Myocardial necrosis in ICU patients with acute non-cardiac disease: a prospective study

Objective: To ascertain if, after an episode of hypotension, unnoticed myocardial necrosis could occur in critical care patients with acute non-cardiac illness and to search for signs of cardiac necrosis.

Design: A prospective observational study.

Setting: General intensive care unit (ICU) at a tertiary level hospital.

Patients: Thirty-one patients in two groups. Group 1 included 19 patients with severe sepsis/septic shock (ACCP/SCCM Consensus Conference). Group 2 included 12 patients with hypovolemic shock.

Interventions: Biochemical markers of myocardial necrosis (cardiac troponin I (cTnI), creatine kinase (CK), creatine kinase MB mass (CKMB) and myoglobin) were measured at 12 h (T1), 24 h (T2) and 48 h (T3) after enrollment. A standard 12-lead ECG was recorded upon enrollment (T0) and at T2. Anomalous Q-waves or ST segment depression or elevation was considered diagnostic for acute myocardial infarction (AMI). A hypotensive episode (arterial systolic pressure < 90 mmHg at heart rate > 100 bpm) was considered moderate if it lasted 30–60 min or severe if longer than 60 min.

Measurements and results: At T0 none of the patients had AMI on ECG. At T2 a non-Q AMI developed in five patients. Increased levels of troponin I, myoglobin, CK and CKMB were found in 74.2%, 96.8%, 74.2% and 67.7% of the patients, respectively. Cardiac troponin I increased in 11 out of 19 septic patients and in all hypovolemic patients. There was a significant difference between the groups (p < 0.05). All biochemical markers increased in relationship to the degree of hypotension with cTnI again showing a significant difference. The longer the hypotensive episode was, the greater was the increase (moderate hypotension: median 1.16; quartiles 0.55–3.44 ng/ml, severe hypotension: median 8.53; quartiles 1.1–20.7 ng/ml; p < 0.05). Abnormal levels of cTnI were more frequent in non-survivors than in survivors (p < 0.05).

Conclusions: Hypotension may cause cardiac damage in critically ill patients with acute non-cardiac diseases as shown by abnormal levels of cTnI. It is likely that a high number of these myocardial necroses may go unnoticed on the ECG.

Key words Shock · Sepsis · Hypovolemia · Cardiac troponin I · Myocardial necrosis
**Introduction**

Critical care patients are exposed to a high degree of non-cardiac stress, which increases myocardial oxygen consumption [1]. At the same time, the myocardial oxygen supply may be reduced by hypotension, tachycardia, hypoxemia, anemia and, in some patients, intrinsic coronary artery disease [2]. An unexpectedly high incidence of clinically unrecognized myocardial injury, according to elevated levels of cardiac troponin I (cTnI), has been reported in the critically ill [3, 4, 5]. Troponin I is a myocardial regulatory protein that is present at increased levels in plasma following myocardial damage [6, 7, 8]. Abnormally high troponin I values are often associated with the occurrence of hypotensive episodes [5, 9] and higher morbidity and mortality rates [4, 5]. Hypovolemia may play a role in troponin release from the cardiomyocytes. Subendocardial hemorrhages and necrosis have been found in the myocardium of severely injured patients after fatal hypovolemic shock [10].

Abnormally high troponin T values have been found in sepsis [11]. Myocardial dysfunction is reported to be an important factor contributing to the high mortality in septic patients [12]. During septic shock the coronary circulation displays abnormalities similar to those of the systemic circulation. A maldistribution of nutritive blood flow and a disturbance in convective and diffusive oxygen delivery (DO₂), as reflected by abnormally high coronary sinus oxygen content and low oxygen extraction, have been reported in both human and animal studies [13, 14, 15]. The resulting imbalance of DO₂ and oxygen consumption (VO₂) can raise the possibility of myocardial ischemia [16, 17]. The results of human post-mortem studies showed the presence of large areas of myofibrillar necrosis in the septic myocardium [18].

The aim of this study is to determine whether critically ill patients with non-cardiac illness sustain “unnoticed” myocardial necrosis after a hypotensive episode of septic or hypovolemic origin.

**Materials and methods**

Patients

We conducted a prospective observational study in a general intensive care unit (ICU) from October 15, 1997 to May 15, 1998. Patients were enrolled in two groups according to the following inclusion criteria: group 1 (G1): patients with severe sepsis/septic shock, as defined by the ACCP/SCCM Consensus Conference [19]; group 2 (G2): patients with hypovolemic shock (arterial hypotension and central venous pressure (CVP) < 5 cmH₂O). Patients who had had external heart massage, defibrillation or electrical cardioversion in the previous 7 days [20], symptoms and/or ECG signs typical of acute myocardial infarction (AMI) at enrollment, complete left branch block on ECG or chest trauma in the previous 7 days [20] were excluded from the study.

**Cardiac markers**

We measured the plasma concentration of cardiac troponin I (cTnI), creatine kinase (CK), creatine kinase MB mass (CKMB) and myoglobin. Blood was taken at 12 h (T1), 24 h (T2) and 48 h (T3) after enrollment (T0); plasma was immediately separated and stored at -20°C until analysis. Because the time between the onset of hypovolemia or sepsis and enrollment varied considerably among patients, the peak values of biochemical markers were considered for data analysis.

The cTnI assay was performed by immunoassay method (OPUS, Dade-Behring Diagnostics). The minimum detection limit of the assay was 0.5 ng/ml (according to the manufacturer information), thus abnormal values were defined as higher than 0.5 ng/ml [21]. The upper limit of the reference range was 2.5 ng/ml [22]. Any blood level above 2.5 ng/ml was considered indicative of acute myocardial injury, while levels below 2.5 ng/ml defined the presence of minor myocardial injury.

The recommended manufacturer lower limits for CK, CKMB (mass) and myoglobin assays were 200 UI/ml, 5 ng/ml and 80 ng/ml, respectively. These values were confirmed by local laboratory experience.

**Hypotension grading**

A hypotensive episode was assessed by arterial systolic pressure (Psyst) lower than 90 mmHg at a heart rate above 100 bpm. Hypotensive episodes were considered non-significant if they lasted less than 30 min, moderate if 30–60 min in duration, and a duration of more than 60 min was considered severe.

**Severity score**

We documented the number and severity of organ dysfunction at T0 according to the Multiple Organ Dysfunction Score (MODS) [23].

**Electrocardiogram**

A standard 12-lead ECG was recorded at T0 and T2. The ECG criteria of Q and non-Q AMI [24] were based on the presence of any new anomalous Q wave (Q < 0.10 mV), or ST segment elevation or depression (≥ 0.10 mV) in at least two of the following leads: a) D2, D3 or aVF; b) V1–V6; c) D1, aV1. Patients with non-specific ST-T segment changes (e.g. left ventricular hypertrophy, drugs) were enrolled only if unmodified with respect to previous baseline traces.

**Clinical diagnosis of acute myocardial infarction**

Localized or radiating substernal or epigastric pain accompanied by weakness, sweating, nausea, vomiting, anxiety or any otherwise unexplained sudden-onset breathlessness or loss of consciousness with cardiovascular collapse was considered compatible with AMI [25].

**Anemia**

Severe anemia was defined as a hemoglobin level of less than 7 g/dl.