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Original Article

The metabolic syndrome and its perioperative complications

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ABSTRACT: ***Objective:*** *The metabolic syndrome is a well-known risk factor for diabetes and cardiovascular disease, but no literature data are currently available on its role as a risk factor in surgical patients.*
Design: *Observational study.*
Patients and methods: *Two hundred patients undergoing major abdominal surgery were studied. The prevalence rate of metabolic syndrome and postoperative complication data were collected and analyzed.*
Results: *Patients with the metabolic syndrome were 29% of all patients studied; this group showed an incidence of morbidity of 31% and of mortality of 3.4%; patients without syndrome were 71%, and showed an incidence of morbidity of 24% and of mortality of 2.1%. Postoperative infections were statistically significantly more frequent among patients with the metabolic syndrome.*
Conclusion: *The metabolic syndrome could constitute a risk factor for postoperative mortality and complications. (Nutritional Therapy & Metabolism 2006; 24: 187-93)*

KEY WORDS: Postoperative mortality, Metabolic syndrome, Postoperative infections

INTRODUCTION

The first report of the metabolic syndrome (MS) was made during the late 1940s by Vague (1). It is a condition in which many different metabolic derangements are associated, including an alteration in glucose metabolism (i.e., insulin resistance) and the pattern of lipids. The cardiovascular landmark of MS is arterial hypertension (2). Visceral obesity is frequently associated (3).

From an epidemiological standpoint, patients with MS are at higher risk of cardiovascular morbidity and mortality (4, 5). This is due not only to the proatherogenic metabolic pattern, but also to a chronic inflammatory state which is part of the syndrome; this may contribute to the genesis of the vascular lesions (6).

The MS is also a well-known risk factor for type 2 diabetes mellitus (7-9). Both conditions share common pathophysiological and clinical features, such as insulin resistance and endothelial dysfunction (10).

Though traditionally a common problem in medical patients, MS is diffused in Western population, so it seems reasonable to find it also in patients who undergo surgical procedures. Its complications – e.g., cardiovascular events – can raise the perioperative risk of these patients. Cardiovascular events and infections are common complications of insulin resistance, and they can adversely affect the clinical course of any surgical patient with MS. Surgical complications may be more common in patients with MS due to endothelial dysfunction which impairs tissue oxygen delivery (10). All of these potential problems can raise the risk of perioperative complications and the need for postoperative intensive care unit admission, thus raising costs.

Despite these facts, no literature data exist regarding MS in the surgical patient, either regarding its prevalence or correlation with perioperative complications.

In light of these considerations, we have done an observational study in which MS has been studied in a population of surgical patients. Its prevalence has been evaluated, together with the incidence of postoperative complications: i.e., infections, cardiovascular events and surgical complications. We assessed the mortality and morbidity risk of patients using the Physiologic and Operative Score for the eNumeration of Mortality and Morbidity (POSSUM), and searched for any statistical difference among scores in the 2 groups: those with and without MS. We tested the correlation between the presence of MS and development of complications in postoperative course.

PATIENTS AND METHODS

This study has been done on a population of elective surgical patients who underwent major abdominal procedures in a 6-month period starting in June 2005. All of the patients included in the study gave their consent, and the study protocol was approved by the local ethics committee.

Patients who underwent laparoscopic or bariatric surgery and patients in severe presurgical conditions (i.e., American Society of Anaesthesiology Physical Status) (ASAps) score of 3 or 4) were excluded from the study population. The diagnosis of the metabolic syndrome was made following the criteria issued by the Adult Treatment Panel III in 2001 (11). These include 3 or more findings including fasting hyperglycemia, arterial hypertension, obesity, hypertriglyceridemia or HDL hypocholesterolemia. On this basis, patients were divided into 2 groups: the MS group with affected patients, and a control group (CG).

Researchers were not the clinicians in charge of the patients, and the study did not alter the usual clinical management of the patients involved. Patients have been followed constantly since their discharge from the operating theater until discharge from hospital, and any complications has been recorded. For the study purposes, complications have been divided into infective, cardiovascular and surgical. Specifically, infections were diagnosed using the criteria of the Centers for Disease Control of Atlanta and those of the Consensus Conference on Sepsis (12, 13), and included pulmonary infections, abdominal sepsis and CVC-related infections. Cardiovascular complications included acute coronary syndrome, acute arrhythmias, acute heart failure, deep venous thrombosis and pulmonary embolism. Surgical complications were defined as the need for reintervention within 72 hours after surgery, as indicated by wound or anastomosis dehiscence, hematoma or gut fistula formation.

Mortality and morbidity risk were assessed using the POSSUM score (14), both in all patients and in the 2 groups separately. Student's t test was employed to determine any statistical difference in scores between the 2 groups.

Metabolic syndrome prevalence, complication incidence and mortality were evaluated in all patients and in the 2 groups – MS and CG. Differences in incidence of complications and mortality in those groups have been tested using the chi-square test ($p<0.005$).

RESULTS

There were 315 patients considered for the study. Of them, 115 were excluded due to 1 or more exclusion criteria (Tab. I). The final patient population was 200. Patients belonging to the MS or CG group did not show statistically relevant differences regarding age, sex, relevant comorbidities and surgical procedures. The prevalence of the metabolic syndrome was 29% for all patients. Distribution of diagnostic criteria for the syndrome in each group and in the whole population is shown in Table II.

POSSUM scores for the whole population were 52.8% and 14.9% for expected morbidity and mortality, respectively. Actual rates were 26% and 2.5%, in the whole population. When evaluated separately for the 2 groups, expected morbidity and mortality rates (POSSUM scores) were 55.2% and 15.5%, in the MS group; and 51.9% and 14.8 %, in the CG group. Actual morbidity and mortality rates were 31% and 3.4%, in the MS group; and 24% and 2.1%, in the CG group. Expected morbidity and mortality rates as predicted by the POSSUM score were statistically higher in the MS group. All of these data, with the demographics of the patients, are summarized in Table III.

In the MS group, incidence of complications was 20.7% for infections, and 5.2% for both surgical and cardiovascular problems. In the CG group, infection incidence was 15.5%, surgical was 2.1% and cardiovascular was 6.3%. The chi-square test ($p<0.005$) revealed that infections were statistically more frequent in the MS than in the CG group (Tab. IV).

TABLE I - DISTRIBUTION OF EXCLUSION CRITERIA AMONG PATIENTS EXCLUDED

Exclusion criteria	Number of patients
Laparoscopic surgery	63
Bariatric surgery	7
ASA 3-4	45
Total	115

ASA = American Society of Anaesthesiology

TABLE II - DISTRIBUTION OF DIAGNOSTIC CRITERIA OF THE METABOLIC SYNDROME IN EACH GROUP AND IN ALL PATIENTS STUDIED

	Group SM	Group CG	All patients
Low HDL	91% (53/58)	29% (42/142)	47% (95/200)
Hyperglycemia	64% (37/58)	8% (12/142)	24% (49/200)
Hypertension	77% (45/58)	33% (47/142)	46% (92/200)
Hypertriglyceridemia	29% (17/58)	4% (6/142)	11% (23/200)
Obesity	41% (24/58)	3% (5/142)	14% (29/200)

Group CG = control group; Group SM = metabolic syndrome group

TABLE III - DEMOGRAPHICS AND MORBIDITY/MORTALITY RATES, EXPECTED AND ACTUAL, IN ALL PATIENTS AND IN THE 2 SEPARATE GROUPS

	Age in years (mean ± SD)	Sex (as percentage of men)	POSSUM morbidity	POSSUM mortality	Actual complication incidence	Actual mortality rate
All patients (n=200)	68.7±12.4	50.5%	52.8%	14.9%	26% (52/200)	2.5% (5/200)
Metabolic syndrome group (n=58)	68.4±11.7	62%	55.2%	15.5%	31% (18/58)	3.4% (2/58)
Control group (n=142)	68.8±13.2	35%	51.9%	14.8%	24% (34/142)	2.1% (3/142)

TABLE IV - DISTRIBUTION OF COMPLICATIONS IN EACH GROUP

	Without complications	Infective complications	Surgical complications	Cardiovascular complications	Mortality
Metabolic syndrome group (n=58)	65.5% (38/58)	20.7% (12/58)	5.2% (3/58)	5.2% (3/58)	3.4% (2/58)
Control group (n=142)	74% (105/142)	15.5% (22/142)	2.1% (3/142)	6.3% (9/142)	2.1% (3/142)

DISCUSSION

The metabolic syndrome includes many metabolic derangements involving glycemic homeostasis, as well as lipid pattern, and clinically it also involves the cardiovascular system. It is a quite common condition among patients, but no data are available on its prevalence in surgical populations. However, its complications badly influence the clinical course of surgical patients, raising their morbidity and mortality risks. Our study found a prevalence of 29% in a series of 200 surgical patients who underwent major abdominal surgery. The mortality and morbidity risk, measured using the POSSUM system, were statistically significantly higher in patients with MS. Incidences of postoperative complications were similar in both groups, except for infections, which were more frequent in the MS group with statistical significance.

The features of the metabolic syndrome are both purely metabolic and clinical. Commonly they include abdominal or visceral obesity, a proatherogenic lipid pattern (i.e., hypertriglyceridemia and/or HDL hypocholesterolemia), arterial hypertension and insulin resistance (i.e., fasting hyperglycemia or glucose intolerance and type 2 diabetes mellitus) (15).

Other clinical or metabolic features are less commonly included in the MS definition. These are nonalcoholic hepatic steatosis (16), microalbuminuria (17, 18), polycystic ovarian syndrome (19), adipocytic dysfunction or endothelial dysfunctions (20-23), and a chronic inflammatory and hypercoagulable state (24-27). In our study population, the main features were low HDL, arterial hypertension and fasting hyperglycemia.

In 2001, the Adult Treatment Panel III (ATP III) issued a definition of MS which is based on a determination of fasting hyperglycemia as the sign of insulin resistance. Other criteria included in the definition are arterial hypertension, visceral obesity, hypertriglyceridemia and HDL hypocholesterolemia. Three or more of these give a diagnosis of MS (11).

This definition, although not the only one (28-30), is quite easy and cheap to apply, especially in an everyday clinical setting, when there is no time to do complicated metabolic determinations and when costs must be kept to a minimum. This is the case of preoperative evaluation. The ATP III criteria meet this need, allowing the clinician to diagnose MS in a way which is both reliable and easy to achieve. This is why we used them to assess prevalence of the syndrome in our patient population.

Insulin resistance is thought to be the key point in MS pathophysiology (31). Insulin-dependant tissues – i.e., adipose and rough muscular tissues – are those in which glucose uptake from the blood stream is linked to insulin-mediated expression of membrane glucose transporters. In MS patients, those tissues are not able to raise their uptake, i.e., they "resist" insulin action. This would lead to a hyperglycemic state if insulin secretion did not increase. Clinically, there is a tendency in these patients to hyperglycemia, which is evident during fasting, and certainly to a hyperinsulinemic state (31). Moreover, the liver of these patients is unable to inhibit gluconeogenesis mediated by insulin. Then, there is both increased production of endogenous glucose and decreased utilization of both endogenous and exogenous glucose. The metabolic syndrome shares these pathophysiological features with type 2 diabetes mellitus. This could justify regarding the former as a risk factor for the latter.

Another feature that the two conditions share is a higher risk for coronary disease. Many reports are found in the literature which show the association between MS and higher cardiovascular risk, in terms of both morbidity and mortality rates. Why this is true is still a matter of debate among Authors (32-36).

Experimental and clinical data show that a chronic inflammatory state is almost always present in patients with MS (37-39). In fact, adipose tissue is able to release Interleukin-6, which stimulates the liver to produce inflammatory mediators and lead to macrophage activation. Activated macrophages can hurt endothelial cells and ease atheroma formation, thus explaining the higher incidence of cardiovascular disease in patients with the syndrome.

As mentioned above, MS prevalence in our study population was 29%. This finding seems slightly higher than that in data from the European general population and is in line with data from the general US population. However, an average of 80% of our patients had cancer and underwent oncologic surgery. Considering the two separate groups, cancer prevalence was 82.7% in the MS group and 78.8% in the CG group. We did not statistically test this difference, but it is interesting to note that recent literature reports suggest a carcinogenic role of MS. Particularly, inflammatory cytokines secreted by adipocytes could be responsible for enhancing reactive oxygen species production, thus inducing cell mutagenesis (40). This finding, which is surely worth further study, could explain why MS tended to appear in a series of surgical patients.

Apart from its supposed role in contributing to carcinogenesis, the high prevalence of MS in surgical patients suggests that this condition might be the basis for developing complications in the surgical aftermath. Patients with MS often do not seem to be sick at the moment of preoperative evaluation, and their personal feelings may be of well-being. They are still free from organ complications. However, the underlying metabolic condition exposes these patients to higher mortality and morbidity rates. We used the POSSUM score to define postoperative risk in our patients. It gives the clinician 2 risk scores: morbidity and mortality risk. Experts think that it tends to overestimate the risk. The main advantage of this score is that it takes into account both patient-related and surgery-related factors, which both influence patient outcome after surgery; and this is why we used it. We found higher risk scores for both morbidity and mortality in the MS group, and this was statistically relevant. This is not surprising, considering that MS patients may show derangements in physiological parameters considered by the POSSUM system (e.g., ECG alterations or hypertension).

We evaluated separately incidence rates for infective, surgical and cardiovascular complications in the two groups, using the chi-square test. Infective complications were statistically ($p<0.005$) more frequent in the MS group (20.7% vs. 15.5% in the CG group), with respiratory infections being most common (41.2% of all infections in the MS group). It is interesting to note that MS is a state of insulin resistance. Affected patients tend to be hyperglycemic. In the postoperative period counterregulatory hormones oppose insulin action, thus impairing insulin resistance (41, 42). These include glucagon, cortisol and endogenous catecholamines. These last can be secreted as part of the neuroendocrine response to surgical trauma and pain (i.e., with poor pain control). Even cytokines secreted as part of the inflammatory response to trauma can play a role acting against insulin action (43). This postoperative hormonal pattern can raise the hyperglycemic tendency in patients with the metabolic syndrome during the first hours after surgery. Among the detrimental effects of hyperglycemia, there is an increased susceptibility to infections (44). This can be due to both glycosylation of immunoglobulins or impaired diapedetic and killing action of neutrophils. Again, this is a feature that MS shares with diabetes mellitus.

The metabolic syndrome should be seen as a metabolic condition of high infective risk, which is even higher in the postoperative period, when hormonal changes enhance the insulin resistance. Therapeutically, these patients need a tight glycemic control, as elsewhere shown in the literature (41, 45-48).

Surgical complications have been considered as any conditions requiring surgical reintervention within 72 hours from the first surgery. This definition included wound or anastomosis dehiscence, gut fistula formation or hematoma evacuation. This sort of complication showed an incidence of 5.2% in the MS group, versus 2.1% of the CG. Although not statistically significant, this difference can be seen again as a consequence of the hyperglycemic state, which interferes with the normal process of wound and tissue healing (49). Moreover, whenever a respiratory infection arose, hypoxia developed, thus further impairing healing. Tight glucose control might help these patients in healing promptly, thus reducing reintervention rates and consequent complications and costs.

Paradoxically, cardiovascular complication incidence was lower in the MS group than in the CG (5.2% vs. 6.3%). This was not statistically significant. This may be surprising, considering the tight link between MS and cardiovascular disease in the general population. As stated above, the syndrome badly influences endothelial function (50), and is associated with a chronic inflammatory state that can hurt vessel walls and promote atherogenesis. Nevertheless, our findings must be read in their clinical setting. Hypertension or hyperglycemia, common among these patients, may have led the clinicians (i.e., the anesthetist) to include them in the given protocols of clinical management for high-risk patients (e.g., perioperative beta-blocker use) (51) or to generally take special care of them. These measures could have lowered the incidence of acute cardiovascular events. We can not exclude the possibility that this result is linked also to the small number of patients, and it would be interesting to conduct a trial on a larger series.

Finally, actual mortality rates were found to be higher in the MS group, 3.4% versus 2.1%. Though the difference was not statistically significant, it is important to point out that complications, especially respiratory infections, may have added an extra burden of mortality to the MS group.

CONCLUSIONS

The metabolic syndrome is a collection of many metabolic alterations which is quite widely diffused in the Western population. Due to its supposed role in contributing to carcinogenesis, it can be even more frequent among patients who need oncologic surgery. The syndrome could raise the risk of postoperative morbidity and mortality linked to infections (particularly pulmonary infections), cardiovascular events or surgical complications.

Making a preoperative diagnose of MS helps the clinician to better define the postoperative risk, so as to plan tighter clinical management for the affected patients.

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