35.
- 243 DeMaria EJ, Murr M, Byrne TK, *et al.* Validation of the obesity surgery mortality risk score in a multicenter study proves it stratifies mortality risk in patients undergoing gastric bypass for morbid obesity. *Ann Surg* 2007; **246**:578–584.
- 244 Thomas H, Agrawal S. Systematic review of obesity surgery mortality risk score: preoperative risk stratification in bariatric surgery. *Obes Surg* 2012; **22**:1135–1140.
- 245 Melendez-Araújo MS, de Matos Arruda SL, de Oliveira Kelly E, de Carvalho KMB. Preoperative nutritional interventions in morbid obesity: impact on body weight, energy intake, and eating quality. *Obes Surg* 2012; **22**:1848–1854.
- 246 Alami RS, Morton JM, Schuster R, *et al.* Is there a benefit to preoperative weight loss in gastric bypass patients? A prospective randomized trial. *Surg Obes Relat Dis* 2007; **3**:141–145.
- 247 Alvarado R, Alami R, Hsu G, *et al.* The impact of preoperative weight loss in patients undergoing laparoscopic Roux-en-Y gastric bypass. *Obes Surg* 2005; **15**:1282–1286.
- 248 Benotti PN, Still CD, Wood GC, *et al.* Preoperative weight loss before bariatric surgery. *Arch Surg* 2009; **144**:1150–1155.
- 249 Liu RC, Sabnis AA, Forsyth C, Chand B. The effects of acute preoperative weight loss on laparoscopic Roux-en-Y gastric bypass. *Obes Surg* 2005; **15**:1396–1402.
- 250 Williams TK, Rosato EL, Kennedy EP, *et al.* Impact of obesity on perioperative morbidity and mortality after pancreaticoduodenectomy. *J Am Coll Surg* 2009; **208**:210–217.
- 251 Huerta S, Dredar S, Hayden E, *et al.* Preoperative weight loss decreases the operative time of gastric bypass at a Veterans Administration hospital. *Obes Surg* 2008; **18**:508–512.
- 252 Riess KP, Baker MT, Lambert PJ, *et al.* Effect of preoperative weight loss on laparoscopic gastric bypass outcomes. *Surg Obes Relat Dis* 2008; **4**:704–708.
- 253 Still CD, Benotti P, Wood GC, *et al.* Outcomes of preoperative weight loss in high-risk patients undergoing gastric bypass surgery. *Arch Surg* 2007; **142**:994–998.
- 254 Leykin Y, Pellis T, Del Mestro E, *et al.* Anesthetic management of morbidly obese and super-morbidly obese patients undergoing bariatric operations: hospital course and outcomes. *Obes Surg* 2006; **16**:1563–1569.
- 255 Frey WC, Pilcher J. Obstructive sleep-related breathing disorders in patients evaluated for bariatric surgery. *Obes Surg* 2003; **13**:676–683.
- 256 Afolabi BA, Novaro GM, Szomstein S, *et al.* Cardiovascular complications of obesity surgery in patients with increased preoperative cardiac risk. *Surg Obes Relat Dis* 2009; **5**:653–656.
- 257 Fried M, Yumuk V, Oppert J-M, *et al.* Interdisciplinary European guidelines on metabolic and bariatric surgery. *Obes Facts* 2013; **6**:449–468.
- 258 Katkhouda N, Mason RJ, Wu B, *et al.* Evaluation and treatment of patients with cardiac disease undergoing bariatric surgery. *Surg Obes Relat Dis* 2012; **8**:634–640.
- 259 Rao A, Tey BH, Ramalingam G, Poh AG. Obstructive sleep apnoea (OSA) patterns in bariatric surgical practice and response of OSA to weight loss after laparoscopic adjustable gastric banding (LAGB). *Ann Acad Med Singapore* 2009; **38**:587–597.
- 260 Malbois M, Giusti V, Suter M, *et al.* Oximetry alone versus portable polygraphy for sleep apnea screening before bariatric surgery. *Obes Surg* 2010; **20**:326–331.
- 261 Chung F, Yang Y, Liao P. Predictive performance of the STOP-Bang score for identifying obstructive sleep apnea in obese patients. *Obes Surg* 2013; **23**:2050–2057.
- 262 Reed K, Pengo MF, Steier J. Screening for sleep-disordered breathing in a bariatric population. *J Thorac Dis* 2016; **8**:268–275.

- 263 Tenório LHS, Santos AC, Câmara Neto JB, *et al.* The influence of inspiratory muscle training on diaphragmatic mobility, pulmonary function and maximum respiratory pressures in morbidly obese individuals: a pilot study. *Disabil Rehabil* 2013; **35**:1915–1920.
- 264 Nagappa M, Mokhlesi B, Wong J, *et al.* The effects of continuous positive airway pressure on postoperative outcomes in obstructive sleep apnea patients undergoing surgery: a systematic review and meta-analysis. *Anesth Analg* 2015; **120**:1013–1023.
- 265 van Huisstede A, Biter LU, Luitwieler R, *et al.* Pulmonary function testing and complications of laparoscopic bariatric surgery. *Obes Surg* 2013; **23**:1596–1603.
- 266 Clavellina-Gaytán D, Velázquez-Fernández D, Del-Villar E, *et al.* Evaluation of spirometric testing as a routine preoperative assessment in patients undergoing bariatric surgery. *Obes Surg* 2015; **25**:530–536.
- 267 Budde AO, Desciak M, Reddy V, *et al.* The prediction of difficult intubation in obese patients using mirror indirect laryngoscopy: a prospective pilot study. *J Anaesthesiol Clin Pharmacol* 2013; **29**:183–186.
- 268 Weil IA, Seicean S, Neuhauser D, *et al.* Use and utility of hemostatic screening in adults undergoing elective, noncardiac surgery. *PLoS One* 2015; **10**:e0139139.
- 269 Thaler HW, Frisee F, Korninger C. Platelet aggregation inhibitors, platelet function testing, and blood loss in hip fracture surgery. *J Trauma* 2010; **69**:1217–1221.
- 270 Madsen DE, Ingerslev J, Sidelmann JJ, *et al.* Intraoperative blood loss during orthognathic surgery is predicted by thromboelastography. *J Oral Maxillofac Surg* 2012; **70**:e547–e552.
- 271 Jámor C, von Pape K-W, Spannagl M, *et al.* Multiple electrode whole blood aggregometry, PFA-100, and in vivo bleeding time for the point-of-care assessment of aspirin-induced platelet dysfunction in the preoperative setting. *Anesth Analg* 2011; **113**:31–39.
- 272 Venkat R, Hannallah JR, Krouse RS, Maegawa FB. Preoperative thrombocytopenia and outcomes of hepatectomy for hepatocellular carcinoma. *J Surg Res* 2016; **201**:498–505.
- 273 Singh I, Achuthan S, Chakrabarti A, *et al.* Influence of preoperative use of serotonergic antidepressants (SADs) on the risk of bleeding in patients undergoing different surgical interventions: a meta-analysis. *Pharmacoevidemol Drug Saf* 2015; **24**:237–245.
- 274 Grzybowski A, Ascaso FJ, Kupidura-Majewski K, Packer M. Continuation of anticoagulant and antiplatelet therapy during phacoemulsification cataract surgery. *Curr Opin Ophthalmol* 2015; **26**:28–33.
- 275 Narouze S, Benzon HT, Provenzano DA, *et al.* Interventional spine and pain procedures in patients on antiplatelet and anticoagulant medications: guidelines from the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of pain Medicine, the international Neuromodulation Society, the north American Neuromodulation Society, and the world Institute of Pain. *Reg Anesth Pain Med* 2015; **40**:182–212.
- 276 Akhavan-Sigari R, Rohde V, Abili M. Continuation of medically necessary platelet aggregation inhibitors-acetylsalicylic acid and clopidogrel-during surgery for spinal degenerative disorders: results in 100 patients. *Surg Neurol Int* 2014; **5**:S376–S379.
- 277 Yamamoto K, Wada H, Sakakura K, *et al.* Cardiovascular and bleeding risk of noncardiac surgery in patients on antiplatelet therapy. *J Cardiol* 2014; **64**:334–338.
- 278 Collyer T, Reynolds H, Truyens E, *et al.* Perioperative management of clopidogrel therapy: the effects on in-hospital cardiac morbidity in older patients with hip fractures. *Br J Anaesth* 2011; **107**:911–915.
- 279 Soo CG, Della Torre PK, Yolland TJ, Shatwell MA. Clopidogrel and hip fractures, is it safe? A systematic review and meta-analysis. *BMC Musculoskelet Disord* 2016; **17**:136.
- 280 Chu EW, Chernoguz A, Divino CM. The evaluation of clopidogrel use in perioperative general surgery patients: a prospective randomized controlled trial. *Am J Surg* 2016; **211**:1019–1025.
- 281 Gribsholt SB, Svensson E, Thomsen RW, *et al.* Preoperative glucocorticoid use and risk of postoperative bleeding and infection after gastric bypass surgery for the treatment of obesity. *Surg Obes Relat Dis* 2015; **11**:1212–1217.
- 282 Dentali F, Marchesi C, Pierfranceschi MG, *et al.* Safety of prothrombin complex concentrates for rapid anticoagulation reversal of vitamin K antagonists. *Thromb Haemost* 2011; **106**:429–438.
- 283 Vitale MA, VanBeek C, Spivack JH, *et al.* Pharmacologic reversal of warfarin-associated coagulopathy in geriatric patients with hip fractures: a retrospective study of thromboembolic events, postoperative complications, and time to surgery. *Geriatr Orthop Surg Rehab* 2011; **2**:128–134.
- 284 Patel MS, Carson JL. Anemia in the preoperative patient. *Med Clin N Am* 2009; **93**:1095–1104.
- 285 Shander A, Knight K, Thurer R, *et al.* Prevalence and outcomes of anemia in surgery: a systematic review of the literature. *Am J Med* 2004; **116**:58–69.
- 286 World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. 2011. <http://www.who.int/vmnis/indicators/haemoglobin.pdf> [Accessed 11 March 2018].
- 287 Rock G, Berger R, Bormanis J, *et al.* A review of nearly two decades in an autologous blood programme: the rise and fall of activity. *Transfus Med* 2006; **16**:307–311.
- 288 Keeler B, Simpson J, Ng S, *et al.* The feasibility and clinical efficacy of intravenous iron administration for preoperative anaemia in patients with colorectal cancer. *Colorectal Dis* 2014; **16**:794–800.
- 289 Calleja JL, Delgado S, Del Val A, *et al.* Ferric carboxymaltose reduces transfusions and hospital stay in patients with colon cancer and anemia. *Int J Colorectal Dis* 2016; **31**:543–551.
- 290 Froessler B, Palm P, Weber I, *et al.* The important role for intravenous iron in perioperative patient blood management in major abdominal surgery: a randomized controlled trial. *Ann Surg* 2016; **264**:41–46.
- 291 Serrano-Trenas JA, Ugalde PF, Cabello LM, *et al.* Role of perioperative intravenous iron therapy in elderly hip fracture patients: a single-center randomized controlled trial. *Transfusion* 2011; **51**:97–104.
- 292 Keeler BD, Simpson JA, Ng S, *et al.* The feasibility and clinical efficacy of intravenous iron administration for preoperative anaemia in patients with colorectal cancer. *Colorectal Dis* 2014; **16**:794–800.
- 293 Delasotta LA, Rangavajjala AV, Frank ML, *et al.* The use of epoetin- α in revision knee arthroplasty. *Adv Orthoped* 2012; **2012**:595027.
- 294 Laffosse J-M, Minville V, Chiron P, *et al.* Preoperative use of epoetin beta in total hip replacement: a prospective study. *Arch Orthop Trauma Surg* 2010; **130**:41–45.
- 295 So-Osman C, Nelissen R, Koopman-van Gemert A, *et al.* A randomised controlled trial on erythropoietin and blood salvage as transfusion alternatives in orthopaedic surgery using a restrictive transfusion policy. *Transfus Altern Transfus Med* 2011; **3**:25–26.
- 296 Na HS, Shin SY, Hwang JY, *et al.* Effects of intravenous iron combined with low-dose recombinant human erythropoietin on transfusion requirements in iron-deficient patients undergoing bilateral total knee replacement arthroplasty (CME). *Transfusion* 2011; **51**:118–124.
- 297 Muñoz M, Gómez-Ramírez S, Cuenca J, *et al.* Very-short-term perioperative intravenous iron administration and postoperative outcome in major orthopedic surgery: a pooled analysis of observational data from 2547 patients. *Transfusion* 2014; **54**:289–299.
- 298 Gombotz H. Patient blood management is key before elective surgery. *Lancet* 2011; **378**:1362–1363.
- 299 Shander A, Van Aken H, Colomina M, *et al.* Patient blood management in Europe. *Br J Anaesth* 2012; **109**:55–68.
- 300 Rineau E, Chaudet A, Chassier C, *et al.* Implementing a blood management protocol during the entire perioperative period allows a reduction in transfusion rate in major orthopedic surgery: a before–after study. *Transfusion* 2016; **56**:673–681.
- 301 Enko D, Wallner F, von-Goedecke A, *et al.* The impact of an algorithm-guided management of preoperative anemia in perioperative hemoglobin level and transfusion of major orthopedic surgery patients. *Anemia* 2013; **2013**:641876.
- 302 Rashiq S, Jamieson-Lega K, Komarinski C, *et al.* Allogeneic blood transfusion reduction by risk-based protocol in total joint arthroplasty. *Can J Anesth* 2010; **57**:343–349.
- 303 Zheng H, Wu J-J, Wang J. Evaluation of effectiveness and analysis of goal-directed blood transfusion in peri-operation of major orthopedic surgery in elderly patients. *Exp Ther Med* 2013; **5**:511–516.
- 304 Phan DL, Rinehart JB, Schwarzkopf R. Can tranexamic acid change preoperative anemia management during total joint arthroplasty? *World J Orthop* 2015; **6**:521–527.
- 305 Walsh T, Palmer J, Watson D, *et al.* Multicentre cohort study of red blood cell use for revision hip arthroplasty and factors associated with greater risk of allogeneic blood transfusion. *Br J Anaesth* 2011; **108**:63–71.
- 306 Monsef JB, Buckup J, Mayman D, *et al.* Targeted preoperative autologous blood donation in total knee arthroplasty reduces the need for postoperative transfusion. *HSS J* 2013; **9**:214–217.
- 307 Pierson JL, Hannon TJ, Earles DR. A blood-conservation algorithm to reduce blood transfusions after total hip and knee arthroplasty. *J Bone Joint Surg Am* 2004; **86**:1512–1518.
- 308 Rondinelli M, Inghilleri G, Pavesi M, *et al.* Efficacy of ferrous bisglycinate chelate for the management of preoperative anaemia in orthopaedic surgical patients: a prospective study. *J Blood Disord Transfus* 2016; **7**:2.
- 309 Beard JR, Officer A, de Carvalho IA, *et al.* The World report on ageing and health: a policy framework for healthy ageing. *Lancet* 2016; **387**:2145–2154.

- 310 Hamel MB, Henderson WG, Khuri SF, Daley J. Surgical outcomes for patients aged 80 and older: morbidity and mortality from major noncardiac surgery. *J Am Geriatr Soc* 2005; **53**:424–429.
- 311 Aldecoa C, Bettelli G, Bilotta F, *et al.* European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. *Eur J Anaesthesiol* 2017; **34**:192–214.
- 312 Griffiths R, Beech F, Brown A, *et al.* Peri-operative care of the elderly 2014: Association of Anaesthetists of Great Britain and Ireland. *Anaesthesia* 2014; **69**:81–98.
- 313 Weimann A, Braga M, Carli F, *et al.* ESPEN guideline: clinical nutrition in surgery. *Clin Nutr* 2017; **36**:623–650.
- 314 Mohanty S, Rosenthal RA, Russell MM, *et al.* Optimal perioperative management of the geriatric patient: a best practices guideline from the American College of Surgeons NSQIP and the American Geriatrics Society. *J Am Coll Surg* 2016; **222**:930–947.
- 315 Inouye SK, Peduzzi PN, Robison JT, *et al.* Importance of functional measures in predicting mortality among older hospitalized patients. *JAMA* 1998; **279**:1187–1193.
- 316 Greer JA, Harvie HS, Andy UU, *et al.* Short-term postoperative functional outcomes in older women undergoing prolapse surgery. *Obstet Gynecol* 2015; **125**:551–558.
- 317 Reisinger KW, van Vugt JL, Tegels JJ, *et al.* Functional compromise reflected by sarcopenia, frailty, and nutritional depletion predicts adverse postoperative outcome after colorectal cancer surgery. *Ann Surg* 2015; **261**:345–352.
- 318 Kwon S, Symons R, Yukawa M, *et al.* Evaluating the association of preoperative functional status and postoperative functional decline in older patients undergoing major surgery. *Am Surg* 2012; **78**:1336–1344.
- 319 Bettelli G. Anaesthesia for the elderly outpatient: preoperative assessment and evaluation, anaesthetic technique and postoperative pain management. *Curr Opin Anaesthesiol* 2010; **23**:726–731.
- 320 Feng MA, McMillan DT, Crowell K, *et al.* Geriatric assessment in surgical oncology: a systematic review. *J Surg Res* 2015; **193**:265–272.
- 321 Dale W, Hemmerich J, Kamm A, *et al.* Geriatric assessment improves prediction of surgical outcomes in older adults undergoing pancreaticoduodenectomy: a prospective cohort study. *Ann Surg* 2014; **259**:960–965.
- 322 Badgwell B, Stanley J, Chang GJ, *et al.* Comprehensive geriatric assessment of risk factors associated with adverse outcomes and resource utilization in cancer patients undergoing abdominal surgery. *J Surg Oncol* 2013; **108**:182–186.
- 323 Kim KI, Park K-H, Koo K-H, *et al.* Comprehensive geriatric assessment can predict postoperative morbidity and mortality in elderly patients undergoing elective surgery. *Arch Gerontol Geriatr* 2013; **56**:507–512.
- 324 Kristjansson SR, Nesbakken A, Jordhøy MS, *et al.* Comprehensive geriatric assessment can predict complications in elderly patients after elective surgery for colorectal cancer: a prospective observational cohort study. *Crit Rev Oncol Hematol* 2010; **76**:208–217.
- 325 Gupta A. Medical management of hip fractures and the role of the orthogeriatrician. *Rev Clin Gerontol* 2012; **22**:261–273.
- 326 Kothari A, Phillips S, Brett T, *et al.* Components of geriatric assessments predict thoracic surgery outcomes. *J Surg Res* 2011; **166**:5–13.
- 327 Kim S-w, Han H-S, Jung H-W, *et al.* Multidimensional frailty score for the prediction of postoperative mortality risk. *JAMA Surg* 2014; **149**:633–640.
- 328 Partridge J, Harari D, Martin F, Dhesei J. The impact of preoperative comprehensive geriatric assessment on postoperative outcomes in older patients undergoing scheduled surgery: a systematic review. *Anaesthesia* 2014; **69**:8–16.
- 329 Indrakusuma R, Dunker M, Peetoom J, Schreurs W. Evaluation of preoperative geriatric assessment of elderly patients with colorectal carcinoma. A retrospective study. *Eur J Surg Oncol* 2015; **41**:21–27.
- 330 Poitras S, Wood K, Savard J, *et al.* Predicting early clinical function after hip or knee arthroplasty. *Bone Joint Res* 2015; **4**:145–151.
- 331 Huisman M, Audisio R, Ugolini G, *et al.* Screening for predictors of adverse outcome in onco-geriatric surgical patients: a multicenter prospective cohort study. *Eur J Surg Oncol* 2015; **41**:844–851.
- 332 Kiran RP, Attaluri V, Hammel J, Church J. A novel nomogram accurately quantifies the risk of mortality in elderly patients undergoing colorectal surgery. *Ann Surg* 2013; **257**:905–908.
- 333 Chang C-M, Yin W-Y, Wei C-K, *et al.* Adjusted Age-Adjusted Charlson Comorbidity Index Score as a risk measure of perioperative mortality before cancer surgery. *PLoS One* 2016; **11**:e0148076.
- 334 St-Louis E, Iqbal S, Feldman LS, *et al.* Using the age-adjusted Charlson comorbidity index to predict outcomes in emergency general surgery. *J Trauma Acute Care Surg* 2015; **78**:318–323.
- 335 Hirano Y, Takeuchi H, Suda K, *et al.* Clinical utility of the Revised Cardiac Risk Index in noncardiac surgery for elderly patients: a prospective cohort study. *Surg Today* 2014; **44**:277–284.
- 336 Potter L, Doleman B, Moppett I. A systematic review of preoperative anaemia and blood transfusion in patients with fractured hips. *Anaesthesia* 2015; **70**:483–500.
- 337 Menzies IB, Mendelson DA, Kates SL, Friedman SM. The impact of comorbidity on perioperative outcomes of hip fractures in a geriatric fracture model. *Geriatr Orthop Surg Rehab* 2012; **3**:129–134.
- 338 Shoair OA, Grasso MP II, Lahaye LA, *et al.* Incidence and risk factors for postoperative cognitive dysfunction in older adults undergoing major noncardiac surgery: a prospective study. *J Anaesthesiol Clin Pharmacol* 2015; **31**:30–36.
- 339 Robinson TN, Wu DS, Pointer LF, *et al.* Preoperative cognitive dysfunction is related to adverse postoperative outcomes in the elderly. *J Am Coll Surg* 2012; **215**:12–17.
- 340 Crepeau AE, McKinney BI, Fox-Ryvicker M, *et al.* Prospective evaluation of patient comprehension of informed consent. *J Bone Joint Surg Am* 2011; **93**:e114.
- 341 Partridge JS, Dhesei JK, Cross JD, *et al.* The prevalence and impact of undiagnosed cognitive impairment in older vascular surgical patients. *J Vasc Surg* 2014; **60**:1002–1011; e3.
- 342 Drevet S, Bioteau C, Maziere S, *et al.* Prevalence of protein-energy malnutrition in hospital patients over 75 years of age admitted for hip fracture. *Orthop Traumatol* 2014; **100**:669–674.
- 343 van Stijn MF, Korkic-Halilovic I, Bakker MS, *et al.* Preoperative nutrition status and postoperative outcome in elderly general surgery patients: a systematic review. *JPEN J Parenter Enteral Nutr* 2013; **37**:37–43.
- 344 Huisman M, Veronese G, Audisio R, *et al.* Poor nutritional status is associated with other geriatric domain impairments and adverse postoperative outcomes in onco-geriatric surgical patients: a multicenter cohort study. *Eur J Surg Oncol* 2016; **42**:1009–1017.
- 345 Revenig LM, Canter DJ, Kim S, *et al.* Report of a simplified frailty score predictive of short-term postoperative morbidity and mortality. *J Am Coll Surg* 2015; **220**:904–911; e1.
- 346 Kenig J, Zychiewicz B, Olszewska U, Richter P. Screening for frailty among older patients with cancer that qualify for abdominal surgery. *J Geriatr Oncol* 2015; **6**:52–59.
- 347 Revenig LM, Canter DJ, Master VA, *et al.* A prospective study examining the association between preoperative frailty and postoperative complications in patients undergoing minimally invasive surgery. *J Endourol* 2014; **28**:476–480.
- 348 Tegels JJ, de Maat M, Hulswé K, *et al.* Value of geriatric frailty and nutritional status assessment in predicting postoperative mortality in gastric cancer surgery. *J Gastrointest Surg* 2014; **18**:439–446.
- 349 Keller DS, Bankwitz B, Nobel T, Delaney CP. Using frailty to predict who will fail early discharge after laparoscopic colorectal surgery with an established recovery pathway. *Dis Colon Rectum* 2014; **57**:337–342.
- 350 Adams P, Ghanem T, Stachler R, *et al.* Frailty as a predictor of morbidity and mortality in inpatient head and neck surgery. *JAMA Otolaryngol Head Neck Surg* 2013; **139**:783–789.
- 351 Tan K-Y, Kawamura YJ, Tokomitsu A, Tang T. Assessment for frailty is useful for predicting morbidity in elderly patients undergoing colorectal cancer resection whose comorbidities are already optimized. *Am J Surg* 2012; **204**:139–143.
- 352 Courtney-Brooks M, Tellawi AR, Scalici J, *et al.* Frailty: an outcome predictor for elderly gynecologic oncology patients. *Gynecol Oncol* 2012; **126**:20–24.
- 353 Robinson TN, Wallace JI, Wu DS, *et al.* Accumulated frailty characteristics predict postoperative discharge institutionalization in the geriatric patient. *J Am Coll Surg* 2011; **213**:37–42.
- 354 Wagner D, DeMarco MM, Amini N, *et al.* Role of frailty and sarcopenia in predicting outcomes among patients undergoing gastrointestinal surgery. *World J Gastrointest Surg* 2016; **8**:27–40.
- 355 Cloney M, D'Amico R, Lebovic J, *et al.* Frailty in geriatric glioblastoma patients: a predictor of operative morbidity and outcome. *World Neurosurg* 2016; **89**:362–367.
- 356 Kua J, Ramason R, Rajamoney G, Chong MS. Which frailty measure is a good predictor of early postoperative complications in elderly hip fracture patients? *Arch Orthop Trauma Surg* 2016; **136**:639–647.
- 357 George EM, Burke WM, Hou JY, *et al.* Measurement and validation of frailty as a predictor of outcomes in women undergoing major gynaecological surgery. *BJOG* 2016; **123**:455–461.
- 358 Kristjansson SR, Rønning B, Hurria A, *et al.* A comparison of two preoperative frailty measures in older surgical cancer patients. *J Geriatr Oncol* 2012; **3**:1–7.

- 359 Lascano D, Pak JS, Kates M, *et al.* Validation of a frailty index in patients undergoing curative surgery for urologic malignancy and comparison with other risk stratification tools. *Urol Oncol* 2015; **33**:426.e1–426. e12.
- 360 Partridge JS, Fuller M, Harari D, *et al.* Frailty and poor functional status are common in arterial vascular surgical patients and affect postoperative outcomes. *Int J Surg* 2015; **18**:57–63.
- 361 King WC, Chen J-Y, Mitchell JE, *et al.* Prevalence of alcohol use disorders before and after bariatric surgery. *JAMA* 2012; **307**:2516–2525.
- 362 Bradley KA, Rubinsky AD, Sun H, *et al.* Prevalence of alcohol misuse among men and women undergoing major noncardiac surgery in the Veterans Affairs healthcare system. *Surgery* 2012; **152**:69–81.
- 363 Harris AH, Reeder R, Ellerbe L, *et al.* Preoperative alcohol screening scores: association with complications in men undergoing total joint arthroplasty. *J Bone Joint Surg Am* 2011; **93**:321–327.
- 364 Bradley KA, Rubinsky AD, Sun H, *et al.* Alcohol screening and risk of postoperative complications in male VA patients undergoing major noncardiac surgery. *J Gen Intern Med* 2011; **26**:162–169.
- 365 Rubinsky AD, Sun H, Blough DK, *et al.* AUDIT-C alcohol screening results and postoperative inpatient healthcare use. *J Am Coll Surg* 2012; **214**:296–305; e1.
- 366 Eliassen M, Grønkvær M, Skov-Ettrup LS, *et al.* Preoperative alcohol consumption and postoperative complications: a systematic review and meta-analysis. *Ann Surg* 2013; **258**:930–942.
- 367 Best MJ, Buller LT, Gosthe RG, *et al.* Alcohol misuse is an independent risk factor for poorer postoperative outcomes following primary total hip and total knee arthroplasty. *J Arthroplasty* 2015; **30**:1293–1298.
- 368 Yu Y-H, Chen AC-Y, Hu C-C, *et al.* Acute delirium and poor compliance in total hip arthroplasty patients with substance abuse disorders. *J Arthroplasty* 2012; **27**:1526–1529.
- 369 Armaghani SJ, Lee DS, Bible JE, *et al.* Preoperative narcotic use and its relation to depression and anxiety in patients undergoing spine surgery. *Spine (Phila Pa 1976)* 2013; **38**:2196–2200.
- 370 Kleinwächter R, Kork F, Weiss-Gerlach E, *et al.* Improving the detection of illicit substance use in preoperative anaesthesiological assessment. *Minerva Anesthesiol* 2010; **76**:29–37.
- 371 Tonnesen H, Kehlet H. Preoperative alcoholism and postoperative morbidity. *Br J Surg* 1999; **86**:869–874.
- 372 Ewing JA. Detecting alcoholism: the CAGE questionnaire. *JAMA* 1984; **252**:1905–1907.
- 373 Saunders JB, Aasland OG, Babor TF, *et al.* Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. *Addiction* 1993; **88**:791–804.
- 374 Neumann T, Linnen H, Kip M, *et al.* Does the Alcohol Use Disorders Identification Test—consumption identify the same patient population as the full 10-item Alcohol Use Disorders Identification Test? *J Subst Abuse Treat* 2012; **43**:80–85.
- 375 Agabio R, Luigi Gessa G, Montisci A, *et al.* Use of the screening suggested by the National Institute on Alcohol Abuse and Alcoholism and of a newly derived tool for the detection of unhealthy alcohol drinkers among surgical patients. *J Stud Alcohol Drugs* 2012; **73**:126–133.
- 376 Martin M, Heymann C, Neumann T, *et al.* Preoperative evaluation of chronic alcoholics assessed for surgery of the upper digestive tract. *Alcohol Clin Exp Res* 2002; **26**:836–840.
- 377 Baxter JL, Alexandrov AW. Utility of cocaine drug screens to predict safe delivery of general anesthesia for elective surgical patients. *AANA J* 2012; **80**:S33–S36.
- 378 Elkassabany N, Speck RM, Oslin D, *et al.* Preoperative screening and case cancellation in cocaine-abusing veterans scheduled for elective surgery. *Anesthesiol Res Pract* 2013; **2013**:149892.
- 379 Oppedal K, Møller AM, Pedersen B, Tønnesen H. Preoperative alcohol cessation prior to elective surgery. *Cochrane Database Syst Rev* 2012;CD008343.
- 380 Rubinsky AD, Bishop MJ, Maynard C, *et al.* Postoperative risks associated with alcohol screening depend on documented drinking at the time of surgery. *Drug Alcohol Depend* 2013; **132**:521–527.
- 381 Hudson KA, Greene JG. Perioperative consultation for patients with preexisting neurologic disorders. *Semin Neurol* 2015; **35**:690–698.
- 382 Sinskey JL, Holzman RS. Perioperative considerations in infantile neuroaxonal dystrophy. *Pediatr Anesth* 2017; **27**:322–324.
- 383 Litman RS, Griggs SM, Dowling JJ, Riazi S. Malignant hyperthermia susceptibility and related diseases. *Anesthesiology* 2018; **128**:159–167.
- 384 Schieren M, Defosse J, Böhmer A, *et al.* Anaesthetic management of patients with myopathies. *Eur J Anaesthesiol* 2017; **34**:641–649.
- 385 King AR, Russett FS, Generali JA, *et al.* Evaluation and implications of natural product use in preoperative patients: a retrospective review. *BMC Complement Altern Med* 2009; **9**:38.
- 386 Adusumilli PS, Ben-Porat L, Pereira M, *et al.* The prevalence and predictors of herbal medicine use in surgical patients. *J Am Coll Surg* 2004; **198**:583–590.
- 387 Sugumaran MC, Cohen JC, Kacker A. Prevalence of over-the-counter and complementary medication use in the otolaryngology preoperative patient: a patient safety initiative. *Laryngoscope* 2012; **122**:1489–1492.
- 388 Tsen LC, Segal S, Pothier M, Bader AM. Alternative medicine use in presurgical patients. *Anesthesiology* 2000; **93**:148–151.
- 389 Hogg LA, Foo I. Management of patients taking herbal medicines in the perioperative period: a survey of practice and policies within Anaesthetic Departments in the United Kingdom. *Eur J Anaesthesiol* 2010; **27**:11–15.
- 390 Lee KP, Nishimura K, Ngu B, *et al.* Predictors of completeness of patients' self-reported personal medication lists and discrepancies with clinic medication lists. *Ann Pharmacother* 2014; **48**:168–177.
- 391 Cordier WS, Steenkamp V. Herbal remedies affecting coagulation: a review. *Pharm Biol* 2012; **50**:443–452.
- 392 McEwen BJ. The influence of herbal medicine on platelet function and coagulation: a narrative review. *Semin Thromb Hemost* 2015; **41**:300–314.
- 393 Vale S. Subarachnoid haemorrhage associated with Ginkgo biloba. *Lancet* 1998; **352**:36.
- 394 Fessenden JM, Wittenborn W, Clarke L. Ginkgo biloba: a case report of herbal medicine and bleeding postoperatively from a laparoscopic cholecystectomy. *Am Surg* 2001; **67**:33–35.
- 395 Rose KD, Croissant PD, Parliament CF, Levin MB. Spontaneous spinal epidural hematoma with associated platelet dysfunction from excessive garlic ingestion: a case report. *Neurosurgery* 1990; **26**:880–882.
- 396 Köhler S, Funk P, Kieser M. Influence of a 7-day treatment with Ginkgo biloba special extract Egb 761 on bleeding time and coagulation: a randomized, placebo-controlled, double-blind study in healthy volunteers. *Blood Coagul Fibrinolysis* 2004; **15**:303–309.
- 397 Kozek-Langenecker SA, Ahmed AB, Afshari A, *et al.* Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology: first update 2016. *Eur J Anaesthesiol* 2017; **34**:332–395.
- 398 Kellermann AJ, Kloft C. Is there a risk of bleeding associated with standardized ginkgo bilobaextract therapy? A systematic review and meta-analysis. *Pharmacotherapy* 2011; **31**:490–502.
- 399 Ang-Lee MK, Moss J, Yuan C-S. Herbal medicines and perioperative care. *JAMA* 2001; **286**:208–216.
- 400 Ortiz JG, Nieves-Natal J, Chavez P. Effects of Valeriana officinalis extracts on [3 H] flunitrazepam binding, synaptosomal [3 H] GABA uptake, and hippocampal [3 H] GABA release. *Neurochem Res* 1999; **24**:1373–1378.
- 401 Kantor ED, Rehm CD, Haas JS, *et al.* Trends in prescription drug use among adults in the United States from 1999–2012. *JAMA* 2015; **314**:1818–1830.
- 402 Hall SA, Chiu GR, Kaufman DW, *et al.* General exposures to prescription medications by race/ethnicity in a population-based sample: results from the Boston Area Community Health Survey. *Pharmacoepidemiol Drug Saf* 2010; **19**:384–392.
- 403 Ward NR, Roth JS, Lester CC, *et al.* Anxiolytic medication is an independent risk factor for 30-day morbidity or mortality after surgery. *Surgery* 2015; **158**:420–427.
- 404 De Baerdemaeker L, Audenaert K, Peremans K. Anaesthesia for patients with mood disorders. *Curr Opin Anesthesiol* 2005; **18**:333–338.
- 405 Jorgensen CCK, Knop J, Nordentoft M, Kehlet H, Lundbeck Foundation Centre for Fast-track, Hip, Knee Replacement Collaborative, Group. Psychiatric disorders and psychopharmacologic treatment as risk factors in elective fast-track total hip and knee arthroplasty. *Anesthesiology* 2015; **123**:1281–1291.
- 406 Auerbach ADV, Vittinghoff E, Maselli J, *et al.* Perioperative use of selective serotonin reuptake inhibitors and risks for adverse outcomes of surgery. *JAMA Intern Med* 2013; **173**:1075–1081.
- 407 Catalani BH, Hamilton CS, Herron EW, *et al.* Psychiatric agents and implications for perioperative analgesia. *Best Pract Res Clin Anaesthesiol* 2014; **28**:167–181.
- 408 Huysse FJ, Touw DJ, Van Schijndel RS, *et al.* Psychotropic drugs and the perioperative period: a proposal for a guideline in elective surgery. *Psychosomatics* 2006; **47**:8–22.
- 409 Castanheira LF, Fresco P, MacEdo AF. Guidelines for the management of chronic medication in the perioperative period: systematic review and formal consensus. *J Clin Pharm Ther* 2011; **36**:446–467.
- 410 Kocsis JH, Friedman RA, Markowitz JC, *et al.* Maintenance therapy for chronic depression: a controlled clinical trial of desipramine. *Arch Gen Psychiatry* 1996; **53**:769–774.

- 411 Cavanagh J, Smyth R, Goodwin G. Relapse into mania or depression following lithium discontinuation: a 7-year follow-up. *Acta Psychiatr Scand* 2004; **109**:91–95.
- 412 Gärtner R, Cronin-Fenton D, Hundborg HH, *et al.* Use of selective serotonin reuptake inhibitors and risk of re-operation due to postsurgical bleeding in breast cancer patients: a Danish population-based cohort study. *BMC Surg* 2010; **10**:3.
- 413 van Haelst IM, Egberts TC, Doodeman HJ, *et al.* Use of serotonergic antidepressants and bleeding risk in orthopedic patients. *Anesthesiology* 2010; **112**:631–636.
- 414 Sayadipour AM, Mago R, Kepler CK, *et al.* Antidepressants and the risk of abnormal bleeding during spinal surgery: a case-control study. *Eur Spine J* 2012; **21**:2070–2078.
- 415 Basile FVB, Basile AR, Basile VV. Use of selective serotonin reuptake inhibitors antidepressants and bleeding risk in breast cosmetic surgery. *Aesthetic Plast Surg* 2013; **37**:561–566.
- 416 Dall MP, Primdahl A, Damborg F, *et al.* The association between use of serotonergic antidepressants and perioperative bleeding during total hip arthroplasty: a cohort study. *Basic Clin Pharmacol Toxicol* 2014; **115**:277–281.
- 417 Schutte HJ, Jansen S, Schafrath MU, *et al.* SSRIs increase risk of blood transfusion in patients admitted for hip surgery. *PLoS One* 2014; **9**:e95906.
- 418 Seitz DP, Bell CM, Gill SS, *et al.* Risk of perioperative blood transfusions and postoperative complications associated with serotonergic antidepressants in older adults undergoing hip fracture surgery. *J Clin Psychopharmacol* 2013; **33**:790–798.
- 419 Bowdle TA. Adverse effects of opioid agonists and agonist-antagonists in anaesthesia. *Drug Saf* 1998; **19**:173–189.
- 420 Strauss J. Psychotropic medication use in older adults. *Int Anesthesiol Clin* 2014; **52**:77–94.
- 421 Rasool FG, Ghafoor R, Lambert D. Antidepressants and antipsychotics: anaesthetic implications. *Anaesth Intensive Care Med* 2011; **12**:166–169.
- 422 Ragheb M. The clinical significance of lithium-nonsteroidal: anti-inflammatory drug interactions. *J Clin Psychopharmacol* 1990; **10**:350–354.
- 423 Lee A, Chui PT, Aun CS, *et al.* Incidence and risk of adverse perioperative events among surgical patients taking traditional Chinese herbal medicines. *Anesthesiology* 2006; **105**:454–461.
- 424 Kudoh A, Takase H, Takazawa T. Chronic treatment with antipsychotics enhances intraoperative core hypothermia. *Anesth Analg* 2004; **98**:111–115.
- 425 Kudoh A, Katagai H, Takase H, Takazawa T. Effect of preoperative discontinuation of antipsychotics in schizophrenic patients on outcome during and after anaesthesia. *Eur J Anaesthesiol* 2004; **21**:414–416.
- 426 Kudoh A, Katagai H, Takazawa T. Antidepressant treatment for chronic depressed patients should not be discontinued prior to anesthesia. *Can J Anesth* 2002; **49**:132–136.
- 427 Jeong BO, Kim SW, Kim SY, *et al.* Use of serotonergic antidepressants and bleeding risk in patients undergoing surgery. *Psychosomatics* 2014; **55**:213–220.
- 428 Doodeman HJ, Kalkman CJ, Egberts T. Antidepressive treatment with monoamine oxidase inhibitors and the occurrence of intraoperative hemodynamic events: a retrospective observational cohort study. *J Clin Psychiatry* 2012; **73**:1103–1109.
- 429 Douketis JDS, Spyropoulos AC, Spencer FA, *et al.* Perioperative management of antithrombotic therapy. Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2012; **141**:e326S–e335S.
- 430 Perrin MJV, Zezi BZ, Ha AC, *et al.* Anticoagulation bridging around device surgery: compliance with guidelines. *Pacing Clin Electrophysiol* 2012; **35**:1480–1486.
- 431 Steib AM, Mertes PM, Marret E, *et al.* Compliance with guidelines for the perioperative management of vitamin K antagonists. *Thromb Res* 2014; **133**:1056–1060.
- 432 Eijgenraam P, ten Cate H, ten Cate-Hoek A J. Practice of bridging anticoagulation: guideline adherence and risk factors for bleeding. *Neth J Med* 2014; **72**:157–164.
- 433 Omran HB, Bauersachs R, Rubenacker S, *et al.* The HAS-BLED score predicts bleedings during bridging of chronic oral anticoagulation. Results from the national multicentre BNK Online bRIDging REGistRY (BORDER). *Thromb Haemost* 2012; **108**:65–73.
- 434 Clark NPW, Witt DM, Davies LE, *et al.* Bleeding, recurrent venous thromboembolism, and mortality risks during warfarin interruption for invasive procedures. *JAMA Intern Med* 2015; **175**:1163–1168.
- 435 Schmitges JT, Trinh OD, Jonas L, *et al.* Influence of low-molecular-weight heparin dosage on red blood cell transfusion, lymphocele rate and drainage duration after open radical prostatectomy. *Eur J Surg Oncol* 2012; **38**:1082–1088.
- 436 Schulman JMM, Majeed A, Mattsson E, *et al.* Strategies and outcomes of periprocedural bridging therapy with low-molecular-weight heparin in patients with mechanical heart valves. *J Thromb Thrombolysis* 2015; **40**:430–436.
- 437 Hammerstingl CO, Omran H. Perioperative bridging of chronic oral anticoagulation in patients undergoing pacemaker implantation: a study in 200 patients. *Europace* 2011; **13**:1304–1310.
- 438 Steinberg BA, Peterson ED, Kim S, *et al.* Use and outcomes associated with bridging during anticoagulation interruptions in patients with atrial fibrillation: findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). *Circulation* 2015; **131**:488–494.
- 439 Siegal DY, Yudin J, Kaatz S, *et al.* Periprocedural heparin bridging in patients receiving vitamin K antagonists: systematic review and meta-analysis of bleeding and thromboembolic rates. *Circulation* 2012; **126**:1630–1639.
- 440 Weltermann AB, Brodmann M, Domanovits H, *et al.* Dabigatran in patients with atrial fibrillation: perioperative and periprocedural management. *Wien Klin Wochenschr* 2012; **124**:340–347.
- 441 Ward CC, Conner G, Donnan G, *et al.* Practical management of patients on apixaban: a consensus guide. *Thromb J* 2013; **11**:27.
- 442 Beyer-Westendorf JG, Gelbricht V, Forster K, *et al.* Peri-interventional management of novel oral anticoagulants in daily care: results from the prospective Dresden NOAC registry. *Eur Heart J* 2014; **35**:1888–1896.
- 443 Ferrandis RC, Castillo J, de Andres J, *et al.* The perioperative management of new direct oral anticoagulants: a question without answers. *Thromb Haemost* 2013; **110**:515–522.
- 444 Ghanbari HP, Phard WS, Al-Ameri H, *et al.* Meta-analysis of safety and efficacy of uninterrupted warfarin compared to heparin-based bridging therapy during implantation of cardiac rhythm devices. *Am J Cardiol* 2012; **110**:1482–1488.
- 445 Sant'anna RTL, Leiria TL, Nascimento T, *et al.* Meta-analysis of continuous oral anticoagulants versus heparin bridging in patients undergoing CIED surgery: reappraisal after the BRUISE study. *Pacing Clin Electrophysiol* 2015; **38**:417–423.
- 446 Di Biase LB, Burkhardt JD, Santangeli P, *et al.* Periprocedural stroke and bleeding complications in patients undergoing catheter ablation of atrial fibrillation with different anticoagulation management: results from the Role of Coumadin in Preventing Thromboembolism in Atrial Fibrillation (AF) Patients Undergoing Catheter Ablation (COMPARE) randomized trial. *Circulation* 2014; **129**:2638–2644.
- 447 Eichhorn WB, Burkert J, Vorwig O, *et al.* Bleeding incidence after oral surgery with continued oral anticoagulation. *Clin Oral Investig* 2012; **16**:1371–1376.
- 448 Kuwahara TT, Takahashi A, Takahashi Y, *et al.* Prevention of periprocedural ischemic stroke and management of hemorrhagic complications in atrial fibrillation ablation under continuous warfarin administration. *J Cardiovasc Electrophysiol* 2013; **24**:510–515.
- 449 Pini RF, Faggioli G, Mauro R, *et al.* Chronic oral anticoagulant therapy in carotid artery stenting: the un-necessity of perioperative bridging heparin therapy. *Thromb Res* 2012; **130**:12–15.
- 450 Chandra AJ, Jazayeri F, Williamson TH. Warfarin in vitreoretinal surgery: a case controlled series. *Br J Ophthalmol* 2011; **95**:976–978.
- 451 Chana RS, Salmon L, Waller A, Pinczewski L. Warfarin management in patients on continuous anticoagulation therapy undergoing total knee replacement. *J Bone Joint Surg Br* 2011; **93**:1497–1502.
- 452 Phillips AD, Dan M, Schaefer N, Randle R. Warfarin cessation is nonessential in patients undergoing total knee arthroplasty: a case-control study. *J Orthop Surg Res* 2015; **10**:16.
- 453 Sporbeck BGB, Georges Bechara F, Hafner HM, *et al.* S3 guidelines for the management of anticoagulation in cutaneous surgery. *J Dtsch Dermatol Ges* 2015; **13**:346–356.
- 454 Essebag VH, Healey JS, Ayala-Paredes F, *et al.* Strategy of continued vs interrupted novel oral anticoagulant at time of device surgery in patients with moderate to high risk of arterial thromboembolic events: the BRUISE CONTROL-2 trial. *Am Heart J* 2016; **173**:102–107.
- 455 Munro J, Booth A, Nicholl J. Routine preoperative testing: a systematic review of the evidence. *Health Technol Assess* 1997; **1**:i–iv; 1–62.
- 456 Johansson T, Fritsch G, Flamm M, *et al.* Effectiveness of noncardiac preoperative testing in noncardiac elective surgery: a systematic review. *Br J Anaesth* 2013; **110**:926–939.
- 457 Li G, Warner M, Lang BH, *et al.* Epidemiology of anesthesia-related mortality in the United States, 1999–2005. *Anesthesiology* 2009; **110**:759–765.

- 458 Greib N, Stojeba N, Dow WA, *et al.* A combined rigid videolaryngoscopy-flexible fibres copy intubation technique under general anesthesia. *Can J Anesth* 2007; **54**:492–493.
- 459 Langeron O, Masso E, Huraux C, *et al.* Prediction of difficult mask ventilation. *Anesthesiology* 2000; **92**:1229–1236.
- 460 Kheterpal S, Martin L, Shanks AM, Tremper KK. Prediction and outcomes of impossible mask ventilation: a review of 50,000 anesthetics. *Anesthesiology* 2009; **110**:891–897.
- 461 Kheterpal S, Healy D, Aziz MF, *et al.* Incidence, predictors, and outcome of difficult mask ventilation combined with difficult laryngoscopy: report from the multicenter perioperative outcomes group. *Anesthesiology* 2013; **119**:1360–1369.
- 462 Meco BC, Alanoglu Z, Yilmaz AA, *et al.* Does ultrasonographic volume of the thyroid gland correlate with difficult intubation? An observational study. *Braz J Anesthesiol* 2015; **65**:230–234.
- 463 Loftus PA, Ow TJ, Siegel B, *et al.* Risk factors for perioperative airway difficulty and evaluation of intubation approaches among patients with benign goiter. *Ann Otol Rhinol Laryngol* 2014; **123**:279–285.
- 464 Bindra A, Prabhakar H, Singh GP, *et al.* Is the modified Mallampati test performed in supine position a reliable predictor of difficult tracheal intubation? *J Anesth* 2010; **24**:482–485.
- 465 Bindra A, Prabhakar H, Bithal PK, *et al.* Predicting difficult laryngoscopy in acromegalic patients undergoing surgery for excision of pituitary tumors: a comparison of extended Mallampati score with modified Mallampati classification. *J Anaesthesiol Clin Pharmacol* 2013; **29**:187–190.
- 466 Mashour GA, Kheterpal S, Vanaharam V, *et al.* The extended Mallampati score and a diagnosis of diabetes mellitus are predictors of difficult laryngoscopy in the morbidly obese. *Anesth Analg* 2008; **107**:1919–1923.
- 467 Calder I. Acromegaly, the Mallampati, and difficult intubation. *Anesthesiology* 2001; **94**:1149–1150.
- 468 Samsoun G, Young J. Difficult tracheal intubation: a retrospective study. *Anaesthesia* 1987; **42**:487–490.
- 469 Khan ZH, Eskandari S, Yekaninejad MS. A comparison of the Mallampati test in supine and upright positions with and without phonation in predicting difficult laryngoscopy and intubation: a prospective study. *J Anaesthesiol Clin Pharmacol* 2015; **31**:207–211.
- 470 El-Ganzouri AR, McCarthy RJ, Tuman KJ, *et al.* Preoperative airway assessment: predictive value of a multivariate risk index. *Anesth Analg* 1996; **82**:1197–1204.
- 471 Cortellazzi P, Minati L, Falcone C, *et al.* Predictive value of the El-Ganzouri multivariate risk index for difficult tracheal intubation: a comparison of Glidescope® videolaryngoscopy and conventional Macintosh laryngoscopy. *Br J Anaesth* 2007; **99**:906–911.
- 472 Khan ZH, Kashfi A, Ebrahimkhani E. A comparison of the upper lip bite test (a simple new technique) with modified Mallampati classification in predicting difficulty in endotracheal intubation: a prospective blinded study. *Anesth Analg* 2003; **96**:595–599.
- 473 Khan ZH, Mohammadi M, Rasouli MR, *et al.* The diagnostic value of the upper lip bite test combined with sternal distance, thyromental distance, and interincisor distance for prediction of easy laryngoscopy and intubation: a prospective study. *Anesth Analg* 2009; **109**:822–824.
- 474 Tremblay M-H, Williams S, Robitaille A, Drolet P. Poor visualization during direct laryngoscopy and high upper lip bite test score are predictors of difficult intubation with the GlideScope® videolaryngoscope. *Anesth Analg* 2008; **106**:1495–1500.
- 475 Benumof JL. *The ASA Difficult Airway Algorithm: new thoughts and considerations. Handbook of Difficult Airway Management.* Philadelphia, PA: Churchill Livingstone; 2000; 31–48.
- 476 Farcon EL, Kim MH, Marx GF. Changing Mallampati score during labour. *Can J Anesth* 1994; **41**:50–51.
- 477 Karkouti K, Rose DK, Wigglesworth D, Cohen MM. Predicting difficult intubation: a multivariable analysis. *Can J Anesth* 2000; **47**:730–739.
- 478 Yamamoto K, Tsubokawa T, Shibata K, *et al.* Predicting difficult intubation with indirect laryngoscopy. *Anesthesiology* 1997; **86**:316–321.
- 479 Vani V, Kamath S, Naik L. The palm print as a sensitive predictor of difficult laryngoscopy in diabetics: a comparison with other airway evaluation indices. *J Postgrad Med* 2000; **46**:75–79.
- 480 Hirmanpour A, Safavi M, Honarmand A, *et al.* The predictive value of the ratio of neck circumference to thyromental distance in comparison with four predictive tests for difficult laryngoscopy in obstetric patients scheduled for caesarean delivery. *Adv Biomed Res* 2014; **3**:200.
- 481 Tao W, Edwards JT, Tu F, *et al.* Incidence of unanticipated difficult airway in obstetric patients in a teaching institution. *J Anesth* 2012; **26**:339–345.
- 482 Schmitt H, Buchfelder M, Radespiel-Tröger M, Fahlbusch R. Difficult intubation in acromegalic patients: incidence and predictability. *Anesthesiology* 2000; **93**:110–114.
- 483 Juvin P, Lavaut E, Dupont H, *et al.* Difficult tracheal intubation is more common in obese than in lean patients. *Anesth Analg* 2003; **97**:595–600.
- 484 Sharma D, Kim LJ, Ghodke B. Successful airway management with combined use of Glidescope® videolaryngoscope and fiberoptic bronchoscope in a patient with Cowden syndrome. *Anesthesiology* 2010; **113**:253–255.
- 485 Türkan S, Ates Y, Cuhruk H, Tekdemir I. Should we reevaluate the variables for predicting the difficult airway in anesthesiology? *Anesth Analg* 2002; **94**:1340–1344.
- 486 Apfelbaum JL, Hagberg CA, Caplan RA, *et al.* Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists task force on management of the difficult airway. *Anesthesiology* 2013; **118**:251–270.
- 487 Moonesinghe SR, Mythen MG, Das P, *et al.* Risk stratification tools for predicting morbidity and mortality in adult patients undergoing major surgery: qualitative systematic review. *Anesthesiology* 2013; **119**:959–981.
- 488 Koo CY, Hyder JA, Wanderer JP, *et al.* A meta-analysis of the predictive accuracy of postoperative mortality using the American Society of Anesthesiologists' physical status classification system. *World J Surg* 2015; **39**:88–103.
- 489 Visser A, Geboers B, Gouma DJ, *et al.* Predictors of surgical complications: a systematic review. *Surgery* 2015; **158**:58–65.
- 490 Parmar CD, Torella F. Prediction of major adverse cardiac events in vascular surgery: are cardiac risk scores of any practical value? *Vasc Endovasc Surg* 2010; **44**:14–19.
- 491 Hooper GJ, Rothwell AG, Hooper NM, Frampton C. The relationship between the American Society of Anesthesiologists physical rating and outcome following total hip and knee arthroplasty: an analysis of the New Zealand Joint Registry. *J Bone Joint Surg Am* 2012; **94**:1065–1070.
- 492 Protopapa K, Simpson J, Smith N, Moonesinghe S. Development and validation of the surgical outcome risk tool (SORT). *Br J Surg* 2014; **101**:1774–1783.
- 493 Kork F, Balzer F, Krannich A, *et al.* Association of comorbidities with postoperative in-hospital mortality: a retrospective cohort study. *Medicine (Baltimore)* 2015; **94**:e576.
- 494 Donati A, Ruzzi M, Adrario E, *et al.* A new and feasible model for predicting operative risk. *Br J Anaesth* 2004; **93**:393–399.
- 495 Sutton R, Bann S, Brooks M, Sarin S. The Surgical Risk Scale as an improved tool for risk-adjusted analysis in comparative surgical audit. *Br J Surg* 2002; **89**:763–768.
- 496 Davenport DL, Bowe EA, Henderson WG, *et al.* National Surgical Quality Improvement Program (NSQIP) risk factors can be used to validate American Society of Anesthesiologists Physical Status classification (ASA PS) levels. *Ann Surg* 2006; **243**:636–641.
- 497 Rao JY, Yeriswamy M, Santhosh M, *et al.* A look into Lee's score: perioperative cardiovascular risk assessment in noncardiac surgeries: usefulness of revised cardiac risk index. *Indian Heart J* 2012; **64**:134–138.
- 498 Andersson C, Wissenberg M, Jørgensen ME, *et al.* Age-specific performance of the revised cardiac risk index for predicting cardiovascular risk in elective noncardiac surgery. *Circ Cardiovasc Qual Outcomes* 2015; **8**:103–108.
- 499 Ford MK, Beattie WS, Wijesundera DN. Systematic review: prediction of perioperative cardiac complications and mortality by the revised cardiac risk index. *Ann Intern Med* 2010; **152**:26–35.
- 500 Davis C, Tait G, Carroll J, *et al.* The Revised Cardiac Risk Index in the new millennium: a single-centre prospective cohort re-evaluation of the original variables in 9,519 consecutive elective surgical patients. *Can J Anesth* 2013; **60**:855–863.
- 501 Bae MH, Jang SY, Choi WS, *et al.* A new revised cardiac risk index incorporating fragmented QRS complex as a prognostic marker in patients undergoing noncardiac vascular surgery. *Am J Cardiol* 2013; **112**:122–127.
- 502 McAlister F, Jacka M, Graham M, *et al.* The prediction of postoperative stroke or death in patients with preoperative atrial fibrillation undergoing noncardiac surgery: a VISION sub-study. *J Thromb Haemost* 2015; **13**:1768–1775.
- 503 Bertges DJ, Goodney PP, Zhao Y, *et al.* The Vascular Study Group of New England Cardiac Risk Index (VSG-CRI) predicts cardiac complications more accurately than the revised cardiac risk index in vascular surgery patients. *J Vasc Surg* 2010; **52**:674–683; e3.
- 504 Moodley Y, Naidoo P, Biccard BM. The South African Vascular Surgical Cardiac Risk Index (SAVS-CRI): a prospective observational study. *S Afr Med J* 2013; **103**:746–750.
- 505 van Diepen S, Youngson E, Ezekowitz JA, McAlister FA. Which risk score best predicts perioperative outcomes in nonvalvular atrial fibrillation patients undergoing noncardiac surgery? *Am Heart J* 2014; **168**:60–67; e5.

- 506 Choi J-H, Cho DK, Song Y-B, *et al.* Preoperative NT-proBNP and CRP predict perioperative major cardiovascular events in noncardiac surgery. *Heart* 2010; **96**:56–62.
- 507 Gillmann H-J, Meinders A, Grohennig A, *et al.* Perioperative levels and changes of high-sensitivity troponin T are associated with cardiovascular events in vascular surgery patients. *Crit Care Med* 2014; **42**:1498–1506.
- 508 Kertai MD, Boersma E, Klein J, *et al.* Optimizing the prediction of perioperative mortality in vascular surgery by using a customized probability model. *Arch Intern Med* 2005; **165**:898–904.
- 509 Peterson B, Ghahramani M, Harris S, *et al.* Usefulness of the myocardial infarction and cardiac arrest calculator as a discriminator of adverse cardiac events after elective hip and knee surgery. *Am J Cardiol* 2016; **117**:1992–1995.
- 510 Smeili LAA, Lotufo PA. Incidence and predictors of cardiovascular complications and death after vascular surgery. *Arq Bras Cardiol* 2015; **105**:510–518.
- 511 Lee TH, Marcantonio ER, Mangione CM, *et al.* Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999; **100**:1043–1049.
- 512 Menendez ME, Neuhaus V, van Dijk CN, Ring D. The Elixhauser comorbidity method outperforms the Charlson index in predicting inpatient death after orthopaedic surgery. *Clin Orthop Relat Res* 2014; **472**:2878–2886.
- 513 Menendez ME, Neuhaus V, Ring D. Inpatient mortality after orthopaedic surgery. *Int Orthop* 2015; **39**:1307–1314.
- 514 Atherly A, Fink AS, Campbell DC, *et al.* Evaluating alternative risk-adjustment strategies for surgery. *Am J Surg* 2004; **188**:566–570.
- 515 Sundararajan V, Henderson T, Perry C, *et al.* New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. *J Clin Epidemiol* 2004; **57**:1288–1294.
- 516 Haynes S, Lawler P. An assessment of the consistency of ASA physical status classification allocation. *Anaesthesia* 1995; **50**:195–199.
- 517 Rushton P, Reed M, Pratt R. Independent validation of the Nottingham Hip Fracture Score and identification of regional variation in patient risk within England. *Bone Joint J* 2015; **97**:100–103.
- 518 Marufu TC, White S, Griffiths R, *et al.* Prediction of 30-day mortality after hip fracture surgery by the Nottingham Hip Fracture Score and the Surgical Outcome Risk Tool. *Anaesthesia* 2016; **71**:515–521.
- 519 Karres J, Heesakkers NA, Ultee JM, Vrouwenraets BC. Predicting 30-day mortality following hip fracture surgery: evaluation of six risk prediction models. *Injury* 2015; **46**:371–377.
- 520 Tsang C, Boulton C, Burgon V, *et al.* Predicting 30-day mortality after hip fracture surgery: evaluation of the National Hip Fracture Database case-mix adjustment model. *Bone Joint Res* 2017; **6**:550–556.
- 521 Kau CY, Kwek E. Can preoperative scoring systems be applied to Asian hip fracture populations? Validation of the Nottingham Hip Fracture Score (NHFS) and identification of preoperative risk factors in hip fractures. *Ann Acad Med Singapore* 2014; **43**:448–453.
- 522 Wiles M, Moran C, Sahota O, Moppett I. Nottingham Hip Fracture Score as a predictor of one year mortality in patients undergoing surgical repair of fractured neck of femur. *Br J Anaesth* 2011; **106**:501–504.
- 523 Gilbert J, Paul SD, Hendel RC, *et al.* Development and validation of a Bayesian model for perioperative cardiac risk assessment in a cohort of 1,081 vascular surgical candidates. *J Am Coll Cardiol* 1996; **27**:779–786.
- 524 Brooke BS, Sarfati MR, Zhang Y, *et al.* Cardiac stress testing during workup for abdominal aortic aneurysm repair is not associated with improved patient outcomes. *Ann Vasc Surg* 2017; **42**:222–230.
- 525 Neary W, Prytherch D, Foy C, *et al.* Comparison of different methods of risk stratification in urgent and emergency surgery. *Br J Surg* 2007; **94**:1300–1305.
- 526 Haga Y, Ikejiri K, Wada Y, *et al.* A multicenter prospective study of surgical audit systems. *Ann Surg* 2011; **253**:194–201.
- 527 Wong D, Oliver C, Moonesinghe S. Predicting postoperative morbidity in adult elective surgical patients using the Surgical Outcome Risk Tool (SORT). *Br J Anaesth* 2017; **119**:95–105.
- 528 Wong G, Ang W, Wong T, Choi S. Surgical Outcome Risk Tool (sort) validation in hepatectomy. *Anaesthesia* 2017; **72**:1287–1289.
- 529 Le Manach Y, Collins G, Rodseth R, *et al.* Preoperative Score to Predict Postoperative Mortality (POSPOM) derivation and validation. *Anesthesiology* 2016; **124**:570–579.
- 530 Dahlke AR, Merkow RP, Chung JW, *et al.* Comparison of postoperative complication risk prediction approaches based on factors known preoperatively to surgeons versus patients. *Surgery* 2014; **156**:39–45.
- 531 Thieme RD, Cutchma G, Chieferdecker MEM, Campos ACL. Nutritional risk index is predictor of postoperative complications in operations of digestive system or abdominal wall? *Arq Bras Cir Dig* 2013; **26**:286–292.
- 532 Karateke F, Ikiz GZ, Kuvvetli A, *et al.* Evaluation of nutritional risk screening-2002 and subjective global assessment for general surgery patients: a prospective study. *J Pak Med Assoc* 2013; **63**:1405–1408.
- 533 Cerantola Y, Valerio M, Hubner M, *et al.* Are patients at nutritional risk more prone to complications after major urological surgery? *J Urol* 2013; **190**:2126–2132.
- 534 Zhou W, Xu X, Yan J, Mou Y. Nutritional risk is still a clinical predictor of postoperative outcomes in laparoscopic abdominal surgery. *Surg Endosc* 2013; **27**:2569–2574.
- 535 Kuppinger D, Hartl WH, Bertok M, *et al.* Nutritional screening for risk prediction in patients scheduled for abdominal operations. *Br J Surg* 2012; **99**:728–737.
- 536 Kuzu MA, Terzioğlu H, Genç V, *et al.* Preoperative nutritional risk assessment in predicting postoperative outcome in patients undergoing major surgery. *World J Surg* 2006; **30**:378–390.
- 537 Canet J, Gallart L, Gomar C, *et al.* Prediction of postoperative pulmonary complications in a population-based surgical cohort. *Anesthesiology* 2010; **113**:1338–1350.
- 538 Copeland G, Jones D, Walters M. POSSUM: a scoring system for surgical audit. *Br J Surg* 1991; **78**:355–360.
- 539 Brooks M, Sutton R, Sarin S. Comparison of surgical risk score, POSSUM and p-POSSUM in higher-risk surgical patients. *Br J Surg* 2005; **92**:1288–1292.
- 540 Whiteley M, Prytherch D, Higgins B, *et al.* An evaluation of the POSSUM surgical scoring system. *Br J Surg* 1996; **83**:812–815.
- 541 Organ N, Morgan T, Venkatesh B, Purdie D. Evaluation of the P-POSSUM mortality prediction algorithm in Australian surgical intensive care unit patients. *ANZ J Surg* 2002; **72**:735–738.
- 542 Bilimoria KY, Liu Y, Paruch JL, *et al.* Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. *J Am Coll Surg* 2013; **217**:833–842; e3.
- 543 Liu Y, Cohen ME, Hall BL, *et al.* Evaluation and enhancement of calibration in the American College of Surgeons NSQIP Surgical Risk Calculator. *J Am Coll Surg* 2016; **223**:231–239.
- 544 Sellers MM, Merkow RP, Halverson A, *et al.* Validation of new readmission data in the American College of Surgeons national surgical quality improvement program. *J Am Coll Surg* 2013; **216**:420–427.
- 545 Cohen ME, Bilimoria KY, Ko CY, Hall BL. Development of an American College of Surgeons National Surgery Quality Improvement Program: morbidity and mortality risk calculator for colorectal surgery. *J Am Coll Surg* 2009; **208**:1009–1016.
- 546 Rodseth RN, Buse GAL, Bolliger D, *et al.* The predictive ability of preoperative B-type natriuretic peptide in vascular patients for major adverse cardiac events: an individual patient data meta-analysis. *J Am Coll Cardiol* 2011; **58**:522–529.
- 547 Biccard B, Lurati Buse G, Burkhart C, *et al.* The influence of clinical risk factors on preoperative B-type natriuretic peptide risk stratification of vascular surgical patients. *Anaesthesia* 2012; **67**:55–59.
- 548 Simmers D, Potgieter D, Ryan L, *et al.* The use of preoperative B-type natriuretic peptide as a predictor of atrial fibrillation after thoracic surgery: systematic review and meta-analysis. *J Cardiothorac Vasc Anesth* 2015; **29**:389–395.
- 549 Buse GAL, Koller MT, Burkhart C, *et al.* The predictive value of preoperative natriuretic peptide concentrations in adults undergoing surgery: a systematic review and meta-analysis. *Anesth Analg* 2011; **112**:1019–1033.
- 550 Rodseth RN, Biccard BM, Le Manach Y, *et al.* The prognostic value of preoperative and postoperative B-type natriuretic peptides in patients undergoing noncardiac surgery: B-type natriuretic peptide and N-terminal fragment of pro-B-type natriuretic peptide: a systematic review and individual patient data meta-analysis. *J Am Coll Cardiol* 2014; **63**:170–180.
- 551 Kopec M, Duma A, Helwani MA, *et al.* Improving prediction of postoperative myocardial infarction with high-sensitivity cardiac troponin T and NT-proBNP. *Anesth Analg* 2017; **124**:398–405.
- 552 Nagele P, Brown F, Gage BF, *et al.* High-sensitivity cardiac troponin T in prediction and diagnosis of myocardial infarction and long-term mortality after noncardiac surgery. *Am Heart J* 2013; **166**:325–332; e1.
- 553 Weber M, Luchner A, Manfred S, *et al.* Incremental value of high-sensitive troponin T in addition to the revised cardiac index for peri-operative risk stratification in noncardiac surgery. *Eur Heart J* 2012; **34**:853–862.
- 554 Biccard B, Naidoo P, De Vasconcellos K. What is the best preoperative risk stratification tool for major adverse cardiac events following elective vascular surgery? A prospective observational cohort study evaluating preoperative myocardial ischaemia monitoring and biomarker analysis. *Anaesthesia* 2012; **67**:389–395.

- 555 Nordling P, Kiviniemi T, Strandberg M, *et al.* Predicting the outcome of hip fracture patients by using N-terminal fragment of pro-B-type natriuretic peptide. *BMJ Open* 2016; **6**:e009416.
- 556 Hietala P, Strandberg M, Kiviniemi T, *et al.* Usefulness of troponin T to predict short-term and long-term mortality in patients after hip fracture. *Am J Cardiol* 2014; **114**:193–197.
- 557 Devereaux P, Biccard BM, Sigamani A, *et al.* Association of postoperative high-sensitivity troponin levels with myocardial injury and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2017; **317**:1642–1651.
- 558 Alcock RF, Kouzios D, Naoum C, *et al.* Perioperative myocardial necrosis in patients at high cardiovascular risk undergoing elective noncardiac surgery. *Heart* 2012; **98**:792–798.
- 559 Thomas KN, Cotter JD, Williams MJ, van Rij AM. Diagnosis, incidence, and clinical implications of perioperative myocardial injury in vascular surgery. *Vasc Endovasc Surg* 2016; **50**:247–255.
- 560 Jarai R, Mahla E, Perkman T, *et al.* Usefulness of preoperative copeptin concentrations to predict postoperative outcome after major vascular surgery. *Am J Cardiol* 2011; **108**:1188–1195.
- 561 Schrimpf C, Gillmann H-J, Sahlmann B, *et al.* Renal function interferes with copeptin in prediction of major adverse cardiac events in patients undergoing vascular surgery. *PLoS One* 2015; **10**:e0123093.
- 562 Mauermann E, Bolliger D, Seeberger E, *et al.* Incremental value of preoperative copeptin for predicting myocardial injury. *Anesth Analg* 2016; **123**:1363–1371.
- 563 Phillips C, Brookes CD, Rich J, *et al.* Postoperative nausea and vomiting following orthognathic surgery. *Int J Oral Maxillofac Surg* 2015; **44**:745–751.
- 564 Kolanek B, Svartz L, Robin F, *et al.* Management program decreases postoperative nausea and vomiting in high-risk and in general surgical patients: a quality improvement cycle. *Minerva Anesthesiol* 2014; **80**:337–346.
- 565 Gan TJ, Diemunsch P, Habib AS, *et al.* Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg* 2014; **118**:85–113.
- 566 Won Y, Yoo J, Chae Y, *et al.* The incidence of postoperative nausea and vomiting after thyroidectomy using three anaesthetic techniques. *J Int Med Res* 2011; **39**:1834–1842.
- 567 Peyton PJ, Wu CY. Nitrous oxide–related postoperative nausea and vomiting depends on duration of exposure. *Anesthesiology* 2014; **120**:1137–1145.
- 568 Abouammoh MA, Abdelhalim AA, Mohamed EA, *et al.* Subtenon block combined with general anesthesia for vitreoretinal surgery improves postoperative analgesia in adult: a randomized controlled trial. *J Clin Anesth* 2016; **30**:78–86.
- 569 Wu Y, Sun H, Wang S, Tseng C-C. Applicability of risk scores for postoperative nausea and vomiting in a Taiwanese population undergoing general anaesthesia. *Anaesth Intensive Care* 2015; **43**:473–478.
- 570 Kim SH, Shin Y-S, Oh YJ, *et al.* Risk assessment of postoperative nausea and vomiting in the intravenous patient-controlled analgesia environment: predictive values of the Apfel's simplified risk score for identification of high-risk patients. *Yonsei Med J* 2013; **54**:1273–1281.
- 571 Allen M, Leslie K, Jansen N. Validation of the postoperative nausea and vomiting intensity score in gynaecological patients. *Anaesth Intensive Care* 2011; **39**:73–78.
- 572 Gärtner R, Kroman N, Callesen T, Kehlet H. Multimodal prevention of pain, nausea and vomiting after breast cancer surgery. *Minerva Anesthesiol* 2010; **76**:805–813.
- 573 Koh IJ, Chang CB, Jeon Y-T, *et al.* Does ramosetron reduce postoperative emesis and pain after TKA? *Clin Orthop Relat Res* 2012; **470**:1718–1727.
- 574 Dewinter G, Teunkens A, Vermeulen K, *et al.* Alizapride and ondansetron for the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic gynaecological surgery: a double-blind, randomised, placebo-controlled noninferiority study. *Eur J Anaesthesiol* 2016; **33**:96–103.
- 575 Fattahi Z, Hadavi SMR, Sahmeddini MA. Effect of ondansetron on postdural puncture headache (PDPH) in parturients undergoing cesarean section: a double-blind randomized placebo-controlled study. *J Anesth* 2015; **29**:702–707.
- 576 Kori K, Oikawa T, Odaguchi H, *et al.* Go-rei-San, a Kampo medicine, reduces postoperative nausea and vomiting: a prospective, single-blind, randomized trial. *J Altern Complement Med* 2013; **19**:946–950.
- 577 Lunn T, Kehlet H. Perioperative glucocorticoids in hip and knee surgery—benefit vs. harm? A review of randomized clinical trials. *Acta Anaesthesiol Scand* 2013; **57**:823–834.
- 578 Thimmasettaiah NB, Chandrappa RG. A prospective study to compare the effects of pre, intra and post operative steroid (dexamethasone sodium phosphate) on post tonsillectomy morbidity. *J Pharmacol Pharmacother* 2012; **3**:254–258.
- 579 Kurz A, Fleischmann E, Sessler D, *et al.* Effects of supplemental oxygen and dexamethasone on surgical site infection: a factorial randomized trial. *Br J Anaesth* 2015; **115**:434–443.
- 580 Dogan R, Erbek S, Gonencer HH, *et al.* Comparison of local anaesthesia with dexmedetomidine sedation and general anaesthesia during septoplasty. *Eur J Anaesthesiol* 2010; **27**:560–964.
- 581 De Oliveira G Jr, Ahmad S, Fitzgerald P, *et al.* Dose ranging study on the effect of preoperative dexamethasone on postoperative quality of recovery and opioid consumption after ambulatory gynaecological surgery. *Br J Anaesth* 2011; **107**:362–371.
- 582 Dahmani S, Brasher C, Stany I, *et al.* Premedication with clonidine is superior to benzodiazepines. A meta analysis of published studies. *Acta Anaesthesiol Scand* 2010; **54**:397–402.
- 583 Pergolizzi JV, Philip BK, Leslie JB, *et al.* Perspectives on transdermal scopolamine for the treatment of postoperative nausea and vomiting. *J Clin Anesth* 2012; **24**:334–345.
- 584 Wang P-K, Tsay P-J, Huang C-C, *et al.* Comparison of dexamethasone with ondansetron or haloperidol for prevention of patient-controlled analgesia-related postoperative nausea and vomiting: a randomized clinical trial. *World J Surg* 2012; **36**:775–781.
- 585 Tang DH, Malone DC. A network meta-analysis on the efficacy of serotonin type 3 receptor antagonists used in adults during the first 24 h for postoperative nausea and vomiting prophylaxis. *Clin Ther* 2012; **34**:282–294.
- 586 Lee A, Chan SK, Fan LT. Stimulation of the wrist acupuncture point PC6 for preventing postoperative nausea and vomiting. *Cochrane Database Syst Rev* 2015; CD003281.
- 587 Alizadeh R, Esmaeili S, Shoar S, *et al.* Acupuncture in preventing postoperative nausea and vomiting: efficacy of two acupuncture points versus a single one. *J Acupunct Meridian Stud* 2014; **7**:71–75.
- 588 Cheong KB, Zhang J-P, Huang Y, Zhang Z-j. The effectiveness of acupuncture in prevention and treatment of postoperative nausea and vomiting: a systematic review and meta-analysis. *PLoS One* 2013; **8**:e82474.
- 589 Lee S, Lee MS, Choi DH, Lee SK. Electroacupuncture on PC6 prevents opioid-induced nausea and vomiting after laparoscopic surgery. *Chin J Integr Med* 2013; **19**:277–281.
- 590 Holmér Pettersson P, Wengström Y. Acupuncture prior to surgery to minimise postoperative nausea and vomiting: a systematic review. *J Clin Nurs* 2012; **21**:1799–1805.
- 591 El-Deeb AM, Ahmady MS. Effect of acupuncture on nausea and/or vomiting during and after cesarean section in comparison with ondansetron. *J Anesth* 2011; **25**:698–703.
- 592 Majholm B, Møller AM. Acupressure at acupoint P6 for prevention of postoperative nausea and vomiting: a randomised clinical trial. *Eur J Anaesthesiol* 2011; **28**:412–419.
- 593 Larson JD, Gutowski KA, Marcus BC, *et al.* The effect of electroacupuncture on postoperative nausea, vomiting, and pain in outpatient plastic surgery patients: a prospective, randomized, blinded, clinical trial. *Plast Reconstr Surg* 2010; **125**:989–994.
- 594 Direkvand-Moghadam A, Khosravi A. Effect of acupressure on post-operative nausea and vomiting in cesarean section: a randomised controlled trial. *J Clin Diagn Res* 2013; **7**:2247.
- 595 Xu M, Zhou S-J, Jiang C-C, *et al.* The effects of P6 electrical acupressure on postoperative nausea and vomiting in patients after infratentorial craniotomy. *J Neurosurg Anesthesiol* 2012; **24**:312–316.
- 596 White PF, Zhao M, Tang J, *et al.* Use of a disposable acupressure device as part of a multimodal antiemetic strategy for reducing postoperative nausea and vomiting. *Anesth Analg* 2012; **115**:31–37.
- 597 Janicki PK, Vealey R, Liu J, *et al.* Genome-wide association study using pooled DNA to identify candidate markers mediating susceptibility to postoperative nausea and vomiting. *Anesthesiology* 2011; **115**:54–64.