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Review Article

Impact of metabolic syndrome in surgical patients: should we bother?

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Abstract

Clinicians inevitably encounter patients who meet the diagnostic criteria for the metabolic syndrome (MetS); these criteria include central obesity, hypertension, atherogenic dyslipidaemia, and hyperglycaemia. Regardless of the variations in its definition, MetS may be associated with adverse outcomes in patients undergoing both cardiac and non-cardiac surgery. There is a paucity of data concerning the anaesthetic management of patients with MetS, and only a few observational (mainly retrospective) studies have investigated the association of MetS with perioperative outcomes. In this narrative review, we consider the impact of MetS on the occurrence of perioperative adverse events after cardiac and non-cardiac surgery. Metabolic syndrome has been associated with higher rates of cardiovascular, pulmonary, and renal perioperative events and wound infections compared with patients with a non-MetS profile. Metabolic syndrome has also been related to increased health service costs, prolonged hospital stay, and a greater need for posthospitalization care. Therefore, physicians should be able to recognize the MetS in the perioperative period in order to formulate management strategies that may modify any perianaesthetic and surgical risk. However, further research is needed in this field.

Key words: anaesthesia; metabolic syndrome; postoperative outcome; surgical procedures

Editor's key points

- In this narrative review, the authors describe the metabolic syndrome, outlining its impact and its recognition.
- They outline management strategies and call for further research in this area.

Metabolic syndrome (MetS) comprises a group of risk factors that include high blood pressure, atherogenic dyslipidaemia (high triglyceride and low high-density lipoprotein–cholesterol concentrations), high fasting glucose concentration, and central obesity.[1] Metabolic syndrome is associated with an increased risk for cardiovascular disease and type 2 diabetes mellitus.[2] Moreover, MetS has been associated with an increased risk of non-cardiac vascular diseases, including stroke, carotid artery disease, peripheral artery disease, chronic kidney disease, atherosclerotic renal artery stenosis, and abdominal aortic aneurysms.[2]

The definition of MetS relies on clinical and laboratory criteria and has been the subject of controversy.[3] The first attempt to define MetS came in 1998 from the World Health Organization.[1] Insulin resistance was suggested to be the major underlying risk factor and a prerequisite for the diagnosis.[1] Nowadays, a generally accepted definition is the one that came from the American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement.[4] It involves the following five diagnostic criteria, any three of which constitute the diagnosis of MetS: increased waist circumference, elevated triglycerides, reduced high-density lipoprotein–cholesterol,[5] elevated blood pressure, and elevated fasting glucose (Table 1). Some individuals or ethnic groups (e.g. Asians, especially South Asians) appear to be susceptible to development of MetS at waist circumferences below those presented in Table 1, which mostly refers to populations in industrialized countries.[6] Although the International Diabetes Federation definition initially considered central (abdominal) obesity as a 'sine qua non' risk factor for establishing the diagnosis of MetS, both the International Diabetes Federation and the American Heart Association/National Heart, Lung, and Blood Institute finally agreed that abdominal obesity should not be a prerequisite feature but rather one of the five equally balanced diagnostic criteria of MetS.[6]

Metabolic syndrome has a high prevalence worldwide that may vary according to the set of diagnostic criteria used (current or older).[7] It is more prominent in countries with Western lifestyles, affecting around 34–39% of the adult population in the USA with roughly equal prevalence in men and women.[8] In Europe, approximately one-quarter of the adult population has MetS, while the percentage in Southeast Asia is less than one-fifth, and this can be attributed in part to differences in the median age of Asian and European populations.[9] In China, the prevalence is relatively low in the general population, and in Japan, it varies considerably according to each study.[9]

Table 1 Criteria for clinical diagnosis of metabolic syndrome (at least three are required).[6] *Waist circumference is measured with a tape in a horizontal plane around the abdomen at the superior point of the iliac crest as defined by the National Cholesterol Education Program's Adult Treatment Panel III guidelines

Clinical measure	Categorical cut-off points
Waist circumference* (European, Caucasian, USA, Canada)	≥102 cm in men ≥88 cm in women
Triglycerides	≥150 mg dl^{-1} (1.7 mmol l^{-1}) or On drug treatment for elevated triglycerides
High-density lipoprotein–cholesterol	<40 mg dl^{-1} (1.0 mmol l^{-1}) in men <50 mg dl^{-1} (1.3 mmol l^{-1}) in women or On drug treatment for low high-density lipoprotein-cholesterol
Blood pressure	≥130 mm Hg systolic blood pressure or ≥85 mm Hg diastolic blood pressure or On antihypertensive drug treatment in a patient with a history of hypertension
Fasting glucose	≥100 mg dl^{-1} (5.6 mmol l^{-1}) or On drug treatment for elevated glucose

Metabolic syndrome is considered a constellation of pathophysiological processes. Currently, it is primarily thought to be caused by adipose tissue dysfunction and insulin resistance, which is associated with abnormalities in insulin secretion, receptor signalling, and impaired glucose disposal. Visceral or intra-abdominal fat is also known to secrete free fatty acids and potentially harmful concentrations of cytokines, such as tumour necrosis factor, leptin, resistin, and plasminogen activator inhibitor, which in turn promote insulin resistance.[10 11] They might also initiate a prothrombotic[12] and pro-inflammatory[13] state that has been reported in patients with MetS.[14] High blood pressure and dyslipidaemia are well documented and modifiable risk factors for atherosclerotic vascular disease. It is unclear whether environmental factors, genetic predisposition, or both are also involved. One key feature of MetS is that each diagnostic component may not stand out on its own because it is not markedly abnormal. However, when these relatively minor abnormalities occur together, there is a substantially increased risk of vascular events. The presence of MetS has been associated with a high risk of vascular and metabolic complications (e.g. future development of diabetes mellitus) independently of its individual diagnostic features. Therefore, the identification of subjects with MetS warrants a holistic management of coexisting risk factors, which is considered the preferable strategy rather than targeting any single characteristic of the syndrome independently. While the pathophysiology of MetS is not yet fully understood, there are concerns of an increased perioperative risk because of the co-morbidities associated with this syndrome, which represent a challenge for the anaesthetist.

The aim of this narrative review is to provide an overview of the literature regarding the impact of MetS on perioperative outcomes in patients undergoing cardiac and non-cardiac surgery.

Search methods

We searched MEDLINE up to October 1, 2014 for relevant publications using combinations of the keywords, such as metabolic syndrome, outcome, perioperative complications, surgery, mortality, morbidity, colon cancer, rectal cancer, liver surgery, orthopaedic surgery, total joint arthroplasty, risk factors, and spinal surgery. We also examined the reference list of the articles identified and selected those we judged relevant. These were included in this narrative review.

Metabolic syndrome and cardiac surgery

Incidence of metabolic syndrome in cardiac surgery patients

The estimated prevalence of MetS in cardiac surgery patients is fairly high (nearly 46%).[15 16] This incidence is almost double that found in the general population (23–28%).[17 18] Hypertension is commonly a diagnostic feature of MetS in cardiac surgery patients (up to 85%).[15] Not all cardiac surgery patients diagnosed with the MetS are obese, but the majority appear to be at least overweight and have increased waist circumference.[6] In a retrospective study[15] of 5304 patients, only 46.5% of those who met the criteria for MetS had a BMI >30 kg m^{-2}, while 12.9% were normal weight (18.5<BMI<24.9); the rest (40.4%) were overweight.[15]

Of note, almost one-third to one-half of those diagnosed with MetS and who undergo coronary artery bypass grafting (CABG) surgery are also diabetic.[15 16] A prospective study[19] including 100 patients demonstrated a similar incidence of obesity (57.5% with BMI >30 kg m^{-2}) and diabetes mellitus (DM; 45%) among patients with MetS.

Metabolic syndrome and mortality in cardiac surgery patients

Metabolic syndrome seems to be an independent predisposing factor for mortality after CABG surgery.[20 21] In the retrospective analysis of 5304 cardiac surgery patients,[15] those with MetS had a 2.4% mortality rate compared with 0.9% for those without MetS. In multivariate analysis, patients with MetS had a three-fold increased probability of death.[15] This increased mortality occurred irrespective of gender and the presence (2.71 *vs* 0.21%, $P<0.0001$) or absence of DM (2.04 *vs* 1%, $P=0.014$), and in this study, DM was not shown to increase overall mortality in the absence of MetS. An observational report studied long-term mortality among 1183 CABG patients and found that MetS increases all-cause and cardiac mortality only in non-diabetic patients (hazard ratio 1.34, $P=0.028$ and 2.31, $P=0.002$, respectively).[16] Conversely, the survival of diabetic patients was not affected by the presence of MetS.[16] This study used a BMI >25 kg m^{-2} instead of waist circumference for assigning patients to the MetS group, and it is unclear whether this modification affected the results. In both retrospective studies, causes of death were also not different between those with and without MetS.[15 16] A small prospective study failed to detect any difference in mortality between those with and without MetS.[19]

Metabolic syndrome and morbidity in cardiac surgery patients

Regarding complications rate, it appears that patients with MetS are more prone to develop renal failure or infection (pneumonia, mediastinitis, or wound infection), compared with those without MetS.[15 19] In one study, patients with MetS had a higher incidence of perioperative stroke (2.3 *vs* 1.4%, $P=0.014$) and similar rates of perioperative myocardial infarction (based on elevations of creatine kinase-MB or troponin I concentrations) compared with patients without MetS.[15] It also seems that patients with MetS have a higher risk for either pre- or postoperative atrial fibrillation (AF) and present increased perioperative resistance to insulin and postoperative cognitive dysfunction compared with patients without MetS (see the section entitled 'Specific anaesthetic considerations in the management of surgical patients with metabolic syndrome').

Metabolic syndrome and valvular decay

One important aspect of MetS is a tendency to accelerated development of a pressure gradient in both native and bioprosthetic valves.[22–24] When studying the progression of aortic stenosis in patients with MetS (using a BMI >30 kg m^{-2} instead of waist circumference), it was reported that stenosis advanced more quickly (−0.14 *vs* −0.08 cm^2 yr^{-1}, $P=0.008$, respectively) than in those without MetS.[22] Metabolic syndrome was an independent predictor of rapid progression of aortic stenosis in terms of aortic valve area and peak gradient, and the relative risk of this adverse outcome was 3.85 in patients with MetS compared with those without MetS. Other investigators reported that although MetS does not change the severity of the aortic stenosis (in terms of mean gradient and aortic valve area), it significantly affects the preoperative left ventricular remodelling in these patients and increases the incidence of postoperative AF.[25] Another study[26] showed that the relative risk for aortic valve calcification was 1.49 for women and 1.70 for men with MetS compared with those without MetS.

Investigating the progression of aortic bioprosthetic valve stenosis retrospectively,[23] one study found that patients with MetS presented a more rapid increase of transprosthetic gradient compared with those without MetS (4 [SD 5] vs 2 [SD 2] mm Hg yr^{-1}, $P<0.001$, respectively when evaluated 3 yr after surgery), a more frequent worsening of prosthetic aortic insufficiency (25 *vs* 12%, respectively) and worse valve haemodynamics (41 *vs* 25%, $P=0.02$, respectively).[23]

A small retrospective study demonstrated that at ~4.5 yr after mitral bioprosthetic valve implantation, patients with MetS had increased transprosthetic valve gradients (6.8 *vs* 4.7 mm Hg, $P=0.007$, respectively) compared with those without MetS.[24]

Metabolic syndrome and stroke

One study,[27] which investigated risk factors for postoperative stroke after cardiac surgery, confirmed that among others, two risk factors of MetS (diabetes and hypertension) were independent risk factors for stroke.[27] Echahidi and colleagues[15] reported a significantly increased rate of stroke (2.3 *vs* 1.4%) and renal failure (12.4 *vs* 6.8%) in patients with MetS undergoing CABG compared with those without MetS.

In summary, patients undergoing cardiac surgery are more likely to have MetS, with or without obesity and DM. Cardiac surgery patients with MetS have higher morbidity and mortality than those without MetS, and they are more likely to develop peri- and postoperative complications. However, larger prospective studies are needed in order to form a definitive opinion.

Metabolic syndrome and non-cardiac surgical procedures

Metabolic syndrome may have a negative impact on outcomes after non-cardiac procedures and increases the risk of adverse peri- and postoperative events.

Metabolic syndrome and general surgery

Based on available data, MetS significantly affects mortality and morbidity rates in general surgery patients. A retrospective study[28] evaluated 3973 patients included in the National Surgical Quality Improvement Program database who underwent liver resection. This study assessed the impact of MetS on the complication rate and 30 day mortality. The presence of MetS was associated with an increased risk of postoperative death [odds ratio (OR) 2.7, 95% confidence interval (CI) 1.5–4.8; $P=0.001$)]. The cumulative incidence of death was 6.9 deaths per 1000 person-days among patients with MetS compared with 2.6 deaths per 1000 person-days among those without MetS.[28] Metabolic syndrome is also related to an increased risk of postoperative complications. Specifically, patients with MetS were at greater risk for infectious, pulmonary, and cardiac complications (OR 1.4, 95% CI 1.02–1.8; $P=0.04$).[28] Furthermore, in elective surgery under general anaesthesia the frequency of hypotension, hypoxaemia, hypertension, bleeding, pain, and postoperative nausea and vomiting is increased (OR 3.31; 95% CI 1.7–6.4; $P<0.05$) in patients with MetS (case–control study, 150 MetS patients, 150 control subjects, $P<0.0001$).[29]

The MetS group ($n=42$, 36.8%) of 114 patients who underwent elective resection of colorectal cancer experienced a higher rate of postoperative complications and a longer length of hospital stay than the non-MetS group (40.5 *vs* 11.1%, $P<0.001$; 11.2 *vs*

8.1 days, $P<0.006$, respectively). It is important to mention that MetS as an entity significantly predicted poor surgical outcomes; this was not true for any of its individual components.[30]

According to the largest retrospective study[31] based on data from 310 208 patients from the American College of Surgeons National Surgical Quality Improvement Program database, patients with MetS (defined as the coexistence of obesity, hypertension, and DM) undergoing non-cardiac surgery are at increased risk for mortality, cardiac adverse events, pulmonary complications, acute kidney injury, stroke and coma, wound complications, and postoperative sepsis. In that study, patients underwent general, vascular, or orthopaedic surgery between 2005 and 2007. Specifically, patients with the modified MetS experienced nearly two- to three-fold higher risk of cardiac adverse events, a 1.5- to 2.5-fold higher risk of pulmonary complications, a two-fold higher risk of neurological complications, and a three- to seven-fold higher risk of acute kidney injury compared with patients of normal weight.[31]

Metabolic syndrome and vascular interventions

Vascular interventions are of specific interest and should be considered as high-risk procedures according to the European Society of Anaesthesiology and Cardiology guidelines.[32–34] The prevalence of MetS is considerable in patients with vascular disease (>30% in patients with carotid artery disease;[35] >50% in those with peripheral arterial disease)[36] and seems to affect mortality and adverse event rates depending on the type of vascular surgery. A retrospective study described the effect of MetS on the outcomes in 921 patients who underwent carotid endarterectomy or carotid stenting.[35] Patients with MetS were more likely to experience a complication than non-MetS patients (23 *vs* 14%, $P=0.001$). There was no difference between MetS and non-MetS patients with respect to patency, restenosis, re-intervention, or survival, but a difference existed for freedom from stroke, myocardial infarction, and major adverse events as evaluated by Kaplan–Meier analysis. Of note, the presence of DM was associated with higher rates of major adverse events and myocardial infarction in MetS patients compared with the non-MetS group.[35] Smolock and colleagues[37] studied 738 patients undergoing superficial femoral artery interventions for symptomatic lower extremity arterial disease. They found that the overall mortality was higher in the MetS group, with patient survival rates of 71 (SD 2) and 53 (SD 3)% at 5 yr in the non-MetS and MetS groups, respectively. Thirty day major adverse cardiac events were equivalent, but the incidence of 30 day major adverse limb events was higher in the MetS group compared with the non-MetS group.[37]

Metabolic syndrome and orthopaedic surgery

Metabolic syndrome may predict adverse outcomes in major orthopaedic surgery. Common perioperative complications after total joint arthroplasties (TJA) include pulmonary embolism (PE), deep vein thrombosis, wound infection, and cardiovascular events.[38–40] An increased risk for PE has been recognized in patients who fulfilled modified MetS criteria and underwent total hip and knee replacement. In one study, patients with MetS had a significantly higher incidence of PE (2.7%, 95% CI 1.8–4.0%) than patients without MetS (1.3%, 95% CI 1.0–1.6%, $P=0.001$), and after adjusting for all other significant risk factors, patients with MetS still had 1.6 times (95% CI 1.01–2.56; $P=0.043$) greater odds for developing PE than those without MetS. Notably, the increasing number of MetS components significantly augmented the incidence of PE by 23% for each additional component of MetS. The most important MetS component was obesity, based on BMI (because waist circumference values were lacking).[41]

Retrospective studies[42 43] observed an increased incidence of in-hospital major complications and significantly higher median hospital charges[43] in MetS compared with non-MetS patients. Surprisingly, the mortality was lower in the MetS group in one of these studies,[43] while the other study did not comment on mortality.[42] Likewise, a higher rate of perioperative cardiovascular complications (AF, pulmonary oedema, arrhythmias, bradycardia, and cardiac arrest) were observed in patients with MetS after TJA compared with those without MetS.[42] A multivariate logistic regression model adjusting for age, sex, race, surgery type, and the presence of risk factors (coronary artery disease, congestive heart failure, cerebrovascular disease, and thromboembolic disease) revealed that the risk of cardiovascular complications after TJA was significantly higher in patients with MetS ($P=0.017$, OR 1.64, 95% CI 1.09–2.46).[42] It has also been reported that patients with uncontrolled diabetes, hypertension, or dyslipidaemia (as components of MetS together with a BMI >30 kg m^{-2}) have increased risk of perioperative complications and increased length of hospital stay after TJA. The rate of postoperative complications was significantly greater in the uncontrolled MetS group (48.6%) than in the well-controlled MetS group (7.9%, $P<0.0001$). Patients with uncontrolled MetS required a mean hospital stay of 7.2 days (95% CI 5.2–9.0) compared with 4.0 days (95% CI 3.6–4.3) for patients with controlled MetS ($P<0.0001$).[40]

In patients who underwent primary posterior lumbar spine fusion surgery, the MetS was identified as a risk factor for perioperative life-threatening complications, increased cost, longer in-hospital stay, and non-routine discharge. Specifically, patients with MetS experienced myocardial infarction, cardiac complications, pneumonia, and pulmonary complications more frequently when compared with non-MetS patients. Patients with MetS were more often discharged to another health-care facility than to their home. Median hospital charges were also higher for MetS *vs* non-MetS patients for posterior lumbar spine fusion.[44]

Metabolic syndrome and bariatric surgery

Bariatric surgery is an acceptable and effective method to manage obesity-related co-morbidities in morbidly obese patients.[45 46] According to the current guidelines, bariatric surgery should be considered in subjects with a BMI ≥35 kg m^{-2} in the presence of metabolic disease including type 2 diabetes mellitus and MetS.[47] Nearly four in five patients undergoing bariatric surgery present with MetS.[48] Co-morbidities (cardiac, pulmonary, metabolic, and hepatic) and complications of morbid obesity in individuals undergoing bariatric surgery may vary and include multiple systems,[49] thus posing particular challenges to the anaesthetist.[50] Hypertension, dyslipidaemia, and hyperglycaemia (i.e. the key components of MetS) respond to bariatric surgery.[47] A recent retrospective study on the largest cohort to date of bariatric surgery patients did not reveal increased rates of perioperative complications in obese patients with MetS compared with those without MetS.[48]

Specific anaesthetic considerations in the management of surgical patients with metabolic syndrome

Metabolic syndrome and atrial fibrillation

Atrial fibrillation is common after cardiac surgery. It carries almost double the morbidity and mortality rate of postoperative cardiac patients without AF[51] and has a significant impact on hospitalization costs.[52] Metabolic syndrome has been associated with increased incidence of AF in the general population.[53 54] One study[53] reported 60 events per 10 000 person-yr in MetS patients and 36 events in patients with no MetS during 15 yr follow-up. They calculated that if MetS could be eliminated with appropriate treatment, as many as 22% fewer AF events would have occurred. In cardiac surgery, AF affects approximately one-third of postoperative cardiac patients (11–40% after CABG and almost 50% after valve surgery).[55–57]

The pathophysiological link between MetS and AF has not been defined. It is speculated that electrical imbalance, which represents the functional component of atrial remodelling, might be targeted by certain factors. In cardiac surgery patients, these could include the increased free fatty acids generated during the lipolytic process as a result of perioperative stress in addition to the inflammatory processes linked to cardiopulmonary bypass and the inflammatory component of the MetS *per se*.[52 58 59]

Echahidi and colleagues,[52] in a retrospective study (5085 cardiac patients), found that AF was slightly more common (29 *vs* 26%) in those with MetS according to National Cholesterol Education Program-Third Adult Treatment Panel criteria than those without MetS, and the incidence increased progressively in parallel with their BMI. Older patients (>50 yr old) presented a significantly higher incidence of postoperative AF (29 *vs* 8%) compared with the younger patient group (<50 yr old). In the older patient group, obesity (BMI >30 kg m^{-2}) and not MetS was found to be significantly associated with AF, whereas in younger patients the presence of MetS doubled the rate of new-onset postoperative AF (from 6 to 12%, P=0.01). Other researchers found contrasting effects of DM and MetS on postoperative AF after cardiac surgery.[60] Hurt and colleagues[60] showed that MetS was not individually predictive of postoperative AF, but DM appeared to be the decisive factor contributing independently to increased postoperative incidence of AF.

Metabolic syndrome and intraoperative hyperglycaemia

Glycaemic control is an important component of perioperative management. While the avoidance of significant hyperglycaemia may decrease perioperative morbidity and mortality, irrespective of the existence of an established diagnosis of DM, concerns have been raised that strict glycaemic control might increase morbidity and mortality mainly as a result of perioperative hypoglycaemia and stroke.[61] A small prospective study in cardiac patients revealed that only those with MetS presented significantly enhanced perioperative insulin resistance that was accompanied by significantly higher values of C-reactive protein.[62] The authors imply a parallel involvement of inflammation and the adverse metabolic state of MetS in the development of insulin resistance. Clinicians should be alert with regard to potentially detrimental effects of immediate postoperative hypoglycaemia as a result of intense intraoperative insulin treatment.[63]

Metabolic syndrome and cognitive dysfunction

There is some evidence that postoperative cognitive function is adversely affected by the presence of MetS in cardiac surgery patients. In a small prospective study of 56 cardiac surgery patients (28 with and 28 without MetS)[64] and 28 coronary patients who did not undergo surgery, verbal and non-verbal memory and executive function were assessed. Patients with MetS had lower scores both before and 1 week after surgery compared with those without MetS or no surgery, especially in recent verbal memory tests (*P*<0.02).[64] Besides, cognitive functions appear also to be more profoundly affected in subjects with MetS compared with their healthier counterparts after non-cardiac surgery.[65]

The results outlined above are documented in a rat model. Using this model, MetS produced greater memory impairment and persistent learning and memory decline after tibial fracture surgery under isoflurane anaesthesia.[66]

Potential treatment options for patients with metabolic syndrome who will require surgery

Available evidence[3 31] suggests that MetS provides a useful tool to recognize surgical patients at increased risk of peri- and postoperative complications. However, there is a paucity of data showing that potential interventions could improve surgery outcome in patients with MetS.

Given that obesity and smoking are main causes of preventable mortality,[67] therapeutic lifestyle changes, incorporating intense behavioural intervention to reduce weight and improve fitness level, are advisable in overweight or obese subjects.[68 69] These interventions could be implemented long before planned surgery in patients with MetS, though their benefit may not be easily quantified. Preoperative nutrition therapy (including calorie restriction and low-carbohydrate consumption) may be considered in order to prepare patients metabolically for the surgical stress; however, the duration and specific measures regarding nutrition need further investigation.[70] In orthopaedic surgery, preoperative assessment of nutrition and optimization of nutritional parameters, including tight glucose control and targeted weight loss, may reduce the risk of perioperative complications, including infection.[71]

Non-alcoholic fatty liver disease is associated with fat accumulation in the liver and insulin resistance and is considered to be the hepatic manifestation of the MetS.[72 73] In this regard, preoperative low-energy diet appears to reduce liver size and facilitate the surgical procedure when surgery must be performed on morbidly obese patients.[74] A short-term (4 weeks) low-carbohydrate diet has been proved to be an effective treatment strategy for patients with non-alcoholic fatty liver disease undergoing mainly bariatric surgery or any foregut operations.[75]

There is evidence that active smoking is associated with the development of MetS, whereas smoking cessation appears to reduce the risk of the syndrome.[76] Indeed, plasma concentrations of adiponectin, an adipocyte-derived plasma protein that is closely related to insulin sensitivity and MetS,[77] increase after smoking cessation.[78] Current smoking is also associated with an elevated risk of mortality in patients undergoing major surgery,[79] while discontinuation of smoking before surgery has a favourable impact on perioperative outcome.[80] Consequently, smoking cessation counselling and interventions should be implemented before surgery for all smokers with metabolic disturbances, such as diabetes, obesity, or dyslipidaemia.[81]

Untreated hypertensive subjects have an increased risk for perioperative stroke, myocardial ischaemia, and renal failure.[32 82–84] While hypertension is not a strong independent predictor for perioperative cardiovascular events in the general population cohort, it is recommended that effective blood pressure control improves the perioperative risk profile by reducing the extent of target organ damage (i.e. heart failure, stroke, and renal dysfunction).[32 85] Lifestyle changes, including at least 30 min moderate aerobic exercise (brisk walking, cycling etc.) 3–4 days per week may improve blood pressure and glycaemic control.[86–88]

Disorders of haemostasis have been documented in subjects with MetS.[12] Indeed, coagulation is enhanced in MetS because of the increased plasma concentrations of fibrinogen, tissue factor and factor VII, which are related to inflammation and central obesity.[12 89–92] These abnormalities, combined with the decreased fibrinolytic activity, in patients with MetS contribute to a greater risk of thrombotic events (arterial and venous).[93 94] Diet and lifestyle changes can affect coagulation and fibrinolysis.[95] However, we need to establish whether commonly used medications (e.g. antihypertensive agents and statins) influence haemostasis in patients with MetS. Obesity and insulin resistance enhance platelet activity in subjects with MetS.[12 96] Finally, the surgical procedure *per se* is associated with platelet activation.[97] Discontinuation of antithrombotic drugs because of concerns regarding perioperative bleeding in patients with MetS may carry an even greater thrombotic risk. This is of major importance in patients with previous coronary stenting.[98] Therefore, it is advisable that antithrombotic treatment should be tailored according to the estimated risk of surgical bleeding *vs* thrombotic complications.

Statins are the principal lipid-lowering agents. Their protective role exceeds their ability to change blood lipid concentrations.[99] These agents appear to have favourable 'pleiotropic' effects on vascular endothelial function, atherosclerotic plaque stability, inflammation, and thrombosis.[100 101] There is no conclusive evidence or guidelines regarding the appropriate time to initiate statin therapy before an elective surgical procedure in statin-naive patients with MetS. However, based on current evidence for patients undergoing vascular surgery[102] we suggest that statins should be started as soon as possible in statin-naive patients with MetS (at least 2 weeks before elective high-risk procedures in order to take advantage of their beneficial extralipid actions). Patients already on a statin should continue treatment throughout the peri- and postoperative periods as soon as oral therapy is recommenced. The intensity and duration of statin treatment in the perioperative period needs to be investigated.[100 103]

The administration of statin therapy (loading dose) in the context of percutaneous coronary interventions[104] or vascular surgery[105] has been shown to affect outcome favourably. Statins should be administered to all patients with vascular disease, whether they are managed conservatively or are undergoing an open surgical or endovascular procedure.[106 107] Furthermore, periprocedural statin administration may help to prevent contrast-induced acute kidney injury in patients undergoing angiography, with or without intervention.[108]

Limitations of this review

Our review should be considered in the light of certain limitations. It is a narrative review, including mostly retrospective observational studies. Moreover, heterogeneity was considerable because of different study outcomes and populations, and diverse methodological processes.

Concluding remarks

Metabolic syndrome has a high prevalence among surgical patients, exceeding 40% in some reports, and may be higher in cardiac surgery patients.

Several, but not all, studies that evaluated the impact of MetS on cardiac and non-cardiac surgery have shown increased mortality among patients with MetS. Most evidence shows that MetS adversely affects perioperative outcomes in both cardiac and non-cardiac surgery. Metabolic syndrome probably contributes to even more perioperative events, with the most common being cardiac, pulmonary, renal, cerebrovascular, thromboembolic, sepsis, and wound infection. Metabolic syndrome has been correlated with a prolonged length of hospital stay after major surgery and a higher need for posthospitalization care, resulting in additional cost. Despite several definitions of MetS currently in use, the recognition of MetS as a group of risk factors for perioperative adverse outcomes urges clinicians to recognize the syndrome, to familiarize themselves with its characteristics, and most importantly, to formulate management strategies that could possibly lead to a reduction of perianaesthetic and perioperative risks. More research in this field is required. Apart from specifically designed studies, the use of registries could prove useful.

Authors' contributions

Study planning: P.T., H.M., G.P.
Manuscript preparation: P.T., A.P., E.L., H.M., D.P.M.
Analysis and interpretation of data: P.T., D.P.M., G.P.
Data collection: A.P., E.L.
Manuscript approval: all authors.

Declaration of interest

None declared.

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