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Cardiovascular Evaluation in General Thoracic Surgery

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INTRODUCTION

In the setting of general thoracic surgery a preoperative cardiovascular risk evaluation is to be considered a mandatory and essential assessment. Cardiac complications are the second most common cause of perioperative morbidity and mortality in the thoracic surgical population. The risk of major postoperative cardiac complications is about 2% to 3% after lung resection[1,2] and, though there are less data, thoracic surgery for noncancerous lesions seems to carry a similar risk [3]. Most frequent complications are arrhythmias and postoperative myocardial infarction. As the majority of pulmonary resection patients are over 60 years old and have a history of cigarette smoking, they represent a potentially high-risk population or may already have a prior diagnosis of heart disease.

The risk of perioperative cardiac complications after non-cardiac surgery is mainly dependent on surgery-related factors, patient-related factors and urgency level of the intervention. Tissue injury and perioperative management generate a stress response : fasting, blood loss, perioperative fluid shifts, autonomic dysregulation and/or hemodynamic derangement (also favoured by more invasive anaesthetic techniques), development of an hypercoagulable state (with secondary potentially increased coronary thrombogenicity or thromboembolic events), change in body core temperature all contribute to stress response and to increase myocardial oxygen demand. Moreover Post-operative lung "adaptations" and complications may themselves generate a ventilation-perfusion mismatch (atelectasis and mucus plugging, altered diffusing capacity, pain-induced hypoventilation, decreased lung compliance), leading to respiratory failure or increased work of breathing with possible consequent imbalance between myocardial oxygen demand and supply which may act as a significant trigger for new-onset arrhythmias, myocardial infarction and may precipitate heart failure.

The role of the cardiologist is to establish the risk of cardiac complications, to suggest adequate cardiac perioperative support (if needed) to reduce the risk or to treat the complications and to critically reassess the patient in a long-term view (preventive cardiology).

PREOPERATIVE CARDIOVASCULAR EVALUATION

When facing a thoracic surgery patient the cardiologist consultant has to answer some questions : Is the intervention an emergency/urgency or is elective? – Is the intervention major or non major thoracic surgery? - Is necessary a cardiac stress testing or a rest evaluation of left ventricular function? - Should the patient undergo a preoperative coronary angiography? - Who should have no testing at all?

The risk of perioperative cardiac complications after non-cardiac surgery is mainly dependent on surgery-related factors, patient-related factors and urgency level of the intervention. Surgery itself carries an established risk of cardiovascular complications (only no intervention involves no perioperative risk!). The European society of cardiology (ESC) [4] and the preceding American heart association/American College of Cardiology (AHA/ACC) [5] guidelines on noncardiac surgery identify three groups according to their estimated 30-day cardiac event rates (cardiovascular death and myocardial infarction) : - low risk (< 1%); – intermediate risk (1-5%); - high risk (> 5%). According to this cardiovascular risk stratification thoracic surgery has to be considered intermediate risk surgery for less invasive procedures (thoracoscopy) and less radical interventions (lobectomy) and high risk surgery for more invasive procedures (pneumonectomy, lung transplantation). Recently the last AHA guidelines [6] has suggested to differentiate interventions in low risk and high risk if expected major adverse cardiovascular events (MACE) are respectively < 1% and > 1%.

Starting with this surgery-related default risk, which patient should undergo specialized preoperative cardiologic testing?

Thoracic societies guidelines all agree to use cardiac risk scores as a screening tool to select patients needing preoperative specialized cardiologic evaluation and/or testing. AHA/ACC and ESC guidelines [4-6] recommend to use Revised Cardiac Risk Index (RCRI) as the preferred risk cardiac scoring tool in noncardiac surgery. RCRI is a validated tool which includes 6 factors with approximately equal prognostic importance (Table 1) [7]. A RCRI ≥ 2 identifies patients with major cardiac complication rates who should undergo additional tests. Therefore, the RCRI has a pivotal role in preoperative decision-making. However, RCRI was originally developed in a generic surgical population including only a limited number of thoracic surgery patients (only 12%); To get through these limitations, Brunelli et al. [1,2] validated a recalibrated RCRI (called the Thoracic-RCRI,Th-RCRI) in a lung resection population showing a good discrimination ability. The Th-RCRI consists of 4 parameters with different prognostic importance : pneumonectomy, 1.5 points; previous ischemic heart disease, 1.5 points; previous stroke or transient ischemic attack, 1.5 points; creatinine > 2 mg/dl, 1 point). Thus, patients with RCRI > 2 and/or Th-RCRI > 1,5 or any cardiac condition requiring medication or a recent/suspected diagnosis of active heart disease or limited exercise capacity (inability to climb two flight of stairs), should be sent for cardiologic consultation.

Medical history for risk factors, clinical examination, drug history and resting 12-lead electrocardiogram should be performed in virtually all thoracic surgery patients. In the field of urgent surgery there is no time to actuate cardiovascular lowering-risk strategies and patients should proceed to intervention. The presence of unstable cardiac conditions (Table 2) requires multidisciplinary discussion (surgeon, anesthesiologist, cardiologist) to individuate the better timing of interventions (cardiac and noncardiac) for each patient.

Determination of functional capacity is the next basic step in patient evaluation; as indices of functional status decrease (i.e. physical deconditioning due to sedentary lifestyle or chronic diseases) greater are perioperative risk of complications and worse is long-term prognosis. Functional status is measured in metabolic equivalents (METs). One MET is a unit of resting oxygen uptake. Previous exercise tests or patient interrogation about daily living activities usually allow an estimate of preoperative functional status [8,9]. A poor functional capacity (≤ 4 METs) identify patients with an increased incidence of perioperative cardiac events. As aforementioned thoracic surgery is an intermediate to high risk procedure. In patients with preoperative good functional capacity (> 4 METs) no further cardiac testing is necessary because in this subset of patients the prognosis is excellent, even in the presence of stable heart disease or risk factors [10]; to reduce the risk of complications a low-dose betablocker may be started in patients with known ischemic heart disease and an angiotensin converting enzyme inhibitor should be considered in patients with heart failure. Assessment of left ventricular function may be considered for patients with ≤ 2 risk factors and poor or unassessable functional capacity. In patients with risk factors (≥ 3) and poor or unknown functional status a pharmacologic stress testing should be performed. Coronary revascularization (coronary artery by-pass graft, CABG, or percutaneous

coronary intervention, PCI) should be reserved to patients with overt signs of extensive inducible ischemia but individualized perioperative management is necessary in order to weigh benefit of the surgical procedure against the predicted adverse outcome of severe coronary artery disease.

Table 1: Clinical risk factors according to the Revised Cardiac Risk Index [7].

• 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 m^2
• Diabetes mellitus requiring insulin therapy
• High-risk type of surgery

Table 2: Unstable cardiac conditions.

• Unstable angina pectoris
• Acute heart failure
• Significant cardia carrhythmias
• Symptomatic valvular heart disease
• Recent myocardial infarction and residual myocardial ischemia

POST OPERATIVE CARDIAC COMPLICATIONS

Arrhythmias

Cardiac arrhythmias are by far the most common cardiac complication after thoracic surgery. The main rhythm disturbances are supraventricular arrhythmias (SA), being ventricular ones less common and prognostically not relevant. Altough frequent, only a minority of SA requires treatment. Atrial fibrillation (AF) is the most concerning SA with a reported incidence between 5% and 22%, generally peaking between 2nd and 4th post-operative days and often requiring medical intervention [11-13]. Atrial flutter should be considered as AF-equivalent. Perioperative AF is associated with higher morbidity, worse short- and long-term survival and longer in-hospital stay [11-16]. Postoperative AF has been associated with older age, male sex, preoperative known history of cardiac disease or history of AF, limited pulmonary reserve, major bleeding, anesthesia; magnitude of pulmonary resection (i.e. less incident in lung transplant and pneumonectomy versus lobectomy) and esophagus resection are strongly related to post-operative AF [16-20]; on the contrary less invasive procedures (i.e. video-assisted thoracoscopic procedures) carry the lowest risk of post-operative AF. Various other medical conditions like pericarditis, lung embolism, pneumonia can trigger AF. Atrial fibrillation generally may result from an irregular atrial response to alteration in atrial refractoriness, slowing of atrial conduction or may be caused directly by multiple functional reentry circuits [21]. AF onset could be favoured by specific factors including electrolyte (in particular hypokalemia) or acid-base disorders, intraoperative

cardiac manipulation, direct cardiac stimulation from perioperative use of cathecolamines or autonomic imbalance from rapid volume depletion, pain, fever, hypo- or hyperglycaemia; surgical handling of lung/esophageal tissues can cause atrial and pericardial irritation or pulmonary veins stimulation (a note site of spontaneous electrical activity that can initiate AF) [22] In new-onset AF the clinician should pay attention to possible pulmonary and cardiac life-threatening complications such as pulmonary embolus, tension pneumothorax and cardiac tamponade. Perioperative AF is often transient and self-limiting. Whenever feasible thoracic epidural anesthesia could act as a non pharmacological prophylactic antiarrhythmic strategy due to its known analgesic effects and its association with decreased sympathetic drive to the heart [23]. The Society of Thoracic Surgeons (STS) [24] guidelines recommend pharmacologic prophylaxis with beta-blockers in patients already beta-blocked before surgery; diltiazem and amiodarone are the drugs of choice for patients not taking beta-blockers before surgery. However amiodarone should be used with caution (not recommended in pneumonectomy, mechanical ventilated patients, significant pre-existing lung disease) and low dosage regimens because of its intrinsic pulmonary toxicity and in order to avoid occurrence of acute respiratory distress syndrome [25]. Magnesium supplementation and/or hypokalemia correction strengthens effectiveness of pharmacological prophylaxis. Once AF has occurred treatment strategies (Figure 1) differ depending on patient's hemodynamic stability. In unstable patients electrically cardioversion should be prompt performed. In stable patients is preferable a rate-lowering strategy unless the arrhythmia is poorly tolerated or AF is ongoing more than 24 hours after initiation of rate control. β-blockers, in particular β1-selective agents, are the best choice for rate control , making sure that moderate-severe chronic obstructive pulmonary disease or active bronchospasms are absent ; diltiazem should be conversely used. Digoxin could be used in combination with β-blockers and diltiazem. In case of rhythm control strategy, amiodarone and flecainide are the drugs of choice (duration of treatment from 1 to 6 weeks postoperatively). Beyond the aforementioned caution of amiodarone, it should be remembered that flecainide is contraindicated in any form of structural heart disease (including ventricular hypertrophy) [26]. Although amiodarone and flecainide are highly effective, in patients with specific controindications for whom rhythm control strategy is indicated, other antiarrhythmic drugs, electrical cardioversion or simple rate control strategy are to be considered. Finally antithrombotic/anticoagulation therapy should be initiated in patients with AF that recurs or persists for more than 48 hours.

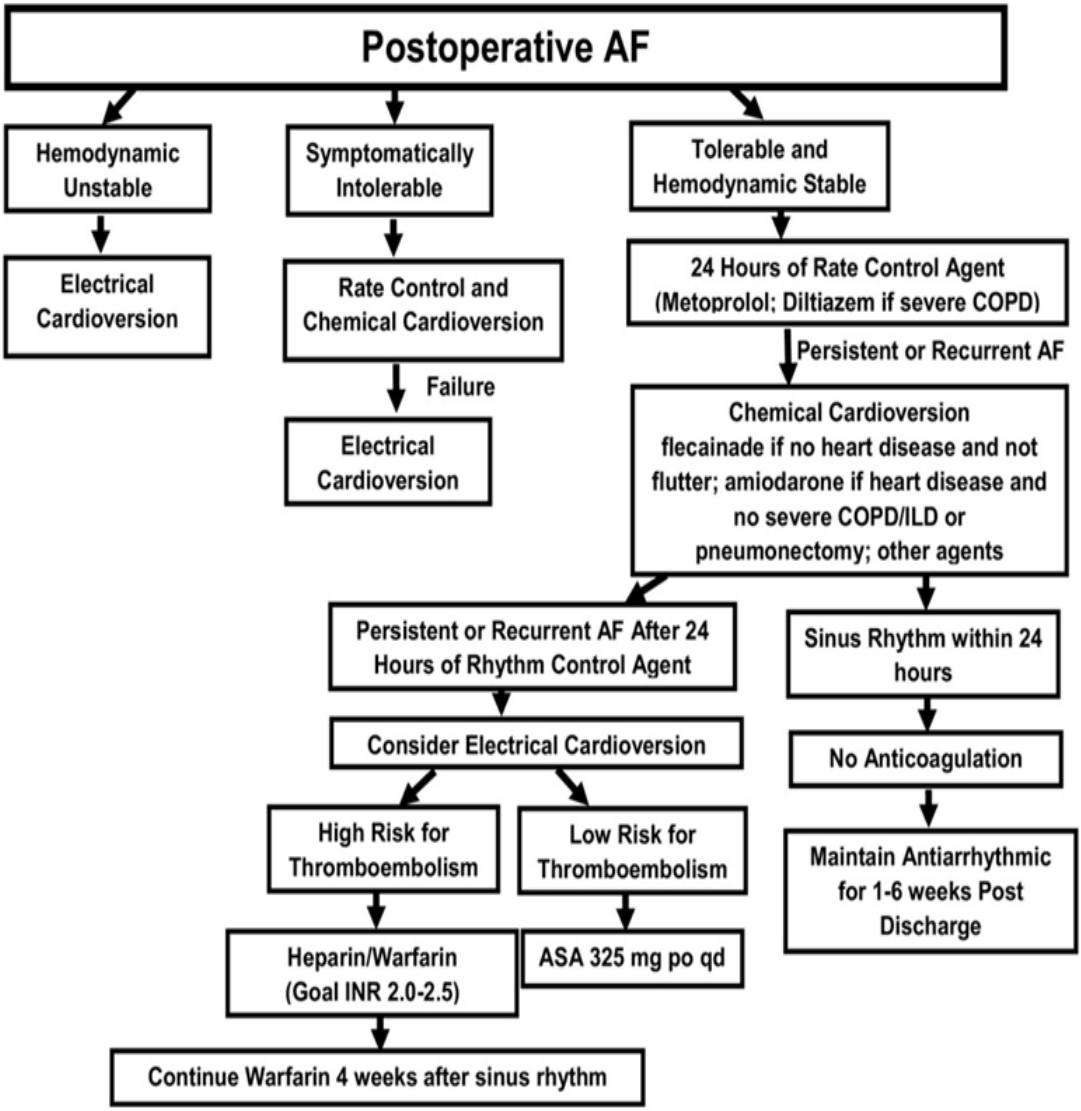

Figure 1: Postoperative atrial fibrillation flowchart proposed by Society of Thoracic Surgeons [24] ASA (acetylsalicylic acid) ; COPD (chronic obstructive pulmonary disease); ILD (interstitial lung disease); INR (international normalized ratio).

Myocardial Ischemia

Acute coronary syndromes after surgery are often a challenging clinical issue. According to third universal definition of acute myocardial infarction (MI) [27], in post-operative scenario we can observe two main types of perioperative myocardial infarction (PMI).

MI type 1 (spontaneous MI)

Spontaneuous MI is characterized by acute thrombosis and occlusion of one or more coronary vessels due to atherosclerotic plaque rupture, ulceration, fissuring, erosion or dissection of a vulnerable plaque; myocardial ischemia can be further worsened by distal microthrombotic embolization and by coronary vasoconstriction induced by underlying endothelial dysfunction or systemic sympathetic activation; increase in luminal shear stress or intraplaque inflammation usually cause plaque rupture. MI type 1 can occur both in patients with known pre-operative severe CAD and patients with non-obstructive CAD or no CAD [28,29]. Some perioperative stressors are believed to contribute to plaque instability:

- Increased levels of circulating cathecolamines (endogen and/or esogen) and cortisol

- Postoperative hypercoagulability and increased platelet reactivity [30,31]

- Increased shear stress favoured by tachycardia, hypertension

MI type 2 (secondary to an ischaemic imbalance)

The perioperative scenery of surgery patients is full of circumstances that can lead to increased myocardial oxygen demand and reduced myocardial oxygen supply; increased sympathetic activity, postoperative pain, withdrawal of betablockers, hypo- or hypervolemia, arterial pressure instability, pulmonary congestion or atelectasis, all can esitate in tachycardia, increased myocardial wall stress, hypotension, coronary vasoconstriction, anemia, hypoxemia; these phenomena build the pathophysiological basis for ischaemic imbalance [32,33]. However in some patients evidence of plaque rupture has been observed in reports with anatomical-pathological correlation. Although obviously worsening ischaemia imbalance, obstructive CAD it's not a necessary prerequisite (Figure 3) [34-36].

In the setting of PMI type 1 the patient is generally symptomatic and electrocardiogram shows ST-segment elevation in the site of coronary obstruction, while PMI type 2 patients can be even asymptomatic and electrocardiogram generally shows ST-segment depression or no ST-segment abnormalities. Numerous clinical studies have shown that PMI occurs most often in the first postoperative days, is asymptomatic and has no ST-segment elevation, being mostly PMI type 2 [32,33;37]. Neverthless pathophisiology of PMI it's not yet well understood and mechanisms of both PMI type 1 (plaque disruption) and PMI type 2 (ischaemic imbalance) may take place : although most PMI occur without ST-segment elevation, clinical studies with angiographic and/or anatomical-pathological correlation have shown signs of plaque disruption up to 55% of patients [34-36;38].

PMI affects both early mortality (in-hospital mortality ranges between 3,5% and 25%) and long-term survival [32,39-41]. Troponin levels identify patients with worse short- and long-term prognosis [42-44]. However the major challenge in PMI is diagnosis. As aforementioned PMI is often asymptomatic, moreover chest pain could be even not assessable in sedated and/

or intubated patients or can be misunderstood for post-surgical pain. ST-segment changes should be interpreted in context and with caution because unspecific changes can derive from many perioperative conditions that can be patient-related (i.e. electrolyte dysorders, hypo- or hyperthermia, hyperventilation, patient decubitus or dressings), surgery-related (i.e. pericarditis, pleural or pericardial effusion, chest trauma), drugs-related (i.e. digitalis effect, antiarrhythmic drugs) or even nurse-related (i.e. different electrocardiogram leads positioning). Also markers of myocardial necrosis require critical interpretation; troponin should be the marker of reference because CK-MB loses sensitivity and specificity in surgery [4]. Neverthless raised troponin levels are observed in many other pathologic conditions (i.e. shock, renal failure, heart failure, sepsis, tachyarrhythmias, critally ill patients). Therefore isolated elevation (in absence of symptoms or dynamic ST-segment changes) of troponin should raise doubt about the diagnosis of PMI. In order to identify occurrence of PMI, postoperative daily electrocardiogram and daily troponin measurement both before and 48-72 hours after surgery may be considered in patients at intermediate to high cardiovascular risk such as thoracic surgery patients [4]. Once PMI is identified all causes of ischaemia imbalance must be treated : tachycardia, hypo- or hypertension, anemia, pain, bleeding. High risk of bleeding generally restricts antithrombotic and/or antiplatelet therapy and coronary intervention to selected cases (evidence of ST-segment elevation, cardiogenic shock or rhythm instability).

Cardiac Herniation

Acute herniation of the heart is a rare but often lethal complication of thoracic surgery; mortality rate usually exceeds 50%, even if managed promptly. Cardiac herniation generally occurs in the immediate postoperative period and almost always in the first 24 hours [45-47]. The basis for this fearsome complication is herniation of the heart through a pericardial defect or dehiscence of a pericardial prosthesis suture and into the empty pleural, typically after a pneumonectomy; the side of the pneumonectomy influences the clinical picture; right-sided herniation induces a sudden torsion of the great vessels with consequent impairment of the venous return to the heart, hesitating in a superior vena cava syndrome with hypotension, cyanosis and shock; in left-sided herniation cardiac rotation is less significative and herniated myocardium is constrained by the edges of pericardial defect, leading to myocardial ischaemia, arrhythmias and/or ventricular outflow obstruction. Coughing, changes in patient position, vomiting or extubation may precipitate cardiac herniation. Primary closure of the pericardial defect or pericardial edges suturing to the myocardium can prevent herniation. Management consists of emergent surgery to reposition the heart and close the pericardial defect.

Right Ventricular Failure

Postoperative right ventricular dysfunction is common after lung resection surgery. The extent of resection negatively influences right ventricle's function [48-50]. The main pathophysiological mechanism advocated is augmentation of pulmonary pressures and resistance or rather right-

ventricular afterload. Adaptation to increased afterload is possible through dilation of ventricle chamber; this allows the right ventricle to reduce wall-tension and oxygen consumption but makes it more preload-dependent [48-50]. Clinical signs of right-heart failure together with echocardiographic evidence of right ventricle dilation and increased estimated pulmonary pressures should lead to targeted treatment. Management consists of preload optimization, support of right ventricular function with inotropic drugs (such as dobutamine and milrinone), decrease of right-ventricular afterload (i.e. with inhaled nitric oxide).

Right to Left Shunt

Patients with patent foramen ovale are at risk of developing right to left shunt due to increase of pulmonary pressure and/or a change in cardiac geometry after lung resection (the shunt increases most after a right pneumonectomy) [51-53]. Platypnea orthodeoxia syndrome (dyspnea and hypoxemia in the upright position) is the main clinical presentation and it tipically occurs late after surgery (within one year) [51]. The mechanism underlying positional nature of shunting is not yet understood. Investigations like arterial blood gas analysis, transthoracic- or transesophageal echocardiography are generally enough to pose the diagnosis; however integration with cardiac catheterization, nuclear medicine lung scanning or cardiac magnetic resonance could be helpful. Percutaneous or surgical closure of the atrial septal defect is the treatment of choice.

Cardiac Tamponade and Pneumopericardium

Tissue injury, underlying lung disease, comorbidities, infections, all can contribute to pericardial effusion. Rapid development of pericardial effusion can result in cardiac tamponade. In the first postoperative days, when the patient is monitored 24 hours a day, equalization of mean diastolic pressures, rising central venous pressure and hypotension can be observed and raise suspicion of cardiac tamponade. Alternatively in no longer monitored patients unexplained or refractory hypotension not responsive to fluid challenge should suggest further cardiac investigation; arrhythmias like atrial fibrillation or severe bradycardia can occur. Rapid cardiac tamponade can manifest as pulseless electrical activity. A transthoracic echocardiogram is a simple and feasible investigation to individuate and estimate pericardial effusion and cardiac tamponade. Urgent percutaneous or surgical pericardiocentesis is the treatment needed for this complication.

A direct communication between a bronchopleural fistula, the bed of the pulmonary artery and the pericardium can result in pneumopericardium. Clinical features are quite similar to cardiac tamponade due to pericardial effusion. Treatment consists of emergent surgery to discontinue air supply to pericardium.

Pulmonary Embolism

Thromboembolic disease is frequent in general thoracic surgery due to relevant presence of malignancies. Cancer and surgery are known to be risk factors for deep venous thrombosis and

lung cancer belongs to the group of malignancies with the highest incidence rates (up to 7%) [54-56]. In particular adenocarcinoma and nonsmall-cell lung cancer carry an high risk of venous thromboembolism than squamous cell lung carcinoma and small-cell lung carcinoma [57,58]. After pneumonectomy thromboembolism can rarely originate from the pulmonary artery stump or may occur because of cancer invasion of the main pulmonary artery, right or left atrium. Main treatment strategy is prevention giving the patient deep venous thrombosis prophylaxis with unfractionated heparin, low molecular weight heparin or factors Xa inhibitor. Diagnosis of deep venous thrombosis is clinical (tumor, rubor, calor, pain of a leg) and can be further confirmed with venous echocolordoppler. Pulmonary embolism is tipically characterized by dyspnea, hypoxemia and hypocapnia, hypotension, chest pain or tightness; it should be noted that in postoperative thoracic patients onset may could be insidious due to concurrent medications (analgesic and/or sedative drugs) , residual lung function. A massive pulmonary embolism may provoke severe hypotension and hemodynamic instability and life-threatening arrhythmias (i.e. atrial fibrillation, atrioventricular blocks, pulseless electrical activity). Once deep venous thrombosis occurred management consists of anticoagulation; in hemodynamic unstable patients emergency embolectomy or fibrinolysis should be considered.

Intra Operative Cardiac Monitoring

Complications may occur during the intervention. Prevention and prompt management of cardiac complications require some intraoperative measures; continuous electrocardiographic monitoring, possibly using multiple leads helps to identify arrhythmias and to detect myocardial ischaemia. Particular attention should be paid during cardiac manipulation. Pulse oximetry consents rapid assessment of blood oxygenation. Invasive and continuous measurement of arterial blood pressure (through catheterization of a peripheral artery) and central venous pressure (CVP) allows immediate identification of sudden changes in hemodynamics as in the case of bleeding or cardiac compression during surgical manipulations. Moreover insertion of a large caliber multiple-lumen CVP catheter allows rapid insertion of a transvenous pacemaker if necessary, insertion of a pulmonary artery catheter (to estimate pulmonary capillary wedge pressure and cardiac output) and infusion of active drugs.

Transesophageal echocardiography (TEE) is useful for intraoperative evaluation and monitoring of cardiac chambers, to estimate ventricular and valvular function and to evaluate wall motion abnormalities. TEE is generally used during lung transplantation but its use in general thoracic surgery is often limited or performed as needed. TEE can reveal compression or infiltration of cardiac structures with more sensitivity than transthoracic echocardiography.

CONCLUSION

General thoracic surgery patients constitute a population with increased cardiovascular risk due to their high prevalence of cigarette smoking and generally older age. Cardiovascular evaluation in general thoracic surgery has to be made in a relevant number of patients. However

advanced cardiologic evaluation (i.e. echocardiogram, stress testing) and prior to surgery coronary revascularization is generally restricted to a minority of patients in whom overt signs of extensive inducible ischemia is identified. Individualized and multidisciplinary management (cardiologist, surgeon, anesthetist) is necessary to identify the best preoperative clinical strategy in terms of risks and benefits. Perioperative monitoring with daily electrocardiogram and troponin measurement is helpful to identify both dysrhythmias (the main postoperative complication) and myocardial ischemia, in a population in whom analgesic drugs and/or sedation could mask or relieve chest pain. In most cases of PMI correction of all potential causes of ischaemia imbalance represents the main strategy together with an individualized medical therapy weighing ischaemic and bleeding risks; coronary intervention should be restricted to selected cases (haemodynamic instability, life-treatening arrhythmias, evidence of ST-segment elevation).

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