The value of biomarkers of myocardial damage or inflammation in off-pump coronary artery bypass (OPCAB) surgery has not yet been established. In a prospective study of 51 consecutive patients scheduled for elective OPCAB surgery, preoperative levels of troponin T, C-reactive protein, interleukin-6, and tumor necrosis factor α were determined. The primary endpoint was the combination of cardiac death or acute myocardial infarction (AMI) within 30 days. Seven patients (14%) presented with an adverse event: 3 cardiac deaths and 6 AMIs. Univariate analysis identified the following adverse event predictors: renal failure (50% vs 11%; P = .028), left ventricular ejection fraction <50% (38% vs 9%; P = .033), preoperative troponin-T level >0.10 ng/dL (43% vs 9%; P = .016), and EuroSCORE rating (7.6 ± 2.5 VS. 5.2 ± 2.6; P = .031). A preoperative troponin-T level >0.10 ng/dL (P = .03) was the only independent adverse event predictor. No significant differences were found with biomarkers of inflammation (P > .05). The presence of a preoperative troponin-T level >0.10 ng/dL is associated with a higher risk of cardiac death or AMI in patients undergoing OPCAB surgery.

Key words: Troponin T. C-reactive protein. Off-pump coronary artery bypass surgery.

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INTRODUCTION

Inflammatory markers such as C-reactive protein (CRP), interleukin 6 (IL-6), and tumor necrosis factor α (TNF-α) are associated with the development of cardiovascular events in patients with acute coronary syndrome (ACS) and also in healthy subjects.

Furthermore, C-reactive protein can predict a higher incidence of cardiovascular complications after percutaneous transluminal coronary angioplasty (PTCA).

Elevated markers of myocardial damage such as troponin T (TrT) point to a worse prognosis in patients with non-ST elevation ACS, as well as in patients undergoing PTCA or peripheral vascular surgery. The prognostic usefulness of these biomarkers in patients who undergo off-pump coronary artery bypass grafting (CABG) has not been studied. The studies published to date have only evaluated patients with extracorporeal circulation and the results have been contradictory.
Biomarkers

During the 24 hours prior to surgery, peripheral blood samples were taken and stored at –80ºC for subsequent analysis. The patients’ treatment was not conditioned by the results of these analyses. Plasma concentrations of TnT were measured (Roche Diagnostics GmbH, Mannheim, Germany) as a marker of myocardial damage: concentrations greater than >0.10 ng/dL were considered pathological. As markers of inflammation, an ultrasensitive C-reactive protein assay (Dade-Behring Inc., Newark, USA) (normal range, 0-0.5 mg/dL) and assays for IL6 (CLB, Amsterdam, The Netherlands) (normal range, 0-1.5 pg/mL) and TNF-α (Biosource Europe S.A., Belgium) (normal range, 50-150 pg/mL) were used.

Adverse Clinical Events

Patient follow-up lasted for the first 30 days after the operation. The primary endpoint was a composite of cardiac death or acute myocardial infarction (AMI). Diagnosis of postoperative AMI was defined as concentrations of the creatine kinase-MB isoenzyme (CK-MB) more than 5 times of the normal value and more than 4% of the total CK fraction.

Statistical Analysis

Continuous variables with a normal distribution were expressed as means (SD) and those not normally distributed as medians (percentiles). Categoric variables were expressed as numbers and percentages. A logistic regression analysis was done to determine the association of the appearance of adverse events with biomarkers, as well as with all the previously described risk factors. The multivariate logistic regression analysis (forward stepwise procedure) included variables with P values less than <0.10 in the univariate analysis. P values less than <0.05 were considered statistically significant.

RESULTS

The baseline clinical characteristics are presented in Table 1. The mean postoperative EuroSCORE11 was greater than >5. Table 2 shows the preoperative levels for the biomarkers. All patients had normal values for CK (50±30 µg/dL) and CK-MB (1.9±1.1 ng/mL), whereas 7 patients (14%) had TnT levels above >0.10 ng/dL.

In the 30 days after the procedure, 3 patients (6%) died, 6 (12%) suffered an AMI, 13 (25%) had postoperative atrial fibrillation, and 7 (14%) had heart failure. The primary composite endpoint of death or AMI occurred in 7 patients (14%). In the univariate analysis (Table 3), the primary endpoint occurred significantly more often in patients with preoperative renal failure (50% vs 11%; P=0.028), left ventricular

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**TABLE 1. Preoperative Clinical Characteristics (n=51)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean±SD Age, years</th>
<th>Men</th>
<th>Diabetic mellitus</th>
<th>Hypertension</th>
<th>Hyperlipidemia</th>
<th>Smokers</th>
<th>Mean±SD BMI</th>
<th>≥30</th>
<th>Living alone</th>
<th>Recent ACS (&lt;1 month)</th>
<th>Prior AMI</th>
<th>Renal failure (creatinine &gt;1.5 mg/dL)</th>
<th>Peripheral vascular disease</th>
<th>Beta-blockers</th>
<th>Mean±SD no. affected vessels per patient</th>
<th>Three affected vessels</th>
<th>LMCA disease</th>
<th>Mean±SD no. grafts per patient</th>
<th>Mean±SD EuroSCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>66±9</td>
<td>38 (75%)</td>
<td>21 (41%)</td>
<td>33 (65%)</td>
<td>31 (61%)</td>
<td>12 (23%)</td>
<td>27.9±3.4</td>
<td>15 (30%)</td>
<td>8 (16%)</td>
<td>38 (74%)</td>
<td>16 (31%)</td>
<td>4 (8%)</td>
<td>9 (18%)</td>
<td>46 (90%)</td>
<td>2.5±0.6</td>
<td>31 (61%)</td>
<td>20 (39%)</td>
<td>1.7±0.6</td>
<td>5.6±2.7</td>
</tr>
</tbody>
</table>

*LVEF indicates left ventricular ejection fraction; BMI, body mass index; ACS, acute coronary syndrome; LMCA, left main coronary artery.

**TABLE 2. Preoperative Biomarker Levels (n=51)**

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Concentration (µg/dL)</th>
<th>range</th>
</tr>
</thead>
<tbody>
<tr>
<td>TnT&gt;0.10 ng/dL</td>
<td>7 (15%) (0.14-1.70)</td>
<td></td>
</tr>
<tr>
<td>CKP, mg/dL</td>
<td>0.24 (0.13-0.83)</td>
<td></td>
</tr>
<tr>
<td>IL6, pg/mL</td>
<td>3.2 (1.6-12.1)</td>
<td></td>
</tr>
<tr>
<td>TNF-α, pg/mL</td>
<td>28.4 (21.4-42.9)</td>
<td></td>
</tr>
</tbody>
</table>

*IL6 indicates interleukin 6; CKP, Creatine protein; TnT, troponin T; TNF, tumor necrosis factor.

Values are expressed as number (%) and range for TnT and median (25 and 75 percentiles) for the remaining variables.

...can affect hemostatic, renal, neurological, and gastrointestinal function.16 Off-pump CABG has become consolidated as an alternative that avoids inflammatory response, although it is more demanding and can affect the quality of the anastomosis.11 It might therefore be more important to monitor markers of inflammation and necrosis in off-pump CABG procedures.

**PATIENTS AND METHODS**

**Study Population**

Patients scheduled for off-pump CABG in 2002 were prospectively included in this study. Patients undergoing emergency procedures, combined surgery, repeat procedures and patients with active infection, those receiving steroid treatment, and alcoholics were excluded because the markers studied may be affected in such cases.
ejection fraction below < 50% (38% vs 9%; \(P=0.033\)), and preoperative TnT greater than > 0.10 ng/dL (43% vs 9%; \(P=0.016\)). The EuroSCORE was significantly higher in patients with the primary endpoint (7.6±2.5 vs 5.2±2.6; \(P=0.031\)). A number of studies have shown that patients with recent ACS, which was not significant as a risk marker in this population. Only a few studies have assessed the usefulness of preoperative CRP in CABG and these studies were done exclusively with CABG with extracorporeal circulation. Guadino et al.\(^\text{17}\) did not find that patients with high preoperative CRP were at greater risk, whereas Milazzo et al.\(^\text{18}\) reported worse long-term prognosis in patients with CRP greater than or equal to ≥ 0.30 mg/dL, and Biancati et al.\(^\text{19}\) found a higher risk of early complications in patients with CRP greater than or equal to ≥ 1 mg/dL. Unlike these studies, we assessed patients undergoing off-pump surgery, which avoids the inflammatory response induced by extracorporeal circulation. In our population, the preoperative concentrations of CRP, IL6, and TNF-α did not show any significant association with mortality or the incidence of AMI in the immediate postoperative period, indicating that inflammatory status generally indicate thrombus formation and complex coronary lesions, associated with a high risk of recurrence.\(^\text{16}\) Thus, preoperative elevation of TnT could identify an unstable coronary process which, although subclinical, might lead to a higher risk of perioperative complications. The prognostic value of TnT was independent of other baseline variables, suggesting that it can be included in risk stratification and that it would add to information provided by traditional risk markers. Troponin T was of greater prognostic value than history of recent ACS, which was not significant as a risk marker in this population.

**DISCUSSION**

A number of studies have shown that patients with clinical suspicion of ACS and TnT concentrations greater than > 0.10 µg/L at the time of admission have a higher rate of cardiac events in both the short and long term.\(^\text{11}\) Preoperative concentrations of TnT have only been assessed for surgery with extracorporeal circulation. Mächler et al.\(^\text{12}\) studied patients with unstable angina and normal CK-MB levels and found that preoperative TnT was of no prognostic value, whereas Carrier et al.\(^\text{13}\) reported that TnT concentrations greater than > 0.02 µg/L were associated with a higher risk of perioperative AMI, and Lyon et al.\(^\text{14}\) found that TnT greater than or equal to ≥ 0.20 ng/dL was associated with higher early and late postoperative mortality.

In our study, the presence of preoperative concentrations of TnT greater than > 0.10 ng/dL was predictive of early cardiac complications. No other studies have been published that assessed the usefulness of preoperative TnT or other markers of myocardial damage in off-pump CABG. The population assessed in our study of off-pump surgery was representative of those undergoing surgery in Spain, and our findings were comparable to previously published studies.\(^\text{15}\) Off-pump of surgery is technically more demanding, and so increased TnT might identify a subgroup of higher risk, with worse tolerance of surgical manipulation and perioperative ischemia. Normal values for TnT are very low, below the limit of sensitivity of the assays used, and so small elevations point to ischemia and myocardial damage.\(^\text{16}\) Our patients had low values of TnT, with a range between 0.14 ng/dL, and 1.70 ng/dL, and normal concentrations of CK-MB. These small elevations generally indicate thrombus formation and complex coronary lesions, associated with a high risk of recurrence.\(^\text{16}\) Thus, preoperative elevation of TnT could identify an unstable coronary process which, although subclinical, might lead to a higher risk of perioperative complications. The prognostic value of TnT was independent of other baseline variables, suggesting that it can be included in risk stratification and that it would add to information provided by traditional risk markers. Troponin T was of greater prognostic value than history of recent ACS, which was not significant as a risk marker in this population.

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| TABLE 3. Analysis of Predictors of Death or Acute Myocardial Infarction (n=51)* |
|-----------------|-----------------|-----------------|-----------------|
|                  | Univariate P    | Multivariate P  | With Event (n=7) | Without Event (n=44) |
| Onsets failure   | 0.06            | 0.18            | 28%             | 4%                |
| LVEF<50%         | 0.049           | 0.18            | 43%             | 11%               |
| LMCA disease     | 0.067           | 0.17            | 71%             | 34%               |
| EuroSCORE        | 0.03            | 0.08            | 7.5±0.50        | 5.25±2.58         |
| TnT>0.1 ng/dL    | 0.016           | 0.03            | 43%             | 9%                |
| CRP>0.3 mg/dL    | 0.080           | 0.12            | 71%             | 36%               |

* LVEF indicates left ventricular ejection fraction; CRP, C-reactive protein; LMCA, left main coronary artery; TnT, troponin T.
CONCLUSION
The presence of increased preoperative concentrations of TnT was associated with a higher risk of a poor outcome in off-pump revascularization surgery, independently of other traditional risk factors. The markers of systemic inflammation did not provide any additional prognostic information.

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