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Obstructive coronary artery disease in patients hospitalized for severe sepsis or septic shock with concomitant acute myocardial infarction

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ABSTRACT

Purpose: It is difficult to differentiate type 1 acute myocardial infarction (AMI) with obstructive coronary artery disease (OCAD) from type 2 AMI in patients admitted for severe sepsis. The aims of this study were to assess the risk factors and prognosis of OCAD in patients admitted to the intensive care unit for severe sepsis with concomitant AMI.
Materials and methods: This is a single-center retrospective cohort study including all consecutive patients who were hospitalized for severe sepsis or septic shock between March 2006 and September 2014 and who underwent coronary angiography in the intensive care unit to identify AMI.
Results: Overall, 78 (5.5%) of 1418 patients hospitalized for severe sepsis underwent coronary angiography to identify concomitant AMI. Thirty-two patients (41%) had OCAD. Following multivariate analysis, the risk factors of OCAD were peripheral vascular disease (odds ratio [OR] = 5.7; 95% confidence interval [CI], 1.1-30.4; $P = .042$) and at least 2 cardiovascular risk factors (OR = 6.7; 95% CI, 1.9-23.8; $P = .003$). Obstructive coronary artery disease was associated with a significant mortality increase at 60 days (OR = 8.1; 95% CI, 1.9-30.2; $P = .004$).
Conclusions: Obstructive coronary artery disease is a poor prognosis factor in patients hospitalized for severe sepsis with concomitant AMI. In this setting, medical treatment should be considered for patients with peripheral vascular disease or with at least 2 cardiovascular risk factors; the need to perform coronary angiography should be considered carefully.

1. Introduction

Myocardial damage is frequently encountered in intensive care unit (ICU) patients admitted for severe sepsis or septic shock; the incidence of myocardial damage in these patients ranges from 12% to 85% [1]. One possible cause of myocardial damage is acute myocardial infarction (AMI), which occurs in up to 36% of patients [2].

In patients hospitalized for severe sepsis or septic shock, myocardial damage rarely appears to be caused by spontaneous coronary artery occlusion (ie, type 1 AMI) [3] and often appears to be associated with an imbalance between the oxygen supply and oxygen demand during shock or respiratory failure (ie, type 2 AMI or ischemic imbalance) [4,5], direct damage caused by endotoxins, difficulties in microvascular coagulation, or clearance insufficiency during renal impairment [6,7].

In clinical practice, it is difficult to differentiate type 1 AMI with obstructive coronary artery disease (OCAD) from type 2 AMI in patients admitted for severe sepsis or septic shock with AMI; no studies have evaluated the OCAD risk factors in this population. The management of type 1 AMI with OCAD and type 2 AMI in patients hospitalized for sepsis is different. In cardiology patients not in the ICU, the presence of cardiovascular risk factors has the most accurate predictive value for OCAD [8]. There are evidence-based guidelines for the assessment of OCAD in hospitalized patients who are not in the ICU and for the determination of the need for coronary angiography and cardiologic medications. Coronary angiography is a risk factor for acute kidney injury, and this complication is associated with increased mortality [9]. Determining the OCAD risk factors in patients admitted to the ICU for severe sepsis with concomitant AMI should facilitate better selection of patients who are most likely to benefit from coronary angiography and cardiologic medications.

The aims of this study were to assess the risk factors and prognosis of OCAD in patients admitted to the ICU for severe sepsis or septic shock with concomitant AMI with no known coronary artery disease.

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2. Material and methods

This observational study was approved by the local Ethics Committee of Félix Guyon University Hospital (R15011). The need for informed consent was waived because of the observational and retrospective nature of the study.

3. Selection of the study sample

This retrospective observational cohort study was conducted in a 23-bed mixed medical/surgical ICU from March 2006 to September 2014 at a French university hospital.

All patients hospitalized for severe sepsis or septic shock and who underwent coronary angiography to diagnose AMI were included in the study.

Concomitant AMI was defined as an elevation in cardiac troponin (cTn) I within 24 hours of ICU admission for severe sepsis or septic shock associated with one of the following criteria: ischemia symptoms, electrographic criteria (new or suspected significant ST-segment T-wave changes, development of pathological Q waves or new left bundle-branch block), or new regional wall motion abnormalities [10].

Severe sepsis was defined as sepsis with sepsis-induced organ dysfunction or tissue hypoperfusion, and *septic shock* was defined as sepsis-induced hypotension persisting despite fluid resuscitation as defined by the Surviving Sepsis Campaign guidelines [11].

During the study period, there was no standardized protocol for coronary angiography, and an AMI examination was performed at the physician's discretion (ICU and cardiology physicians).

Obstructive coronary artery disease was defined as stenosis greater than 50% of the diameter of the left main coronary artery or stenosis greater than 70% of the diameter of a major epicardial vessel or branch vessel that was greater than 2.0 mm in diameter.

No coronary artery disease was defined as stenosis of less than 20% in any vessel.

Percutaneous coronary interventions were typically performed on hemodynamically and significant lesions in vessels greater than 1.5 mm. In clinical practice, decisions regarding percutaneous coronary interventions were at the discretion of the physician performing the coronary angiography.

The exclusion criteria were admission after cardiac arrest, previous known coronary artery disease, AMI not examined by coronary angiography, extracorporeal membrane oxygenation, hospitalization after cardiac surgery, or cardiopulmonary bypass surgery.

4. Data collection

The patients' characteristics and cardiovascular risk factors were recorded. The cardiovascular risk factors were defined as follows: hypertension requiring medical therapy, diabetes mellitus, age at least 65 years, hyperlipidemia currently treated with medication, smoking (≥5 cigarettes per day as a mean in the month before admission), or previous smoking (≥5 cigarettes per day as a mean more than 1 month before admission) [12].

Electrocardiography was systematically performed within 24 hours of admission. The following elements were recorded: heart rate, rhythm, ST-segment depression or elevation greater than 0.5 mm, prominent T-wave flattering or inversion greater than 1 mm and Q wave at least 0.03 second and at least 0.01 mV deep in at least 2 contiguous leads, and left bundle-branch block.

Upon admission, cTnI was systematically measured in all patients. Blood samples were analyzed using a Cobas Roche cTnI assay. When cTnI greater than 0.2 μg/L was observed, physicians were encouraged to obtain additional cTnI measurements to determine the cTnI peak.

Transthoracic echocardiography was systematically performed within 24 hours of admission. The following elements were recorded: left ventricular systolic ejection fraction and left ventricular regional wall motion abnormalities.

Diagnoses of AMI were made prospectively; and electrocardiography, coronary angiography, and diagnoses of AMI were retrospectively reviewed and validated by CB and JBE, who are experts in cardiology.

The microorganisms and infection sites were also recorded.

5. Outcome measurements

The primary aim of the study was to assess OCAD risk factors, and the secondary aims were to assess if OCAD is associated with increased mortality over a 60-day period and to evaluate the effect of percutaneous intervention on mortality in patients with OCAD.

The causes of death were also recorded. Cardiovascular death includes death resulting from an AMI, sudden cardiac death, death due to heart failure, death due to stroke, death due to cardiovascular hemorrhage, and death due to other cardiovascular causes.

6. Statistical analysis

The results are expressed as the total number (percentage) of categorical variables and as the median [25th-75th percentiles] for continuous variables. Continuous variables were compared using the nonparametric Mann-Whitney test. Categorical variables were compared using the χ^2 test or Fisher exact test, as appropriate. Risk factors found to be predictive of OCAD in the bivariate analysis with $P < .1$ were entered into a multivariate logistic regression analysis using backward selection with a criterion of $P < .05$. A receiver operator characteristic curve was determined to evaluate the capacity of the number of cardiovascular risk factors to predict OCAD. Collinearity between independent risk factors was tested; in cases of collinearity between risk factors, the most clinically relevant factor was selected to construct the multivariate model. Survival functions in the ICU were estimated using the Kaplan-Meier method and compared using the log-rank test. A P value < .05 was considered significant. Analyses were performed using SAS statistical software (8.2; SAS Institute, Cary, NC).

7. Results

7.1. Patient characteristics

During the study period, 1418 patients were admitted to the ICU for severe sepsis or septic shock. Of these patients, 121 (8.5%; 95% confidence interval [CI], 7.1-10) had concomitant AMI upon admission. Forty-three patients were excluded from the analysis: 6 for admission after cardiac arrest, 10 for previous known coronary artery disease, 11 for AMI not explored by coronary angiography, 4 for extracorporeal membrane oxygenation, and 12 for hospitalization after cardiac surgery. The remaining 78 patients constituted the cohort (Fig. 1).

The main characteristics of the patients are presented in Table 1.

The median age of the patients was 62 [52-72], with a median Simplified Acute Physiology Score 2 of 57 [42-72].

The infection sites were pulmonary and abdominal in 50 (64.1%) and 14 cases (17.9%), respectively. The most frequently isolated microorganisms were Enterobacteriacae (25 cases), gram-positive cocci (16 cases), and nonfermenting gram-negative bacilli (9 cases).

7.2. Ischemic features

The median values of cTnI at admission and peak were 1.72 [0.20-3.98] μg/L and 8.64 [2.59-25.8] μg/L, respectively. The most frequent abnormalities identified on electrocardiography were ST-segment depression (20.5%) and prominent T-wave inversion (33.3%). The median left ventricular ejection fraction, as evaluated by transthoracic echocardiography, was 45% [30%-55%], and 26 patients (33.3%) had abnormalities in left ventricular kinetics. Two patients (2.6%) had chest pain (Table 2).