

ROUTINE PREOPERATIVE TESTING IN ADULTS UNDERGOING ELECTIVE NON-CARDIOTHORACIC SURGERY



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ROUTINE PREOPERATIVE TESTING IN ADULTS UNDERGOING ELECTIVE NON-CARDIOTHORACIC SURGERY

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- The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.
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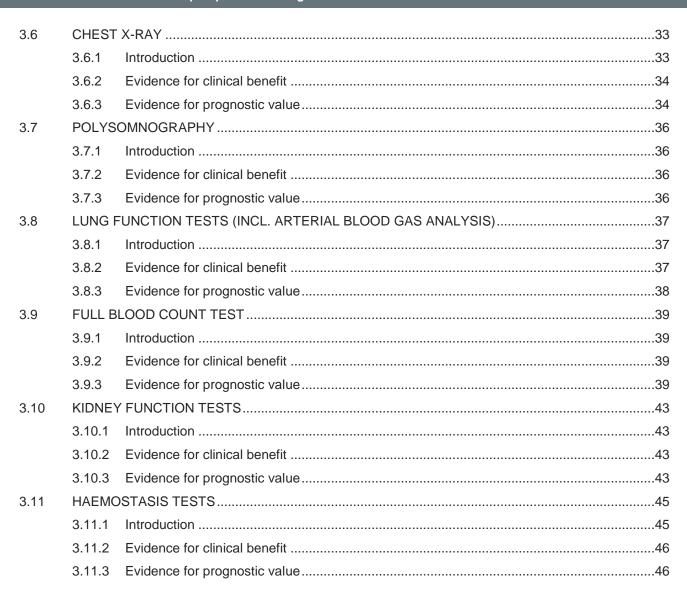


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LIST OF ABBREVIATIONS

| ABBREVIATION | DEFINITION |
|--------------|---|
| 95%CI | 95% confidence interval |
| AAA | Abdominal Aortic Aneurysm |
| ACC | American College of Cardiology |
| ACE | Angiotensin Converting Enzyme |
| AHA | American Heart Association |
| AHI | Apnoea-hypopnoea index |
| aPTT | Activated Partial Thromboplastin Time |
| ASA | American Society of Anesthesiologists |
| AST | Aspartate Aminotransferase |
| AT | Anaerobic Threshold |
| CEBAM | Belgian Centre for Evidence-Based Medicine |
| COPD | Chronic Obstructive Pulmonary Disease |
| CPET | Cardiopulmonary Exercise Testing |
| CPG | Clinical Practice Guideline |
| DARE | Database of Abstracts of Reviews of Effects |
| ECG | Electrocardiogram |
| EEG | Electroencephalography |
| eGFR | Estimated Glomerular Filtration Rate |
| EMG | Electromyography |
| EOG | Electro-oculography |
| ESA | European Society of Anaesthesiology |
| ESC | European Society of Cardiology |
| EVAR | Endovascular Aneurysm Repair |
| FEV1 | Forced Expiratory Volume in 1 second |
| FRC | Functional Residual Capacity |
| FVC | Forced Vital Capacity |



GRADE Grades of Recommendation, Assessment, Development and Evaluation

HbA1c Glycated Haemoglobin

HR Hazard Ratio

HTA Health Technology Assessment

ICU Intensive Care Unit

INR International Normalized Ratio

KCE Belgian Healthcare Knowledge Centre

MA Meta-analysis

MACE Major Adverse Cardiovascular Events
MELD Model For End-Stage Liver Disease

MVV Maximal Voluntary Ventilation

NICE National Institute for Health and Care Excellence
NIHDI National Institute for Health and Disability Insurance

NRKP / CNPQ National Council for Quality Promotion

OIS Optimal Information Size

OR Odds Ratio

OSA Obstructive Sleep Apnoea
PCNL Percutaneous Nephrolithotomy

PT Prothrombin Time

PTT Partial Thromboplastin Time

RBC Red Blood Cell

RCT Randomized Controlled Trial

RR Relative Risk

RRR Relative Risk Reduction
SD Standard Deviation

SIRS Systemic Inflammatory Response Syndrome



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SR Systematic Review
SUN Serum Urea Nitrogen
TLC Total Lung Capacity

VC Vital Capacity

VCO₂ Carbon Dioxide Production

 $\begin{array}{ccc} \text{VE} & & \text{Minute Ventilation} \\ \text{VO}_2 & & \text{Oxygen consumption} \\ \text{WBC} & & \text{White Blood Cell} \end{array}$



■ SCIENTIFIC REPORT

1 INTRODUCTION

1.1 Background

In 2004, KCE developed a first clinical practice guideline (CPG) on preoperative testing. This guideline contained recommendations on the use of specific preoperative tests for patients scheduled for elective non-cardiothoracic surgery, and the perioperative use of beta blocking agents. In June 2005, the National Council for Quality Promotion (NRKP/CNPQ) provided every Belgian hospital with feedback about their use of preoperative tests. This feedback was accompanied by a summary of the 2004 KCE guideline. Furthermore, based on the 2004 KCE guideline the NIHDI (RIZIV/INAMI) developed an online tool that allows to evaluate which preoperative tests are required for a specific patient, a tool that is still in use (http://www.riziv.fgov.be/nl/professionals/individuelezorgverleners/artsen/k waliteit/feedback/Paginas/preop-flowchart-praktische-wegwijzer-onderzoeken.aspx#.V4T0CGfoupo; accessed on July 12th 2016).

1.2 The need for a(n) (update of the) guideline

The 2004 KCE guideline was not yet developed following the current methodological standards, including the GRADE approach. Furthermore, given the age of the guideline, many recommendations carry the risk of being outdated. Finally, the feedback report of the NRKP/CNPQ showed a large variability between hospitals, and this situation has likely not changed.

1.3 Scope

As was the case in the 2004 KCE guideline, this guideline will focus on adult patients (i.e. 18+) undergoing elective non-cardiothoracic surgery. However, the scope was enlarged to include patients with ASA classification 4 too (Table 1).



Table 1 - ASA classification

| ASA grade | Definition |
|-------------|--|
| ASA grade 1 | A normal healthy patient. |
| ASA grade 2 | A patient with mild systemic disease (e.g. current smoker, social alcohol drinker, pregnancy, obesity [BMI 30-40 kg/m²], well-controlled diabetes or hypertension, mild lung disease). |
| ASA grade 3 | A patient with severe systemic disease (e.g. poorly controlled diabetes or hypertension, COPD, morbid obesity [BMI ≥40 kg/m²], active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, end-stage renal disease undergoing regularly scheduled dialysis, history [>3 months] of myocardial infarction, cerebrovascular attack, transient ischemic attack, or coronary artery disease/stents). |
| ASA grade 4 | A patient with severe systemic disease that is a constant threat to life (e.g. recent [< 3 months] myocardial infarction, cerebrovascular attack, transient ischemic attack, or coronary artery disease/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, diffuse intravascular coagulation, acute respiratory disease or end-stage renal disease not undergoing regularly scheduled dialysis). |
| ASA grade 5 | A moribund patient who is not expected to survive without the operation (e.g. ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction). |
| ASA grade 6 | A declared brain-dead patient whose organs are being removed for donor purposes. |

Source: American Society of Anesthesiologists, https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system, accessed on July 12th 2016

Since a recent *KCE* has read for you already focused on the perioperative use of beta blocking agents,² the present guideline will only deal with the use of preoperative tests. A detailed list of preoperative tests addressed in this guideline is provided in chapter 2.3. However, situations where these tests are used for technical information that is needed perioperatively are out of scope (e.g. lung or liver function tests to estimate the remnant function after resection).

For each preoperative test, a clear distinction will be made according to the ASA classification and the type of surgery. Since there is no widely accepted and validated system for classifying the stressfulness of operative procedures, this guideline adopted a simple scale (Table 2) that was also used in the 2004 KCE guideline ¹ and the recently updated NICE guideline.³ Transplant surgery and cardiothoracic surgery are out of scope, as is emergency surgery.



Table 2 – Surgery grades and examples 1,3

| linor | Intermediate | Major or complex |
|--|---|--|
| Excising skin lesion Excising Bartholin gland Draining breast abscess Carpal tunnel release Nasal septum deviation repair Circumcision Hydrocele repair Cataract surgery | Primary repair of inguinal hernia Excising varicose veins in the leg Tonsillectomy or aden(otonsill)ectomy Knee arthroscopy Resection of submandibular gland Conisation Eardrum repair Caesarean section Laparoscopic cholecystectomy | Total abdominal hysterectomy Mastectomy Endoscopic resection of prostate Lumbar discectomy Thyroidectomy Total joint replacement Colonic resection Radical neck dissection Nephrectomy Neurosurgery |



1.4 Remit of the guideline

1.4.1 Overall objectives

This guideline provides recommendations based on current scientific evidence for preoperative testing of adult patients undergoing elective non-cardiothoracic surgery. Clinicians are encouraged to interpret these recommendations in the context of the individual patient situation, values and preferences.

The guidelines are based on clinical evidence and may not always be in line with the current criteria for NIHDI reimbursement of diagnostic and therapeutic interventions. The NIHDI may consider adaptation of reimbursement/funding criteria based on these guidelines.

In view of the currently anticipated variability in the use of preoperative tests across hospitals, this guideline may lead to less overuse and variability, and to a decrease in healthcare costs.

1.4.2 Target users of the guideline

This guideline is intended to be used by all care providers involved in the preoperative management of adult patients undergoing elective non-cardiothoracic surgery, including anaesthesiologists, surgeons, cardiologists, radiologists, clinical biologists, primary care physicians (non-exhaustive list). It can also be of interest for patients and their families, hospital managers and policy makers.

1.5 Statement of intent

Clinical guidelines are designed to improve the quality of health care and decrease the use of unnecessary or harmful interventions. This guideline has been developed by clinicians and researchers for use within the Belgian healthcare context. It provides advice regarding the care and management of adult patients undergoing elective non-cardiothoracic surgery.

The recommendations are not intended to indicate an exclusive course of action or to serve as a standard of care. Standards of care are determined on the basis of all the available clinical data for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Variations, which take into account individual circumstances, clinical judgement and patient choice, may also be appropriate. The information in this guideline is not a substitute for proper diagnosis, treatment or the provision of advice by an appropriate health professional. It is advised, however, that significant deviations from the national guideline are fully documented in the patient's file at the time the relevant decision is taken.

1.6 Funding and declaration of interest

KCE is a federal institution funded for the largest part by INAMI/RIZIV, but also by the Federal Public Service of Health, Food chain Safety and Environment, and the Federal Public Service of Social Security. The development of clinical practice guidelines is part of the legal mission of the KCE. Although the development of guidelines is paid by KCE's budget, the sole mission of the KCE is providing scientifically valid information. KCE has no interest in companies (commercial or non-commercial i.e. hospitals and universities), associations (e.g. professional associations, unions), individuals or organisations (e.g. lobby groups) that could be positively or negatively affected (financially or in any other way) by the implementation of these guidelines. All clinicians involved in the Guideline Development Group (GDG) or the peer-review process completed a declaration of interest form. Information on potential conflicts of interest is published in the colophon of this report. All members of the KCE Expert Team make yearly declarations of interest and further details of these are available upon request.

2 METHODOLOGY

2.1 Introduction

During the pre-assessment before the actual start of this project, NICE already started the update of their guideline, and a draft guideline was available at that time.³ It was therefore decided to adapt the NICE guideline using the ADAPTE methodology (see below, chapter 2.4). Further details about KCE and the guideline development methodology are available at https://kce.fgov.be/content/kce-processes.

Several steps were followed to elaborate this guideline. Firstly, clinical questions were developed (some were adopted from the NICE guideline, some were added) and the inclusion and exclusion criteria were defined in collaboration with members of the GDG. Secondly, a literature review was conducted for those clinical questions that were not included in the NICE guideline. Thirdly, on the basis of the results of the literature review (either from NICE, or from KCE), recommendations were formulated and graded according to the GRADE approach.

2.2 The Guideline Development Group

This guideline was developed as a result of a collaboration between multidisciplinary groups of practising clinicians and KCE experts. The composition of the GDG is documented in Appendix 1. Guideline development and literature review expertise, support, and facilitation were provided by the KCE expert team.

The roles assigned to the GDG were:

- To define the clinical questions, in close collaboration with the KCE expert team and stakeholders;
- To identify critical and important outcomes;
- To provide feedback on the selection of studies and identify further relevant manuscripts which may have been missed;
- To provide feedback on the content of the guideline;

- To provide judgement about indirectness of evidence;
- To provide feedback on the draft recommendations;
- To address additional concerns to be reported under a section on 'other considerations'.

2.3 Clinical research questions

In the NICE guideline, several preoperative tests are already discussed.³ Most of these tests were also included in the present guideline, but some additional tests were added.

The selection of preoperative tests was made by the members of the GDG, representatives of professional organizations and patient representatives during an initial stakeholder meeting held at KCE on February 29, 2016. For all preoperative tests, the following two questions were formulated:

- Clinical benefit: What is the clinical effectiveness of <u>routinely</u> using the test preoperatively in improving patient outcomes in adults undergoing elective non-cardiothoracic surgery?
- Prognostic value: Does the preoperative test predict prognosis in adults undergoing elective non-cardiothoracic surgery?

All-cause mortality was considered as the critical outcome, while all other outcomes were considered as important (cardiac events, quality of life, complications, length of stay, readmission, intensive care unit admission).

The CPG addresses the following preoperative tests:

- Resting electrocardiogram;
- Resting echocardiogram;
- Cardiopulmonary exercise testing;
- Chest radiograph;
- Polysomnography;
- Lung function tests and arterial blood gas analysis;
- Full blood count tests:



- Kidney function tests;
- Haemostasis tests:
- Glycated haemoglobin test (HbA1c);
- Liver function tests;
- Urinalysis;
- Stress echocardiography;
- Myocardial scintigraphy;
- Coronary CT angiography.

2.4 General approach

The ADAPTE methodology generally includes three major phases:^a

- 1. **Set-up Phase:** In which an outline of the necessary tasks to be completed prior to beginning the adaptation process (e.g., identifying necessary skills and resources) is prepared.
- Adaptation Phase: In which guideline developers move from the selection of a topic to the identification of specific clinical questions; search for and retrieve guidelines; assess the consistency of the evidence considered, its quality, validity, content and applicability; decide how to best adapt the evidence found; and prepare a draft of the adapted guideline.
- 3. Finalization Phase: Guides guideline developers through getting feedback on the document from stakeholders who will be impacted by the guideline, consulting with the source developers of guidelines used in the adaptation process, establishing a process for review and updating of the adapted guideline and the process of creating a final document.

In view of the availability of the NICE guideline, no additional search for guidelines was conducted, although members of the GDG also provided some recent relevant guidelines as background information. For those topics for which NICE conducted a(n) (update of their original) literature search (i.e. resting electrocardiogram, resting echocardiogram, cardiopulmonary exercise testing, polysomnography, lung function tests, arterial blood gas analysis, full blood count test, kidney function tests, haemostasis tests and glycated haemoglobin test), no new searches were performed for this project.

For all other tests a new literature search was conducted in MEDLINE, Embase and The Cochrane Library (Cochrane Database of Systematic Reviews, DARE and HTA database). Members of the GDG were also consulted to identify additional relevant evidence that may have been missed by the search.

2.5 Literature search and study selection

2.5.1 Databases and date limits

A systematic review of literature was conducted in the following databases:

- The Cochrane Database of systematic reviews (http://www.cochrane.org)
- Medline (http://www.ncbi.nlm.nih.gov/pubmed)
- Embase (<u>http://www.embase.com/</u>)

For each research question a search strategy (see Appendix 2) was developed and adapted to each database. All databases were searched from 2011 to present, with no language restriction. For Embase, conference papers and duplicates from Medline were excluded. The search results were then imported in Endnote.

http://www.g-i-n.net/document-store/working-groupsdocuments/adaptation/adapte-resource-toolkit-guideline-adaptation-2-0.pdf; accessed on September 6th, 2016



2.5.2 Search strategy

A combination of appropriate MeSH terms and free text words was used (Appendix 2). The PICOs and the search strategy corresponding to the research questions are documented in Appendix 2.

The number of articles by database is provided in Appendix 2.

Studies were screened on **title and abstract** with the PICO in- and exclusion criteria. In case of doubt the content experts were consulted. First, the titles and abstracts of the identified studies were checked and irrelevant studies were eliminated. In a second step, the remaining papers were screened by reading their **full-text**. If no full-text was available, the study was excluded for the final recommendations. Reference lists of the selected studies were hand searched for additional relevant manuscripts.

2.5.3 Study design

- Inclusion criteria for the study design:
 - Therapeutic studies: systematic reviews, meta-analyses, RCTs.
 - Prognostic studies: systematic reviews, meta-analyses, RCTs, comparative studies with multivariate analysis Articles in Dutch, English, and French were included.
- Exclusion criteria for study design
 - Narrative review;
 - Cadaver/animal studies;
 - Case reports;
 - Studies presented as conference abstract only. If no full-text was available, the study was not taken into account for the final recommendations.

An iterative approach was followed:

- First, a search for systematic reviews and meta-analyses was performed;
- Second, the selected evidence synthesis was updated by a search for all relevant primary studies (RCTs and comparative studies) published after the search date of the selected SR/MA.

To be included, a systematic review had to:

- address at least one of the research questions;
- evaluate at least one of the selected (critical and important) outcomes;
- search MEDLINE and at least one other electronic database;
- include an assessment of risk of bias for each primary study.

If more than one systematic review was identified for a particular research question, the focus was on the most complete systematic review(s).

To be included a primary study had to:

- be an RCT or a comparative studies with multivariate analysis;
- address at least one of the research questions;
- evaluate at least one of the selected (critical and important) outcomes.

The process used for the selection of relevant studies is detailed in Appendix 2.



2.6 Quality appraisal

2.6.1 Clinical practice guidelines

The AGREE II instrument was used to evaluate the methodological quality of the NICE guideline³ and the guidelines provided by the GDG (see *other considerations*). Each guideline was scored by a single KCE expert. In case of doubt, a second KCE expert was consulted.

2.6.2 Systematic reviews

Selected (systematic) reviews were critically appraised by a single KCE expert using the AMSTAR checklist

(http://amstar.ca/Amstar Checklist.php).4 In case of doubt, a second KCE expert was consulted.

2.6.3 Primary articles

Critical appraisal of each study was performed by a single KCE expert. In case of doubt, a second KCE expert was consulted.

The quality appraisal of RCTs for therapeutic interventions was performed using the "Cochrane Collaboration's tool for assessing risk of bias" ⁵ (see appendix). For each criterion the definitions as described in the Cochrane Handbook were used. If applicable, risk of bias for the items regarding detection bias and attrition bias were assessed per class of outcomes (e.g. subjective and objective outcomes). In the end, each study was labelled as low risk of bias, unclear risk of bias or high risk of bias according to the criteria described in the Cochrane Handbook.

Study limitations in observational studies were evaluated using a checklist developed by the KCE (http://processbook.kce.fgov.be/node/156).

The tools used for the quality appraisal are reported in Appendix 3.1 while the results of the quality appraisal are presented in Appendix 3.2.

2.7 Data extraction

For each systematic review, the search date, publication year, included studies and main results were extracted. For RCTs and observational studies, the following data were extracted: publication year, study population, study intervention, and outcomes.

Data extraction was performed by one reviewer and entered in evidence tables using standard KCE templates.

All evidence tables are reported in Appendix 4.

Meta-analyses were not performed.

2.8 Grading evidence

For each recommendation, we provided its strength and the quality of the supporting evidence.⁶ According to GRADE, for interventional studies we classified the quality of evidence into 4 categories: high, moderate, low, and very low (Table 3 and Table 4). The quality of evidence reflects the extent to which a guideline panel's confidence in an estimate of the effect was adequate to support a particular recommendation.

GRADE for guidelines was used, meaning that the evidence across all outcomes and across studies for a particular recommendation was assessed. The following quality elements for intervention studies were evaluated: study limitations, inconsistency, indirectness, imprecision and publication bias.

For RCTs, quality rating was initially considered to be of high level (Table 3). The rating was then downgraded if needed based on the judgement of the different quality elements. Each quality element considered to have serious or very serious risk of bias was rated down -1 or -2 points respectively. Judgement of the overall confidence in the effect estimate was also taken into account. We considered confidence in estimates as a continuum and the final rating of confidence could differ from that suggested by each separate domain.⁷



Observational studies were by default considered low level of evidence (Table 3 and Table 4). However, the level of evidence of observational studies with no threats to validity can be upgraded for a number of reasons:

- 1. Large magnitude of effects: The larger the magnitude of effect, the stronger becomes the evidence. As a rule of thumb, the following criteria were proposed by GRADE:
 - a. Large, i.e. RR >2 or <0.5 (based on consistent evidence from at least 2 studies, with no plausible confounders): upgrade 1 level
 - b. Very large, i.e. RR >5 or <0.2 (based on direct evidence with no major threats to validity): upgrade 2 levels
- 2. All plausible confounders: all plausible confounding from observational studies or randomized trials may be working to reduce the demonstrated effect or increase the effect if no effect was observed
- 3. Dose-response gradient: The presence of a dose-response gradient may increase our confidence in the findings of observational studies and thereby increase the quality of evidence.

The general principles used to downgrade the quality rating are summarized in Table 3. Decisions on downgrading with -1 or -2 points were based on the judgement of the assessors.

Due to current methodological limitations of the GRADE system for prognosis, GRADE was not formally applied to this type of evidence and no GRADE tables were created. However, the general GRADE principles were used to arrive at a quality rating too, taking into account that, due to the very serious indirectness of evidence, the maximally possible quality rating was low.

Table 3 – A summary of the GRADE approach to grading the quality of evidence for each outcome

| Source of body of evidence | Initial rating of quality of a body of evidence | Factors that may decrease the quality | Factors that may increase the quality | Final quality of a body of evidence |
|----------------------------|---|--|---|-------------------------------------|
| Randomized trials | High | Risk of bias Inconsistency | Large effect Descriptions | High (⊕⊕⊕⊕) |
| | | 2. Inconsistency | 2. Dose-response | Moderate (⊕⊕⊕⊝) |
| Observational studies | Low | 3. Indirectness | 3. All plausible residual | Low (⊕⊕⊝⊝) |
| | | 4. Imprecision5. Publication bias | confounding would reduce the demonstrated effect or would suggest a spurious effect if no effect was observed | Very low (⊕⊖⊝) |

Source: Guyatt GH, Oxman AD, Sultan S, Glasziou P, Akl EA, Alonso-Coello P, et al. GRADE guidelines: 9. Rating up the quality of evidence. J Clin Epidemiol. 2011;64(12):1311-6.

Table 4 – Levels of evidence according to the GRADE system

| Quality level | el Definition Methodological Quality of Supporting Evidence | |
|----------------------|---|---|
| High | We are very confident that the true effect lies close to that of the estimate of the effect. | RCTs without important limitations or overwhelming evidence from observational studies. |
| Moderate | We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. | RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies. |
| Low | Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. | RCTs with very important limitations or observational studies |
| Very low | We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect. | or case series. |

Source: Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol. 2011;64(4):401-6.

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Table 5 – Downgrading the quality rating of evidence using GRADE

| Quality element | Reasons for downgrading |
|-----------------|---|
| Limitations | For each study reporting the selected outcome, possible risk of bias introduced by lack of allocation concealment, lack of blinding, lack of intention-to-treat analysis, loss of follow-up and selective outcome reporting were assessed. Additionally, other limitations such as stopping early for benefit and use of unvalidated outcome measures were taken into consideration. Level of evidence was downgraded if studies were of sufficiently poor quality. Downgrading was omitted if studies with low risk of bias were available that lead to similar conclusions as the studies with a high risk of bias. |
| Inconsistency | Downgrading the level of evidence for inconsistency of results was considered in the following situations: point estimates vary widely across studies, confidence intervals show minimal or no overlap, the statistical test for heterogeneity shows a low p-value or the P is large. If large variability in magnitude of effect remained unexplained, the quality of evidence was rated down. |
| Indirectness | Quality rating was downgraded for indirectness in case the trial population or the applied intervention differed significantly from the population or intervention of interest. Also, the use of surrogate outcomes could lead to downgrading. A third reason for downgrading for indirectness occurred when the studied interventions were not tested in a head-to-head comparison. |
| Imprecision | Evaluation of the imprecision of results was primarily based on <u>examination of the 95%CI</u> . Quality was rated down if clinical action would differ if the upper versus the lower boundary of the 95%CI represented the truth. In general, 95%Cis around relative effects were used for evaluation, except when the event rate was low in spite of a large sample size. To examine the 95%Cis, the clinical decision threshold (CDT) was defined. When the 95%CI crossed this clinical decision threshold, the quality level was rated down. A relative risk reduction (RRR) of 25% was defined as CDT by default and adapted if deemed appropriate e.g. in case of a low risk intervention. |
| | Even if 95%Cis appeared robust, level of evidence could be rated down because of fragility. To judge fragility of results, it is suggested to calculate the number of patients needed for an adequately powered (imaginary) single trial, also called the <u>optimal information size (OIS)</u> . If the total number of patients included in a systematic review was less than the calculated OIS, rating down for imprecision was considered. For calculations, a RRR of 25% was used, unless otherwise stated. When the OIS could not be calculated, a minimum of 300 events for binary outcomes and a minimum of 400 participants for continuous outcomes were used as a rule of thumb. |
| Reporting bias | Quality rating was downgraded for reporting bias if publication bias was suggested by analysis using funnel plots or searching of trial registries. Publication bias was also suspected if results came from small, positive industry-sponsored trials only. |



2.9 Formulation of recommendations

Based on the retrieved evidence, the first draft of recommendations was prepared by the KCE experts. This first draft was, together with the evidence tables, circulated to the guideline development group 2 weeks prior to the face-to-face meetings (February 29, 2016; May 2, 2016; June 20, 2016). Recommendations were changed if important new evidence supported this change. Based on the discussion meetings a second draft of recommendations was prepared and once more circulated to the guideline development group for final approval.

The strength of each recommendation was assigned using the GRADE system (Table 6). The strength of recommendations depends on a balance between all desirable and all undesirable effects of an intervention (i.e., net clinical benefit), quality of available evidence, values and preferences, and estimated cost (resource utilization). For this guideline, no formal cost-effectiveness study was conducted. Factors that influence the strength of a recommendation are reported in Table 7.

Table 6 – Strength of recommendations according to the GRADE system

| System | | | |
|--------|--|--|--|
| Grade | Definition | | |
| Strong | The desirable effects of an intervention clearly outweigh the undesirable effects (the intervention is to be put into practice), or the undesirable effects of an intervention clearly outweigh the desirable effects (the intervention is not to be put into practice). | | |
| Weak | The desirable effects of an intervention probably outweigh the undesirable effects (the intervention probably is to be put into practice), or the undesirable effects of an intervention probably outweigh the desirable effects (the intervention probably is not to be put into practice). | | |

Source: Andrews JC, Schunemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. J Clin Epidemiol. 2013;66(7):726-35.

Table 7 - Factors that influence the strength of a recommendation

| Factor | Comment | |
|---|---|--|
| Balance between desirable and undesirable effects | The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted. | |
| Quality of evidence | The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted. | |
| Values and preferences | The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted. | |
| Costs (resource allocation) | The higher the costs of an intervention, i.e. the greater the resources consumed, the lower the likelihood that a strong recommendation is warranted. | |

Sources: Schünemann HJ, Jaeschke R, Cook DJ, Bria WF, El-Solh AA, Ernst A et al. An Official ATS Statement: Grading the Quality of Evidence and Strength of Recommendations in ATS Guidelines and Recommendations. Am J Respir Crit Care Med 2006: 174:605–14.

Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B et al. Grading Strength of Recommendations and Quality of Evidence in Clinical Guidelines – Report From an American College of Chest Physicians Task Force. Chest 2006; 129:174-81.

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A strong recommendation implies that most patients would want the recommended course of action. A weak recommendation implies that the majority of informed patients would want the intervention, but many would not. Specifically, a strong negative recommendation means the harms of the recommended approach clearly exceed the benefits whereas a weak negative recommendation implies that the majority of patients would not want the intervention, but many would. In the case of a weak recommendation, clinicians are especially required to spend adequate time with patients to discuss patients' values and preferences. Such an in-depth discussion is necessary for the patient to make an informed decision. This may lead a significant proportion of patients to choose an alternative approach. Fully informed patients are in the best position to make decisions that are consistent with the best evidence and patients' values and preferences.

For policy-makers, a strong recommendation implies that variability in clinical practice between individuals or regions would likely be inappropriate whereas a weak recommendation implies that variability between individuals or regions may be appropriate, and use as a quality of care criterion is inappropriate.⁹

We offer the suggested interpretation of "strong" and "weak" recommendations in Table 8.

Table 8 - Interpretation of strong and conditional (weak)* recommendations

| Implications | Strong recommendation | Weak recommendation | |
|-------------------|--|--|--|
| For patients | Most individuals in this situation would want the recommended course of action, and only a small proportion would not. | , , | |
| | Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences. | | |
| For clinicians | Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. | , | |
| For policy makers | The recommendation can be adopted as policy in most situations. | Policy-making will require substantial debate and involvement of various stakeholders. | |

^{*} the terms "conditional" and "weak" can be used synonymously

Source: Andrews JC, Schunemann HJ, Oxman AD, Pottie K, Meerpohl JJ, Coello PA, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. J Clin Epidemiol. 2013;66(7):726-35.



2.10 External review

2.10.1 Healthcare professionals

The recommendations prepared by the guideline development group were circulated to Professional Associations (Table 9). Each association was asked to assign one or two key representatives to act as external reviewers of the draft guideline. All expert referees made declarations of interest.

Globally, 9 external experts were involved in the evaluation of the clinical recommendations. All invited panellists received the scientific reports for all research questions and were asked to score each recommendation on a 5-point Likert scale indicating their level of agreement with the recommendation, with a score of '1' indicating 'completely disagree', '2' 'somewhat disagree', '3' 'unsure', '4' 'somewhat agree', and '5' 'completely agree' (the panellists were also able to answer 'not applicable' if they were not familiar with the underlying evidence). If panellists disagreed with the recommendation (score '1' or '2'), they were asked to provide an explanation supported by appropriate evidence. Scientific arguments reported by these experts were used to adapt the formulation or the strength of the clinical recommendations. In Appendix 6, an overview is provided of how their comments were taken into account.

Table 9 - List of Professional Associations invited

- Collegium Chirurgicum
- European Society of Anaesthesiology (ESA)
- Society for Anesthesia and Resuscitation of Belgium (BVAR/SBAR)
- Belgian Society of Radiology (BSR)
- European Association of Urology (EAU)
- Société Scientifique de Médecine Générale (SSMG)
- Belgische Vereniging van Ziekenhuisdirecteurs
- Groupement des Gynécologues Obstétriciens de Langue Française de Belgique (GGOLFB)
- Vlaamse Vereniging voor Obstetrie en Gynaecologie (VVOG)

2.10.2 Patient representatives

Associations of patient representatives were contacted to invite patient representatives to take part in both stakeholder meetings (Feb 29, 2016 & Oct 4, 2016). A key role for patient representatives is to ensure that patients' views and experiences inform the group's work.

The two patient representatives were asked the following questions:

- Have important considerations from a patients' perspective been missed in the formulation of our recommendations?
- Do we need to add information that could assist patients in making clear choices when doctors discuss treatment options with them?

No other (or formal) methods were used to include patients' views and experiences.

2.11 Final validation

As part of the standard KCE procedures, an external scientific validation of the report was conducted prior to its publication. This validation was done in two phases. First, the scientific content was assessed by two clinicians on Oct 28, 2016 (cf. names in the colophon). Second, the methodology was validated making use of the AGREE II checklist. This validation process was chaired by CEBAM on Nov 7, 2016 (cf. names in the colophon).



3.1 Introduction

Several RCTs have evaluated the effectiveness of batches of preoperative tests in adult patients undergoing cataract surgery¹⁰⁻¹² or general elective surgeries. 10, 11 Three RCTs on cataract surgery suggested that routine testing with electrocardiography, complete blood count, and/or a basic metabolic panel did not reduce the risk of intraoperative (OR = 1.02, 95%CI 0.85 to 1.22) or postoperative medical adverse events (OR = 0.96, 95%CI 0.74 to 1.24) when compared to selective or no testing. 12 There was no difference in cancellation of surgery between those with preoperative medical testing and those with no or limited preoperative testing (2 RCTs, RR = 1.00 and 0.97, respectively). 10, 12 One RCT compared per protocol ECG, chest X-ray, basic metabolic panel, complete blood count, coagulation tests, and sickle cell testing with no testing in adult patients undergoing a variety of surgeries. 10, 11 No difference was found in intraoperative events (RR = 1.0, 95%CI 0.4 to 3.0) or postoperative morbidity (RR = 1.24, 95%CI 0.66 to 2.35). Hospital revisits within 7 days were significantly more frequent in the testing group compared with no testing (RR = 0.4, 95%CI 0.2 to 0.9). None of these studies reported on the effectiveness of specific tests, and therefore they only provide indirect evidence for the research questions in this guideline.

In the updated NICE guideline, some general principles are also discussed.³ The importance of a good history taking and clinical assessment is out of question, and was already recommended by the KCE 2004 guideline.¹ In particular, NICE recommends to ensure that the results of any preoperative tests undertaken in primary care are included when referring people for surgical consultation.³ In addition, NICE recommends to take into account any medicines people are taking when considering whether to offer any preoperative test.

Disclaimer

Most of the chapters below should be read together with the NICE guideline³ for those who search for a full understanding of the literature (including the evidence tables and GRADE tables).

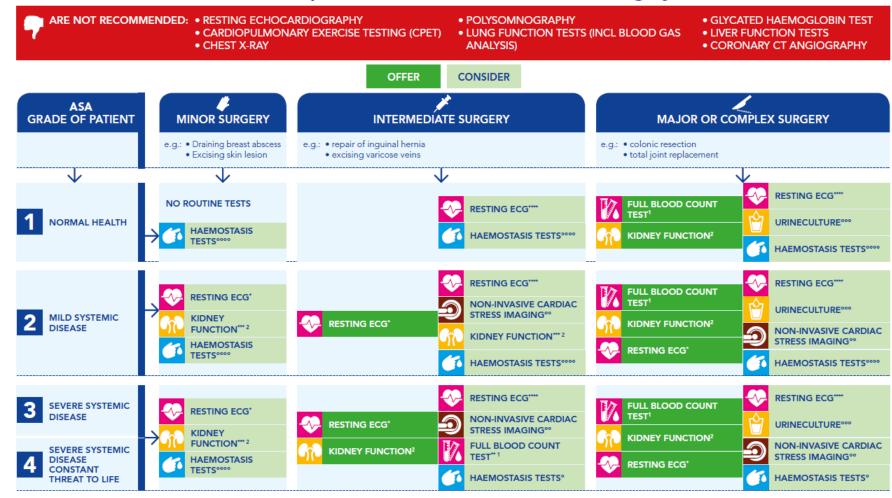
3.2 General algorithm

See next page.

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WHICH ROUTINE TESTING SHOULD BE PERFORMED

in adults prior to elective non-cardiothoracic surgery



in case of clinical risk factors according to the cardiac risk index
 in case of cardiovascular or renal disease, if symptoms were





^{***} when renal impairment is suspected

^{****} if older than 65v

[°] in case of a chronic liver disease or a history of abnormal bleeding, spontaneous, or after trauma or surgery

in case of clinical risk factors according to the cardiac risk index and of a poor functional capacity

ooo in case of urological or prosthesis surgery

oooo history of abnormal bleeding, spontaneous, or after trauma or surgery

¹ Red blood cells (hemoglobin, hematocrit and count), white blood cells (count and formula) and platelets.

Creatinine, DFG, sodium and potassium.



3.3 Resting electrocardiogram

3.3.1 Introduction

Resting electrocardiogram (ECG) is a non-invasive test used to assess known cardiovascular diseases or to detect previously undiagnosed cardiovascular diseases. In the preoperative setting, resting ECG also provides a standard against which to measure changes in the postoperative period.

In the KCE 2004 guideline¹ a resting ECG was recommended for the following indications:

- ASA 1 patients above the age of 50 years;
- ASA 2 and 3 patients with cardiovascular, renal and/or respiratory comorbidities and in case of treatment with specific drugs (neuroleptic agents, tricyclic antidepressants, cardiac glycosides, antiarrhythmic drugs, cardiotoxic chemotherapy).

3.3.2 Evidence for clinical benefit

NICE did not identify relevant clinical studies comparing patients' outcomes with or without preoperative resting ECG were identified.³

3.3.3 Evidence for prognostic value

Seven cohort studies were retrieved by NICE to assess the prognostic value of preoperative resting ECG.³

Non-cardiac, non-vascular surgery

One prospective cohort (Biteker 2012) in 660 patients found a prolonged QT interval to be an independent predictor of perioperative cardiovascular events (adjusted OR = 1.043, 95%CI 1.03 to 1.06). The level of evidence is low because of high risk of bias mainly due to design, short follow-up and exclusion of high-risk surgery.

Elective surgery

One prospective cohort study (Fritsch 2012) in 1363 patients reported a higher risk of perioperative complications (OR = 2.814, 95%CI 1.36 to 5.82) in patients with an abnormal preoperative ECG than those with a normal one. Perioperative complications under study were cardiac, cerebrovascular, respiratory and bleeding complication.

Hip fracture surgery

Two papers analysed resting ECG in patients with hip fracture surgery.

The first one is a single centre prospective cohort (Koike 1999) in 114 patients. The authors found a non-significant higher risk of one-year mortality (RR = 1.54, 95%Cl 0.95 to 2.49) in patients with an abnormal preoperative ECG than patients with a normal ECG. Because the confidence interval includes both benefit and harms, imprecision was considered to be serious.

The second paper (Kyo 1993) retrospectively analysed a cohort of 427 elderly patients undergoing femoral neck fracture surgery. The survival analysis showed a HR of 2.66 (95%Cl 1.54 to 4.59) for patients with an abnormal ECG in comparison with other patients.

Major vascular surgery

Long-term survival was studied in a retrospective cohort (Landesberg 2007) including 624 patients in one center. At any time, approximately twice as many patients with ST segment depression (> 0.5 mm) died compared to those without ST segment depression (HR =1.94, 95%CI 1.48 to 2.54).

Non-cardiac surgery

Two prospective cohort studies were found.

Firstly, a prospective cohort study (Liu 2002) in 513 geriatric surgical patients found that the risk of postoperative cardiac complications was the same in patients with abnormal ECG as those with normal ECG (OR = 0.63, 95%CI 0.28 to 1.42). Due to serious imprecision and high risk of bias, the level of evidence was very low.



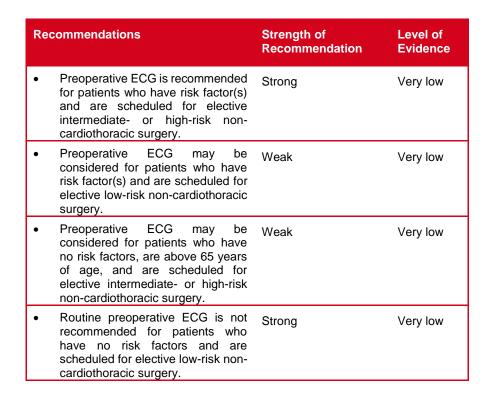
Secondly, a multicentre prospective cohort study (Van Klei 2007) including 2 967 patients found a postive association between right bundle branch block and postoperative myocardial infarction risk (OR = 2.1, 95%Cl 1.0 to 4.41), while left bundle branch block was associated with a higher risk of postoperative myocardial infarction (OR = 3.1, 95%Cl 1.0 to 9.61) and death during admission (OR = 3.5, 95%Cl 1.3 to 9.42). The level of evidence was very low for all outcomes except for death during admission (low level of evidence).

Conclusions

- There is no evidence on the effect of resting preoperative ECG on clinical outcome.
- Evidence on the prognostic value shows that an abnormal preoperative ECG is associated with an increased risk of perioperative cardiovascular events and mortality (low to very low quality).

Other considerations

| Factor | Comment |
|---|---|
| Balance between clinical benefits and harms | There is no evidence comparing patients' outcomes with or without preoperative resting ECG. The ability to predict postoperative complications or other outcomes is unclear. |
| | It is unclear from prognostic studies whether there was any impact on the decision to continue with surgery as planned, based on the test results. If surgery is delayed in order to optimize the cardiac function, there is a need to consider any potential consequences of delaying surgery. |
| | In the absence of strong evidence, other evidence sources become informative too. Both the ESC/ESA and ACC/AHA guidelines contain recommendations about the use of a preoperative resting ECG, ^{13, 14} and are reasonably consistent and largely in line with the grid provided in the NICE 2016 guideline. ³ Because of clarity reasons and better consistency between the recommendations and the available evidence, the ESC/ESA recommendations were adopted and translated in the grid below. |
| Quality of evidence | The prognostic evidence is mainly low to very low, since it is often unclear whether test results led to management changes prior to surgery. |
| Costs (resource allocation) | NICE did not identify economic evaluations that addressed this review question. |
| Patients values and preferences | No additional considerations made. |
| Changes to the NICE recommendations | Compared to the NICE guideline a slightly different approach (more liberal for some categories, more restrictive for others) was taken, because age and cardiac risk factors were more consistently taken into account. |



| | Surgery grade | | |
|------------|--|--|--|
| ASA grade | Minor | Intermediate | Major/complex |
| ASA 1 | Do not offer | Consider if >65y | Consider if >65y |
| ASA 2 | Consider if risk factors according to the revised cardiac risk index * | Offer if risk factors according to the revised cardiac risk index *, consider if >65y without risk factors | Offer if risk factors according to the revised cardiac risk index*, consider if >65y without risk factors |
| ASA 3 or 4 | Consider if risk factors according to the revised cardiac risk index * | Offer if risk factors according to the revised cardiac risk index *, consider if >65y without risk factors | Offer if risk factors according to the revised cardiac risk index*, consider if >65y without risk factors |

^{*} Clinical risk factors according to revised cardiac risk index: ischaemic heart disease (angina pectoris and/or previous myocardial infarction), heart failure, stroke or transient ischaemic attack, renal dysfunction (serum creatinine >170 μmol/L or 2 mg/dL or a creatinine clearance of <60 mL/min/1.73 m²), diabetes mellitus requiring insulin therapy.¹⁴

Examples

- A 72-year old woman who is in perfect health is planned for excision of a basal cell carcinoma of the nose. A preoperative resting electrocardiogram is not indicated.
- A 54-year old woman who is in perfect health is planned for a thyroidectomy because of a multinodular goitre with tracheal compression. A preoperative resting electrocardiogram is not indicated.
- A 61-year old male who has well-controlled type 2 diabetes (treated with bedtime insulin) is planned for an inguinal hernia repair. A preoperative resting electrocardiogram is indicated.





3.4 Resting echocardiography

3.4.1 Introduction

Resting echocardiography is a non-invasive test used, in the preoperative setting, to predict the heart response to the physiological stress of surgery and to formulate a safe perioperative management plan for the patient.

In the KCE 2004 guideline ¹ no evidence was found for a preoperative resting echocardiography, and it was only recommended for symptomatic ASA 3 and 4 patients (recent heart failure, insufficiently recompensated heart failure and/or dyspnoea).

In the NICE 2016 guideline the following recommendations were included:³

- Do not routinely offer resting echocardiography before surgery.
- Consider resting echocardiography if the person has:
 - a heart murmur and any cardiac symptom (including breathlessness, pre-syncope, syncope or chest pain) or
 - signs or symptoms of heart failure.

Before ordering the resting echocardiogram, carry out a resting electrocardiogram (ECG) and discuss the findings with an anaesthetist.

3.4.2 Evidence for clinical benefit

NICE identified three non-randomized studies that assessed the clinical benefit of resting echocardiography as a preoperative test in altering perioperative management for adults with mild to severe comorbidities (ASA ≥ 2) undergoing major or complex non-cardiac elective surgery.³

Hip fracture surgery

A retrospective study in 60 patients (Guryel 2004) – older than 65 years – admitted to the hospital with a fractured neck of the femur demonstrated that preoperative echocardiography not significantly increased the risk of delayed to surgery (RR = 1.93, 95%Cl 0.59 to 6.27) in comparison with no preoperative resting echocardiography. The quality of evidence is very low because of high risk of bias and serious imprecision.

Bariatric surgery

An observational study (Poso 2014) in 46 morbidly obese subjects scheduled for bariatric surgery showed that the mean length of hospital stay was 0.7 days higher (95%Cl 0.13 to 1.53) in patients undergoing preoperative resting echocardiography than in those that did not. No patient died after 30 days in both the intervention and control group. This evidence carries a high risk of bias.

Non-cardiac surgery

A large retrospective observational study (Wijeysundera 2011) in 70 996 adults analysed the 30-day mortality, length of hospital stay and surgical site infection in patients undergoing preoperative resting echocardiography and in patients that did not undergo it. There were no differences in 30-day mortality (RR = 1.14, 95%Cl 1.02 to 1.27) and surgical site infection (RR = 1.03, 95%Cl 0.98 to 1.08) between the two groups. In the preoperative resting echocardiography group, the mean length of stay of hospital stay was 0.31 days higher (95%Cl 0.17 to 0.45) than in the control group. High risk of bias was identified for this evidence.

3.4.3 Evidence for prognostic value

No evidence was identified.

Conclusions

 Evidence of very low quality suggests that there is no clinical benefit with routine echocardiography testing in elective hip fracture surgery, bariatric surgery and non-cardiac surgery.



| Factor | Comment |
|---|---|
| Balance between clinical benefits and harms | The surgery can be delayed due to the additional time required for a patient to have a resting echocardiography. The potential risk of poorer perioperative outcomes is not offset by any clinical benefit. |
| Quality of evidence | The quality of evidence is very low because of high risk of bias and imprecision. |
| Costs (resource allocation) | NICE did not identify economic evaluations that addressed this review question. |
| Patients values and preferences | No additional considerations made. |
| Changes to the NICE recommendations | No reason was found to change the first NICE 2016 recommendation. ³ However, since the second recommendation is not applicable to routine testing (but rather on clinical indication), it was not adopted for our guideline. |

| Re | commendations | Strength of Recommendation | Level of Evidence |
|----|---|----------------------------|----------------------|
| • | Resting echocardiography is not routinely recommended before elective non-cardiothoracic surgery. | Strong | Very low |

| | Surgery grade | | |
|------------|---------------|--------------|---------------|
| ASA grade | Minor | Intermediate | Major/complex |
| ASA 1 | Do not offer | Do not offer | Do not offer |
| ASA 2 | Do not offer | Do not offer | Do not offer |
| ASA 3 or 4 | Do not offer | Do not offer | Do not offer |

Examples

- A 68-year old male with an implanted pacemaker and without symptoms of heart failure is planned for total hip replacement. A preoperative resting echocardiography is not indicated.
- A 61-year old male who has a history of myocardial infarction two years ago is planned for a knee arthroscopy. During the preoperative clinical assessment the man complains about worsening dyspnoea and peripheral oedema. A resting echocardiography is indicated, not as a routine preoperative test, but as part of the diagnostic work-up of heart failure.



3.5 Cardiopulmonary exercise testing

3.5.1 Introduction

In the preoperative setting, cardiopulmonary exercise testing (CPET) is used to assess the patient's functional capacity and the tolerance to physiological stress due to surgery. This test typically uses a cycle ergometer to measure the patient's cardiac, respiratory and metabolic variables during exercise that simulates the surgery conditions.

In the KCE 2004 guideline¹ this test was not addressed.

In the NICE 2016 guideline the test was addressed, but no recommendation was made.³ Because of some inconsistencies in the description of the evidence by NICE, some of the original articles were consulted to write the text below.

3.5.2 Evidence for clinical benefit

NICE identified one retrospective cohort study (Goodyear 2013) that studied the clinical effectiveness of CPET as a preoperative test in improving patient outcomes in adults and young people with mild to severe comorbidities undergoing major to complex non-cardiac elective surgery.³

Open abdominal aortic aneurysm surgery

In this retrospective cohort study, 203 patients undergoing open abdominal aortic aneurysm (AAA) surgery were compared according to whether they received preoperative CPET or not. Median length of hospital stay and 30-day mortality were significantly lower in patients that received CPET and in a historical control in comparison with those that did not receive preoperative CPET (median length of stay [95%CI]: CPET 10 days [10.3 to 13.5] vs. no CPET 13 days [13.9 to 19.0]; 30-day mortality: RR = 0.32; 95%CI 0.11 to 0.94).

Endovascular aneurysm repair (EVAR) in abdominal aortic aneurysm surgery

The same study showed that, in 84 EVAR AAA patients, median length of hospital stay was shorter in the CPET group (4 days [95%CI 4.6 to 6.7]) than in the control group (6 days [95%CI 5.3 to 8.6]). In contrast, 30-day mortality

was not significantly higher in patients with CPET than those without CPET (Peto OR = 3.91, 95%Cl 0.05 to 329.71).

3.5.3 Evidence for prognostic value

NICE included sixteen observational studies that evaluated patient outcomes after surgery in adults or young people with mild or severe comorbidities undergoing major to complex non-cardiac elective surgery.³ However, the five studies on lung resection are not discussed here (out of scope).

Abdominal aortic aneurysm repair surgery

Anaerobic threshold (AT)

Three cohort studies showed inconsistent results regarding the prognostic value of AT for mortality in patients with AAA surgery. While a cohort study in 130 patients (Barakat 2015) demonstrated that AT was no predictor of 30-day mortality (very low quality), two other studies reported that a lower AT was predictive of increased mortality (low quality). The first study (Hartley 2012) showed that a lower AT was predictive of 30-day mortality, but was not predictive of 90-day mortality. The second study (Carlisle 2007) reported that a lower AT was predictive of survival at 35 months. In addition, a fourth study including 102 patients, which we supposed to be Thompson 2011, showed that AT was a marker able to predict death.

Barakat 2015 showed that AT was a predictor of cardiac and pulmonary complications (low quality), while Thompson 2011 did not find any association between AT and cardiac, respiratory or cerebrovascular events. A lower AT was also identified as a predictor of major complications in two studies (Prentis 2012, Thompson 2011). In contrast, AT was not a predictor of major complications in 101 patients included in the same study but undergoing endovascular aneurysm repair (very low quality).

VO₂

Two overlapping prospective studies (Grant 2015 [N=506] and Hartley 2012 [N=415]) reported that a peak $VO_2 < 15$ ml/kg/min reduced the survival rate measured by 90-day mortality (low quality) and 3-year survival (moderate), but was not predictive of 30-day mortality (low quality). This last finding was confirmed by a study in 130 patients (Barakat 2015) showing that peak VO_2



was no predictor of 30-day mortality. That same study found no predictive value of peak VO₂ for cardiac or pulmonary complications (very low quality).

VE/VO₂

A prospective cohort study (Barakat 2015) in 130 patients reported that VE/VO₂ had no predictive value for 30-day mortality, cardiac or pulmonary complications (very low quality). VE/VO₂ had no predictive value for death, cardiac, cerebrovascular and respiratory complications or major complications in a study including 102 patients (Thompson 2011).

VE/VCO₂

Two prospective cohort studies with a total of 636 patients showed that a lower VE/VCO₂ was predictive of an increased 3-year survival (Grant 2015) and survival at 35 months (Carlisle 2007). However, two studies in 232 patients (Barakat 2015, Thompson 2011) reported no predictive value of VE/VCO₂ for mortality. In addition, no predictive value was found for cardiac, pulmonary or cerebrovascular complications in the same studies. Also, no association was found between VE/VCO₂ and major complications in two studies (Prentis 2012, Thompson 2011).

Overall, quality of evidence is very low.

Several sub-threshold CPET

Grant 2015 et al. showed in a cohort of 506 patients that patients with zero or one sub-threshold CPET variables had a 3-year survival of 86.4% compared with 59.9% in patients with three sub-threshold CPET variables. ¹⁵ In the subset of patients included by Hartley, patients with at least 2 CPET-derived values below the defined thresholds had a significantly increased risk of both 30- and 90-day mortality (very low quality evidence). ¹⁶

Colorectal surgery

In a prospective cohort study, the relationship between preoperative CPET – as a measurement of fitness status – and in-hospital morbidity was investigated in 136 patients undergoing major colonic surgery. The authors found that a 1.0 ml/kg/ml increase in VO₂ at lactate threshold was associated with a more than 20% reduction in the odds of complication (adjusted OR = 0.77, 95%Cl 0.66 to 0.89, p<0.0005) and a 2.0 ml/kg/ml increase with a more or less 40% reduction (adjusted OR = 0.60, 95%Cl 0.45 to 0.80, p<0.001). Quality of evidence is low.

Pancreaticoduodenectomy

Anaerobic threshold:

Two cohort studies – one retrospective (Ausania 2012), one prospective (Junejo 2014) – studied in a total of 267 patients the predictive value of AT. AT was not found to be predictive of in-hospital mortality or cardiorespiratory complications (very low level of evidence). However, inconsistency between the 2 studies was found for the effect of AT on all complications. Ausania 2012 desmontrated that the postoperative complication rate was significantly lower in patients with a high AT in comparison with those with a lower AT (AT>10.1 kg/ml/min: 38.5% versus AT≤10.1 kg/ml/min: 70%, p=0.013), while Juneja 2014 did not find any predictive value of AT for all complications (adjusted OR [95%CI] 1.07 [0.83-1.39], p=0.06). The quality of evidence is very low.

In addition, one cohort study (Ausania 2012) showed that patients with a high AT had a shorter hospital stay than the other patients (median hospital stay in days [range]: AT>10.1 kg/ml/min: 17.5 [8-99] versus AT≤10.1 kg/ml/min: 29.4 [12-54], p=0.001). In the same study, AT was predictive of pancreatic leak (adjusted OR [95%CI]: 5.79 [1.62-20.69], p=0.007). The level of evidence is low due to serious imprecision.

VO₂:

The previously mentioned prospective cohort comprising 143 patients (Junejo 2014) reported that VO_2 max was not predictive of in-hospital mortality (adjusted OR [95%CI] 1.03 [0.77-1.38]), 30-day mortality (adjusted OR [95%CI] 1.32 [0.91-1.91]) or cardiopulmonary complication (adjusted OR [95%CI] 1.0 [0.86-1.16]). Serious imprecision and high risk of bias lead to a very low level of evidence.

Ventilatory equivalence of carbone dioxyde (VE/VCO₂):

Junejo 2014 reported that a higher VE/VCO₂ was predictive of an increased 30-day mortality (adjusted OR [95%CI] 1.35 [1.03-1.77]) and in-hospital mortality (adjusted OR [95%CI] 1.26 [1.05-1.51]). The quality of evidence is low due to high risk of bias. According to the same authors, a higher VE/VCO₂ is not predictive of all complications (adjusted OR [95%CI] 0.97 [0.89-1.06]) or cardiopulmonary complications (adjusted OR [95%CI] 0.98 [0.90-1.07]). For the latter two outcomes, imprecision was considered to be serious because the confidence intervals included both benefit and harms.



Hepatic resection

A prospective cohort study (Junejo 2012) in 108 patients undergoing hepatic resection showed that $Ve/VCO_2 \ge 34.5$ is predictive for cardiopulmonary complications (adjusted OR [95%CI] 3.45 [1.31-9.14], p=0.013) or any complication (adjusted OR [95%CI] 3.97 [1.44-10.95], p=0.008). Level of evidence was low.

Bariatric surgery

One prospective cohort study (McCullough 2006) including 109 patients demonstrated that peak VO₂ was a significant predictor of complications (Peak VO₂ < 15.8 ml kg⁻¹ml⁻¹ – adjusted OR [95%CI] 12.89 [1.14 to 145.76] or Peak VO2 as continuous variable – adjusted OR [95%CI] 1.61 (per unit decrease) [1.19 to 2.18], p=0.002). Level of evidence is considered as low because of a high risk of bias.

Radical cystectomy

Prentis 2013 showed in 82 patients that a lower AT was predictive for major postoperative morbidity (adjusted OR [95%CI] 0.74 [0.57 to 0.96]) and increased length of stay after radical cystectomy (adjusted OR [95%CI] 0.47 [0.28 to 0.79]). The level of evidence was low.

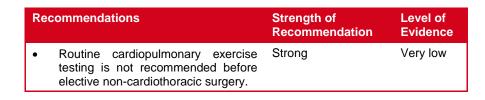
Major elective surgery

In a prospective cohort study (Snowden 2010) comprising 123 patients undergoing major elective surgery, the predictive value for any complications of two preoperative tests was compared: objective measurement of cardiopulmonary function as AT versus an algorithm based on activity assessment. AT measurement significantly improved prediction for occurrence of more than one complication compared with an algorithm-based activity assessment (adjusted OR [95%CI] 0.44 [0.30 to 0.64], p<0.0001). The level of evidence was moderate.

Conclusions

- The clinical benefit of CPET in patients undergoing AAA surgery is unclear, because the only retrieved study showed a decrease in length of inpatient stay, but inconsistent results for 30-day morality when different surgical techniques are considered.
- Based on the available evidence, the prognostic value of CPET is unclear because, on the one hand, conflicting results were found for mortality in patients undergoing abdominal aortic aneurysm repair or pancreaticoduodenectomy, and on the other hand, the predictive value of CPET for complications varied according to the type of surgery.

| Factor | Comment |
|---|--|
| Balance between clinical benefits and harms | CPET is considered as safe test, as risky as a mild-moderate exercise. Experienced physiologists or clinicians must interpret CPET results to avoid misleading decisions regarding suitability for surgery. All CPET measures need to be considered according patient's pathology. |
| Quality of evidence | Clinical evidence is based on one retrospective study that shows serious limitation. The prognostic value of CPET was based on non-randomised prospective cohort studies. |
| Costs (resource allocation) | NICE retrieved one economic study (Goodyear 2013) showing that using CPET as a risk stratification strategy prior to AAA surgery was more effective and less costly in the open surgery arm compared to no testing. |
| Patients values and preferences | No additional considerations made. |
| Changes to the NICE recommendations | Not applicable |



| | Surgery grade | Surgery grade | | |
|------------|---------------|---------------|---------------|--|
| ASA grade | Minor | Intermediate | Major/complex | |
| ASA 1 | Do not offer | Do not offer | Do not offer | |
| ASA 2 | Do not offer | Do not offer | Do not offer | |
| ASA 3 or 4 | Do not offer | Do not offer | Do not offer | |

Example

 A 52-year old woman with severe COPD is planned for a total abdominal hysterectomy. Preoperative cardiopulmonary exercise testing is not indicated.

3.6 Chest X-ray

3.6.1 Introduction

Chest X-ray can detect diseases of the lungs, pleura, heart, major vasculature, mediastinum, chest wall and diaphragm. In the preoperative setting, chest X-ray is used to assess known chronic medical conditions or to detect previously undiagnosed diseases. Conditions that are frequently detected in this setting include chronic obstructive pulmonary disease (COPD), heart failure, tuberculosis and lung cancers. However, chest X-ray involves exposure to a dose of radiation and are of questionable benefit in asymptomatic individuals, in whom the rate of abnormality detection is low.

In the KCE 2004 guideline ¹ the following recommendations were included:

- Not routinely recommended for ASA 1 patients;
- Can be considered (on clinical indication) for ASA 2 and 3 patients with respiratory, cardiovascular or renal comorbidity.

In the NICE 2016 guideline, routine chest X-rays before surgery were not recommended.³

The topic was covered by the NICE guideline of 2004, but was not updated in the new guideline of 2016. One systematic review of Johanssen et al.¹¹ however, updated the evidence of this guideline with a search dating from the search of the guideline onwards. First we summarise the findings of the NICE guideline and then the findings of the update of Johansson and our update of the Johansson systematic review. The NICE guideline identified 29 papers, mainly case series.



3.6.2 Evidence for clinical benefit

None of the papers in the original NICE review compared the health outcomes for patients who had preoperative chest X-rays with patients who did not.

The systematic review of Johanssen et al.¹¹ identified 2 cohort studies assessing the clinical utility of chest X-ray in patients without pulmonary clinical symptoms in preparation of elective surgery. Neither of the two studies investigated the association between the test and changes in clinical management or 30-day mortality. Postoperative pulmonary complications occurred in 2.7-58.3% of the patients. Neither study showed a significant association between abnormal tests and postoperative pulmonary complications. In our update we did not identify comparative studies.

3.6.3 Evidence for prognostic value

The original NICE review identified 29 case series. The frequency of the three outcomes varied greatly across case series: an abnormal chest X-ray result was recorded in 0.3% to 65.7% of patients. A change in clinical management was recorded in 0% to 13.3% of patients. A postoperative complication was recorded in 0% to 8.8% of patients. Predictive value of abnormal findings was difficult to judge from the body of evidence due to the heterogeneity of the studies, with different definitions of what actually was an abnormal finding.

In the update we identified 2 low-quality studies on the prognostic value of chest X-ray, and none on clinical impact:

• In a prospective cohort study, Fritsch et al. 19 included 1 363 patients (56.1% female) scheduled for elective surgery in a secondary care hospital. Regression analysis was performed in order to identify the strongest predictors for perioperative complications. No statistically significant association between abnormalities on chest X-ray and postor intraoperative complications were found (OR = 2.516, 95%CI 0.862 to 7.347, p=0.091). Main limitation was the fact that preoperative testing was not performed according to a strict algorithm, but was rather based on individual practice of a perioperative physician. It is also unclear what the added value was of the logistic regression in assessing prognostic value of a test. Impact on clinical practice was not assessed.

De la Matta et al.²⁰ conducted a prospective study of 309 smokers with at least 20 pack-years of cumulative smoking who were candidates for transurethral resection of urinary bladder tumours. The patients were classified in 2 groups according to radiographic findings. Radiographic findings were associated with a higher incidence of perioperative complications (p=0.02), need for further preoperative consultations (p<0.01), longer delay in completing the pre-anaesthesia study (p<0.01), longer mean (SD) hospital stay (3.43 [3.17] days vs. 2.50 [1.77] days, p<0.001), and longer duration of surgery (p<0.001). Attitudes did not change in relation to radiographic findings during or after surgery. Abnormal findings on chest X-ray were found in 144 of the 309 patients (43%). Chest X-ray correctly classified only 3.54% of the patients with complications (predictive value). The authors concluded that the predictive value of chest X-ray for cardiopulmonary complications is low and findings do not influence intra- or postoperative attitudes.

We excluded 2 studies because they were conducted either in a middle-income country (Brazil) ²¹ or in a low-income country (Pakistan). ²²

Conclusions

- There is no evidence that a chest X-ray before surgery has an impact on clinical outcomes.
- Chest X-ray findings are poor predictors of postoperative complications and do not alter clinical practice.



| Factor | Comment | |
|---|--|--|
| Balance between clinical benefits and harms | Chest X-rays involve exposure to a dose of radiation and are of questionable benefit in asymptomatic individuals, they are poor predictors of complications, do not change clinical practice and there is no evidence that they have any impact on outcomes. No reason was found to change the NICE 2016 recommendation (although it was somewhat rephrased). ³ | |
| Quality of evidence | There is only observational evidence of low quality. The main problem with the observational studies is the fact that chest radiographs are not performed systematically but left at the discretion of the clinician. This may bias the findings, it is plausible however that this bias would favour chest X-ray. | |
| Costs (resource allocation) | NICE only provided cost information. Because of the minimal clinical benefit, NICE considered it unlikely that a chest X-ray is a cost-effective preoperative test. | |
| Patients values and preferences | No additional considerations made. | |
| Changes to the NICE recommendations | No reason was found to change the NICE 2016 recommendation (although it was somewhat rephrased). ³ | |

| Recommendations | Strength of Recommendation | Level of Evidence |
|--|----------------------------|----------------------|
| Chest X-ray before elective non- cardiothoracic surgery without clinical indication is not recommended. | Strong | Low |

| | Surgery grade | Surgery grade | | |
|------------|---------------|---------------|---------------|--|
| ASA grade | Minor | Intermediate | Major/complex | |
| ASA 1 | Do not offer | Do not offer | Do not offer | |
| ASA 2 | Do not offer | Do not offer | Do not offer | |
| ASA 3 or 4 | Do not offer | Do not offer | Do not offer | |

Examples

- A 52-year old woman with severe COPD is planned for a total abdominal hysterectomy. Preoperative chest X-ray may be indicated on clinical grounds.
- A 57-year old male smoker is planned for a transurethral resection of the prostate. He has no cardiopulmonary symptoms. Preoperative chest X-ray is not indicated.





3.7 Polysomnography

3.7.1 Introduction

Polysomnography is used to diagnose and monitor treatment responsiveness in obstructive sleep apnoea (OSA) and other sleep disorders. Formal polysomnography is conducted in a hospital setting and pulse involves monitorina parameters includina oximetry. electroencephalography (EEG), surface electromyography (EMG), respiratory effort, electro-oculography (EOG) and electrocardiography (ECG) during a night's sleep. Simpler sleep studies may also be performed by issuing an individual with a sleep study device to use in their own home. In the preoperative setting, polysomnography is used to diagnose OSA and institute appropriate management with the aim of reducing postoperative morbidity and mortality. Polysomnography is non-invasive and safe, with the only recognised complication being self-limiting skin irritation from electrodes.

In the KCE 2004 guideline¹ this test was not addressed.

The NICE 2016 guideline only included two research recommendations:³

- Does preoperative screening of people who are at risk of obstructive sleep apnoea (OSA) with polysomnography identify those at higher risk of postoperative complications?
- Does treating OSA perioperatively improve outcomes?

3.7.2 Evidence for clinical benefit

NICE³ identified one non-randomised observational study (Chung 2008) comprising 416 obese patients aged 18 years or older who had an ASA physical status of 1-4 and were scheduled to undergo elective procedures in general surgery, gynaecology, orthopaedics, urology, plastic surgery, ophthalmology, or neurosurgery. The study demonstrated no clinical benefit of preoperative polysomnography on postoperative respiratory complications, 13 cardiac complications, neurological complications, unplanned ICU admission, and readmission within 30 days, compared to no preoperative polysomnography, but all confidence intervals were too wide to exclude a beneficial effect.

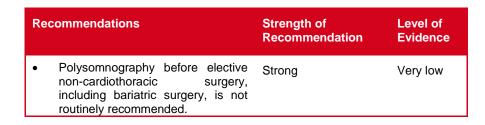
3.7.3 Evidence for prognostic value

One retrospective study (Weingarten 2011) on polysomnography prior to bariatric surgery reported no increased risk in pulmonary complications (OR = 1.00, 95%Cl 0.44 to 2.30, p=0.992), surgical complications (OR = 1.33, 95%Cl 0.79 to 2.25, p=0.284) or other complications (OR = 0.79, 95%Cl 0.49 to 1.25, p=0.310) during surgery in those 29 who tested with an apnoea-hypopnoea index (AHI) of 5 or greater. The same retrospective study also reported no increased risk in postoperative complications in those who tested with an AHI of 5 or greater (OR = 0.86, 95%Cl 0.59 to 1.29, p=0.47).

Conclusions

 Clinical benefit and prognostic value is not demonstrated in the two observational studies that were found, but cannot be excluded either.

| Factor | Comment |
|---|--|
| Balance between clinical benefits and harms | Clinical benefit and prognostic value are unproven. There are no indications that preoperative polysomnography would be harmful, apart from time lost if there is a waiting list. |
| Quality of evidence | Studies were considered of poor quality and underpowered. They were also underpowered so a clinical meaningful effect could not be excluded. |
| Costs (resource allocation) | Only cost information was included in the NICE guideline, ³ and a research question was set out to obtain the clinical evidence needed to indicate whether or not polysomnography represents an efficient use of NHS resources. |
| Patients values and preferences | No additional considerations made. |
| Changes to the NICE recommendations | Not applicable. |



| | Surgery grade | Surgery grade | | |
|------------|---------------|---------------|---------------|--|
| ASA grade | Minor | Intermediate | Major/complex | |
| ASA 1 | Do not offer | Do not offer | Do not offer | |
| ASA 2 | Do not offer | Do not offer | Do not offer | |
| ASA 3 or 4 | Do not offer | Do not offer | Do not offer | |

Example

 A 45-year old man with a BMI of 42 kg/m² and symptoms of obstructive sleep apnoea is planned for a laparoscopic gastric bypass.
 Polysomnography is indicated on clinical grounds, but does not need to be planned preoperatively.

3.8 Lung function tests (incl. arterial blood gas analysis)

3.8.1 Introduction

Lung function tests can assess lung volumes, capacities, rates of flow and gas exchange, enabling the diagnosis and monitoring of respiratory diseases. In the preoperative setting, lung function tests are used to assess individuals with known or suspected respiratory disease. Tests used include spirometry, which measures inhaled and exhaled lung volumes and flow over time, as well as more sophisticated tests to measure static lung volumes and the diffusing capacity of the lungs. Arterial blood gas analysis is also considered as a potential lung function test.

In the KCE 2004 guideline¹ lung function tests were not considered routine tests, unless for ASA 3 patients with chronic or acute respiratory disease. Blood gas analysis was not listed in the 2004 guideline because of the specific scope (no ASA 4 patients or thoracic surgery).

In the NICE 2016 guideline the following recommendations were included:³

- Do not routinely offer lung function tests or arterial blood gas analysis before surgery.
- Consider seeking advice from a senior anaesthetist as soon as possible after assessment for people who:
 - are ASA grade 3 or 4 due to known or suspected respiratory disease and
 - o are having intermediate or major or complex surgery.

3.8.2 Evidence for clinical benefit

No relevant studies were identified concerning the benefit of lung function tests were identified.³



3.8.3 Evidence for prognostic value

Bariatric surgery

One prospective cohort study (Hamoui 2006) of 146 patients investigated the following pulmonary test measures: vital capacity (VC), functional residual capacity (FRC) and total lung capacity (TLC), forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1), maximal voluntary ventilation (MVV), and pO₂. They reported that for each 10% decrease in vital capacity, the risk of postoperative complications increased more than two-fold. The remaining tests were not found to predict risk of complications.

Cancer surgery

One retrospective cohort study (Jeong 2013) of 538 patients compared abnormal with normal lung function tests. They reported an increased risk of postoperative surgical complications in those with abnormal findings. However, lung function tests were not predictive of postoperative systemic complications.

Conclusions

- There is no evidence on the effect of lung function tests on clinical outcome.
- Evidence on prognostic value is limited and inconsistent.

| Factor | Comment |
|---|--|
| Balance between clinical benefits and harms | There was no evidence that lung function tests alter clinical outcome. The ability to predict postoperative complications or other outcomes was very limited. |
| Quality of evidence | There was only very limited prognostic evidence for two types of surgery bariatric surgery and gastric cancer surgery. The prognostic evidence is problematic since it is often unclear whether test results led to management changes prior to surgery or whether the physician was aware of the test results prior to surgery. Studies only adjusted for a minimum number of characteristics at best, and in some studies it was unclear which factors were accounted for. |
| | Study results were not consistent; Some studies reported lung function tests to be an independent predictor, and others not, of complications. |
| Costs (resource allocation) | No economic evaluations were identified by NICE for lung function testing. |
| Patients values and preferences | No additional considerations made. |
| Changes to the NICE recommendations | The (first) NICE 2016 recommendation was adopted (but rephrased somewhat). ³ The second NICE recommendation was not adopted since it refers to testing on clinical grounds. |

| Recommendations | Strength of Recommendation | Level of Evidence |
|--|----------------------------|----------------------|
| Lung function tests (including arterial blood gas analysis) are not routinely recommended before elective non- cardiothoracic surgery. | Strong | Very low |

| | Surgery grade | Surgery grade | | |
|------------|---------------|---------------|---------------|--|
| ASA grade | Minor | Intermediate | Major/complex | |
| ASA 1 | Do not offer | Do not offer | Do not offer | |
| ASA 2 | Do not offer | Do not offer | Do not offer | |
| ASA 3 or 4 | Do not offer | Do not offer | Do not offer | |

Example

 A 57-year old male smoker is planned for a transurethral resection of the prostate. He has no cardiopulmonary symptoms. Preoperative lung function tests are not indicated.

3.9 Full blood count test

3.9.1 Introduction

The full blood count test can be used in the preoperative setting to detect anaemia, bleeding disorders, inherited and acquired haematological disorders, and the effects of other systemic diseases.³ The results may be used to plan the use of blood products and blood salvage techniques in the perioperative period. A full blood count test involves the red blood cells (haemoglobin, haematocrit and count), the white blood cells (count and differentiation) and the platelet count.

In the KCE 2004 guideline¹ haemoglobin testing was recommended for ASA 1 patients with anaemia or recent blood loss, and for ASA 2-3 patients with (a history) of anaemia, recent blood loss or kidney disease.

3.9.2 Evidence for clinical benefit

NICE did not identify clinical studies comparing preoperative full blood count testing with no preoperative full blood count testing.³

3.9.3 Evidence for prognostic value

NICE identified ten studies that evaluated preoperative full blood count testing as a predictor of outcome after surgery.³

All elective surgeries

One retrospective cohort study (N=7679) compared patients with and without preoperative anaemia (Beattie 2009). Surgery included vascular and oncology surgery in head and neck, urology, thoracic, hepatobiliary, general, and gynaecological procedures. The authors reported an increased risk of mortality at 90 days for patients with anaemia (adjusted OR = 2.36, 95%CI 1.57 to 3.55), and this association held when those with severe anaemia (adjusted OR = 1.79, 95%CI 1.17 to 2.74) or those who received red blood cell transfusions (adjusted OR = 3.04, 95%CI 1.80 to 5.13) were excluded from the analysis (moderate quality).



Orthopaedic surgery

Each of the studies in this category compared those with and without preoperative anaemia.

One prospective cohort study of 4940 patients (Jans 2014) reported an increased risk of peri- or postoperative red blood cell transfusion (adjusted OR = 4.7, 95%CI 3.8 to 5.1), length of stay over 5 days (adjusted OR = 2.50, 95%CI 1.90 to 3.29) and readmission at 90 days (adjusted OR = 1.4, 95%CI 1.1 to 7.8) in those with preoperative anaemia (moderate quality).

One retrospective cohort study of 15222 patients (Greenky 2012) reported an increased risk of periprosthetic joint infections in those with anaemia (propensity-adjusted OR = 1.95, 95%Cl 1.41 to 2.70) (low quality). This study also reported no clear difference in 30- or 90-day mortality between those with (OR = 0.59, 95%Cl 0.10 to 3.53) and without preoperative anaemia (OR = 1.54, 95%Cl 0.50 to 4.73) (very low quality), although an increased risk of mortality at 1 year was seen for those with anaemia (OR = 1.81, 95%Cl 1.00 to 3.29) (low quality).

One prospective study of 191 patients (Jamsen 2015) reported no clear increased risk of postoperative hyperglycaemia among those with anaemia (adjusted OR = 3.90, 95%CI 0.91 to 16.71) (low quality).

One retrospective cohort study of 605655 patients (Yoshihara 2014) reported an increased risk of peri- or postoperative allogenic blood transfusion among those with preoperative anaemia (hip: OR = 2.03, 95%CI 1.86 to 2.22; knee: OR = 2.70, 95%CI 2.52 to 2.91) (low quality).

Vascular surgery

One retrospective cohort study of 1211 patients (Dunkelgrun 2008) compared those with and without preoperative anaemia. They reported an increased risk of major adverse cardiac events at 30 days in those with anaemia, and this risk increased with severity of anaemia (severe anaemia: OR = 4.70, 95%CI 2.60 to 8.50) (moderate to low quality).

One retrospective cohort study of 1773 patients (Amaranto 2011) compared levels of preoperative white blood cell (WBC) count within the normal range. They reported an increased risk of postoperative complications (adjusted OR = 1.32, 95%CI 1.11 to 1.58), major adverse events (adjusted OR = 1.67, 95%CI 1.23 to 2.27) and death (adjusted OR = 1.82, 95%CI 1.12 to 2.96) for those with higher WBC count undergoing endovascular surgery

(moderate quality). However, no clear difference in risk of these outcomes with variation in WBC count within the normal range was observed for those undergoing open surgery (moderate to low quality). Note that the overall odds ratio for death in the open cohort masked an effect that both low and high values of preoperative WBC count in the open cohort were predictive of an increased risk of death.

Cancer surgery

One retrospective cohort study of 327 patients (Bedke 2012) investigated the preoperative WBC count at three different thresholds. They reported that WBC count was predictive of survival when using the threshold of 9.5 per microliter (HR = 1.91, 95%CI 1.10 to 3.32) (very low quality).

One retrospective study of 223 patients (Wang 2015) investigated the preoperative platelet count at a threshold of 178×10^9 /l, which was reported to be predictive of overall survival (OR = 1.54, 95%Cl 1.04 to 2.29) (low quality).

Non-cardiac surgery

One retrospective cohort study of 316644 patients (Glance 2014) investigated the effect of increased preoperative platelet count on the incidence of blood transfusion, death and major complications. They stratified results according to preoperative platelet count and compared each of the following with normal platelet counts: moderate-to-severe thrombocytopenia, mild thrombocytopenia, low-to-normal platelet count and thrombocytosis.

They reported the following findings:

- Mild thrombocytopenia, moderate-to-severe thrombocytopenia, and thrombocytosis were each associated with increased risk of blood transfusion (low quality).
- Mild and moderate-to-severe thrombocytopenia were also associated with increased risk of 30-day mortality (low quality).
- Moderate-to-severe thrombocytopenia was associated with increased risk of postoperative pulmonary and renal complications (low quality).
- Mild thrombocytopenia was associated with increased risk of renal complications (low quality).

- Thrombocytosis was associated with increased risk of with pulmonary, renal, sepsis, wound and thromboembolic complications (low quality).
- There was no clear association between platelet count and cardiac complications, central nervous system complications or graft failure (very low quality).

Conclusions

- There is no evidence on the effect of full blood count tests on clinical outcome.
- Evidence of low to very low quality suggests that the absence of anaemia is associated with lower rates of postoperative mortality or complications.
- The evidence relating to platelet count is limited to one study of low quality.

| Factor | Comment |
|---|---|
| Balance between clinical benefits and harms | The majority of the evidence used full blood count testing to identify people with anaemia. There was only one study relating to platelet count. Furthermore, the evidence was restricted to major surgery and higher ASA grades. In the majority of studies, people without anaemia had better outcomes with regards to mortality, infections, length of stay and readmission rates. One study reported that people with anaemia had received more blood transfusions, which seems to indicate a change in management in relation to testing. |
| Quality of evidence | The evidence was mainly of low or very low quality. The ideal evidence would have been testing as an intervention rather than a prognostic factor. However, no such evidence was identified. The prognostic evidence is problematic since it is often unclear whether test results led to management changes prior to surgery or whether the physician was aware of the full blood count results prior to surgery. Even though we restricted evidence to studies using multivariable analyses to identify test results as independent footopy leading to proteursial outcomes. |
| | independent factors leading to postsurgical outcomes, some studies only adjusted for a minimum number of characteristics, and in other studies it was unclear which factors were accounted for. For instance, red blood cell transfusions were either not reported as an outcome or not adjusted for in the analyses, which makes results difficult to interpret. No evidence was identified for people with lower ASA grades for minor elective surgery. Therefore the evidence is not generalizable to all people covered in the remit of the guideline. |
| Costs (resource allocation) | No economic evaluations were identified by NICE for lung function testing. |
| Patients values and preferences | No additional considerations made. |
| Changes to the NICE recommendations | No reason was found to change the grid available in the NICE 2016 guideline. ³ |

| Recommendations | Strength of Recommendation | Level of Evidence |
|---|----------------------------|----------------------|
| Preoperative full blood count testing is not routinely recommended in patients undergoing elective minor non- cardiothoracic surgery. | Strong | Very low |
| Preoperative full blood count testing is not routinely recommended in patients undergoing elective intermediate non-cardiothoracic surgery, although it can be considered in patients with ASA 3-4. | Weak | Very low |
| Preoperative full blood count testing is recommended in patients undergoing elective major or complex non-cardiothoracic surgery. | Strong | Very low |

Red blood cells (haemoglobin, haematocrit and count), the white blood cells (count and differentiation) and platelet count.

| | Surgery grade | Surgery grade | | |
|------------|---------------|--|---------------|--|
| ASA grade | Minor | Intermediate | Major/complex | |
| ASA 1 | Do not offer | Do not offer | Offer | |
| ASA 2 | Do not offer | Do not offer | Offer | |
| ASA 3 or 4 | Do not offer | Consider for patients with cardiovascular or renal disease if any symptoms not recently investigated | Offer | |

Examples

- A 43-year old woman in normal health is planned for varicose vein stripping. A preoperative full blood count test is not indicated.
- A 55-year old man with well-controlled hypertension is planned for left hemicolectomy. A preoperative full blood count test is indicated.
- A 55-year old man with end-stage renal disease is planned for repair of an inguinal hernia. He complains about fatigue. A preoperative full blood count test can be considered if not recently done.



3.10.1 Introduction

Kidney function tests involve sampling venous blood to test for creatinine, electrolytes (sodium and potassium) and sometimes urea to examine the functional status of the kidneys.³ Estimated glomerular filtration rate is also frequently reported. In the preoperative setting the test may be used to establish a baseline for the patient, to inform prediction of postoperative risks and to plan medical management in the perioperative period.

In the KCE 2004 guideline ¹ kidney function tests were recommended for ASA 1 patients aged 60 years and above (undergoing major surgery) and for ASA 2-3 patients aged 60 years and above, with kidney disease, or treated with specific drugs (e.g. digoxin, laxantia, diuretics). In case of major surgery, kidney function tests were also recommended for ASA 2 and 3 patients with COPD, diabetes or cardiovascular disease (including severe hypertension).

3.10.2 Evidence for clinical benefit

NICE did not identify clinical studies comparing preoperative kidney function testing with no preoperative kidney function testing.³

3.10.3 Evidence for prognostic value

Three studies evaluated preoperative kidney function testing as a predictor of outcome after surgery:³

One retrospective cohort study of 881 patients undergoing carotid endarterectomy (AbuRahma 2013) compared those with an eGFR value of <60 ml/minute/1.73m² with those with higher values. They reported an increased risk for the composite outcome of postoperative mortality or stroke among those with eGFR <60 ml/minute/1.73m² (adjusted OR = 3.70, 95%CI 1.30 to 10.53) (low quality).

- One retrospective cohort study of 155 patients undergoing endovascular abdominal aortic aneurysm repair (Soong 2008) also compared those with an eGFR value of <60 ml/minute/1.73m² with those with higher values. They reported an increased risk of perioperative mortality and postoperative renal failure (adjusted OR = 0.07, 95%Cl 0.03 to 0.21) among those with eGFR <60 ml/minute/1.73m², but there is considerable uncertainty for the mortality outcome (adjusted OR = 0.25, 95%Cl 0.03 to 2.32).</p>
- One post-hoc analysis of a prospective study of 2 323 patients undergoing non-cardiac surgery (Mases 2014) compared those with an eGFR value of >90 ml/minute/1.73m² with those with lower values. They reported a general increase in risk of all-cause mortality and major adverse cardiovascular and cerebrovascular events (MACE) with declining eGFR, but the effect only reached statistical significance with an eGFR < 30 ml/minute/1.73m² (very low quality).

Conclusions

- There is no evidence on the effect of kidney function tests on clinical outcome.
- Evidence of low to very low quality suggests that a normal eGFR (>60 ml/minute/1.73m²) is associated with lower rates of post- or perioperative mortality or post-surgical renal failure.





| Factor | Comment |
|---|--|
| Balance between clinical benefits and harms | Three studies using blood kidney function testing prior to major surgery were identified. All of the studies associated an increased glomerular filtration rate (eGFR) >60 ml/minute/1.73 m² with lower rates of postor perioperative mortality or post-surgical renal failure. If acute kidney injury is suspected, performing a kidney function test would assist in planning the patient's management post-surgery and should be considered in this population. For example, the higher the age, the higher the risk of having chronic renal impairment, which is a risk factor for postoperative acute renal impairment. |
| Quality of evidence | Only observational studies were identified by NICE. The ideal evidence would have been testing as an intervention rather than a prognostic factor. However, no such evidence was identified. The prognostic evidence is problematic since it is often unclear whether test results led to management changes prior to surgery or whether the physician was aware of the test results prior to surgery. |
| | Studies using multivariable analyses were searched to identify test results as independent factors leading to postsurgical outcomes. In one study it was unclear which variables were used in the multivariable analysis. A further study did not adjust for variables in the analysis, but as the eGFR measure accounts for other factors (such as age and race) the study was included. No evidence was identified for people with lower ASA grades for minor elective surgery. The evidence is therefore not generalizable to all people covered in the remit of the guideline. |
| Costs (resource allocation) | NICE did not identify economic evaluations that addressed this review question. |
| Patients values and preferences | No additional considerations made. |
| Changes to the NICE recommendations | The GDG was of the opinion that the NICE 2016 grid needed a change on a few places: ³ |

| Factor | Comment | |
|--------|---|--|
| | Major or complex surgery: because of the type of surgery, the postoperative risk of having renal impairment is higher, and preoperative testing is needed to take precautions if necessary. | |
| | Minor surgery, ASA 2-4: several circumstances are imaginable where the postoperative risk of having renal impairment is higher (e.g. treatment with ACE inhibitor or AT2 inhibitor), and preoperative testing should at least be considered then. | |

| _ | | | |
|-----|---|----------------------------|----------------------|
| Red | commendations | Strength of Recommendation | Level of Evidence |
| • | Kidney function tests* are recommended in all patients undergoing elective major or complex non-cardiac surgery and in patients with ASA 3-4 undergoing elective intermediate non-cardiothoracic surgery. | Strong | Very low |
| • | Kidney function tests* are not recommended in patients with ASA 1 undergoing elective minor or intermediate non-cardiothoracic surgery. | Strong | Very low |
| • | Kidney function tests* are recommended if renal function impairment is suspected in patients with ASA 2 undergoing elective minor or intermediate non-cardiothoracic surgery and in patients with ASA 3-4 undergoing elective minor non-cardiothoracic surgery. | Strong | Very low |

^{*} Creatinine, eGFR, sodium and potassium.

| | Surgery grade | | |
|------------|---|---|---------------|
| ASA grade | Minor | Intermediate | Major/complex |
| ASA 1 | Do not offer | Do not offer | Offer |
| ASA 2 | Consider in people in whom renal function impairment is suspected | Consider in people in whom renal function impairment is suspected | Offer |
| ASA 3 or 4 | Consider in people in whom renal function impairment is suspected | Offer | Offer |

Examples

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- A 43-year old woman in normal health is planned for varicose vein stripping. A preoperative kidney function test is not indicated.
- A 68-year old man with well-controlled hypertension treated with an ACE inhibitor is planned for a knee arthroscopy. In view of his age and ACE inhibitor treatment, he has an increased risk of chronic renal function impairment, and a preoperative kidney function test can be considered.

3.11 Haemostasis tests

3.11.1 Introduction

Haemostasis tests involve sampling venous blood to detect congenital and acquired coagulation disorders and to examine the effects of anticoagulant drugs. In the preoperative setting, the test may be used to establish a baseline for the patient and may be used to plan the use of blood products and blood salvage techniques in the perioperative period.

In the KCE 2004 guideline¹ a distinction was made between general and epidural/locoregional anaesthesia. For patients undergoing general anaesthesia, haemostasis tests were not recommended for ASA 1-2 patients, but recommended for ASA 3 patients with kidney disease planned for intermediate or major surgery. For patients undergoing epidural/locoregional anaesthesia, haemostasis tests were not recommended for ASA 1 patients, but recommended for ASA 2-3 patients with kidney disease, liver disease of chronic alcoholism.

In the NICE 2016 guideline the following recommendations were included:3

- Do not routinely offer haemostasis tests before surgery.
- Consider haemostasis tests in people with chronic liver disease having intermediate or major or complex surgery.
 - o If people taking anticoagulants need modification of their treatment regimen, make an individualized plan in line with local guidance.
 - If clotting status needs to be tested before surgery (depending on local guidance) use point-of-care testing.





In the systematic review for the 2003 guideline, NICE did not identify studies comparing the health outcomes for patients who had preoperative haemostasis tests with patients who did not.¹⁸ However, they did identify fifteen papers that evaluated changes in clinical management for either prothrombin or partial thromboplastin tests. Of these, ten papers observed changes in clinical management experienced by patients. Six studies defined a change in clinical management as a patient requiring a blood transfusion and the other four papers used broader, and varying, definitions.

Johansson et al. did not identify studies that investigated the association of haemostasis testing and changes in clinical management.¹¹

Our update identified one such study. Sousa Soares et al. prospectively included 800 patients with ASA 1 undergoing minor-medium elective surgeries. Of these, 709 (88.6%) underwent preoperative coagulation tests and 11 (1.6%) had abnormal results. In eight patients these abnormal results led to a change in management, without further details provided in the article.

3.11.3 Evidence for prognostic value

In the systematic review for the 2003 guideline, NICE identified fourteen papers aimed to estimate the frequency of postoperative complications experienced by patients and six reported the specific complications that were observed (complications were not observed in eight case series).

Three of the six papers reported peri- or postoperative bleeding as the only postoperative complication experienced by patients and three adopted broader definitions of postoperative complications.

Johansson et al. identified six studies using a multivariate analysis to investigate the incidence of adverse events and morbidity, whereas three studies reported on mortality. ¹¹ Of these, only two studies found a correlation between an abnormal platelet count and an abnormal INR test and the outcomes 'adverse events' or 'morbidity' in patients undergoing elective abdominal surgery. In addition, one study found a correlation between an abnormal prothrombin time and an abnormal platelet count and mortality in patients undergoing miscellaneous surgeries.

Our update identified four additional studies using a multivariate analysis:

- One retrospective cohort study of 8 645 patients undergoing outpatient plastic surgery procedures compared those with abnormal preoperative laboratory test results with those with normal test results.²³ The following laboratory tests were evaluated: hematocrit, white blood cell (WBC) count, platelet count, sodium, serum urea nitrogen (SUN), creatinine, partial thromboplastin time (PTT), prothrombin time (PT), international normalized ratio (INR), albumin, total bilirubin, aspartate aminotransferase (AST), and alkaline phosphatase. The use of preoperative testing was not associated with major postoperative complications (0.42% vs 0.21%, p=0.178) or wound complications (2.1% vs 1.7%, p=0.150). Multivariate analysis showed that neither the performance of preoperative testing nor the presence of abnormal results was associated with postoperative complications. This was also true for haemostasis tests analysed as a separate group.
- One large retrospective cohort study of 2 020 533 patients undergoing elective, non-cardiac surgery evaluated three preoperative haemostatic tests (INR, aPTT and platelet count) and compared patients with abnormal test results with those with normal results.²⁴ Compared to patients with three normal test results, patients who had one abnormal test result were more likely to have perioperative RBC transfusion (OR=1.9; 95%CI 1.86-1.93), to return to the operating room (OR=1.8; 95%CI 1.8-1.9), higher 30-day mortality (OR=3.0; 95%CI 2.8-3.1) and unplanned readmission (OR=1.6; 95%CI 1.5-1.6). Patients with two or three abnormal test results had the highest odds for poor outcomes (perioperative RBC transfusion: OR=2.8, 95%CI 2.7-2.8; return to operating room: OR=3.0, 95%CI 2.9-3.1; 30-day mortality: OR=6.7, 95%CI 6.4-7.0; unplanned readmission: OR=2.2, 95%CI 2.1-2.3).
- One large retrospective cohort study of 636 231 patients undergoing major surgery evaluated the relationship between the INR result and outcome.²⁵ The adjusted odds ratio for major bleeding as compared to INR <1 was as follows: 1.22 (95%CI 1.18-1.25) for INR 1-1.49, 1.48 (95%CI 1.40-1.56) for INR 1.5-1.9, and 1.49 (95%CI 1.39-1.60) for INR ≥2. The adjusted odds ratio for 30-day mortality was 1.51 (95%CI 1.41-1.62) for INR 1-1.49, 2.31 (95%CI 2.122.52) for INR 1.5-1.9, and 2.81 (95%CI 2.563.10) for INR ≥2.</p>

One retrospective cohort study included 11 804 adult patients who had undergone neurosurgery.²⁶ The relationship between three preoperative haemostatic tests (INR, aPTT and platelet count) and periand postoperative outcomes was evaluated. Compared to patients with three normal test results, patients who had one abnormal test result were more likely to have intraoperative RBC transfusion (OR=1.9; 95%CI 1.5-2.4) and to return to the operating room (OR=1.7; 95%CI 1.3-2.3), and to have a higher 30-day mortality (OR=4.7; 95%CI 3.3-6.8). Patients with two or three abnormal test results had the highest odds for poor outcomes (intraoperative RBC transfusion: OR=3.6. 95%CI 2.3-5.5; postoperative RBC transfusion: OR=8.5, 95%CI 1.9-39.0; return to operating room: OR=2.4, 95%CI 1.4-4.1; 30-day mortality: OR=13.1, 95%Cl 7.9-21.7). Patients with a history indicative of potentially abnormal haemostasis had statistically significant higher odds of experiencing each of the poor outcomes (intraoperative RBC transfusion: OR=2.4, 95%CI 2.0-2.9; postoperative RBC transfusion: OR=3.2, 95%CI 1.1-8.9; return to operating room: OR=2.0, 95%CI 1.6-2.5; 30-day mortality: OR=8.2, 95%CI 6.1-11.0). Patients with a history indicative of potentially abnormal haemostasis also had statistically significant higher odds of having abnormal haemostasis tests (abnormal INR: OR=5.1, 95%CI 4.0-6.5; abnormal aPTT: OR=2.4, 95%CI 1.9-3.1; low platelet count: OR=3.6, 95%CI 2.9-4.4).

Conclusions

- There is no direct evidence that carrying out preoperative haemostasis tests would, or would not, improve health outcomes for patients.
- Evidence of low to very low quality suggests that an abnormal haemostasis test result is associated with a higher risk for postoperative mortality or major bleeding, although study results are conflicting.

| Factor | Comment |
|---|--|
| Balance between clinical benefits and harms | Haemostasis tests are safe, and preoperative test results appear to be prognostic for postoperative mortality and major bleeding, although the evidence is conflicting. Patients suffering from chronic liver failure have an increased risk of bleeding and this may require monitoring prior to intermediate and major or complex surgery. ³ People with antecedent(s) of abnormal bleeding, either spontaneously or after trauma or surgery, also have an increased risk of bleeding and this may require monitoring prior to intermediate and major or complex surgery. When epidural anaesthesia is planned, routine haemostasis tests are not necessary, unless in people with antecedent(s) of abnormal bleeding, either spontaneously or after trauma or surgery, and in people with chronic liver disease having elective intermediate or major or complex non-cardiothoracic surgery. People taking anticoagulants such as coumarins need monitoring of haemostasis tests on clinical grounds. |
| Quality of evidence | The evidence is limited to cohort studies, of which some included a very large population and were of fair quality. |
| Costs (resource allocation) | In individuals who are not on anticoagulants or who do not suffer from chronic liver disease, the prevalence of abnormalities identified by haemostasis testing that would alter management is low. ³ Therefore, it would not be costeffective to perform this test routinely. However, it is likely to be cost-effective to perform haemostasis tests on patients with increased risk of related complications. |
| Patients values and preferences | No additional considerations made. |
| Changes to the NICE recommendations | No reasons were found to change the NICE 2016 recommendations (although the second recommendation was simplified). |
| | |

| Recommendations | Strength of Recommendation | Level of Evidence |
|--|----------------------------|----------------------|
| Haemostasis tests are not routinely recommended before elective non- cardiothoracic surgery. | Strong | Very low |
| In people with antecedent(s) of abnormal bleeding, either spontaneously or after trauma or surgery, and in people with chronic liver disease having elective intermediate or major or complex non-cardiothoracic surgery, one will consider haemostasis tests. | Weak | Very low |

| | Surgery grade | | |
|------------|---------------|---|---|
| ASA grade | Minor | Intermediate | Major/complex |
| ASA 1 | Do not offer | Do not offer | Do not offer |
| ASA 2 | Do not offer | Do not offer | Do not offer |
| ASA 3 or 4 | Do not offer | Consider in people with chronic liver disease | Consider in people with chronic liver disease |

Examples

- A 75-year old woman with well-controlled diabetes and hypertension is planned for cataract surgery. Preoperative haemostasis tests are not indicated.
- A 51-year old man with alcoholic liver disease is planned for total knee replacement. Preoperative haemostasis tests can be considered.
- A 43-year old woman in normal health is planned for varicose vein stripping. She complains about frequent nose bleeds, heavy menstrual bleedings and bruises. Preoperative haemostasis tests will certainly need to be considered.
- A 72-year old man is taking coumarins for a chronic atrial fibrillation. He is planned for a resection of a skin lesion. Preoperative haemostasis tests should be ordered on clinical grounds.

3.12 Glycated haemoglobin test (HbA1c)

3.12.1 Introduction

The glycated haemoglobin (HbA1c) test is a venous blood test used to diagnose diabetes mellitus and monitor glucose control in patients known to have diabetes. In the preoperative setting, the test may be used in those with known diabetes and may also be used to screen for previously undiagnosed diabetes. The information from the test may be used to alter diabetes management both pre- and perioperatively, with the aim of reducing postoperative morbidity and mortality.

In the KCE 2004 guideline¹ this test was not addressed.

In the NICE 2016 guideline the following recommendations were included:3

- People with diabetes who are being referred for surgical consultation from primary care should have their most recent HbA1c test results included in their referral information.
- Offer HbA1c testing to people with diabetes having surgery if they have not been tested in the last 3 months.
- Do not routinely offer HbA1c testing before surgery to people without diagnosed diabetes.

In addition, one research recommendation was included: Does optimisation of HbA1c in people with poorly controlled diabetes improve surgical outcomes?³

3.12.2 HbA1c in diabetes

3.12.2.1 Evidence for clinical benefit

NICE did not find relevant clinical studies comparing preoperative HbA1c testing with no preoperative HbA1c testing in patients diagnosed with diabetes.³

3.12.2.2 Evidence for prognostic value

Four retrospective cohort studies (Afsar 2012, Chrastil 2015, Dronge 2006, Harris 2013) looked at the level of HbA1c as a predictor of outcome after surgery:

- One retrospective cohort found preoperative HbA1c >7% to be a predictor of primary arteriovenous fistula failure (OR = 2.79; 95%CI 1.31-5.32) in multivariate analysis.
- One retrospective cohort found preoperative HbA1c <7% to be a predictor of 90-day mortality (OR = 1.37; 95%CI 0.82-2.29) in multivariate analysis (adjusted for 38 variables). The same study found preoperative HbA1c <7% to be an independent predictor of complications (OR = 1.22; 95%CI 1.01-1.47) and a weak predictor of total number of complications (OR = 1.18; 95%CI 0.97-1.43) in multivariate analysis (adjusted for 38 variables).
- Another retrospective cohort found that preoperative HbA1c >7% was not predictive of periprosthetic joint infections (HR = 0.86; 95%CI 0.68-1.09). However, the same study found preoperative HbA1c >7% to be a weak predictor of death (HR = 1.30; 95%CI 1.08-1.56).
- One retrospective cohort study found preoperative HbA1c <7% to be a predictor of reduced postoperative infections after non-cardiac surgery (OR = 2.13; 95%CI 1.23-3.69) in multivariate analysis.

Conclusions

- There is no evidence on the effect of HbA1c on clinical outcome in patients with diabetes.
- There is inconsistent evidence on the prognostic value of HbA1c in patients with diabetes.



| Factor | Comment |
|---|---|
| Balance between clinical benefits and harms | The studies were in patients undergoing different surgery types, but many surgery types were not included, so generalisation of the results is difficult. It is unclear from these studies whether there was any impact on the decision to continue with surgery as planned, based on the test results. If surgery is delayed in order to optimise control of the patient's diabetes, there is a need to consider any potential consequences of delaying surgery. |
| Quality of evidence | Only retrospective studies were identified by NICE. The studies all conducted multivariate analysis, but adjusted for different confounders. |
| | There was inconsistency in outcomes. For example, the evidence concerning postoperative infection in non-cardiac surgery included one study that showed HbA1c was an independent predictor of postoperative infection, and one study that did not show a predictive ability of HbA1c on postoperative infection. |
| Costs (resource allocation) | NICE did not identify economic evaluations that addressed this review question. |
| Patients values and preferences | No additional considerations made. |
| Changes to the NICE recommendations | No reasons were found to change the NICE 2016 recommendations. |

| Recommendations | Strength of Recommendation | Level of Evidence |
|--|----------------------------|----------------------|
| People with diabetes who are being referred for elective non- cardiothoracic surgery from primary care should have their most recent HbA1c test results included in their referral information. | Weak | Low |
| HbA1c testing is recommended in people with diabetes having elective non-cardiothoracic surgery if they have not been tested in the last 3 months. | Weak | Low |

Example

 A 71-year old women with a recent myocardial infarction (<3 months) and well-controlled diabetes is planned for a mastectomy. HbA1c was tested during hospitalisation for her myocardial infarction. Preoperative HbA1c testing is not indicated.



3.12.3.1 Evidence for clinical benefit

NICE did not find relevant clinical studies comparing preoperative HbA1c testing with no preoperative HbA1c testing in patients without diagnosed diabetes.³

3.12.3.2 Evidence for prognostic value

One prospective observational study (Gustafsson 2009) looked at the level of HbA1c as a predictor of outcome after surgery. The main surgical procedures within this surgery were anterior resection, abdominoperineal resection, total colectomy, right hemicolectomy, left hemicolectomy, and other resection. Patients in this study were grouped based on the preoperative measurements of HbA1c: 31 patients were found to have HbA1c above the normal range (over 6%) and 89 patients had HbA1c within the normal range (4.5–6%). The study demonstrated that for patients undergoing major colorectal surgery, preoperative HbA1c at a 6% threshold could predict postsurgical complications but not length of hospital stay or infection after surgery.

Conclusions

- There is no evidence on the effect of HbA1c on clinical outcome in patients with undiagnosed diabetes.
- There is only limited evidence on the prognostic value of HbA1c in patients with undiagnosed diabetes.

Other considerations

| Factor | Comment | |
|--|---|--|
| Balance between clinical benefits and harms | - The available evidence to tee immed to conclude that | |
| Quality of evidence Only one prospective study of fair quality was ide by NICE. | | |
| Costs (resource allocation) | NICE did not identify economic evaluations that addressed this review question. | |
| Patients values and preferences | No additional considerations made. | |
| Changes to the NICE recommendations No reasons were found to change the NICE recommendations. | | |

| Recommendations | Strength of Recommendation | Level of Evidence |
|---|-------------------------------|----------------------|
| HbA1c testing is not recommended before elective non-cardiothoracic surgery in people without diabetes. | Strong | Low |

| | Surgery grade | Surgery grade | | |
|------------|---------------|---------------|---------------|--|
| ASA grade | Minor | Intermediate | Major/complex | |
| ASA 1 | Do not offer | Do not offer | Do not offer | |
| ASA 2 | Do not offer | Do not offer | Do not offer | |
| ASA 3 or 4 | Do not offer | Do not offer | Do not offer | |

Example

 A 71-year old women with a recent myocardial infarction (<3 months) and well-controlled hypertension is planned for a mastectomy. She does not have a history of diabetes. Preoperative HbA1c testing is not indicated.



3.13 Liver function tests

3.13.1.1 Introduction

Liver function tests are often used before liver surgery, but this is out of scope of this report, which is the role of preoperative liver function tests in surgical interventions in general.

This test was not addressed by the KCE 2004 guideline $^{\rm 1}$ or the NICE guidelines. $^{\rm 3,\,18}$

3.13.1.2 Evidence for clinical benefit

No studies were found assessing clinical benefit.

3.13.1.3 Evidence for prognostic value

Johanssen et al.¹¹ identified seven studies analysing the correlation between liver test results and perioperative mortality and morbidity. All studies used a cohort study design, either prospective or retrospective and were very heterogeneous. Only one study found a correlation between an abnormal total bilirubin, aspartate aminotransferase, or alkaline phosphatase and mortality. One study provided data on the accuracy and positive predictive value of liver testing for 24-hour mortality. The accuracy of alkaline phosphatase testing was 91.1% with a positive predictive value of 0.2%. The accuracy of aspartate aminotransferase testing was 91.7% with a positive predictive value of 0.17%. The accuracy of total bilirubin testing was 93.6% with a positive predictive value of 0.23%. They concluded that there is no valid evidence supporting routine (unselective) liver tests in asymptomatic patients.

In the update one study was identified, that was excluded after full-text examination, being in a tropical low income setting that was not sufficiently comparable to the Belgian setting.²⁷

Conclusions

• There is insufficient evidence supporting routine (unselective) use of preoperative liver tests in asymptomatic patients.

| Factor | Comment | |
|---|---|--|
| Balance between clinical benefits and harms | There is no evidence of clinical benefit. Evidence consisted of case series where most failed to show a correlation with postoperative outcome. The one study assessing prognostic accuracy found a very low predictive value. The evidence is limited to case series with a very low lovel of suidence. | |
| Quality of evidence | The evidence is limited to case series with a very low level of evidence. | |
| Costs (resource allocation) | No economic evaluations were retrieved. | |
| Patients values and preferences | No additional considerations made. | |
| Changes to the NICE recommendations | Not applicable. | |

| Recommendations | Strength of Recommendation | Level of Evidence |
|--|----------------------------|----------------------|
| Routine preoperative liver function testing without clinical indication is not recommended before elective non- cardiothoracic surgery. | Strong | Very low |

| | Surgery grade | gery grade | | |
|------------|---------------|--------------|---------------|--|
| ASA grade | Minor | Intermediate | Major/complex | |
| ASA 1 | Do not offer | Do not offer | Do not offer | |
| ASA 2 | Do not offer | Do not offer | Do not offer | |
| ASA 3 or 4 | Do not offer | Do not offer | Do not offer | |

Examples

- A 43-year old woman in normal health is planned for varicose vein stripping. Preoperative liver function testing is not indicated.
- A 71-year old women with a recent myocardial infarction (<3 months) and well-controlled diabetes is planned for a mastectomy. Preoperative liver function testing is not indicated.
- A 65-year old man is planned for resection of a solitary colorectal liver metastasis. Preoperative liver function testing may be indicated, but for technical (operative) reasons.

3.14 Urinalysis

3.14.1 Introduction

Urinalysis is a safe test, without known risks, that provides information on physical, chemical and microscopic components of urine. In the preoperative setting, urine culture may be used to detect urinary tract infections, while physical and chemical analyses may be used to detect renal diseases and poorly controlled diabetes.

The KCE 2004 guideline¹ recommended urine culture when urogenital system surgery or hip replacement surgery are performed, whatever the ASA score.

NICE included the test in their 2003 guideline, ¹⁸ but didn't perform a new literature search for the 2016 update. ³ Therefore, a new search was done for this guideline. The NICE 2016 guideline included the following recommendations:

- Do not routinely offer urine dipstick tests before surgery.
- Consider microscopy and culture of midstream urine sample before surgery if the presence of a urinary tract infection would influence the decision to operate.

3.14.2 Urine culture

3.14.2.1 Evidence for clinical benefit

No studies were found assessing clinical benefit.



3.14.2.2 Evidence for prognostic value

Urinary tract surgery

Kidney

Percutaneous nephrolithotomy

Four studies reported the occurrence of postoperative outcomes according the results of preoperative urine culture.

A first study included 198 patients undergoing percutaneous nephrolithotomy (PCNL).²⁸ Systemic inflammatory response (SIRS) (defined as 2 or more conditions including body temperature <36°C or >38°C, heart rate >100 beats per minute, respiratory rate >20 breaths per minute and/or leukocyte count >12 000 white blood cells per µl or <4 000 white blood cells per µI) occurred in 20 patients (9.8%). A positive preoperative renal pelvic urine culture was not associated with the occurrence of SIRS (OR = 1.74, 95%CI 0.62-4.21).

Using the same definition of SIRS (except for heart rate threshold: >90 beats per minute), a second study also found no association between SIRS and a positive preoperative renal pelvic urine culture (p=0.629) in 303 patients undergoing PCNL.²⁹ SIRS was observed in 27.4% of patients. Moreover, no association was found between SIRS and a positive preoperative bladder urine culture (p= 0.221). In a multivariate logistic regression analysis, stone burden (≥ 8 cm²), recurrent urinary tract infection and infection stone were associated with SIRS (OR = 2.80, 95%CI 1.27-6.18; OR = 2.08, 95%CI 1.03-4.20; and OR = 15.75, 95%CI 1.75-141.56, respectively). In addition, sepsis was diagnosed in 7.6% of patients. Multivariate analysis did not show any association between positive preoperative urine culture and sepsis (OR = 1.03, 95%CI 0.18-5.73).

A third multicentre study assessed the risk factors associated with the occurrence of postoperative fever among 5 354 patients with renal calculi treated by PCNL.30 Postoperative fever was used as a proxy for postoperative infection. After controlling for confounding factors, preoperative urine culture was associated with an increased risk of postoperative fever (OR = 2.12, 95%CI 1.69-2.65).

Finaly, one study analysed preoperative predictive factors of treatment failure in 169 patients with bilateral obstructive renal or ureteral calculi and undergoing PCNL or antegrade ureteroscopy.31 Treatment failure was defined as a progression of renal function to chronic kidney disease stage 5 or requirement of renal replacement therapy. Multivariate analysis showed that treatment failure was statistically high in patients with a positive preoperative culture (OR = 4.96, 95%CI 1.68-14.63).

Laparoscopic nephrectomy

In a small prospective study including 77 patients undergoing laparoscopic simple nephrectomy for benign conditions, positive urine culture was not found to be a predictive factor for intraoperative difficulty assessed by the surgeon on 10-point scale.32

Prostate

A multicentre prospective cohort study ³³ assessed the risk of postoperative infectious complications (febrile urinary tract infection or bacteriuria) in 424 patients with symptomatic benign prostatic hyperplasia or prostate cancer who underwent transurethral resection of the prostate or (open/laparoscopic) prostatectomy. All patients received intravenous antibiotics at surgery. Univariate analysis showed that recent urinary tract infection and preoperative urinary tract infection were no predictive factors for infectious complications (OR = 1.16, 95%CI 0.56-2.40; and OR = 1.30, 95%CI 0.62-2.71, respectively). In multivariate analysis, diabetes mellitus, post-void residuals and operative time were identified as predictive for infectious complications.

Other surgeries

A multicentre retrospective cohort study in 2 497 patients undergoing total hip or knee arthroplasty showed that asymptomatic bacteriuria is an independent risk factor for prosthetic joint infection.³⁴ Subgroup analysis showed that patients with asymptomatic bacteriuria had a significantly higher rate of prosthetic joint infection regardless of whether they received preoperative antibiotic treatment or not.



3.14.3 Biochemical and other urinary tests

3.14.3.1 Evidence for clinical benefit

No evidence was identified.

3.14.3.2 Evidence for prognostic value

Urinary tract surgeries

Kidney

Bilateral obstructive renal or ureteral calculi

Treatment failure – defined as a progression of renal function to chronic kidney disease stage 5 or requirement of renal replacement therapy – was studied in 169 patients undergoing PCNL or antegrade ureteroscopy.³¹ Multivariate analysis showed that treatment failure was statistically high in patients with proteinuria measured with urine dipstick (OR = 2.07, 95%CI 1.19-3.58).

Other surgeries

Preoperative asymptomatic leucocyturia was not a predictive factor of early prosthetic joint infections in 739 patients undergoing primary total knee or hip arthroplasty (adjusted OR = 1.04, 95%CI 0.138-7.833).³⁵ However, these results must be interpreted with caution because of the monocentric retrospective design and the low event rate (only 7 out of 739 patients had early prosthetic joint infections).

Conclusions

- No evidence was found regarding the clinical benefit of urinalysis.
- The prognostic evidence about the association between a positive preoperative urine culture and postoperative infections is conflicting in patients undergoing urogenital surgery.
- In patients undergoing hip or knee arthroplasty, preoperative asymptomatic leucocyturia was not a predictive factor of early prosthetic joint infections, although asymptomatic bacteruria was. Preoperative antibiotic treatment of asymptomatic bacteriuria did not affect the occurrence of prosthetic joint infection.

Other considerations

Factor Comment

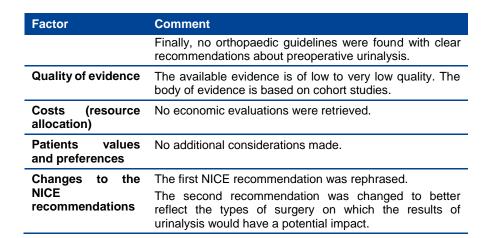
Balance between clinical benefits and harms

There is no evidence comparing patients' outcomes with or without preoperative urinalysis. The prognostic evidence about the association between a positive preoperative urine culture and postoperative infections is conflicting in patients undergoing urogenital surgery.

In the absence of strong evidence, other evidence sources also become informative.

First, the European Association of Urology recommends that: "In diagnostic and therapeutic procedures not entering the urinary tract (clean procedures), asymptomatic bacteriuria is generally not considered as a risk factor, and screening and treatment are not considered necessary. On the other hand, in procedures entering the urinary tract and breaching the mucosa, particularly in endoscopic urological surgery, bacteriuria is a definite risk factor. In case of absence of bacteriuria, the procedure in the present guidelines is usually classified as clean-contaminated, while the presence of bacteriuria, obstruction and drainage catheters, define the procedure as contaminated. A urine culture must therefore be taken prior to such interventions and in case of asymptomatic bacteriuria, preoperative treatment should be given." ³⁶ Second, the NICE 2016 guideline does not recommend

Second, the NICE 2016 guideline does not recommend routine dipstick urine testing in asymptomatic patients and considers urinalysis in specific patient groups.³



| Re | commendations | Strength of Recommendation | Level of Evidence |
|----|---|----------------------------|----------------------|
| • | Routine preoperative urinalysis and urine culture is not recommended before elective non-cardiothoracic surgery. | Strong | Very low |
| • | Preoperative urine culture can be considered in patients undergoing elective urinary tract or prosthetic joint surgery. | Weak | Very low |

Examples

- A 57-year old male smoker is planned for a transurethral resection of the prostate. Preoperative urinalysis can be considered.
- A 51-year old man with alcoholic liver disease is planned for total knee replacement. Preoperative urinalysis can be considered.
- A 55-year old man with well-controlled hypertension is planned for left hemicolectomy. Preoperative urinalysis is not indicated.

3.15 Non-invasive cardiac stress imaging

3.15.1 Stress echocardiography

3.15.1.1 Introduction

Stress echocardiography using exercise or pharmacological (dobutamine, dipyridamole) stress combines information on left ventricular function at rest, heart valve abnormalities and the presence and extent of stress-inducible ischaemia.¹⁴

In the KCE 2004 guideline¹ this test was not addressed, nor in the NICE guidelines.^{3, 18}

3.15.1.2 Evidence for clinical benefit

One randomised study³⁷ compared preoperative stress testing (N=46) with no testing (N=53) in 99 patients undergoing elective abdominal aortic, infrainguinal and carotid vascular surgery. Before randomisation patients were stratified according to specified clinical predictors and according to the type of vascular surgical procedure planned. Minor clinical predictors included advanced age, abnormal electrocardiogram (left ventricular hypertrophy, left bundle-branch block, ST-T abnormalities), rhythm other than sinus rhythm, history of stroke or transient ischemic attack, or uncontrolled systemic hypertension. Intermediate clinical predictors included mild stable chronic angina, a history of known myocardial infarction or Q waves on a preoperative electrocardiogram (ECG), compensated or prior congestive heart failure, or a history of diabetes mellitus (insulin or noninsulin dependent). Patients with high-risk clinical predictors such as unstable coronary syndromes, severe valvular disease, or decompensated congestive heart failure were excluded. Of 46 patients randomized to preoperative stress testing, 41 (89%) patients underwent dobutamine stress echocardiography, whereas the remaining 5 patients underwent dobutamine (N=4) or adenosine thallium scintigraphy (N=1). Patients were followed up until 12 months postoperatively. One non-cardiac death (respiratory failure) occurred on postoperative day 7 in a patient randomized to no stress test who had undergone aortobifemoral revascularization. There were no cardiac deaths before hospital discharge. Before hospital discharge there were 3 (4%) nonfatal adverse postoperative cardiac outcomes including congestive heart failure in 1 patient randomized to cardiac stress testing and elevated troponin I levels in 2 patients who did not undergo stress testing. In the group of patients who underwent cardiac stress testing, the positive predictive value of cardiac events was 0%, and the negative predictive value was 92%. One patient randomized to no stress test had an episode of congestive heart failure 1 month postoperatively, and 1 patient had a presumed cardiac death 9 months postoperatively (unwitnessed arrest).

3.15.1.3 Evidence for prognostic value

Four meta-analyses evaluated the prognostic accuracy of preoperative stress echocardiography, ³⁸⁻⁴¹ of which the reviews of Beattie et al. and Kertai et al. were the most recent and comprehensive. In view of the heterogeneity of the included studies, the results of the meta-analysis of Beattie et al. are less trustworthy, and therefore only ranges of results are reported here. In 18 studies in patients undergoing vascular surgery Beattie et al. reported a sensitivity between 29% and 97% and a positive likelihood ratio between 1.14 and 39.8.³⁸ Kertai et al. reported a pooled sensitivity of 74% (95%CI 53-94%) for dipyridamole stress echocardiography (4 studies) and a pooled specificity of 86% (95%CI 80-93%) in a population undergoing major vascular surgery.³⁹ For dobutamine stress echocardiography (8 studies), a pooled sensitivity of 85% (95%CI 74-97%) and specificity of 70% (95%CI 62-79%) was found.³⁹ In a mixed population (3 studies) Beattie et al. reported a sensitivity between 90% and 98% and a positive likelihood ratio between 2.05 and 2.69.³⁸

Four additional primary studies were identified:

Palombo et al. prospectively included 91 patients with at least one risk factor for coronary artery disease (family history of myocardial infarction, age >70 years, history of smoking, history of myocardial infarction, hypertension, reduced exercise capacity, cerebrovascular disease, diabetes requiring pharmacological therapy, renal failure) who underwent elective abdominal aortic repair.⁴² Stress echocardiography was positive in 9 cases, including 7 presenting critical coronary artery disease on the basis of coronary angiography. One non-fatal myocardial infarction occurred in one patient (1.1%) with a positive stress echocardiography and non-critical single-vessel disease. Sensitivity, specificity, positive predictive value and negative predictive value for the prediction of major cardiac events (heart failure, fatal or

- non-fatal myocardial infarction, and major ventricular arrhythmia) were found to be 100%, 91%, 11% and 100%, respectively.
- Schouten et al. retrospectively included 77 consecutive patients with at least three risk factors for coronary artery disease (age >70 years, angina pectoris, myocardial infarction, heart failure, stroke, renal failure, diabetes mellitus) who underwent elective abdominal aortic repair (endovascular: N=39; open: N=38). Three (8%) patients in the open repair group died within 30 days after surgery, whereas in the endovascular group all patients survived. The incidence of the combined endpoint of cardiovascular death or nonfatal MI for patients in the open group was 13% versus 0% in the endovascular group. Patients with no, or only limited, stress-induced myocardial ischemia at preoperative dobutamine stress echocardiography had a lower incidence of perioperative myocardial infarction than patients with extensive stress-induced ischemia (3% vs 21%, p=0.03).
- Yokoshima et al. retrospectively included 122 consecutive patients who were scheduled for non-cardiac intermediate risk surgery. 44 All patients had intermediate predictors of coronary artery disease (mild angina pectoris, prior myocardial infarction, compensated or prior congestive heart failure, diabetes mellitus). Perioperative cardiac events were defined as events during the operation or within 1 month postoperatively, including fatal arrhythmias, heart failure, angina pectoris, myocardial infarction and cardiac death. Eight perioperative cardiac events occurred, including two deaths. Sensitivity, specificity, positive predictive value and negative predictive value for the prediction of perioperative cardiac events were 100%, 52%, 13%, and 100%, respectively, for standard dobutamine stress echocardiography, and 100%, 76%, 23%, and 100%, respectively, for semiquantitative dobutamine stress echocardiography.
- Lerakis et al. included 611 patients who underwent bariatric surgery. 45 Of these, adequate baseline imaging quality of preoperative dobutamine stress echocardiography was achieved in 590 patients. Seven patients had a positive dobutamine stress echocardiography, and 5 of these underwent subsequent coronary angiography. Only 1 patient (with previous history of coronary artery disease) was found with significant coronary artery disease which was managed medically. Nonsignificant coronary artery disease was found in 2 patients, the

remaining 2 patients had normal coronary arteries. Angiography was deferred in 1 patient who proceeded to surgery on medical treatment. One patient declined surgery. There were 3 deaths (all due to sepsis) during hospitalization, resulting in a 30-day mortality of 0.5%. Two of these patients had a negative preoperative DSE, the remaining patient had a negative preoperative technetium scan. There was no difference in mortality based on preoperative dobutamine stress echocardiography results

(negative dobutamine stress echocardiography 0.19%, positive dobutamine stress echocardiography 0%, inconclusive dobutamine stress echocardiography 1.8%, p=0.36).

Conclusions

- The available evidence of very low quality does not allow to draw a firm conclusion about the effect of preoperative dobutamine stress echocardiograpy on postoperative outcome.
- The available prognostic studies reported a wide range of estimates of prognostic accuracy, rendering a conclusion very difficult.

3.15.2 Myocardial scintigraphy

3.15.2.1 Introduction

A myocardial scintigraphy is a type of nuclear medicine procedure where an amount of a radionuclide is used during the procedure to assist in the examination of the tissue under study in order to evaluate the heart's function and blood flow. A radionuclide is used as a "tracer," it travels through the blood stream and is taken up (absorbed) by the healthy heart muscle tissue. On the scan, the areas where the radionuclide has been absorbed will show up differently than the areas that do not absorb it (due to possible damage to the tissue from decreased or blocked blood flow). A stress myocardial perfusion scan the heart is stressed by exercise or medication. Myocardial perfusion scintigraphy was originally developed as a two-dimensional planar imaging technique, but SPECT acquisition has since become the clinical standard in current practice.⁴⁶

In the KCE 2004 guideline¹ this test was not addressed, nor in the NICE quidelines.^{3, 18}

3.15.2.2 Evidence for clinical benefit

No direct evidence on the clinical benefit of preoperative myocardial perfusion scan was identified.

3.15.2.3 Evidence for prognostic value

The reviews of Beattie et al.³⁸ and Kertai et al.,³⁹ mentioned in the previous section, evaluated the diagnostic accuracy of both planar and SPECT myocardial perfusion scan. Beattie et al. reported a diagnostic likelihood ration of 1.83; 95%CI 1.59-2.10; P = 0.001) and an area under the ROC curve of 0.75; 95% CI, 0.70-081. Kertai et al reported a pooled sensitivity of 83% (95%CI 77% to 89%) and a pooled specificity of 49 % (95%CI 41% to 57%). Both reviewers report that the test characteristics are inferior to stress echocardiography. Quality of primary studies however is low.

In the update, we assessed the full text of 2 additional validation studies^{47,48}, but we excluded them because both had incomplete and inconsistent verification of positive SPECT results, as it was unclear on what grounds some underwent additional examinations, including coronary angiography and why part of patients with positive results did or did not undergo surgery and were merely excluded from the analysis, making the results impossible to interpret. It must be noted that studies in the above mentioned systematic reviews suffer from the same problems.

Conclusions

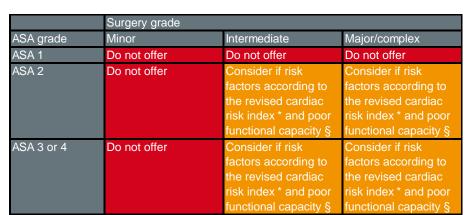
- There is no evidence for clinical benefit of preoperative myocardial scintigraphy.
- Meta-analysis suggests that prognostic characteristics are inferior to stress echocardiography, but quality of the evidence is low.



| Factor | Comment |
|---|--|
| Balance between clinical benefits and harms | The vast majority of studies evaluating preoperative stress echocardiography and scintigraphy was carried out in a population undergoing vascular surgery. One small RCT found no effect of preoperative dobutamine stress echocardiography on postoperative outcome, but because the estimate is very imprecise, a firm conclusion is difficult. The available prognostic studies reported a wide range of estimates of prognostic accuracy, rendering a conclusion very difficult. |
| | In the absence of strong evidence, other evidence sources become informative too. Both the ESC/ESA and ACC/AHA guidelines contain recommendations about the use of a preoperative non-invasive cardiac stress imaging, ^{13, 14} and are reasonably consistent. ESC/ESA recommend stress imaging before high-risk surgery in patients with more than two clinical risk factors (according to the revised cardiac risk index) and poor functional capacity (defined as < 4 metabolic equivalents). Stress imaging may be considered before high- or intermediate-risk surgery in patients with one or two clinical risk factors and poor functional capacity (<4 METs). ACC/AHA combine these two recommendations in one overall recommendation, stating that it is reasonable for patients at elevated risk for non-cardiac surgery with poor functional capacity to undergo either dobutamine stress echocardiography or scintigraphy if it will change management. Finally, both ESC/ESA and ACC/AHA state that routine stress imaging is not recommended before low-risk surgery (regardless of the patient's clinical risk). |
| Quality of evidence | The RCT is of fair quality, but the effect estimates are very imprecise due to the low occurrence of postoperative events, rendering the quality of evidence very low. Quality of primary observational studies is low, both suffering from verification bias and not systematic testing of all eligible persons, making it |

| Factor | Comment |
|-------------------------------------|---|
| | unclear if testing was not done based on clinical suspicion, which is not the scope of this report. |
| Costs (resource allocation) | No economic evaluations were retrieved. |
| Patients values and preferences | No additional considerations made. |
| Changes to the NICE recommendations | Not applicable. |

| Red | commendations | Strength of Recommendation | Level of Evidence |
|-----|---|----------------------------|----------------------|
| • | Non-invasive stress imaging can be considered for patients at elevated risk before elective non-cardiothoracic surgery with poor functional capacity, if it will change management. | Weak | Very low |
| • | Routine noninvasive stress imaging is not recommended before elective low-risk non-cardiothoracic surgery, regardless of the patient's clinical risk. | Strong | Very low |



^{*} Clinical risk factors according to revised cardiac risk index: ischaemic heart disease (angina pectoris and/or previous myocardial infarction), heart failure, stroke or transient ischaemic attack, renal dysfunction (serum creatinine >170 µmol/L or 2 mg/dL or a creatinine clearance of <60 mL/min/1.73 m²), diabetes mellitus requiring insulin therapy.¹⁴

§ Poor functional capacity is defined as < 4 metabolic equivalents (METs), i.e. the inability to climb two flights of stairs or run a short distance (100 m on level ground at 3-5 km/h).¹⁴

Examples

- A 54-year old woman who is in perfect health is planned for a thyroidectomy because of a multinodular goitre with tracheal compression. Preoperative non-invasive stress imaging is not indicated.
- A 61-year old male who has well-controlled type 2 diabetes (treated with bedtime insulin) is planned for an inguinal hernia repair. He walks daily for one hour. Preoperative non-invasive stress imaging is not indicated.
- A 61-year old male who has a history of myocardial infarction two years ago is planned for a knee arthroscopy. During the preoperative clinical assessment the man complains about worsening dyspnoea and peripheral oedema. He is unable to climb stairs. Preoperative non-invasive stress imaging can be considered.
- An 85-year old woman is planned for cataract surgery. She walks with a walker. Preoperative non-invasive stress imaging is not indicated.

3.16 Coronary CT angiography

3.16.1 Introduction

Coronary CT angiography is a noninvasive modality that excludes or finds coronary artery disease. It does not need any induction of cardiac stress.

In the KCE 2004 guideline¹ this test was not addressed, nor in the NICE guidelines.^{3, 18}

3.16.2 Evidence for clinical benefit

No clinical studies were found comparing preoperative coronary CT with no coronary CT in patients undergoing elective non-cardiac surgery. Two studies reported on changes in management:

- Budde et al. included 28 patients who underwent abdominal aortic aneurysm repair and had a preoperative thoraco-abdominal electrocardiography-gated 64-detector-row CT angiography.⁴⁹ On CT, 17 patients (61%) had significant coronary disease (>50% stenosis) including left main (N=4), single (N=7) and multiple (N=6) vessel disease. Based on CT findings, patient management would have been changed in 4 out of the 28 patients (14%; 95%Cl 1-27%) by adding coronary angiography. In five patients who underwent coronary artery bypass grafting previously, CT did not change management but confirmed graft patency.
- Watanabe et al. included 120 patients planned for lung cancer resection who underwent preoperative 3D-CT angiography.⁵⁰ Seventy-one patients had normal findings, and forty-nine patients showed coronary stenosis on 3D-CT angiography. Among the latter 49 patients, 24 with slight stenosis underwent lung tumor resection, 23 had coronary angiography for severe stenosis before lung surgery and 2 were not eligible for lung resection because of very severe coronary stenosis, corresponding to a change in management in 21% of the patients.



3.16.3 Evidence for prognostic value

Only one study evaluated the prognostic value of coronary CT in patients undergoing elective non-cardiac surgery. Hwang et al. included 844 patients who underwent coronary CT for screening of coronary artery disease before non-cardiac surgery.⁵¹ Clinically determined revised cardiac risk index was compared with the extent and severity of coronary artery disease assessed by coronary CT. Perioperative major cardiac event (PMCE), defined as cardiac death, myocardial infarction, or pulmonary edema within 30 days postoperatively, developed in 25 patients (3.0%). Significant coronary CT findings were defined as >3 any lesions with ≥1 (diameter stenosis ≥70%) stenosis based on the relationship between the severity of coronary artery disease and PMCE risk. The risk of PMCE was 14.0% in patients with significant CT findings compared to 2.2% in patients without significant CT findings regardless of revised cardiac risk index score. On the basis of revised cardiac risk index and coronary CT, the risk of PMCE could be estimated with a sensitivity, specificity, positive predictive value, and negative predictive value of 76%, 73%, 8%, and 99%, respectively.

Conclusions

- There is no evidence on the clinical benefit of coronary CT in patients undergoing elective non-cardiac surgery. There is limited evidence that coronary CT leads to a change in management (in about 14-21% of patients).
- There is only limited evidence on the prognostic value of coronary CT in patients undergoing elective non-cardiac surgery.

| Factor | Comment |
|---|--|
| Balance between clinical benefits and harms | The available evidence is too limited to conclude that coronary CT can indicate the likelihood of death and/or perioperative complications. Only few studies are available that demonstrated that perioperative management was altered in some way based on the test, but it is unclear how this impacted on patient outcomes. |
| Quality of evidence | The evidence is limited to retrospective cohort studies. |
| Costs (resource allocation) | Catalan et al. compared the cost-effectiveness of initial preoperative coronary 64-slice CT vs. invasive coronary angiography based on four studies in a population undergoing cardiac surgery. ⁵² 71.2% of the coronary angiographies and 3.56% of the post-angiography complications could have been avoided by an initial preoperative CT with a saving of €411/patient. |
| Patients values and preferences | No additional considerations made. |
| Changes to the NICE recommendations | Not applicable. |

| Recommendations | Strength of Recommendation | Level of Evidence |
|---|----------------------------|----------------------|
| Preoperative coronary CT is not routinely recommended in patients undergoing elective non- cardiothoracic surgery. | Strong | Very low |



| | Surgery grade | | |
|------------|---------------|--------------|---------------|
| ASA grade | Minor | Intermediate | Major/complex |
| ASA 1 | Do not offer | Do not offer | Do not offer |
| ASA 2 | Do not offer | Do not offer | Do not offer |
| ASA 3 or 4 | Do not offer | Do not offer | Do not offer |

Example

 A 71-year old women with a recent myocardial infarction (<3 months) and well-controlled diabetes is planned for a mastectomy. Preoperative coronary CT is not indicated.

4 IMPLEMENTATION AND UPDATING OF THE GUIDELINE

4.1 Implementation

4.1.1 Multidisciplinary approach

In this report we focused on the effectiveness of specific (medical) interventions, without taking into account the organization of health services. In clinical practice, a multidisciplinary approach by different health care professionals should be encouraged. This approach should not only cover the medical needs of the patient but also their psychosocial needs.

4.1.2 Patient-centered care

The choice of an intervention should not only consider medical aspects but also patient preferences. Patients should be well and timely informed about all diagnostic and treatment options and the advantages and disadvantages they offer.

4.1.3 Barriers and facilitators for implementation of this guideline

During the stakeholders meeting, the potential barriers and facilitators related to the use of this guideline were discussed:

- Clinical inertia is probably the most important barrier for implementation that was identified. For many years, a large battery of lab tests, ECG and chest X-ray were the minimum for a preoperative assessment, and still many practitioners adhere to these habits.
- Availability of tests and/or expertise was not considered to be a barrier for implementation, since all recommended tests are available in all Belgian hospitals.

To improve the implementation of this guideline, an accompanying app was developed for iOS and Android. The app is easy-to-use in daily practice, and mostly avoids clinical judgement, so that it can also be used by nurses and trainees. Also patients can consult the app and confront practitioners with the preoperative tests recommended by the app.

The identification of potential barriers and facilitators related to the use of this guideline is limited to a discussion held during the stakeholders meeting. More sophisticated methods could be used, but this would go beyond the scope of this project. More information on the identification of barriers and facilitators in guidelines implementation can be found in a recent KCE-report (see KCE website).

4.1.4 Actors of the implementation of this guideline

Clinical guidelines are developed according to standardised principles, based on scientific information regularly updated from the international literature. KCE formulates recommendations addressed to specific audiences (clinicians, decision-makers, sickness funds, NIHDI, professional organizations, hospital managers...). KCE is not involved in the decision making process itself, or in the execution of the decisions.

As stated above, an accompanying app was developed for iOS and Android. In addition, the content of this guideline is intended to be disseminated by scientific and professional organisations. They will also play a key role in dissemination that makes use of diverse channels such as websites or sessions of continuing education (LOK/GLEM).

4.2 Monitoring the quality of care

This guideline should be considered as a starting point to develop quality improvement programs that target all caregivers concerned.

It can be used as a tool to support health policies to improve the quality of care, e.g. through the support of actions to increase caregivers' awareness and to improve their practice, or through the development (or revision) of sets of process and outcome quality indicators.

4.3 Guideline update

In view of the rapidly evolving evidence, this guideline should be updated every 5 years. If, in the meantime, important new evidence would become available, this should be taken into consideration.

The KCE processes foresee that the relevance of an update would be yearly assessed for each published guideline by the authors. Decisions are made on the basis of new scientific publications on a specific topic (e.g. Cochrane reviews, RCTs on medications or interventions). Potential interest for groups of health practitioners is also considered in this process.

This appraisal leads to a decision on whether to update or not a guideline or specific parts of it to ensure the recommendations stay in line with the latest scientific developments.



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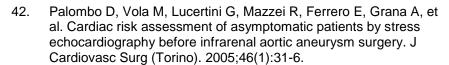
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