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Metabolic Syndrome and Perioperative Complications During Elective Surgery Using General Anesthesia

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ABSTRACT

Introduction: Metabolic Syndrome (MS) is a cluster of alterations associated to high risk of cardiovascular diseases and diabetes mellitus. Although Metabolic Syndrome is a public health issue, little has been studied about its impact in the anesthetic-surgical scene.
Aims: To analyze the correlation level between MS and perioperative complications, in patients under programmed surgery with general anesthesia technique in Cartagena, Colombia.
Materials and methods: A case control study was designed, where 300 patients were enrolled: 150 cases and 150 controls. Socio-demographic, hemodynamics and respiratory variables, as well as surgical complications (hypotension, hypertension, hypoxemia, bleeding, moderated-severe pain and post chirurgical nausea-vomiting) were registered. Fisher's exact test and X2, where appropriated were employed to compare categorical data. A logistic regression model was applied to calculate correlation between variables.
Results: Surgical complications were more frequent in cases group (P<.001). Differences in age and ASA physical status were also found (P<.05). MS was correlated to perioperative complications (OR: 3.31; P<.05). ASA III physical status was another risk factor to post chirurgical complications development (OR: 4.01; P<.05). None mortality case was reported.
Conclusions: In a comparison with healthy population, Metabolic Syndrome represented a risk factor to perioperative complications development. According to results, further prevention and approach guidelines in order to reduce perioperative complications associated to Metabolic Syndrome.

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Síndrome metabólico y complicaciones perioperatorias durante cirugías programadas con anestesia general

Palabras clave:
Resistencia a la insulina
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Medicina

RESUMEN

Introducción: El síndrome metabólico es un conjunto de alteraciones asociadas a un alto riesgo de enfermedades cardiovasculares. Aunque representa un problema de salud pública, poco se conoce de su impacto en situaciones como la anestésica-quirúrgica.
Objetivo: Analizar la correlación entre síndrome metabólico y complicaciones perioperatorias en pacientes de cirugía programada con anestesia general en Cartagena, Colombia.
Material y métodos: Se diseñó un estudio de casos y controles, con 300 pacientes: 150 casos y 150 controles. Se registraron variables sociodemográficas, hemodinámicas, respiratorias, complicaciones perioperatorias (hipotensión, hipertensión, hipoxemia, sangrado, dolor moderado-severo y náuseas o vómitos postoperatorios). Se emplearon la prueba exacta de Fisher o la de la χ^2, según fuera apropiado, para la comparación de grupos. Se aplicó un modelo de regresión logística univariable, para estimar el grado de correlación entre las variables.
Resultados: Las complicaciones perioperatorias fueron más frecuentes en el grupo de casos ($p < 0,001$). Hubo diferencias significativas en edad y estado físico según la Asociación Americana de Anestesiólogos (ASA) ($p < 0,05$). El síndrome metabólico se correlacionó con complicaciones perioperatorias (*odds ratio* [OR] = 3,31). El estado físico ASA III fue factor de riesgo de complicaciones postoperatorias (OR = 4,01).
Conclusiones: El síndrome metabólico es un factor de riesgo de complicaciones perioperatorias. El estudio indica que hay que implementar estrategias de intervención sanitarias con vistas a la prevención y el manejo del síndrome metabólico en el ámbito quirúrgico, lo que conlleva reducción de las complicaciones perioperatorias asociadas.

Introduction

The metabolic syndrome (MS) is known as a set of clinical pathological entities associated with insulin resistance. The concept of insulin resistance was described by Himsworth more than 60 years ago, and postulated as a potential etiologic factor in different metabolic diseases.[1]

Insulin resistance, defined as a state of diminished physiological response to insulin concentrations,[2] appears to be the result of excess abdominal adipose tissue, and increased secretion of free fatty acids (FFAs) and pro-inflammatory factors, including tumor necrosis factor alpha (TNFα), IL-6 and other adipocytokines; this results in a defective glucose transport in skeletal muscle, and abnormal lipid metabolism.[3-5] This phenomenon is associated with the development of metabolic disorders such as arterial hypertension, dyslipidemia, obesity and type 2 diabetes mellitus. Although the pathophysiology has not been described fully, these metabolic abnormalities, when taken together, increase morbidity and mortality from cardiovascular diseases.[6-8]

The grouping into a syndrome of the metabolic consequences of insulin resistance was initially proposed in 1988.[9] In 2003, the American Association of Clinical Endocrinology (AACE) unified criteria for the diagnosis of the metabolic syndrome, emphasizing the importance of the oral glucose tolerance test.[10] These new criteria were added to those established by the WHO[11] and ATP III[12] and provided a broader diagnostic definition. The International Diabetes Federation (IDF) recognized the need for a simple tool that could be readily applied and used universally for diagnosing the syndrome. Consequently, in 2006, the IDF consensus group proposed new criteria (essential and additional), for the definition of the metabolic syndrome, recognizing the ethnic identity and variations in the identification of obesity, and focused on the prediction of vascular coronary disease and diabetes.[7]

With some degree of similarity, both the metabolic syndrome as well as the perioperative period are characterized by a state of insulin resistance that manifests in the form of hyperglycemia, which triggers other metabolic disorders that have a negative effect on final organ function through different pathophysiological mechanisms.[3,13-15].

In seriously ill patients, hyperglycemia has a negative effect on their perioperative course.[16]. Achieving a state of euglycemia appears to be beneficial in certain clinical situations,[17,18] although there is no agreement regarding the ideal target for blood sugar, the duration of the therapy, or the modality. Drug therapy, exercise and nutrition to improve insulin sensitivity appear to be promising, although further evaluation is warranted in order to confirm their perioperative effectiveness in risk reduction.[18]

Currently, there is a growing number of reports of metabolic syndrome patients in national and international series.[2,8] Patients considered as having metabolic syndrome have been studied at length according to the baseline risk

for cardiovascular events[6-8] in conventional activities or situations. However, to this date, there are no conclusive studies in the literature regarding the behavior of these types of patients during surgery under general anesthesia, which means that the risk for this population during this form of anesthesia is unknown.

The objective of this study was to analyze the degree of correlation between metabolic syndrome as defined by the IDF, and perioperative complications in patients undergoing elective surgery under general anesthesia in a surgery service in the district of Cartagena, Colombia.

Material and methods

Case-control study of patients scheduled for surgery under general anesthesia between March 2008 and March 2009, in the surgery service of the San Juan de Dios University Clinic in the district of Cartagena de Indias, Colombia. The subjects of the study were patients of both genders, over 18, with an ASA (American Society of Anesthesiologists) physical status stage between I and III,[19,20] and low or intermediate surgical risk and no active cardiac conditions in accordance with the classification of the American College of Cardiology and the American Heart Association (ACC/AHA) for patients with heart disease undergoing non-cardiac surgery.[21] Not included were patients who refused the proposed anesthesia technique or whose procedure had been postponed in accordance with the ACC/AHA guidelines, and patients who were admitted for emergency surgery.

There was a total of 300 patients of both genders who underwent surgery under general anesthesia, and they were included in the study and assigned to the two groups: (1) Cases (150 patients diagnosed with metabolic syndrome according to the 2005 guidelines of the International Diabetes Federation[7]); and (2) Controls (150 patients without metabolic syndrome). Although the minimum sample size in each group was 75 patients, 150 patients were studied in each group in order to increase the power and accuracy of the statistical models. This estimation was done using a 23% probability of exposure to the syndrome,[22,23] and the confidence interval and the relative error selected were 95% and 0.29, respectively. Patient selection was based on simple randomized sampling.

All patients were interviewed before receiving anesthesia, the physical condition ASA score was determined, and the data were entered in a single data collection form. The variables studied in the perioperative period were ASA score, surgical risk of the procedure according to the ACC/AHA guidelines; perioperative complications, both intra- as well as post-operative hypotension (≥30% drop with respect to the mean baseline arterial pressure on admission), hypoxemia (≥10% reduction of the peripheral oxyhemoglobin baseline saturation recorded on admission with a pulse oximeter), bleeding (loss of 30% of blood volume for the patient type and weight), moderate-to-severe pain (>4 on the verbal numerical pain scale after management with non-steroidal anti-inflammatory agents, opioids or infiltration of the surgical wound with local anesthetic according to the institutional protocol for pain management for each surgical procedure), post-operative nausea and vomiting (after prophylactic management according to the institutional protocol for each surgical procedure or individual patient risk), and mortality.

Conventional non-invasive continuous monitoring was performed (surface electrocardiovisoscope, pulse oximetry, respiratory rate, temperature, non-invasive blood pressure, mean arterial pressure, end-tidal carbon dioxide levels). Anesthesia was given by the surgical team on call, without altering the quality or type of anesthesia determined by the treating anesthesiologist.

The anesthesia technique, monitoring with the usual devices, anesthetic supplies and human resources employed were all the same for both groups. The anesthesiologist's judgment prevailed for decision-making regarding interventions before, during and after surgery. Finally, the data collection form was filled concomitant with the preparation of the anesthesia record and during patient stay in the post-anesthesia care unit (PACU).

The data were described using central trend measurements. Categorical variables were compared using the χ^2 or Fisher's exact test, as appropriate. A multiple logistic regression model was applied to estimate the correlation between metabolic syndrome and perioperative complications. Socio-demographic, clinical and anthropometric data were also included as independent variables. The procedure was adjusted stepwise backward to 0.25. Confidence intervals (CI) of 95% were used, and a *P* value <.05 was considered as significant.

The research procedure was approved by the medical ethics and research review board of Cartagena University and of the Healthcare Service Provider (CUSJD). All the subjects participating in the study signed the institutional informed consent for the surgery and the anesthesia technique, as well as the informed consent for inclusion in the research project. The risk classification for the patients in the study, in accordance with Resolution 2378 of June 27, issued by the Ministry of Social Protection, was "no risk".[24]

Results

Table 1 shows the results of the demographic variables for the subjects analyzed in this study. Although the groups were heterogeneous, no significant differences were found for the age range between 41 and 50 years (*P*=.45), ASA III physical status (*P*=.36) and the frequency of excess weight (*P*=.17). Interestingly, a significant difference was found in the frequency of perioperative complications between the two groups (*P*<.0001).

Regarding the distribution of the type of general anesthesia given to the subjects participating in the study, 189 was balanced anesthesia, 95 was pure inhaled anesthesia, 12 was total intravenous anesthesia (TIVA) and 4 was combined.

Table 2 describes the perioperative complications in both groups of patients. There were significant differences between the group of cases and the control group (*P*=.0001), with the frequency of perioperative complications being greater among patients who fulfilled all the criteria for metabolic syndrome. In the group of cases, hypo- and hypertension were the most

Table 1 – Socio-demographic, anthropometric and clinical distribution

	Without MS	SM	*P* value
Age range			
18-30	30	2	<.0001
31-40	57	13	.0001
41-50	24	30	.4526
51-60	14	19	.0202
61-70	15	41	.0001
71-80	10	45	<.0001
Gender			.7217
Female	91	89	
Male	59	61	
ASA physical status			
I	97	2	<.0001
II	45	135	<.0001
III	8	13	.3658
Comorbidities			
Hypertriglyceridemia	3	124	<.0001
Low HDL	2	61	<.0001
Hypertension	8	91	<.0001
Hyperglycemia	1	43	<.0001
Excess weight	44	56	.1777
Obesity	11	70	<.0001
Postoperative complications	16	47	<.0001

ASA: American Society of Anesthesiologists; HDL: high density lipoproteins; MS: metabolic syndrome. Source: the authors.

frequent complications, with significant differences when the proportions for these complications were compared with the control group. It is worth noting that two or more concomitant complications may be found in the same individual patient in each of the study groups.

The statistical analysis using the univariate logistic regression to determine potential associations between the independent variables such as the presence of metabolic syndrome, ASA II and III physical status, excess weight, and perioperative complications assigned in turn as a dependent variable, showed a positive odds ratio (OR) for the relationship between metabolic syndrome and perioperative complications (OR=3.31; CI, 1.7-6.4; *P*<.05), indicating an association between suffering from metabolic syndrome and experiencing these types of complications.

Additionally, the CI for this OR does not cover neutrality, indicating that it is statistically significant (*P*<.05). Consequently, there is an association between the variables described and perioperative complications, ruling out the possibility that this finding might be attributed to chance, the presence of bias, or confounding variables.

Although the regression model used showed an odds ratio lower than one in the association between excess weight and postoperative complication (OR=0.63; CI, 0.32-1.23; *P*=.18), the confidence interval for this odds ratio comprises neutrality, indicating that it is not statistically significant (*P*>.05). The relationship between excess weight and its strength of association with perioperative complications is an issue requiring further study. In our group, we have begun to work in this regard by proposing epidemiological research methods that may help elucidate possible causality.

ASA III physical status is a risk factor associated with postoperative complications, as shown in table 3, with a positive OR and confidence intervals far from 1 (OR=4.5; CI, 1.07-19.6; *P*=.039).

ASA I physical status is a protective factor for perioperative complications in patients undergoing elective surgery under general anesthesia (OR=0.17; CI, 0.06-0.46; *P*<.05).

There were no deaths in the study population.

Discussion

The results of this study show that, in the context of surgery, metabolic syndrome represents a risk factor for the development of perioperative complications (Table 3). Although there is no evidence of impact on mortality on the surgical patient, there is associated morbidity that may increase the impact of the metabolic syndrome on prognosis. Likewise, its emergence as a risk factor in the perioperative period suggests the need for modifications in the approach to these patients by the surgical team. Along these same lines, it is known that in the past few years there has been an increase in the number of cases of metabolic syndrome in the world,[6,22] together with a change in the epidemiological pattern, and it is now found at an increasingly younger age.[25,26] Given its relation with cardiovascular disease, the growing prevalence of metabolic syndrome has been reflected in increased morbidity and mortality due to diseases such as acute coronary syndrome, acute myocardial infarction, and cerebrovascular disease.[21,27,28]

The high frequency of hypo- and hypertension in the group of cases, when compared with the control group (Table 2), is consistent with the deterioration of the cardiovascular response reported in patients with metabolic syndrome subjected to stressful events. This association was reported by Campillo et al[27] in a cross-sectional study that included 149 patients with metabolic syndrome admitted to the intensive care unit, where they observed an increase in the risk of dying from cardiogenic shock, hemorrhagic stroke, ischemic cerebrovascular disease and mesenteric thrombosis in the group of patients. Consequently, the hemodynamic status of the patient with metabolic syndrome is a factor of special interest during surgical procedures under general anesthesia, and because of the impossibility to infer causality from the results of this study, the understanding of the pathophysiological mechanisms might provide tools for the prevention and management of these types of complications.

Several factors, modifiable and non-modifiable, influence the development of metabolic syndrome.[6,11,12,29] Sedentary life style and a diet high in carbohydrates and fats have been the focus of prevention strategies, given their association with obesity and insulin resistance.[6,11,30,31] Both conditions favor the development of a prolonged pro-inflammatory state[4,5] that may affect immune modulation during surgery and favor

Table 2 – Description of the perioperative complications

Complication	MS (n=150)			No MS (n=150)			
	Intra	Post	Total	Intra	Post	Total	P value
Hypotension	21	0	21	2	1	3	.0001
Hypoxemia	2	2	4	0	0	0	.122
Hypertension	10	1	11	2	0	2	.019
Bleeding	5	0	5	1	1	2	.447
Pain (M/S)	N/A	13	13	N/A	8	8	.365
PONV	N/A	7	7	N/A	3	3	.335
Total	38	25	63	6	13	19	.0001

M/S: moderate-to-severe; MS: metabolic syndrome; N/A: not applicable; PONV: post-operative nausea and vomiting; Post: post-operative complications; Trans: intra-operative complications.
Note that complications are not exclusive, considering that patients might present two or more simultaneous complications. No cases of hypercapnia were reported in any of the groups. Comparisons were done using the exact Fisher test. Source: the authors.

Table 3 – Correlation analysis between perioperative complications and metabolic syndrome

Covariables	Coefficient	Standard error	Raw OR	Adjusted OR[a]	CI	P value
Presence of metabolic syndrome	1.3407	0.3177	3.8216	3.3165[b]	1.70-6.44	<.05
Presence of excess weight	–0.9194	0.3122	0.3987	0.6365[b]	0.32-1.23	.18
ASA I	–1.8881	0.4853	0.1514	0.1778[c]	0.06-0.46	<.05
ASA II	0.7106	0.3182	2.0353	0.8919	0.40-1.96	.77
ASA III	1.4693	0.4533	4.3462	4.019	1.56-10.33	<.05

ASA: physical status according to the American Society of Anesthesiologists; CI: confidence interval; OR: odds ratio.
[a]OR adjusted for age, gender, metabolic syndrome, excess weight and ASA stage.
[b]OR adjusted for ASA III.
[c]OR adjusted only for excess weight (no patient with metabolic syndrome can be ASA I).
Logistic regression model for perioperative complications. Perioperative complications were interpreted as dependent variables. Perioperative complications were interpreted as dependent variables. Adjusted by stepwise reward to 0.25. Source: the authors.

the occurrence of complications such as those observed in this study. The inflammatory response during surgery has been studied previously,[32] and the alteration in the production of inflammation factors such as TNFα and some cytokines,[3-5] reported in patients with metabolic syndrome, might explain in part the mechanism whereby the risk of complications increases in these patients when they are taken to surgery under general anesthesia.

Accordingly, modifiable factors appear as an option not only to reduce morbidity and mortality in patients with metabolic syndrome, but also to lower the risk of perioperative complications. This is what behavior showed to accomplish in this study, acting as a protective factor of ASA I physical status (table 3), and adding benefits and value to preventive measures geared at lowering weight in obese patients and modifying life style before the surgical procedure.

The comparison between the groups showed evidence that patients with no metabolic syndrome are significantly younger and are in better physical condition (table 1). Although it may initially be a selection bias during sampling (one of the possible weaknesses of this study) it is important to highlight that this trend is consistent with the epidemiological behavior of the syndrome, which is more frequent in patients over 50, explaining why the sample distribution might be representing a phenomenon associated with the presence of metabolic syndrome.[33] Contrary to what could be expected, the regression analysis showed that age in itself did not represent a risk factor for the development of perioperative complications. For this reason, the high rate of observed adverse events in the metabolic syndrome group is not considered to be due to the advanced age of the subjects who, because of the effects of aging, would then have a lower response to the surgical insult (table 3). In this regard, differences in the frequency of obesity between the groups could be considered as a determining factor for increased risk, since it includes most of the cases of visceral obesity (one of the components of the metabolic syndrome), and has been generally associated with perioperative complications.[34,35]

In conclusion, this study showed a direct correlation between metabolic syndrome and the development of perioperative complications in elective surgery scheduled for general anesthesia. These results point to the need of designing and implementing new prevention and intervention strategies to reduce the risk for patients with metabolic

syndrome undergoing surgery. Likewise, these results are an encouragement for further studies on the effects of metabolic syndrome in the context of surgery and anesthesia, and their underlying mechanisms.

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Conflict of interests

The authors state that they have no conflict of interest in relation to this work.

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