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IMPACT OF A CLUSTERED METABOLIC CONDITION ON RECOVERY AFTER A MAJOR CARDIAC EVENT

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SUMMARY – This study examined the clinical implications of a metabolic dysfunction profile in patients undergoing emergency cardiac procedures for severe myocardial events. Individuals were categorized based on specific metabolic health indicators defined by established clinical guidelines. Their in-hospital experiences, complications, and recovery outcomes were assessed, along with short-term follow-up data.

Despite expectations that metabolic abnormalities would worsen the course of the illness, patients with and without these conditions demonstrated comparable short-term trajectories. Differences in critical events or recovery benchmarks were minimal. The findings raise questions about the utility of current diagnostic criteria for metabolic syndrome in predicting outcomes during acute coronary interventions, suggesting that some risk factors may be underrepresented in existing models.

Key words: *Metabolic syndrome X; Myocardial infarction*

Introduction

The concurrence of metabolic risk factors for endothelial dysfunction and atherosclerotic cardiovascular disease, which include abdominal obesity, hyperglycemia, dyslipidemia, and hypertension, suggests the existence of metabolic syndrome. Other names used for this constellation of findings are syndrome X, insulin resistance syndrome, 'deadly quartet', or obesity dyslipidemia syndrome[1,2]. According to a recent paper by Mottillo *et al*.[3], the metabolic syndrome is associated with a 2-fold increase in cardiovascular outcomes and 1.5-fold increase in all-cause mortality. Studies are needed to investigate whether or not the prognostic significance of the metabolic syndrome exceeds the risk associated with the sum of its individual components. Furthermore, additional studies should elucidate the mechanisms by which the metabolic syndrome increases cardiovascular risk. The overall prevalence of metabolic syndrome is estimated to be around 20% with an age-dependent increase and increase over time[4].

There are several definitions of the metabolic syndrome[1-3,5]. The criteria provided for the definition of the metabolic syndrome/insulin resistance syndrome (MS/IRS) according to the American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE)[6,7] are:

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1) triglycerides >1.69 mmol/L,
2) HDL cholesterol <1.04 mmol/L in men and <1.29 in women,
3) elevated blood pressure (≥130/85 mm Hg),
4) 2-hour post-glucose challenge >7.78 mmol/L and fasting glucose between 6.11 and 7.00 mmol/L,
5) overweight/obesity (body mass index ≥25 kg/m^2), and
6) other risk factors including:
   - family history of type 2 diabetes, hypertension, or CVD,
   - polycystic ovary syndrome,
   - sedentary lifestyle,
   - advancing age, and
   - ethnic groups having high risk for type 2 diabetes or cerebrovascular disease.

Diagnosis depends on clinical judgment with two or more of the first four criteria listed above. This definition has been designed to help physicians predict and prevent serious complications from a number of related conditions grouped in the cluster, even if the underlying pathophysiology may not be completely understood. The differences from other definitions may be summarized as follows: 1) the MS/IRS is used to describe the cluster of abnormalities that are more likely to occur in insulin resistant/hyperinsulinemic individuals; 2) the MS/IRS is differentiated from type 2 diabetes; 3) body mass index, rather than waist circumference, is used as the index of obesity, and viewed as a physiological variable that increases insulin resistance, rather than as a criterion for the diagnosis of MS/IRS; 4) ethnicity is introduced as an important risk factor for insulin resistance, and non-Caucasian ancestry identified as an increasing risk of MS/IRS; 5) other factors have been identified that increase the risk of developing MS/IRS, including family history of type 2 diabetes, hypertension, cerebrovascular disease, polycystic ovary syndrome, gestational diabetes, and acanthosis nigricans; and 6) fasting plasma glucose concentrations are used to identify individuals with type 2 diabetes, and the plasma glucose concentration 2 h after 75-g oral glucose load is introduced as a more sensitive measure of the risk of MS/IRS.

Using the AACE/ACE[6,7] definition for MS/IRS, the main objectives of this study were:

- to calculate the incidence of MS/IRS among consecutive patients with acute ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI) and to compare the results with literature data;
- to evaluate the severity of heart disease and acute STEMI in patients with MS/IRS and to compare the results with patients without the syndrome; and
- to evaluate the prognosis of acute STEMI in patients with MS/IRS and to compare the results with patients without the syndrome.

Patients and Methods

Study population

This retrospective study included 385 consecutive patients having suffered acute STEMI and treated with primary PCI in Kerckhoff Heart Center, Bad Nauheim, Germany, over a two-year period. Data were collected from hospital registry. The diagnosis of STEMI was established and primary PCI performed using the European Cardiac Society criteria[8,9]. In brief, patients with an episode of chest pain within the last 48 hours and ST-elevation on electrocardiography (ECG) in at least two consecutive leads were included.

Methods

After primary PCI patients were hospitalized at cardiology department with continuous monitoring including clinical, ECG, laboratory and echocardiography. Six months after discharge, the authors collected data on major adverse cardiovascular events (MACE) (restenosis, reinfarction, cardiac and non-cardiac rehospitalization, mortality, coronary artery bypass graft (CABG) and cerebrovascular insult (CVI rate)) during patient examination, by checking medical documentation or by telephone contact with patient family members or family physicians.

Using the AACE/ACE[6,7] definition of MS/IRS, study patients were divided into two groups (with and without MS/IRS) and compared according to the severity of their heart disease and prognosis. The severity of heart disease and acute STEMI were estimated

using clinical findings (angina pectoris before primary PCI, dyspnea, all ECG verified rhythm abnormalities, heart failure, cardiogenic shock, cardiac arrest and artificial respiration), cardiac laboratory marker values (creatine phosphokinase (CPK), cardiac troponin T (cTnT)), echocardiography (left ventricular ejection fraction (LVEF)) and coronarography findings (culprit vessel, number of significantly narrowed coronary arteries, diameter and length of stents) and number of hospital days. The prognosis was estimated using intrahospital reinfarction and re-PCI, as well as MACE during six-month follow-up.

Angiography and PCI were performed by the standard technique on a monoplane system (Axiom Artis, Siemens, Erlangen, Germany) as recommended in current guidelines[9]. Patients received 70 IE/kg unfractionated heparin, 500 mg aspirin, a loading dose of 600 mg clopidogrel and in most cases a GPIIb/IIIa inhibitor. Serum biomarkers were assessed as commercially available. Echocardiography was performed according to the clinical standard and in accordance with recommendations related to current echocardiography guidelines[10].

Statistical analysis

Statistical analysis was performed by using the SPSS for Windows 15 software. Nominal (categorical) variables were analyzed by using Pearson χ^2-test and Fisher's exact test, and quantitative variables by using Mann-Whitney test. The level of significance was set at $P<0.05$.

Ethical standards

The study was performed in accordance with ethical standards laid down in the Declaration of Helsinki and was approved by the appropriate institutional review committee.

Results

The mean age of study patients was 63.0 years and 70.3% of them were male. The anterior myocardial wall was affected in 41.1% and inferior wall in 58.9% of study patients. Out of 385 patients, 192 patients fulfilled the criteria for MS/IRS (men 50.9% and women 37.5%), while 193 patients did not meet these

Table 1. Severity of acute ST-elevation myocardial infarction

Finding	Characteristics	Metabolic syndrome	No metabolic syndrome	*P*
Clinical presentation	Angina pectoris (%)	95.1	93.3	0.172
	Dyspnea (%)	3.9	8.8	0.065
	Hospital days	6.48 (±4.31)	6.48 (±4.59)	0.709
Intrahospital complications	Rhythm abnormalities (%)	3.9	3.6	0.785
	Heart failure (%)	1.0	1.0	1.000
	Cardiogenic shock (%)	2.9	2.6	1.000
	Cardiac arrest (%)	6.8	5.2	0.990
	Mechanical ventilation (%)	8.7	5.7	0.325
	Reinfarction (%)	0.5	1.6	0.623
	Re-PCI* (%)	2.1	2.1	1.000
Laboratory	Mean maximal cardiac troponin T (ng/mL)	4.00 (±3.40)	4.46 (±3.21)	0.657
	Mean maximal creatinine phosphokinase (U/L)	1619.7 (±1475.4)	1928.7 (±2166.3)	0.399
Echocardiography	Mean LVEF** (%)	45.65 (±9.79)	45.69 (±9.53)	0.991
Coronarography	Mean number of stenosed vessels	1.69 (±0.87)	1.74 (±0.92)	0.619
	Mean stent diameter (mm)	3.28 (±0.40)	3.21 (±0.39)	0.118
	Mean stent length (mm)	14.39 (±4.93)	14.96 (±4.51)	0.214

*Re-PCI = repetition of percutaneous coronary intervention; **LVEF = left ventricular ejection fraction

Table 2. Prognosis of acute ST-elevation myocardial infarction

Finding	Characteristics	Metabolic syndrome	No metabolic syndrome	*P*
MACE*	Reinfarction (%)	1.4	1.6	0.623
	Restenosis (%)	17.5	13.3	0.382
	Rehospitalization (cardiac) (%)	27.1	25.9	0.624
	Rehospitalization (non-cardiac) (%)	7.2	6.7	0.527
	Cerebrovascular insult (%)	1.9	0.5	0.372
	Urgent CABG**	1	0	–
	Mortality (%)	6.3	6.2	0.990
	Total (%)	30.7	30.7	1.000

*MACE = major adverse cardiovascular events; **CABG = coronary artery bypass graft

criteria. There were no statistically significant age or sex differences between the two patient groups.

Data on the severity of acute STEMI and prognosis in both patient groups are shown in Tables 1 and 2, respectively. Patients with MS/IRS had similar or worse results on all severity parameters except for the incidence of dyspnea, reinfarction rate, cardiac laboratory markers (cTnT and CK), and the number and length of coronary artery stenosis. The same held for the parameters of prognosis except for the reinfarction rate. None of these differences reached statistical significance.

Discussion

Most people with metabolic syndrome suffer thrombotic complications superimposed to atherosclerotic and inflammatory arterial vascular lesions. Altered cardiac remodeling together with altered adhesion and coagulation mechanisms appears suitable to explain decreased functional performance of infarcted organs, and decreased success of acute (reduced fibrinolytic response, no reflow phenomenon) and long term intervention strategies for vessel patency (PCI, CABG) in these patients. That is why studies revealed high incidence of metabolic syndrome in patients with acute myocardial infarction (AMI), as well as more serious findings and prognosis of AMI in these patients[11,12]. Investigators mostly used criteria for metabolic syndrome established by the National Cholesterol Education Program expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) (NCEP ATP III)[5]. There are no reports evaluating AACE/ACE definition[6,7] using coronary artery disease.

Using NCEP ATP III criteria, patients with metabolic syndrome had two- to threefold increased risk of subclinical or clinically overt cardiovascular disease. Using these criteria, Yilmaz *et al.*[13] and Zeller *et al.*[14] found metabolic syndrome in 49% and 46% of AMI patients without ST-elevation and unselected population of AMI patients, respectively, significantly more common in women. Two thirds of young patients with premature myocardial infarction had metabolic syndrome[15]. Similar incidence of MS/IRS was found in the present study, with a slightly higher incidence in men.

Patients with metabolic syndrome had increased infarct size, more extensive coronary artery disease, and poor myocardial perfusion grade[13,16-18]. Bohmer *et al.*[19] found no association of the presence of metabolic syndrome with related biomarkers or the size of myocardial infarction. In this study, lower cohort serum concentrations of cardiac markers (cTnT, CK) and less extended coronary artery disease were recorded in patients with MS/IRS, however, without statistical significance. According to Piatti *et al.*[18], insulin resistance is an independent predictor of early in-stent restenosis, which was not found in the present study (the same incidence of early in-stent restenosis). However, a higher incidence of late in-stent restenosis was found in patients with MS/IRS. According to literature data[20,21], metabolic syndrome is also a strong predictor of recurrent ischemic coronary events, but without correlation with either early or re-infarction during follow up in the present study. Metabolic

syndrome appeared to be associated with worse in-hospital complications and outcome, especially with a higher risk of severe heart failure[14,21,22]. Results of the present study suggested a higher incidence of rhythm abnormalities, cardiogenic shock, and cardiac arrest in MR/IRS group (without statistical significance), while the incidence of heart failure and the mean left ventricular ejection fraction were the same in both patient groups.

Using metabolic score as a simple metabolic risk marker, Raposo *et al*.[23] found a statistically significant relation between this score and outcome at one-year follow up after non-ST elevation acute coronary syndromes. Using the NCEP ATP III[5] definition of metabolic syndrome, Iribaren *et al*.[24] conclude that the presence of this syndrome imparts a high risk of early-onset clinical coronary disease, but the prognostic information associated with the syndrome is not greater than the sum of its parts. The authors of this article found the same incidence of MACE in general in the two groups of study patients during six-month follow up, with nonsignificant differences in some components.

Using the AACE/ACE definition for MS/IRS, the authors did not find the expected significant influence of this syndrome on the severity and prognosis during six-month period in patients having suffered acute STEMI and treated with primary PCI. From the interventional cardiologists' point of view, one of the explanations could be that early invasive treatment of acute STEMI attenuates the risk of metabolic syndrome. However, there are several open questions in metabolic syndrome in general, i.e. the lack of clarity of definition, multiple different patient phenotypes, the lack of consistent evidence base, unclear pathogenesis uniting the syndrome components, and the fact that cardiovascular risk associated with the syndrome is not greater than the sum of its individual components[24-27]. Among all these issues, anthropometry as an additional problem seems to be one of the major ones in the AACE/ACE definition[6,7] Body mass index used in this definition is an inferior anthropometric parameter in comparison to waist circumference or waist-to-hip ratio in verification of abdominal obesity and cardiovascular risk[28,29]. That is why it is necessary to emphasize the importance of the waist and hip circumference measurement in all patients with coronary disease, especially in risk stratification of patients with AMI. Also, the MS/IRS diagnosis dependence on clinical judgment may result in lower accuracy and investigation of different patient populations in different studies.

In conclusion, evaluating the AACE/ACE[6,7] definition for MS/IRS in patients with acute STEMI treated with primary PCI, the authors found no statistically significant differences in the severity and prognosis between patients with and without the syndrome. The main reasons for such unexpected results may lie in many open questions in this definition (primarily the absence of waist-to-hip ratio) and metabolic syndrome in general.

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