

Metabolic Syndrome in Patients undergoing Coronary Artery Bypass Graft: Prevalence and a Marker of Morbidity/Mortality during Hospitalization and 30 days after Hospital Discharge

Eduardo Pimenta, Oswaldo Passarelli Junior, Flávio Borelli, Márcio G. Sousa, Carlos Gun, Vivian Amato, Celso Amodeo, Leopoldo Soares Piegas

Division of Arterial Hypertension and Nephrology of the Instituto Dante Pazzanese de Cardiologia de Sao Paulo - Sao Paulo, SP, Brazil

Summary

Objectives: To compare the morbidity and mortality of patients with and without metabolic syndrome (MS) (according to the First Brazilian Guidelines for Diagnosis and Treatment of MS) undergoing coronary artery bypass graft (CABG) during hospitalization and after 30 days.

Methods: A total of 107 patients who underwent CABG with no associated procedures were assessed between August and October 2005; 74 (69.2%) of them had MS. Criteria of in-hospital outcome were: acute atrial fibrillation (AF), prolonged mechanical ventilation (MV), need for transfusion of blood products, number of hours spent in the ICU, length of hospital stay (days), respiratory and surgical wound infection, and death. For 30 days, the combination of events such as the need for readmission to hospital, surgical wound infection and death was assessed.

Results: The mean age was 60.6 ± 9.7 years, and the group with MS presented a higher body mass index and body surface, and a higher prevalence of diabetes. No statistically significant difference was observed in the occurrence of in-hospital events such as AF (15.2% vs 16.2%), MV (3.0% vs 2.7%), number of units of blood products used (3.2 ± 2.7 vs 2.6 ± 2.9), length of ICU stay (53.7 ± 27.3 vs 58.9 ± 56.5), length of hospital stay (9.2 ± 8.7 x 8.5 ± 8.5), respiratory infection (6.1% vs 2.7%), surgical wound infection (3.0% vs 5.4%), and mortality rate (3.0% vs 0.0%). The occurrence of combined events in 30 days was similar in both groups (12.2% vs 20.3%, $p = \text{NS}$).

Conclusion: Patients with MS did not have increased morbidity and mortality when undergoing CABG, however they had a higher trend of occurrence of surgical wound infection.

Key words: Metabolic syndrome; coronary artery bypass graft; morbidity; mortality; prevalence; length of stay.

Introduction

The metabolic syndrome (MS) is an association of cardiovascular risk factors that is closely related to increase of insulin resistance. Its prevalence varies according to the criteria used and to the population studied, ranging between 10.7% in Korean¹ women and 84% in men with diabetes mellitus in Finland and Sweden².

Patients with MS have a four-fold increase in the risk of death due to coronary artery disease and up to a three-fold increase in the risk of all-cause mortality^{3,4}. These individuals present a higher risk of coronary⁵ events and also a worse post-event outcome, such as larger extension of the area affected by an acute myocardial infarction (MI)⁶ and frequent left ventricular dysfunction⁷.

However, the prevalence of individuals with MS among those patients undergoing coronary artery bypass graft (CABG) and its impact on the perioperative and late postoperative

clinical course are still unknown. The purpose of this study was to evaluate the prevalence of MS in patients who had undergone coronary artery bypass graft, as well as its role as a prognostic marker of adverse events in the immediate postoperative period and 30 days later.

Methods

We prospectively evaluated 107 patients who underwent CABG between August and October 2005. Patients were considered to be affected by MS according to the I Brazilian Guidelines for Diagnosis and Treatment of Metabolic Syndrome⁸ if they had at least three of the following findings: blood pressure $>130/85$ mmHg or use of antihypertensive medications; fasting glucose levels >110 mg/dl or previous diagnosis of diabetes mellitus; triglycerides >150 mg/dl or treatment with lipid lowering drugs; HDL cholesterol <40 mg/dl in men or <50 mg/dl in women and abdominal circumference >102 cm in men or >88 cm in women. Abdominal circumference was measured horizontally in the midline between the iliac crest and the lower margin of the costal arch at the end of expiration.

We evaluated demographic data such as age, weight, height

Mailing Address: Eduardo Pimenta •

Rua das Camélias, 357 - 04048-060 – São Paulo, SP

E-mail: espimenta@cardiol.br

Manuscript received June 29, 2006; revised manuscript received July 14, 2006; accepted July 14, 2006.

and sex, body mass index (BMI), body surface (BS), renal function and history of smoking and previous acute myocardial infarction. BS was obtained through Dubois⁹ equation [BS = (weight^{0.425} x height^{0.725}) x 0.007184] - weight in kilograms and height in centimeters. BMI was obtained by dividing weight (in kilograms) by the square of the height (in meters). Renal function was expressed as creatinine clearance and it was calculated by the Cockcroft & Gault¹⁰ formula, using preoperative serum creatinine. A patient who smoked at least one cigarette per day in the last year was considered a smoker. The history of acute myocardial infarction was collected in medical records.

The variables that could interfere in the postoperative course, such as perfusion time, anoxia time and left ventricular function were also analyzed. Left ventricular function was evaluated by contrast ventriculography and it was considered a severe dysfunction if the ejection fraction was <0.35.

Patients with chronic atrial fibrillation, chronic renal failure undergoing dialysis and those who had undergone procedures associated with CABG, such as valve replacement or repair and resection of left ventricle aneurism were excluded from the study.

The parameters of intra-hospital progression evaluated included the occurrence of acute atrial fibrillation, prolonged mechanical ventilation (>48h), transfusion of blood products (in units), parenteral use of vasoactive drugs, surgical reintervention, time spent at the intensive care unit (hours), length of hospital stay (days), respiratory infection, infection of surgical wound (sternum or lower limbs), stroke and death. The 30-day follow-up period included the evaluation of the following isolated events, as well as their combination: re-admission to hospital, infection of surgical wound and death. The indication for the use of vasoactive drugs was a systolic blood pressure lower than 90mmHg and refractory to volume replacement. The use of blood products was indicated in the presence of serum hemoglobin levels lower than 10mg/dl or a coagulation disorder with active bleeding. The diagnoses of respiratory infection and surgical wound infection were considered in face of the need of antibiotic therapy at the discretion of the assisting physician.

The statistical analysis was carried out in two stages; the first one included the univariate analysis to test the relationship between each of the possible factors of worst postoperative progression. A significance of 0.10 was used in the univariate analysis to select which variables would be considered for the models of logistic regression, and the tests used were Fisher's exact test, chi square, Student's t test and Mann-Whitney. The second stage consisted of carrying out the logistic regression for the selected variables.

Results

The mean age of 107 patients was 60.6±9.7 years, with 81 (75.7%) males. The prevalence of MS was 69.2% in the general population, and it was higher among women (80.8%) than men (65.4%). Demographic and surgical data are displayed in Table 1, where we can observe that individuals with MS presented higher BMI, larger body surface and a higher prevalence of diabetes mellitus. Renal function estimated by creatinine

clearance was more preserved in patients with MS.

Factors related to the surgical procedure, such as anoxia time and perfusion time were similar in the two groups. The presence of severe ventricular dysfunction, which is associated with worse perioperative progression, also did not present any difference.

Clinical progressions during hospitalization and during the 30-day follow-up in the two groups are displayed in tables 2 and 3. Events such as atrial fibrillation and surgical wound infection, as well as the length of stay in the intensive care unit were more pronounced in patients with MS, although there was no statistical significance. The need of transfusion of blood products, prolonged mechanical ventilation, use of vasoactive drugs, respiratory infection, length of hospital stay, surgical re-intervention e death were similar in the groups. There was only one death among patients without MS.

Patients with MS presented higher need of re-hospitalization and higher incidence of surgical wound infection during the 30-day follow-up after CABG, although these findings were not statistically significant. There were no cases of stroke and death in the two groups and the incidence of combined events was higher in patients with MS (not statistically significant).

MS was not an independent factor for any of the progression criteria in the multivariate analysis.

Discussion

This is the first study reporting the prevalence of MS in patients undergoing CABG. Similarly, some studies evaluated the prevalence of MS in patients with acute coronary syndrome. The prevalence of MS was 46% in 633 patients diagnosed with acute myocardial infarction admitted to hospitals in France⁷. Clavijo et al reported 55.7% patients with MS among individuals with acute myocardial infarction who underwent primary angioplasty excluding the patients with diabetes mellitus⁶. In both studies there was a higher prevalence of MS among women - the same as in the current study. However, the prevalence of MS in the general population studied was higher in our study (69.2%). This difference observed in our population can be explained by the high incidence of diabetic patients who present coronary lesions in multiple arteries more frequently¹¹.

Mild to moderate renal failure is a risk factor for worse postoperative progression in patients undergoing CABG¹² and after acute myocardial infarction¹³. Although some of the components of MS are risk factors for the decrease in renal function, these patients presented higher rates of glomerular filtration. This finding can be explained by the younger age of the population with MS, since this factor interferes in the calculation of the creatinine clearance. Another possible explanation is that the patients with diabetes mellitus were in the initial stages of diabetic nephropathy, which promotes increased glomerular filtration.

Several studies discussed the association between postoperative clinical course and obesity according to BMI, but the findings were conflicting. Elahi et al¹⁴ evaluated the occurrence of hospital events in 3,002 patients undergoing CABG. The risk of complications such as stroke, atrial

Table 1 - Demographic characteristics, past medical history and variables related to surgery

	without MS (n = 33)	with MS (n = 74)	p
Men/women	28/5	53/21	NS
Age (years)	62.8±10.23	59.7±9.3	NS
BMI (kg/m ²)	24.6±3.1	28.9±4.2	<0.0001
Body surface (m ²)	1.7±0.1	1.8±0.2	0.001
Creatinine clearance (ml/min)	64.2±20.2	81.8±28.8	<0.0001
Preoperative hemoglobin (g/dl)	14.1±1.7	14.3±1.6	NS
Hypertension (%)	75.8	90.5	NS
Diabetes mellitus (%)	6.1	52.1	<0.0001
Dyslipidemia (%)	45.5	60.8	NS
Smoking (%)	27.3	17.6	NS
Previous MI (%)	48.5	41.9	NS
Severe LV dysfunction (%)	6.1	12.2	NS
Time of anoxia (min)	55.8±17.4	54.3±17.7	NS
Time of perfusion (min)	76.5±24.3	78.4±25.4	NS

MI - myocardial infarction, BMI - body mass index; LV - left ventricle.

Table 2 - Events in the hospitalization phase

	without MS	with MS	p
Transfusion of blood products (units)	3.2±2.7	2.6±2.9	NS
Prolonged mechanical ventilation (%)	3.0	2.7	NS
Use of vasoactive medications (%)	39.4	32.4	NS
Atrial fibrillation (%)	15.2	16.2	NS
Respiratory infection (%)	6.1	2.7	NS
Surgical wound infection (%)	3.0	5.4	NS
Length of stay at ICU (hours)	53.7±27.3	58.9±56.5	NS
Length of hospital stay (days)	9.2±8.7	8.5±8.5	NS
Surgical re-intervention (%)	6.1	2.7	NS
Death (%)	3.0	0	NS

ICO - intensive care unity.

Table 3 - Events in the postoperative 30-day follow-up

	without MS (%)	with MS (%)	p
Re-hospitalization	6.1	10.8	NS
Surgical wound infection	6.1	9.5	NS
Death	0	0	NS
Combined events	12.2	20.3	NS

MS - metabolic syndrome.

arrhythmia, renal insufficiency, surgical wound infections in the chest and lower limbs, prolonged mechanical ventilation and hospitalization longer than seven days was higher in patients with BMI >40kg/m². The increase in complication rates raised the cost in the amount of £1750 compared with

the patients with BMI <30 kg/m², although there were no deaths in this group of patients. Some authors used obesity as a risk factor and their findings were similar to those in this study. Thus, Moulton et al. concluded that obesity is not a risk factor for adverse events after cardiac surgery, except for the

increased number of superficial surgical wound infections and the higher incidence of atrial arrhythmias¹⁵. Likewise, Brandt et al¹⁶, when analyzing 500 patients with obesity defined as BMI >30kg/m², did not find increased morbidity/mortality after CABG in obese patients during hospitalization when compared with non-obese patients, although there was a trend to a higher incidence of surgical wound infections in the chest and lower limbs in obese individuals.

Other studies showed that obesity was a protective factor for CABG. Overweight (BMI between 25 and 30 kg/m²) and obese patients (BMI >30 kg/m²) who participated in the ARTS study and underwent CABG, during the mean follow-up of three years, presented a lower need of a new revascularization procedure and lower incidence of major cardiac or cerebrovascular events (death, stroke, transient ischemic attack, sustained neurological deficit and nonfatal acute myocardial infarction) when compared with non-obese patients (BMI <25kg/m²)¹⁷.

The analysis of studies involving obesity as a risk factor is due to the inexistence of studies about MS. However, this comparison can be performed since obesity is a risk factor for many of the components of MS, and also because it is a state of relative insulin resistance¹⁸. The conflicting findings are partly due to disagreement between the criteria adopted,

the characteristics of the populations and the methodological strategies used. None of the studies evaluated the factors inherent to the surgical procedure.

The presence of MS is also related with graft patency. Yilmaz et al¹⁹ showed that the risk of occlusion or significant injury to the graft performed with a saphenous vein is twice more frequent in patients with MS in a period shorter than five years after the surgery.

This study is limited by the small number of patients enrolled and consequently by the low number of events.

Thus, this study allows us to suggest that the prevalence of MS in patients undergoing coronary artery bypass graft is high. However, there was no significant difference in perioperative morbidity/mortality, both during hospitalization and during the postoperative 30-day follow-up, despite the trend of increased number of events such as surgical wound infection, atrial fibrillation and need of re-hospitalization after hospital discharge.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Oh Jy, Hong YS, Sung YA, Barrett-Connor E. Prevalence and factor analysis of metabolic syndrome in an urban Korean population. *Diabetes Care*. 2004; 27 (8): 2027-32.
2. Isomaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care*. 2001; 24 (4): 683-9.
3. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA*. 2002; 288(21): 2709-16.
4. Hu G, Qiao Q, Tuomilehto J, Balkau B, Borch-Johnsen K, Pyorala K for the DECODE Study Group. Prevalence of the metabolic syndrome and its relation to all-cause and cardiovascular mortality in nondiabetic European men and women. *Arch Intern Med*. 2004; 164(10): 1066-76.
5. Girman CJ, Rhodes T, Mercuri M, Pyorala K, Kjekshus J, Pedersen TR, et al for the 4S Group and the AFCAPS/TexCAPS Research Group. The metabolic syndrome and risk of major coronary events in the Scandinavian Simvastatin Survival Study (4S) and the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS). *Am J Cardiol*. 2004; 93(2): 136-41.
6. Clavijo LC, Pinto TL, Kuchulakanti PK, Torguson R, Chu WW, Satler LF, et al. Metabolic syndrome in patients with acute myocardial infarction is associated with increased infarct size and in-hospital complications. *Cardiovasc Revasc Med*. 2006; 7: 7-11.
7. Zeller M, Steg PG, Ravisy J, Laurent Y, Janin-Manificat L, L'Huillier I, et al. Prevalence and impact of metabolic syndrome on hospital outcomes in acute myocardial infarction. *Arch Intern Med*. 2005; 165: 1192-8.
8. Sociedade Brasileira de Hipertensão, Sociedade Brasileira de Cardiologia, Sociedade Brasileira de endocrinologia e Metabologia, Sociedade Brasileira de Diabetes, Sociedade Brasileira de Estudos da Obesidade. I Diretriz Brasileira de Diagnóstico e Tratamento da Síndrome Metabólica. *Arq Bras Cardiol*. 2005; 84 (supl 1): 1-28.
9. DuBois D, DuBois EF. A formula to estimate the approximate surface area if height and weight be known. *Arch Intern Med*. 1916; 17: 863-71.
10. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976; 16: 31-41.
11. Ledru F, Ducimetière P, Battaglia S, Courbon D, Beverelli F, Guize L, et al. New diagnostic criteria for diabetes and coronary artery disease: insights from an angiographic study. *J Am Coll Cardiol*. 2001; 37(6): 1543-50.
12. Cooper WA, O'Brien SM, Thourani VH, Guyton RA, Bridges CR, Szczech LA, et al. Impact of renal dysfunction on outcomes of coronary artery bypass surgery: results from the Society of Thoracic Surgeons National Adult Cardiac Database. *Circulation*. 2006; 113(8): 1063-70.
13. Pimenta E, Ramos RF, Gun C, Santos ES, Timerman A, Piegas LS. Renal function outcome in acute myocardial infarction as a prognostic factor of in-hospital events and at one-year follow-up. *Arq Bras Cardiol*. 2006; 86(3): 170-4.
14. Elahi MM, Chetty GK, Sosnowski AW, Hickey MS, Spyt TJ. Morbid obesity increases perioperative morbidity in first-time CABG patients – should resources be redirected to weight reduction. *Int J Cardiol*. 2005; 105: 98-9.
15. Moulton MJ, Creswell LL, Mackey ME, Cox JL, Rosenbloom M. Obesity is not a risk factor for significant adverse outcomes after cardiac surgery. *Circulation*. 1996; 94: 1187-92.
16. Brandt M, Harder K, Walluscheck KP, Schöttler J, Rahimi A, Möller F, et al. Severe obesity does not adversely affect perioperative mortality and morbidity in coronary artery bypass surgery. *Eur J Cardiothorac Surg*. 2001; 19: 662-6.
17. Gruberg L, Mercado N, Milo S, Boersma E, Disco C, van Es GA, et al for the Arterial Revascularization Therapies Study Investigators. Impact of body mass index on the outcome of patients with multivessel disease randomized to either coronary artery bypass grafting or stenting in the ARTS trial: the obesity paradox II? *Am J Cardiol*. 2005; 95: 439-44.
18. Turhan H, Yetkin E. Obesity-related increased perioperative morbidity in CABG patients: does metabolic syndrome affect the perioperative outcomes? *Int J Cardiol*. 2006; 110: 273-4.
19. Yilmaz MB, Guray U, Guray Y, Biyikoglu SF, Tandongan I, Sasmaz H, et al. Metabolic syndrome negatively impacts early patency of saphenous vein grafts. *Coron Artery Dis*. 2006; 17(1): 41-4.