

Argentine Consensus Statement of Cardiovascular Risk Evaluation in Noncardiac Surgery / Brief Version

Director

Dr. Juan Krauss^{MTSAC}

Coordinator:

Dr. Fernando Botto^{MTSAC}

Secretaries:

Dr. Luciano Lucas

Dr. Rodrigo Bagnati^{MTSAC}

Writing Committee:

Dr. Diego Arakaki

Dr. Patricia Avellana

Dr. Fernando Belcastro^{MTSAC}

Dr. Augusto Lavalle Cobos^{MTSAC}

Dr. Mario Racki^{MTSAC}

INDEX

1. Introduction, 159
2. Preoperative assessment of clinical/surgical cardiovascular risk, 160
3. Strategies that can modify the outcomes, 168
4. Specific clinical situations, 173
5. References, 175

Abbreviations

CF	Clase funcional	AMI	Myocardial Infarction
ECG	Electrocardiogram	HF	Heart Failure
COPD	Chronic obstructive pulmonary disease	ACE Inhibitors	Angiotensin converting enzyme inhibitors
GRADE	Grading of Recommendations Assessment, Development, and Evaluation	RCRI	Revised Cardiac Risk Index
aHR	Adjusted hazard ratio	RAAS	Renin-angiotensin-aldosterone system

1. INTRODUCTION

About 200 million noncardiac surgeries are performed worldwide each year, with nearly 100 million conducted in subjects over 45 years of age. (1) For this reason, the preoperative assessment of cardiovascular risk is a common issue for clinicians, cardiologists and anesthesiologists.

About 2 million patients die within 30 days post-surgery due to various complications, the most frequent of cardiovascular origin, particularly related to acute ischemic events. (2, 3) As a result, cardiovascular risk assessment is central to improve clinical and surgical outcomes through different types of perioperative measures.

For several years, the international scientific societies have generated and renewed recommendations, often based on pathophysiological criteria, on the extrapolation of decisions from the non-operative clinical context and on observational studies with biases and insufficient sample sizes. This consensus will demonstrate the difficulties to generate recommendations in the perioperative period, given the lack or suboptimal quality of the existing scientific evidence.

Naturally, it is important to emphasize that a consensus is a guideline of recommendations that are not dogmatic and constitute an advice for the “average” patient, with no intention to replace the doctor’s judgment in the “individual” patient. The recommended diagnostic and therapeutic measures may be affected by the avail-

ability and expertise of the attending physician's environment and may change over time in accordance with the emergence of new scientific evidence.

1.1 Methodology of the review

The Writing Committee defined the topic index and conducted a systematic review of every aspect, with literature search, article selection and data collection based on pre-established criteria, to assess all randomized, observational studies of significant importance and existing meta-analyses.

Traditional concepts related to the type of evidence were applied in the diagnosis and risk stratification area. Moreover, in the therapeutic area, the recently created GRADE (Grading of Recommendations Assessment, Development, and Assessment) system, clearly structured to develop systematic reviews and clinical guidelines, and of growing incorporation by several international scientific societies, was applied to qualify the evidence accumulated and to generate recommendations. (4)

To analyze the potential benefits of the treatments evaluated, multiple meta-analyses were performed with different endpoints for the different treatments. To develop this consensus, the Writing Committee included as critical endpoints total mortality, myocardial infarction (AMI) and perioperative stroke. Total mortality instead of cardiovascular mortality was chosen, given the difficult adjudication of the latter.

2. PREOPERATIVE ASSESSMENT OF CLINICAL/SURGICAL CARDIOVASCULAR RISK

Preoperative assessment of cardiovascular risk in noncardiac surgery aims to guide perioperative management of diagnostic methods and therapeutic indications necessary to mainly reduce short-term cardiovascular complications.

Assessment should be simple, accessible, fast and as cheap as possible in order to avoid exceeding the complexity and even the risks of the surgical intervention per se, nor delay it unnecessarily, especially in indications tending to cure or prevent serious disease progression as, for example, cancer, vascular diseases, infections, etc.

Preoperative assessment of the clinical/surgical risk should progressively incorporate, 1) the clinical condition of the patient, 2) the degree of surgical risk during the procedure, and 3) the results of the additional studies requested.

2.1 Clinical condition of the patient

Clinical variables arising from patient interrogation and physical examination are very useful elements, and have been the center of attention for many years. Different authors have developed multivariate scores to predict cardiovascular risk, from the Goldman et al. study published in 1977, (5) later modified by other authors, to the Revised Cardiac Risk Index (RCRI) published by Lee et al in 1999, (6) externally validated and showing improvement in predicting events. For this reason, it was incorporated by the 2007 AHA/ACC 2007 (7) and 2009 ESC (8) guidelines, and as a result has been the most widespread to date.

In the analysis of the methodology used to develop the best qualified scores (prospective recruitment, inclusion of various types of surgery, event monitoring), significant limitations are observed. First, sample sizes were modest (including between 455 and 2,893+ patients), and the number of cardiovascular events was small (between 30 and 66). Therefore, the number of independent predictors obtained according to the evaluated score (between 5 and 13) is exaggerated considering that 12 to 15 events per predictor are required to rely on the statistical model. Second, the analysis of the ROC curve for sensitivity and specificity showed values around 0.75, a fact which assumes an incorrect risk classification in 1 out of 4 patients, and determines a modest prediction. Third, some risk factors and endpoints used had different definitions, and furthermore, the latter (especially perioperative infarction) had suboptimal monitoring. Finally, these scores are not very applicable today as they were developed between 15 and 38 years ago, before the rise of many current advances in surgical and anesthetic techniques.

Concerning other methods or disseminated scores, especially among anesthesiologists, we can quote the classification of the American Society of Anesthesia (ASA), which assesses the patient's general physical condition or illness degree. (9) There is very controversial evidence regarding the relation of this scale with postoperative outcomes, so that although useful to describe among peers the general state of a patient, including important decisions such as postponing a surgery in extreme cases, its routine use is not recommended as a cardiovascular risk stratification system in clinical practice.

Even though RCRI has shown the best estimate of cardiovascular events in an unselected adult population undergoing noncardiac surgery, it has limitations as it was performed in a single center, with exclusion of emergency cases and those with hospital stay <2 days, stroke was not considered as endpoint and AMI was defined according to CK-MB.

A systematic review published in 2010 assessed the ability of RCRI to predict cardiovascular complications and death after vascular and nonvascular noncardiac surgery. (10) It showed a moderate ability to discriminate patients at low versus high risk, especially with poor prediction of events after vascular surgery, and to predict

mortality. The authors mention the paucity of studies with adequate power and quality, and the high heterogeneity in the analysis.

To date, the most important evidence regarding independent predictors of perioperative risk arises from a large multicenter and international prospective study called VISION (Vascular events In noncardiac Surgery patients cOhort evaluation), recently published by PJ Devereaux et al., which included 15,133 patients submitted to a wide range of noncardiac surgery in subjects >45 years, who had at least one night of hospitalization. Inclusion was prospective, with objectives, prespecified risk factors and endpoints, with systematic monitoring of postoperative troponin T, central and blind event adjudication, and primary analysis based on 30-day mortality, with 282 primary events adjudicated (30-day mortality rate of 1.9%, 95% CI 1.7-2.1%). (2) While the first publication focused on the importance of monitoring with troponin there are 11 independent clinical predictors of death at 30 days:

- 1- Age >65 years. Category 65 to 74 years (adjusted hazard ratio [aHR] 1.67, 95% CI 1.18-2.36) and >75 years (aHR 3.03, 95% CI 2.20-4.18).
- 2- Recent high risk coronary artery disease (aHR 3.12, 95% CI 1.71-5.68).
- 3- History of peripheral vascular disease (aHR 2.13 95% CI 1.47-3.10).
- 4- History of heart failure (aHR 1.60 95% CI 1.09-2.36).
- 5- History of stroke (aHR 2.01 95% CI 1.42-2.84).
- 6- History of chronic obstructive pulmonary disease (COPD) (aHR 2.15 95% CI 1.61-2.89).
- 7- Active cancer (aHR 2.38 95% CI 1.79-3.18).
- 8- Urgent/emergency surgery (aHR 4.62 CI 95 % 3.57-5.98).
- 9- Major general surgery (aHR 3.25 95% CI 1.64-6.45).
- 10- Major vsular surgery (aHR 2.38 95% CI 1.04-5.47).
- 11- Major neurosurgery (aHR 3.72 95% CI 1.68-8.20).

As can be seen through the adjusted HRs, the presence of any predictor doubles, triples and even quadruples (urgent/emergency) mortality compared with its absence.

For the proposed assessment of clinical/surgical cardiovascular risk indicated in **section 2.4** of this consensus, we have assembled a list of major and minor criteria based on VISION independent predictors, to which we have incorporated risk predictors arising from other studies and also from the panel of participating cardiologists' criteria (e.g., severe valvular disease, renal failure, diabetes and stable coronary artery disease, cutoff age modification, etc.).

2.2 Degree of surgical risk

2.2.1 Type of surgery

All surgical procedures produce some degree of stress that favors four situations: 1) an increase in myocardial oxygen demand induced by tachycardia and changes in blood pressure; 2) a hypercoagulable state given by imbalance between prothrombotic and fibrinolytic factors; 3) increased friction forces inside the coronary arteries ("shear stress"); and 4) an inflammatory and hypoxic condition generated by neurohumoral changes. There are also other specific surgical factors that may cause ischemia, myocardial injury and heart failure: need for urgent or emergency surgery, location, aggressiveness and duration of the procedure. Undoubtedly, major noncardiac surgery represents a myocardial stress, which can lead to coronary thrombosis and ischemic complications caused by the combination of these mechanisms.

Patients in planned vascular surgery represent a subgroup with panvascular atherosclerotic disease, i.e., whether the planned surgery is aortic, of the lower limb arteries or even from the carotid arteries, an additional risk is added due to the coexistence of coronary artery disease, diabetes, renal failure and advanced age. For these reasons, procedures that a priori impress as less risky (e.g. peripheral angioplasty or infrainguinal surgery) may present severe postoperative complications.

The Section 2.4 table shows risk of death and AMI at 30 days according to the type of surgery, divided into 3 categories (high >5%, intermediate between 1 and 5%, and low <1%) taken from the guidelines of the European Society of Cardiology (ESC), (8) and modified for this consensus including VISION study data and the panel of experts' advice.

2.2.2 Type of anesthesia

Most used anesthetics cause vasodilation through the reduction of sympathetic tone, and thus cause systemic hypotension. Consequently, the main objective during surgery is to maintain adequate perfusion of vital organs. Therefore, preoperative detection of severe cardiovascular disease that may complicate the perioperative period is essential.

The scope of this agreement is limited to preoperative cardiovascular management recommendations; therefore, it does not specifically include the selection of the anesthetic or surgical technique, leaving them to the cri-

teria of the anesthesiologist and surgeon, once the result of the risk assessment is reported by the cardiologist.

2.2.3 Time of surgery

A surgical urgent or emergency situation involves an incidence of 30-day mortality nearly 5 times higher than elective surgery, according to the VISION study. (2) In this study, surgery within 24 hours was considered an emergency, and between 24 and 72 hours of the acute event an urgency. Undoubtedly, the magnitude of the adverse consequences largely respond to the clinical and hemodynamic instability presented by these patients at the time of the intervention, given the impossibility of treating and stabilizing them previously to improve surgical aggression tolerance.

Urgent or emergency surgeries only allow a superficial cardiac assessment. However, a quick and simple assessment can influence intra and postoperative monitoring, and medical indications adjusted to the patient's conditions to reduce the risk. For example, the assessment of ventricular function by Doppler echocardiography can be useful in perioperative management.

Additionally, the presence of myocardial ischemia, or a history of ischemic heart disease can lead intra- and postoperative monitoring towards the assessment of myocardial injury markers, more frequent electrocardiograms (ECG) or ST segment monitoring.

In less urgent situations where the risk of the underlying disease exceeds that of surgery, combined with the patient's condition, the indication can be considered semi-elective, and the intervention is advisable even without full assessment of the patient. This applies, for example, to malignancies, when surgery is necessary to define healing feasibility. Any surgery delay in an attempt to stabilize the patient (such as studies and treatments, that are sometimes complex) may jeopardize the patient's prognosis more than the risk of surgery itself, given the potential progress of the tumoral process.

2.3 Complementary studies

2.3.1 Electrocardiogram

The higher the cardiovascular risk of the patient and of surgery, the greater the value of ECG to predict short- and long-term events. Paradoxically, this benefit may be canceled in elderly populations due to the low specificity as a result of the high prevalence of abnormalities.

On the other hand, its usefulness is lower in low-risk surgeries and in young patients without comorbidities in whom the probability of finding ECG abnormalities is very low and hence the benefit is also very low.

Recommendations for preoperative ECG indication

Class I

- 1- Patients with at least one major or minor criterion listed in Section 2.4. (Level of evidence A)
- 2- Patients in moderate or high risk planned surgery of the Table presented in Section 2.4. (Level of evidence: B)

Class II-a

- 1- Patients with any cardiac disease or arrhythmia not listed in the mentioned list. (Level of evidence: C)

Class II-b

- 1- Patients without major or minor criteria of the mentioned list, or any other known heart disease or arrhythmia. (Level of evidence: B)

2.3.2 Chest X-ray:

Due to the low diagnostic yield, difficulty in identifying patients at increased risk, lack of prognostic value to help reduce perioperative risk, cost and association to potential adverse effects (radiation); this consensus does not recommend the systematic indication of chest X-ray in the preoperative assessment of noncardiac surgery. On the contrary, selective indication based on the characteristics of the individual patient or surgical procedure is suggested.

Recommendations for preoperative chest x-ray indication

Class I

- 1- None

Class II-a

- 1- Patients with respiratory signs or symptoms of unidentified origin. (Level of evidence: B)

2- Patients in planned thoracic, thoraco-abdominal or upper abdominal surgery. (Level of evidence: B)

Class II-b

- 1- Patients with advanced age (>70 years) (Level of evidence B)
- 2- Patients with history of heart failure. (Level of evidence: B)
- 3- Patients with history of chronic lung disease (level of evidence B)

Class III

- 4- Systematic indication of chest x-ray for all patients in planned noncardiac surgery (Level of evidence C)

2.3.3 Functional myocardial ischemia evocative tests

Myocardial ischemic evocative testing allows having more information during preoperative assessment. This is particularly true in patients at high cardiovascular risk who will undergo moderate or high risk surgeries, in those with unassessed ischemic symptoms, and those in planned vascular surgery or other high risk surgery.

The indication of functional preoperative tests should follow the general clinical criteria applied in non-operative scenarios. For the purposes of this agreement, section 2.4 establishes a methodology suggested for the definition of clinical and surgical risk and recommendations including functional test indication. Globally, their use is suggested in patients with stable, symptomatic or low functional class cardiovascular history.

Conventional exercise testing is the most available method, with a modest sensitivity and specificity for the combined outcome of infarct and death (74% and 69%, respectively), with a high negative predictive value (98%), and a diagnostic accuracy similar to that of other methods. (11) However, it is common for patients with moderate and high risk to present baseline ECG abnormalities that hamper result interpretation, and who also fail to reach the ideal ischemic threshold due to their inability of performing vigorous exercise.

Studies of myocardial perfusion and stress echocardiography are excellent alternatives when a patient can exercise, while the modalities of myocardial perfusion with dipyridamole and dobutamine stress echo are ideal for those who cannot. It is also important to emphasize the need to indicate pharmacological studies when the patient has complete left bundle branch block or pacemaker, particularly with dipyridamole.

The information gathered by multiple meta-analyses shows a similar diagnostic ability of nuclear medicine studies compared with exercise or pharmacological stress echocardiography, perhaps with a slightly higher specificity of ultrasound studies, which do not expose the patient to radiation. (12-11)

These findings should not be interpreted dichotomously, i.e. "with" or "without" ischemia. In general, we could say that patients with <20% ischemic myocardial segments have the same results as those without ischemia. The risk of AMI or death gradually increases above 20% of ischemic segments, showing a strong association with complications when ischemia affects more than 30% of myocardial segments. (13)

It is important to emphasize that only 24% of patients had ischemia >20%, (13) and that there is evidence indicating that more than 30% of cardiovascular events occur in patients with negative ischemia. (12) Therefore, in order to obtain a better diagnostic yield an adequate selection of patients is necessary.

In conclusion, the indication of preoperative functional tests should follow the general clinical criteria applied in non-preoperative scenarios. For the purposes of this consensus, a suggested methodology to define the clinical/surgical risk and recommendations including the indication of functional tests is seen in section 2.4. Globally, it is recommended to perform functional tests in patients with stable cardiovascular disease who are symptomatic or with low functional class

Recommendations for preoperative indication of functional tests

Class I

None

Class II-a

- 1- Patients with moderate or high clinical/surgical that meet minor criteria of the list, numbered from 1 to 6, as defined in section 2.4. (Level of evidence A)
- 2- Low clinical/surgical risk patients that meet minor criteria of the list, numbered from 1 to 6, who have angina or dyspnea in FC 1-2, or who live with a low FC (less than 4 METs), as defined in section 2.4. (Level of evidence: C)

Class II-b

- 1- Patients with any degree of risk that meet some minor criterion of the list, numbered from 7 to 10. (Level of evidence C)
- 2- Low clinical/surgical risk patients that meet minor criteria of the list, numbered from 1 to 6, who are asymp-

omatic and with good FC (4 METs or more). (Level of evidence: C)

Class III

1- Patients at high cardiovascular risk defined by major criteria. (Level of evidence: C)

2.3.4 Color Doppler echocardiography

Although the information available in the noncardiac surgery scenario is scarce and contradictory, there would be an association between echocardiographic variables such as ventricular systolic and/or diastolic dysfunction, left ventricular hypertrophy and moderate to severe valve disease, and increased risk of perioperative complications. Among these variables, systolic ventricular dysfunction accumulates the highest level of evidence. (14)

There are few studies evaluating the incremental predictive value of echocardiography on clinical risk factors and those attempting to show that the information provided by this method favorably affects perioperative management reducing complications are practically non-existent.

Indication of systematic echocardiography for the assessment of cardiovascular risk in noncardiac surgery is not recommended. Indications must be made based on history, symptoms, physical exam and ECG findings.

Recommendations for preoperative color Doppler echocardiography

Class I

1- Patients with (Level of evidence C):

- Decompensated heart failure.
- History of heart failure without previous echocardiogram or with functional class changes subsequent to its performance.
- Presence of murmur with risk criteria, without previous echocardiogram, or with functional class changes subsequent to its performance.

Class II-a

1- Patients with (Level of evidence C):

- Suspected or confirmed AMI sequel without prior echocardiogram.
- Significant ECG abnormalities not previously assessed by echocardiogram (new Q waves, left ventricular hypertrophy, complete bundle branch blocks, ST-segment abnormalities).

Class III

1- Systematic indication in patients under 70 years with no history of heart failure or AMI, with no grade II or higher murmur, and without significant ECG abnormalities. (Level of evidence: C)

2.4 Evaluation and reporting of clinical/surgical cardiovascular risk

This consensus proposes three stages for assessing clinical/surgical cardiovascular risk:

Step 1: To evaluate **preoperative clinical risk**, in 3 categories: high, moderate and low.

Step 2: To evaluate **risk according to the type of surgery**, in 3 categories: high, moderate and low.

Step 3: To evaluate **clinical/surgical risk** combining the clinical risk defined in step 1 and the risk of surgery defined in step 2, thus obtaining 3 categories: high, moderate and low risk.

High risk (> 5%)	Moderate risk	Low risk (<1%)
- Aortic (surgery and endovascular repair)	- Abdominal, not included in major general	- Breast
- Peripheral vascular	- Carotid endarterectomy	- Endocrine
- Major vascular, other	- Peripheral angioplasty	- Ophthalmologic
- Major thoracic *	- Therapeutic endoscopic procedures	- Minor gynecological
- Major general ø	- Head and neck	- Plastic
- Major neurosurgery	- Major orthopedic ψ	- Minor orthopedic
	- Major urological or gynecological λ	- Minor urological
		- Endoscopic diagnostic procedures
		- Dental

STEP 1: Evaluation of preoperative clinical risk

Major Criteria

- 1- Urgent or emergency surgery
- 2- Recent high risk coronary heart disease (AMI occurrence, acute coronary syndrome or angina in FC 3 or 4 | in the 6 months prior to surgery.)
- 3- Suffering from severe aortic or mitral stenosis

Minor Criteria

- 1- Age >70 years
- 2- Diabetes mellitus
- 3- History of peripheral vascular disease
- 4- History of stable coronary heart disease
- 5- History of congestive heart failure or ejection fraction <40%
- 6- History of stroke
- 7- Suffering from severe aortic stenosis or mitral regurgitation
- 8- Severe COPD
- 9- Active cancer
- 10- Chronic renal failure (creatinine ≥ 2.0 mg/dL)

Preoperative clinical risk categories

A- High clinical risk

- 1- If there is 1 or more major criteria, regardless of the existence of minor criteria
- 2- If there are 2 or more minor criteria

B- Moderate clinical risk

- 1- If there is one minor and no major criterion

C- Low clinical risk

- 1- There is no major or minor criterion

STEP 2: Surgical risk evaluation (death or AMI at 30 days)

*Major thoracic surgery: pneumonectomy, lobectomy, mediastinal tumor resection, major chest wall resection.

⊖ Major general surgery: complex visceral resection, liver, pancreas or kidney transplantation, partial or total colectomy, stomach surgery or other intra-abdominal surgery and major resections of head and neck for non-thyroid tumor

Ψ Major orthopedic surgery: major pelvis or hip surgery, internal fixation of femur, knee replacement, and suprapatellar and infrapatellar amputation (but above the foot)

λ Major urological or gynecological surgery: nephrectomy, ureterectomy, bladder resection, retroperitoneal tumor resection, bladder reduction, radical hysterectomy, prostatectomy or transurethral prostatectomy

STEP 3: Evaluation of clinical/surgical risk and recommendations

A. In the presence of HIGH clinical risk defined by a major criterion, clinical/surgical risk should be considered HIGH for any type of surgery. However, in the presence of LOW risk surgeries, clinical judgment should prevail before continuing with the following recommended behaviors.

Recommendations

- In case of urgent or emergency surgery, proceed to surgery. Preoperative ECG and Doppler echocardiography may be useful for intra- and postoperative management, provided that their implementation does not delay the procedure. Troponin measurements are suggested on days 1 and 2 after surgery, and consultation with the cardiologist within the first 48 hours after surgery.
- In case of recent high risk coronary disease, it is recommended to indicate coronary angiography and eventual revascularization, if not performed so far. If the patient was revascularized, it would be wise to postpone noncardiac surgery until 3 months of the acute episode, except that drug eluting stent placement demand slonger times (see the "special situations" section), and provided that this is not detrimental considering the underlying disease (e.g., cancer).
- In case of severe aortic or mitral stenosis, its resolution is recommended before noncardiac surgery.
- If the clinical criteria for low-risk surgery (or any other risk) has decided not to treat the aforementioned

valve or severe coronary artery disease prior to noncardiac surgery, an appointment with the cardiologist is recommended after surgery to continue with the most appropriate management of the situation.

B. In the absence of major criteria, clinical/surgical risk should be defined according to the clinical risk established by the number of minor criteria and type of surgery according to the following table.

Variable	Low risk surgery	Moderate risk surgery	High risk surgery
Low clinical risk	LOW	LOW	MODERATE
Moderate clinical risk	LOW	MODERATE	HIGH
High clinical risk	LOW	HIGH	HIGH

Recommendations:

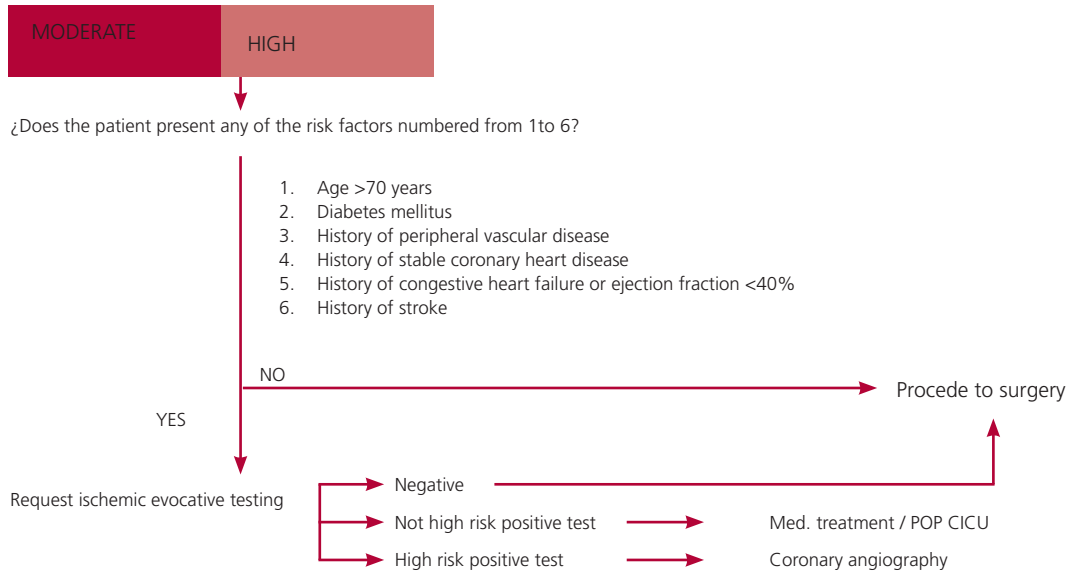
1- Moderate or high clinical/surgical risk

- In the presence of a minor criterion of the list numbered between 1 and 6, functional exercise or pharmacological ischemic evocative testing should be requested.
 - High ischemic risk result according to Table 1. It is recommended to indicate coronary angiography and eventual revascularization before noncardiac surgery.
 - Positive result for ischemia but with no Table 1 high-risk criteria. It is recommended to indicate anti-ischemic medication (including beta-blockers) and aspirin, inform the anesthesiologist and the surgeon (in the risk report), and suggest assessing troponin on postoperative days 1 and 2. Request interconsultation with the cardiologist within the first 48 hours after surgery, and program post-discharge follow-up.
 - Normal result: keep the treatment the patient was already receiving if deemed appropriate and proceed to surgery without further studies. Troponin assessment is suggested on postoperative days 1 and 2.
- If there is only a minor criterion of the list numbered between 7 and 10, or there is no minor criterion, it is recommended to proceed to surgery without further studies. It is advisable to apply appropriate medical criteria for the preoperative treatment of the described comorbidities, such as hydration in renal failure, hemodynamic assessment in valvular regurgitation (it would be useful to have a color Doppler echocardiography obtained within the last 6 months) and review of bronchodilator therapy in COPD.

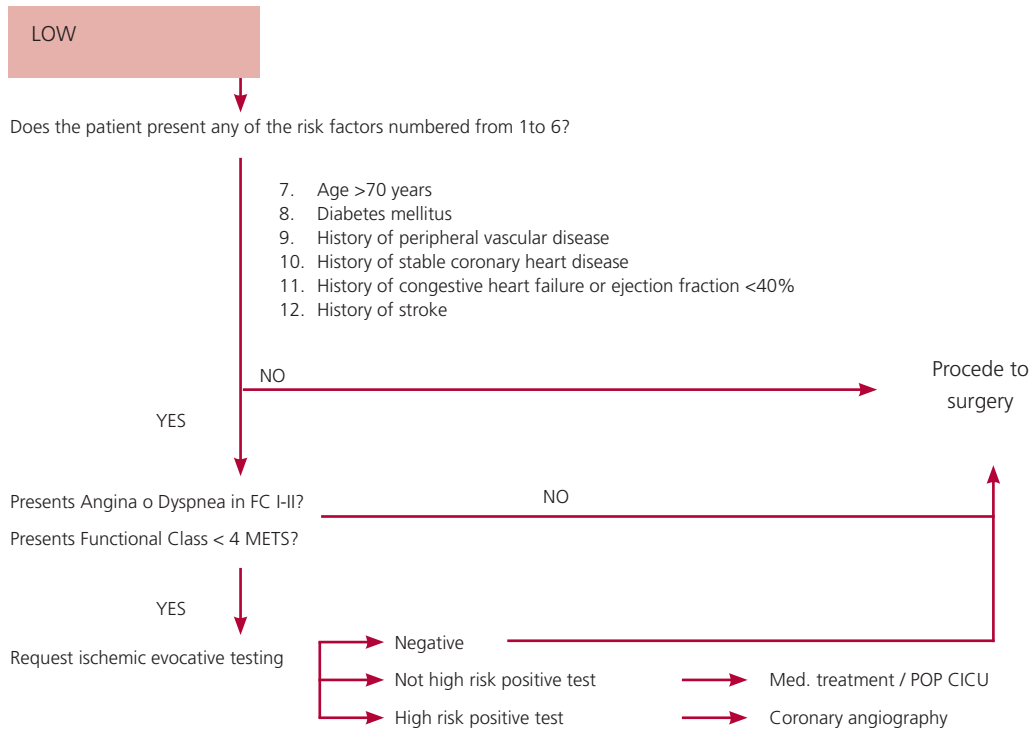
2- If the clinical/surgical risk is Low:

- If the patient has a minor criterion of the list numbered between 1 and 6, and is stable (asymptomatic for angina or dyspnea) with preserved functional capacity (4 METs), he may proceed to surgery without further studies.
- If the patient has a minor criterion of the list numbered between 1 and 6, and has FC 1-2 angina or dyspnea or is asymptomatic but lives with a low FC (less than 4 METs), exercise or pharmacological ischemic evocative testing is suggested.
 - Positive high ischemic risk result according to Table 1. It is advisable to indicate coronary angiography and eventual revascularization before or after noncardiac surgery according to clinical judgment. If revascularization after the procedure is recommended, it is advisable to indicate anti-ischemic drugs (including beta-blockers) and aspirin in the perioperative period and inform the anesthesiologist and the surgeon (in the risk report). If possible, it would be useful to assess troponin on postoperative days 1 and 2 if the patient remains hospitalized, request interconsultation with the cardiologist within the first 48 hours after surgery, and program post-discharge follow-up.
 - Positive result for ischemia with no high-risk criteria according to Table 1. It is advisable to indicate anti-ischemic drugs (including beta-blockers) and aspirin in the perioperative period, inform the anesthesiologist and the surgeon (in the risk report), and suggest troponin assessment on postoperative days 1 and 2 if the patient remains hospitalized. After surgery, program a follow-up appointment with the cardiologist.

Clinical/surgical risk



Clinical/surgical risk



- Normal result: keep the treatment the patient was already receiving if deemed appropriate and proceed to surgery without further studies
- If there is only a minor criterion of the list numbered between 7 and 10, or there is no minor criterion, it is recommended to proceed to surgery without further studies. It is advisable to apply appropriate medical criteria for preoperative treatment of the described comorbidities, such as hydration in renal failure, hemodynamic assessment in valve regurgitation (it would be useful to have a color Doppler echocardiography obtained within the last 6 months) and review of bronchodilator therapy in COPD.

Table 1. High ischemic risk in myocardial ischemic evocative testing

Parameter
One of the following:
1- Emergence of ST-segment changes and/or angina at very low load (<3 METs) or at low HR (<100 bpm)
2- ST-segment depression >5 mm.
1- ST-segment elevation without Q, >2 mm in any area.
2- Presence of complex sustained ventricular arrhythmia.
3- Rapidly progressive angina to 10/10 intensity.
4- Intra-exertion BP drop >20 mm Hg.
5- Transient dilation of the left ventricular chamber
6- Increased lung uptake of radioisotope
7- Ischemic area >20%

Simplified recommendations according to estimated clinical/surgical risk

3. STRATEGIES THAT CAN MODIFY THE OUTCOMES

The experience of the surgical team, the choice of surgical approach and anesthetic technique, and perioperative care may significantly influence immediate and long-term outcomes. Therefore, especially in cases of extreme risk, the intervening surgeon, the anesthesiologist and the cardiologist should discuss the therapeutic possibilities, ranging from less invasive procedures to a non-surgical management of the causal disease. Even, in some occasions, it will be preferable to postpone the surgical decision until completing studies and stabilizing the patient. However, the spirit of this consensus favors “not delaying any noncardiac surgery when there is risk of progress or complications of the underlying disease”, except in cases of very high cardiovascular risk, established by a clearly treatable reason according to available scientific evidence.

The most frequent cardiovascular complications in patients with heart disease undergoing major procedures are related to perioperative myocardial ischemia, frequently caused by surgical stress. For this reason, most measures are aimed at its diagnosis, the anti-ischemic treatment provided and the improvement of conditions which favor its occurrence (anemia, hypovolemia, hypoxia, etc).

3.1 Pharmacological indications in the perioperative period

We performed systematic reviews for each of the perioperative pharmacological indications, selecting available large randomized, observational studies, and determining the quality of the evidence applying GRADE. (4) In this abridged version only the studies used will be mentioned and the conclusions of the respective meta-analyses presented. For more information on the works included, the selection criteria, the evaluation of their quality and the values of each meta-analysis, please refer to the complete version of this guideline.

3.1.1 Aspirin

The balance between the potential benefit and the risk of hemorrhage is crucial in the decision to continue or discontinue aspirin in patients with chronic prescription, or else its perioperative initiation in the face of elevated cardiovascular risk in those who were not previously receiving it.

Our meta-analysis included 23,959 patients, with 1,043 deceased, 698 AMI, 103 stroke and 795 major hemorrhage cases. There were no differences in the rate of death (RR 0.98, 95% CI 0.87-1.10), AMI (RR 1.05, 95% CI 0.70-1.59) and stroke (RR 1.02, 95% CI 0.69-1.50) when ASA versus control were compared in the perioperative period. Conversely, a significant increase in the rate of major hemorrhage was observed (RR 1.24, 95% CI 1.08-1.42) with the use of ASA. Only moderate heterogeneity was observed in AMI (I^2 43%), whereas the rest of the analyses were not heterogeneous.

According to GRADE, the quality of the evidence was high for mortality and hemorrhage, and moderate for AMI and stroke.

In conclusion, there are no benefits with the perioperative use of ASA in terms of death, AMI and stroke, and there is high risk of major hemorrhage. Therefore, it is necessary to interrupt ASA whenever the surgical timing allows it.

The POISE-2 study showed that ASA should be interrupted at least 3 days before, and restarted 7 days after surgery in patients in whom it was previously indicated. (19)

Publications included in the meta-analysis: PEP, (15) Oscarsson et al., (16) STRATAGEM, (17) APAP, (18) and POISE-2. (19)

RECOMMENDATIONS ON THE USE OF ASPIRIN

Class I

1- *In patients receiving chronic ASA (for AMI, stroke, coronary heart disease, and carotid artery or peripheral artery disease) it is recommended to interrupt it 3 or more days before noncardiac surgery, and restart it not before 1 week after the procedure (Level of evidence A)*

Class II-a

1- *In patients with history of percutaneous coronary intervention, either with drug-eluting stents (within 12 months) or bare-metal stents (within 6 weeks) it is recommended to administer low-dose ASA (75-100 mg) during the perioperative period (Level of evidence C)*

2- *In patients who suffered an ACS in the last 12 months and who are not included in the above point, it is recommended, once the risk-benefit evaluation is performed (thrombosis/bleeding), to consider low-dose ASA (75-100 mg) during the perioperative period (Level of evidence C)*

3- *Indicate ASA in the postoperative period to patients undergoing acute ischemic events (AMI or stroke), provided the hemorrhagic risk allows it and with the surgical team agreement (Level of evidence C)*

Class III

1- *Indicate aspirin to patients not receiving it chronically or do not interrupt it in those that take it due to their history (AMI, stroke, coronary heart disease, carotid or peripheral artery disease) and who are not contemplated in the IIa indications (Level of evidence A)*

3.1.2 Betablockers

During the last years several clinical trials and meta-analyses have been published about the indication of betablockers during the perioperative period of noncardiac surgery, which have been incorporated to the clinical guidelines of different scientific societies. However, to date, certain aspects have not been duly clarified on their use in the perioperative period.

Over a total of 9,988 patients, 267 of whom died, our meta-analysis showed a significant increase of overall mortality with betablockers (RR 1.31, 95% CI 1.03-1.66), without evidence of statistical heterogeneity in the results ($I^2=0$). In the case of AMI, over a total of 460 cumulative events, a significant reduction was observed (RR 0.76, 95% CI 0.63-0.91) with betablocker use, whereas in the case of stroke, it was significantly increased (RR 2.21, 95% CI 1.34-3.66) with their indication.. Also, the cumulative analysis of these two events did not evidence heterogeneity.

Evidence classification using GRADE showed moderate quality for the endpoint of mortality at 30 days, and high quality for AMI at 30 days after surgery

This consensus suggests, in patients receiving chronic betablocker treatment, especially those with ischemic heart disease with inducible ischemia, treatment continuation during the perioperative period. In those cases where myocardial ischemia is detected in the preoperative evaluation, we suggest initiating betablockers with dose titration, at least 5 to 7 days before the noncardiac surgery. In both situations, although there is potential risk of intraoperative hypotension, we believe that the medical criterion should guide with caution the indication or interruption of the last dose/s corresponding to the hours prior to surgery, for each individual patient.

Publications included in the meta-analysis: DIPOM, (20) MaVS, (21) BBSA, (22) and POISE. (3)

RECOMMENDATIONS ON THE USE OF BETABLOCKERS

Class I

None

Class II-a

- 1- In patients with chronic prescription of betablockers due to stable coronary heart disease with inducible ischemia, acute coronary syndrome during the last year, hypertension, atrial fibrillation (control of HR) or heart failure, it is recommended to continue their administration during the perioperative period, maintaining or interrupting the last dose/s corresponding to the hours prior to surgery, according to the medical criterion for each individual patient (Level of evidence C)
- 2- In patients not receiving betablockers in whom inducible myocardial ischemia or high response atrial fibrillation is detected during the preoperative evaluation, initiate betablocker treatment with dose titration for at least 5 to 7 days before surgery, and continue their administration during the perioperative period, maintaining or interrupting the last dose/s corresponding to the hours prior to surgery, according to the medical criterion for each individual patient (Level of evidence C)

Class III

- 1- Initiate betablocker treatment on the day of surgery, prior to its initiation, independently of the pathology to be treated (Level of evidence A)

3.1.3 Statins

Our meta-analysis included 3 trials and no significant differences were found with respect to mortality or stroke at 30 days post-surgery, with RR 0.80 (95% CI 0.35-1.84) and 0.56 (95% CI 0.17-1.79), respectively. Use of statins significantly reduced only non-fatal AMI, with RR 0.54 (95% CI 0.34-0.86). Regarding the evidence GRADE rating, we should point out the low quality for each of the endpoints considered.

It is also necessary to emphasize that there is no evidence with respect to statin continuation or interruption in patients using them chronically, as they have been excluded from the studies. For this reason, this consensus favors maintaining their use throughout the perioperative period.

Publications included in the meta-analysis: Durazzo et al., (23) DECREASE III, (24) and DECREASE IV. (25)

RECOMMENDATIONS ON THE USE OF STATINS

Class I

None

Class II-a

- 1- Continue treatment with statins during the perioperative period in patients who receive them chronically (Level of evidence C)
- 2- Indicate statins before noncardiac surgery in patients in whom significant atherosclerotic disease was detected in any territory (coronary, carotid, aortic or peripheral) during the preoperative evaluation, and are candidates for secondary prevention. (Level of evidence C)

Class III

- 1- Indicate statins prior to noncardiac surgery in patients not receiving them chronically and who have no diagnosis of dyslipidemia or significant atherosclerosis in any arterial territory (Level of evidence C)

3.1.4 Renin-angiotensin-aldosterone system (RAAS) inhibitors

The meta-analysis evaluating mortality at 30 days found no benefit with RAAS inhibitors, (RR 1.77, 95% CI 0.44-7.09), and an elevated heterogeneity with $I^2=84\%$. No data were reported on AMI and stroke. According to GRADE, the evidence quality is very low.

A meta-analysis on hypotension induced by these drugs showed a significant reduction of severe hypotension episodes (RR 0.39, 95% CI 0.17-0.92) upon their interruption, with significant heterogeneity ($I^2=80\%$).

Based on the information emerging from other hypotensive drugs, this consensus statement discourages their use on the day of surgery, prior to the intervention. In fact, our meta-analysis observed hypotension with RASS inhibitors, though the studies selected had significant methodological limitations.

Publications included in the meta-analysis: Turan et al. (26) and Railton et al. (27)

RECOMMENDATIONS ON THE USE OF RAAS INHIBITORS

Class I

None

Class II-a

- 1- *Interrupt preoperative ACEI or ARB dose in chronically treated patients on the day of surgery, and resume it as soon as possible during the postoperative period, when hemodynamic conditions are stable (Level of evidence C)*
- 2- *Initiate ACEI or ARB treatment according to medical criterion in patients who in the preoperative evaluation were diagnosed with hypertension or severe ventricular dysfunction, provided they are interrupted on the day of surgery, as stated in 1 (Level of evidence C)*

Class III

- 3- *Initiate ACEI or ARB treatment on the day of noncardiac surgery (Level of evidence C)*

3.1.5 Calcium blockers

The meta-analysis showed that use of calcium blockers did not reduce mortality (RR 0.59, 95% CI 0.17-2.02) or AMI (RR 0.19, 95% CI 0.02-1.68) at 30 days post-surgery, with no observed heterogeneity.

According to GRADE, there is scarce and low quality evidence on the use of calcium blockers in the perioperative period of noncardiac surgery, and therefore we cannot develop specific recommendations. However, extrapolating pathophysiological concepts observed with other hypotensive drugs (ACEI, ARBs and beta-blockers), and considering the trend towards hypotension observed with calcium blockers in the scarce existing evidence, this consensus statement recommends not taking them on the day of surgery, prior to the intervention.

Publications included in the meta-analysis: Amar et al., (28) Godet et al., (29) Retamal et al., (30) Van Mieghem et al. (31) and Caramella et al. (32)

RECOMMENDATIONS ON THE USE OF CALCIUM BLOCKERS

Class I

None

Class II-a

- 1- *In patients receiving chronic calcium blockers, continue their administration during the perioperative period, interrupting, only on the day of surgery, the dose prior to the intervention (Level of evidence C)*
- 2- *Initiate treatment with calcium blockers in patients with inducible myocardial ischemia or strong suspicion of coronary vasospasm during the preoperative evaluation, interrupting, only on the day of surgery, the dose prior to the intervention, and resuming it during the perioperative period (Level of evidence C)*

Class III

- 3- *Initiate calcium blockers in the preoperative period of noncardiac surgery in patients not receiving them chronically, starting on the day of surgery, prior to the intervention (Level of evidence C)*

3.1.6 Anticoagulants

Patients with chronic administration of either classic (acenocoumarol, warfarin) or new (dabigatran, rivaroxaban, apixaban) oral anticoagulants, should consult a hematologist specialized in coagulation, at least 5 days before surgery, to receive indications on the interruption, possible substitution therapy and anticoagulation resumption.

3.1.7 Infective endocarditis prophylaxis

Since currently there is a great scientific debate on infective endocarditis prophylaxis, and this aspect has not

been one of the main objectives of this consensus, we suggest the reader to refer to clinical guidelines published on this topic in the last years. (33, 34)

3.1.8 Venous thromboembolism prophylaxis

Please refer to the 2009 Thromboembolic Disease Consensus Statement of the Argentine Society of Cardiology. (35)

3.2 Indication for coronary angiography and prophylactic coronary revascularization

The burden of coronary heart disease is a powerful risk predictor. The surgical setting (inflammation, hypoxia, hypercoagulability) may promote plaque rupture followed by thrombosis and vasospasm, mainly in non-significant lesions, or it may trigger ischemia in pre-existing fixed lesions, leading to infarction in the context of tachycardia, hyper or hypotension, anemia or hypoxemia.

A meta-analysis of the most outstanding publications was performed to analyze the importance of coronary angiography and the possibility of prophylactic coronary revascularization. The following studies were included: CARP, (36) Monaco et al., (37) and Illuminati et al. (38) The DECREASE-V study (39) was excluded due to the recent banning by the Erasmus University. The three trials collectively included 1,144 patients, evidencing no significant differences in mortality (RR 0.63, 95% CI 0.13-3.09), AMI incidence (RR 0.50, 95% CI 0.11-2.24), or stroke (RR 0.79, 95% CI 0.21-2.97) at 30 days post-surgery. Heterogeneity was significant for death and AMI (I² 67% and 66%, respectively), given by the different methodological characteristics of the studies.

In conclusion, based on limited and low quality evidence, it can be speculated that revascularization of severe coronary lesions does not improve the risk of suffering perioperative ischemic complications, compared with the conservative treatment adopted prior to noncardiac surgery, in patients with stable coronary heart disease.

Regarding “unstable” patients, the VISION trial demonstrated that high risk “recent” coronary heart disease, defined as unstable angina, AMI or FC 3-4 angina during the last 6 months, was an independent predictor of death at 30 days after noncardiac surgery. (2) Conversely, stable coronary heart disease was not an independent predictor of death, supporting the concept that severe lesions do not represent the main mechanism leading to perioperative AMI, and therefore their revascularization should not be mandatory prior to noncardiac surgery.

Recommendations to perform coronary angiography and prophylactic coronary revascularization

Class I

- 1- In patients with “recent high risk coronary heart disease” (acute coronary syndrome or FC 3-4 angina in the last 6 months) who will undergo intermediate or high risk noncardiac surgery, and have no prior coronary angiography or coronary revascularization. (Level of evidence C)
- 2- In patients with severe valve disease and concomitant coronary artery disease, in whom valve disease treatment is planned prior to noncardiac surgery. (Level of evidence C)

Class II-a

- 1- In patients with functional tests indicative of high ergometric risk (Table I) or with pharmacological tests (stress-echo, gamma camera) evidencing extensive ischemia (Table I), who will undergo intermediate or high risk noncardiac surgery, provided the latter can be postponed for to 6-12 weeks (considering exclusive use of bare-metal stents), without risk of progression or complication of the underlying disease. If the noncardiac surgery can be postponed between 6 and 12 months without damage, then drug-eluting stents may be considered in the case of percutaneous coronary intervention. (Level of evidence C)
- 2- In patients with multislice CT scan showing severe left main coronary artery stenosis (Level of evidence C)

Class II-b

- 1- In patients with functional or pharmacological tests detecting myocardial ischemia but without the high risk criteria described in Table I (Level of evidence C)

Class III

- 1- In patients with or without stable coronary heart disease in FC 1-2 without prior ischemia detected by functional or pharmacological tests. (Level of evidence C)

2- In clinically stable patients with severe coronary heart disease established by multislice CT scan (excluding severe left main coronary artery stenosis) without prior ischemia detected by functional or pharmacological tests. (Level of evidence C)

3- In patients whose noncardiac surgery may not be postponed for more than 6 weeks due to risk of progression or complication of the underlying disease. (Level of evidence C)

3.3 Perioperative monitoring

There is evidence indicating that most perioperative infarctions are asymptomatic and that postoperative myocardial injury detected by biomarkers has an adverse prognostic value. (2, 40, 41)

The Myocardial Injury after Noncardiac Surgery (MINS) entity has been recently defined and is represented by ischemic troponin T elevation during the early postoperative period, not requiring presence of symptoms or ECG ischemic abnormalities. MINS, adjusted by preoperative and postoperative risk variables, was shown to be an independent predictor of death at 30 days, reaching 34% of the population attributable risk (PAR)

According to this evidence, it would be advisable to perform troponin dosage in the first 2 or 3 postoperative days in noncardiac surgeries performed in subjects with, at least, increased cardiovascular risk. The cause of elevated troponin should be investigated, the most frequent being myocardial ischemia, followed by sepsis and pulmonary embolism. In case of myocardial injury of assumed ischemic etiology, it is minimally suggested to correct the potential causes of hypoxia, anemia, tachycardia, hypertension, pump failure, etc., and evaluate the need for aspirin, betablockers and statins, as in the non-operative context. Additionally, avoiding early discharge and performing intensive monitoring during 24 to 48 hours could also be a sensible measure due to the higher risk of short-term death.

4. SPECIFIC CLINICAL SITUATIONS

4.1 Heart valve diseases

A murmur detected in the presurgical evaluation should alert on the presence of heart valve disease. Its evaluation, as well as that of ventricular function, justifies color Doppler echocardiography, especially prior to intermediate and high risk surgeries.

4.1.1 Aortic stenosis

In the presence of severe symptomatic aortic stenosis, an elective surgery should be postponed or cancelled until aortic valve replacement is performed, provided this decision does not significantly worsen the underlying disease in elective surgery, according to adequate clinical/surgical criteria.

When the risk of the valvular procedure is higher than that of noncardiac surgery, or the patient refuses to undergo the procedure, or it is not advisable to postpone the noncardiac intervention until after the valvular surgery, an option could be to perform a percutaneous balloon valvuloplasty or a percutaneous valve implantation, and proceed with the noncardiac surgery when this is possible. The remaining option is to perform the noncardiac surgery despite the severe aortic stenosis, accepting the increased risk.

Asymptomatic patients with severe stenosis pose a problem for which there are divergent opinions, although most recommend the preoperative resolution of the heart valve disease due to the risk of sudden death, heart failure and acute pulmonary edema associated with general anesthesia or the intervention itself. Considering that a number of patients are "pseudo-asymptomatic" by self-limitation, an exercise stress test is recommended, whenever possible, to assess functional reserve and symptoms. (42)

4.1.2 Mitral stenosis

Non-severe mitral stenosis is usually well tolerated, whereas severe mitral stenosis justifies valvuloplasty or prior surgery in patients who will undergo moderate or high risk surgeries. The possibility of a percutaneous procedure (valvuloplasty) seems advisable, provided it is suitable. (42)

4.1.3 Aortic and mitral regurgitation

Chronic heart valve diseases due to volume overload are usually well tolerated, particularly in patients with preserved systolic function. The decrease in heart rate tends to increase regurgitation and ventricular diameters, whereas tachycardia is better tolerated. It is recommended to establish the etiology of mitral regurgitation, as the risk is higher when the origin is ischemic-necrotic. (42)

Heart valve prostheses:

Patients with normally functioning prostheses should only require guidance on the prophylaxis against bacterial endocarditis and anticoagulation control. Patients with high thromboembolic risk should continue with intravenous or subcutaneous heparin until 6 to 12 hours before the procedure and resume it in the early post-

operative period. Nevertheless, this consensus statement recommends a visit to the hematologist before surgery so that all the indications concerning coagulation management are carried out. In case of prosthetic dysfunction, each case in particular should be evaluated according to its etiology and severity.

4.3 Cardiac arrhythmias

The presence of cardiac arrhythmia is no contraindication per se to perform noncardiac surgery. If the arrhythmia can worsen the clinical status of the patient (for example, due to heart failure secondary to atrial fibrillation of high ventricular response), the procedure should be prevented until usual measures in the non-surgical context are installed to control the arrhythmia and reduce risks. Regarding chronic antiarrhythmic medication (amiodarone, flecainide, propafenone, etc.) there is no reason or evidence pointing to their systematic interruption.

Anticoagulation management for specific arrhythmias should follow the surgeon's criteria (according to the type of surgery and the associated bleeding risk) and the hematologist's opinion, who will indicate the postponement times depending on the anticoagulant used, or else the reversal of anticoagulation, and if necessary, the indication as bridge of a plan with shorter half-life anticoagulants.

4.2.1 Patient with arrhythmia detected at the presurgical evaluation

As previously mentioned, only a decompensated arrhythmia can postpone a surgery. The detection of a rhythm disorder should guide the diagnosis and treatment of an underlying heart disease, similarly to the non-surgical context; thus, the reader should refer to the corresponding consensus.

Advanced and/or symptomatic conduction disorders normally do not represent great risk. Preoperative pacemaker implantation follows the same general recommendations as in the non-surgical context. A transient pacemaker is indicated in patients who must receive a permanent pacemaker that, due to the surgical urgency, could not be previously implanted. For further information, please refer to urgent cardiac stimulation guidelines.

4.3 Heart failure

History of heart failure (HF) or cardiomyopathy is associated with increased perioperative risk in noncardiac surgery. Both the RCRI score as the VISION trial established HF as an independent predictor of perioperative risk. (2, 6)

Preoperative clinical stability in patients with ventricular dysfunction has a favorable prognostic impact compared with the presence of decompensated HF during the preoperative evaluation. In this case, all elective surgeries should be postponed to treat and stabilize the patient.

Ventricular function assessment is recommended, in case this has not been recently done. In this sense, Doppler echocardiography, in addition to ventricular function data, provides complementary structural information.

As general concept, it can be established that systolic function indices are a good complement of the clinical history and physical exam, but their systematic evaluation in patients without history of HF or other clinical findings should not be the initial approach to define risk. Neither would it be necessary in patients with history of HF who are currently stable and with ventricular function data obtained within the last year.

4.4 Coronary artery stents and double antiaggregation therapy

Angioplasty with stent placement is currently the most used myocardial revascularization strategy. Although it is a safe procedure, it is not exempt from complications, as the dreaded stent thrombosis, whose most important predictor is premature interruption of dual antiplatelet therapy, followed by the need for noncardiac surgery. (43-44) In turn, surgery per se increases the risk of thrombosis by generating a prothrombotic state, as previously detailed.

This establishes a difficult to manage subgroup where surgery cannot be postponed and the minimum times of dual antiplatelet therapy have not been accomplished, which would be 4 to 6 weeks for bare-metal stents and 6 months to 1 year for drug-eluting stents. (45)

There is no solid evidence supporting the conducts to assume in patients who will be subjected to noncardiac surgery during the period in which dual antiplatelet therapy is indicated after angioplasty.

It is important to emphasize that there are new treatments, as bridge therapy with reversible drugs or with short half-life, or the new drugs still under study which might have an important role in these circumstances. However, there is still no firm evidence supporting their use, and hence no recommendation can be provided. (45)

Ideally, when there is no choice but to perform the surgery and interrupt one or both antiplatelet therapies, it would be prudent, whenever possible, to perform it in centers with 24-hour available hemodynamic facilities. In case of stent thrombosis, primary angioplasty is the treatment of choice, either for the degree of reperfusion achieved, as for the lower bleeding risk compared with thrombolytic drugs.

In brief, existing evidence, though weak, seems to demonstrate that the greater impact on the decrease of

major adverse events is given by the time elapsed between angioplasty and the surgical procedure, with an inverse relationship evidencing that with longer times the incidence of events is lower.

Conflicts of interest

None declared. (See author's conflicts of interest forms in the web / Supplementary Material).

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