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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 abtracts 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 $\geq$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

PImax 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. *How, when and by whom should patients be evaluated pre-operatively?*		
• 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 2C	16–19 20
• We recommend the implementation of functional measures such as level of independence, frailty and level of anxiety in pre-operative evaluation.	1B	21–27,31
• 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.	2C	32
• 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.	1C	33,34
1.2. *How should the patient be informed about peri-operative risks?*		
• We recommend the inclusion of information in every pre-operative consultation, as it is very important to patients.	1B	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. Specific clinical conditions		
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
Diabetes		
• 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
Obesity		
• 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
Coagulation disorders		
• 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-operaitve 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
Anaemia and pre-operative blood conservation strategies		
• 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
The geriatric patient		
• 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

(*continued*)

Recommendation	Grade	References
• 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.	1B	311,312,314,339–341
• Depression is frequent in the elderly and is related to increased complications. We recommend that depression is assessed by validated tools.	1B	311,314
• 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
• 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
• Malnutrition is frequent, often underevaluated 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
• 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		
• 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
• 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
• 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
• We recommend that the AUDIT-C and the AUDIT score are not interchangeable for detection of AUD in pre-operative assessment.	1C	370
• We suggest that the NIAAA-4Q tool can be used pre-operatively to identify AUD.	2C	375
• 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
• No suggestion can be given on the timing, duration and intensity of alcohol cessation.	2A	379
• 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		
• 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
• 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
• 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		
• 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
• We suggest stopping herbal medicines 2 weeks prior to surgery.	2B	391,399
• 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		
• We suggest that patients chronically treated with TCA should undergo comprehensive cardiac evaluation prior to anaesthesia.	2B	404,408
• We recommend that antidepressant treatment for chronically depressed patients should not be discontinued prior to anaesthesia.	1B	424
• We suggest that there is insufficient evidence for discontinuation of SSRI treatment peri-operatively.	2B	409,420,421
• 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
• We suggest that antipsychotic medication is continued in patients with chronic schizophrenia peri-operatively.	2B	408
• We suggest stopping lithium administration 72 h prior to surgery.		
• 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
• We suggest that lithium therapy is continued in patients undergoing minor surgery under local anaesthesia.	2C	408
• We suggest stopping herbal medicine 2 weeks prior to surgery.	2B	399
Peri-operative bridging of anticoagulation therapy		
• 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
• 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
• In pacemarker and defibrillator devices implantation, we recommend continuing VKA therapy in preference to 'bridging' therapy with LMWH.	1B	444,445
• 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?		
• 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.		
• Details of this should be documented in the patient chart.	1A	458
• 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
• 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
• We recommend that the Mallampati classification alone should no longer be considered capable of predicting the laryngoscopic view with precision.	1B	461,464–467
• 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
• 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
• 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
• 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
• We suggest that difficult videolaryngoscopy cannot easily be predicted, as only a few studies have addressed this question so far.	2C	461,463,471
• 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		
• We recommend using ASA-PS to stratify mortality risk in patients undergoing noncardiac surgery.	1B	487,488,491–496
• 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
• 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
• We suggest using the Nottingham Hip Fracture Score to stratify peri-operative mortality risk in patients undergoing surgery for hip fractures.	2C	517–522
• We recommend using the STOP BANG questionnaire to assess the risk of OSAS and postoperative complications.	1C	103–106
Biomarkers		
• 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
• 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
• 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*		
• We recommend implementing a PONV guideline according to the local clinical setting.	1B	569–571
• We recommend the inclusion of a pre-operative PONV score in the pre-anaesthetic evaluation.	2B	569
• 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
• 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 nececessary for the performance of pre-operative evaluation: nurse, general practioner, 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] TerMine[12]) 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 abtracts 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 status[24] and sensory deficits.[25] The Timed Up and Go (TUG) score predicts postoperative complications in patients over 74 years of age[26] 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/miorcardiacarrest). 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 to1.26, $P = 0.29$). 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 (FEV_1)/ functional vital capacity (FVC) <70%] and airflow reversibility (ΔFEV_1 >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 FEV_1 of 85.2% or less and smoking history as independent predictors for the need for peri-operative bronchodilator therapy.[83] Finally, a low FEV_1 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 complications [85] 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, specific[98] 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 FEV_1, 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, stoping 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 outcomes[131] 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] steroids[140] 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 Hb[146] 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 GFR[152] 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 perioperative infection[156] and intra-operative hydroxyethyl starch (HES) administration[157] 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 remifentanil 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 maintainance 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 surgery [185] and major complications after abdominal surgery,[186] the other found that pre-operative HbA1c did not predict complications after gastric bypass surgery[187] 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 guidance[192] 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 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 glycolysated 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 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 laparascopic 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 ß-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] nephrectomy[226] 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 surgery[232] and oesophagectomy.[233] In particular, superobesity (weight >150 kg)[234] or a BMI more than 50 kg min^{-2} [199,200,235,236] are predictors of adverse outcomes. In obese sufferers of metabolic syndrome[237] 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 VO_2 levels was associated with increased short-term complications (renal failure, unstable angina) after bariatric surgery.[204] Abnormalities in ECG, FEV_1 less than 80% [199] and reduced vital capacity are all predictors of postoperative 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 smoking[234] 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 oximetry[260] 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 IMT[263] 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 laparascopic 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 perioperatively 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 study[271] 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 x 10^9 l^{-1}) had an OR of 1.35 (95% CI 1.01 to 1.83) and 125 patients with severe thrombocytopenia (<100 x 10^9 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-operaitve 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 betwen 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 to1.71). 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 $100 \times 10^9 l^{-1}$ mortality, septic complications, renal failure and septic shock had a significantly higher incidence in comparison to a platelet count above $100 \times 10^9\ l^{-1}$.

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 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-operaitve 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 stay [284] 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 ($<12\ g\ dl^{-1}$ for women, $<13\ g\ dl^{-1}$ 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 discharge[289] 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 that 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 wth 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 comorbities 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 $>24\,g\,day^{-1}$ for women and $>36\,g\,day^{-1}$ for men[366]) 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 nondepolarising 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 ß-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 alpha$_1$-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 endogeneous noradrenaline in high concentration causing hypertension, whereas direct acting sympathomimetics may exert an enhanced effect due to receptor hypersensititvity 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 resuts 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 withn 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 fibirillation patients with a $CHADS_2$ 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 $CHADS_2$ score $\leq$4, patients treated for >3 months for a nonrecurrent VTE) taking VKA, treatment (acenocumarol, 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 producedures 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.[433,437] The data were collected from the BRAVE registry (Bonn Registry for Alternative Peri-Procedural 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 $CHADS_2$ 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 Fibrilallation (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 infaction, 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 ($CHADS_2$ >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 surgery[450] 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 anesthetist. However, these clinical tests, and in particular *one* clinical test standing alone, does not provide sufficient sensitivity and specifity 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 maintainenance 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 53 041 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 fibreoptic 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, fibreoptic 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 fibreoptic 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, Samsoon and Young[468] 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

Benumof[475] 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 labour[476] 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 aiway 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 predefined 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 predefined 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 sytematic 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 fibriliation.[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 periperative 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 scores 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 perioperative 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-] 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 perioperative 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-HT_3 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. HT_3-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 HT_3-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.

Corticosteriods 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-HT_3 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 N_2O and using TIVA instead of balanced anaesthesia together with postoperative opioid saring 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 surgery[1] 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
Anticholinerics	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 anaesthesiologist 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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