Surgical revascularization and perioperative management in patients with non-ST-elevation acute coronary syndromes

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Abstract

Purpose: The management and surgical revascularization treatment of patients with acute coronary syndromes (ACS) have undergone great evolution over the past decade. The objective of the present study was therefore to analyze the outcome and predictors of survival in patients unresponsive to maximal non-surgical treatment referred to emergency coronary artery bypass grafting (CABG) with ACS.

Material and methods: Between October 1999 and September 2004, a total of 3571 CABG patients underwent primary isolated CABG at our institution. Out of these, non-ACS (N-ACS) was present in 3124 patients (group 1), 386 patients (group 2) had non-ST-elevation ACS (NSTE-ACS), whereas 61 patients (group 3) had ST-elevation ACS (STE-ACS). Clinical data, in-hospital morbidity and mortality were prospectively recorded and studied retrospectively in the groups.

Results: Left main stem stenosis was observed in 25%, 32%, and 41%, respectively (P < 0.02). Previous myocardial infarction was found in 33%, 43%, and 73% (P < 0.001). Overall in-hospital mortality was 1.5% in group 1, 4.2% in group 2, and 13.0% in group 3 (P < 0.001). Logistic regression and receiver operating characteristic analyses identified cTnI as the strongest preoperative predictor significantly related to in-hospital mortality. A preoperative cTnI level above 1.5 ng/ml was the best single predictor for in-hospital mortality amongst patients with ACS.

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Conclusions: The present study clearly demonstrates a significant difference of in-hospital morbidity and mortality between patients with ACS undergoing CABG. A more precise patient's risk stratification on admission and improvements in the perioperative management with adjunctive pharmacological therapies and the use of intraaortic balloon counter pulsation may improve patients' outcome.

Key words: coronary artery bypass grafting, acute coronary syndromes, perioperative management, outcomes.

Introduction

To date, patients undergoing coronary artery bypass grafting (CABG) with acute coronary syndromes (ACS) ranging from unstable angina or acute myocardial infarction (AMI) without ST-segment elevations up to evolving AMI with persistent ST--segment elevations, offer a challenge from the standpoint of diagnosis, treatment, and prognosis, as the clinical manifestations vary considerably. The differences between the entities of ACS are related to the symptoms severity, the initial electrocardiographic pattern, and the degree of acute myocardial cellular necrosis, as expressed by cardiac troponins elevation as a biochemical marker of irreversible myocardial necrosis [1-3]. Patients with ST-elevation acute myocardial infarction have been clearly identified to have an increased risk of suffering death in hospital and, moreover, to have an increased adverse prognosis in the setting of percutaneous coronary intervention [4,5] as well as in patients undergoing emergency CABG [6,7]. However, the reasons for higher adverse prognosis and increased mortality rates in patients with non-ST-elevation ACS (NSTE-ACS) associated with 'minor myocardial damage' resulting in minor elevations of cardiac troponins are not fully understood. Nonetheless, the surgical revascularization in

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patients with ACS has, so far, an important indication based on the obstructive coronary artery lesion; all of them considered of high risk according to the ACC/AHA guidelines [8-10].

The outcomes of patients with ACS undergoing CABG surgery during their hospitalization are expected to be worse than of non-ACS (N-ACS) patients [11,12]. Although there is a plethora of data regarding the outcomes of CABG in general, there are less of contemporary data regarding the frequency and outcomes of CABG among a wide spectrum of patients refferd to CABG due to ACS, although surgical revascularization treatment and management of ACS patients have undergone a great evolution over the past decade [9,12].

The objective of the present study was therefore to analyze the outcome and predictors of survival in patients unresponsive to maximal non-surgical treatment referred to emergency CABG due to ACS at our institution.

Material and methods

Patient population and data collection

From 1999 to 2004, a total of 3510 consecutive patients who underwent primary isolated CABG at the West-German Heart Center Essen were prospectively studied. Of these, 3124 patients had N-ACS (Group 1), whereas a NSTE-ACS (Group 2) was preoperatively identified in 386 CABG patients. NSTE-ACS was supposed to be present if patients had symptoms indicative of an ACS within the preceding 24 hours like new onset of chest pain or accelerating chest pain within the previous 24 hours occurring at rest or with minimal exertion, alleviated by nitroglycerin and/or rest in the absence of ST-segment elevation of >1 mm on the electrocardiogram or with an elevated serum level of cardiac troponin I (cTnI) or creatine kinase (CK) on admission. Informed consent was obtained for all patients and the study protocols were approved by the Institutional Review Board of the West-German Heart Center Essen. Patients were excluded from the study, if any of the following criteria were present: (1) preoperative myocardial infarction with ST-segment elevation on the electrocardiogram (STEMI); (2) new onset left bundle branch block; (3) reoperations; (4) any concomitant heart surgery besides CABG. All clinical data were prospectively recorded and documented with more than 1800 variables per case using a database tool according to the "Heidelberger Verein zur Multizentrischen Datenanalyse e.V." (HVMD) [13].

The primary study endpoint for comparison between the two groups were in-hospital mortality, defined as all cause of death within 30 days after surgery or during the same time period of hospitalization. Secondary study endpoints were postoperative major adverse events (MAE) during the period of hospitalization including: (1) perioperative myocardial infarction (PMI); (2) low cardiac output syndrome (LOS) with high-dose inotropic support with or without requiring the use of an intraaortic balloon counterpulsation; (3) stroke, and minor adverse events like; (4) new-onset ventricular arrhythmias; (5) major bleeding; (6) necessity for rethoracotomy and (7) postoperative renal failure requiring temporary hemodialysis. Perioperative myocardial infarction was considered to have occurred, if one of the following diagnostic criteria were present: (1) a postoperaive cTnI serum level above 10.5 ng/ml within the first 24 hours after CABG, as previously described [14]; (2) the appearance of ST-segment deviations at the J point in two or more contiguous leads with cut-off points ≥ 0.2 mV in leads V1, V2, or V3 and ≥ 0.1 mV in other leads or T-wave abnormalities in two or more contiguous leads or the development of new Q-waves [2]. LOS was present, if high-dose inotropic support was necessary in the postoperative course during hospital stay with or without the need of an intraaortic balloon couterpulsation (IABP).

Preoperative risk stratification

In patients with an established diagnosis of ACS, the management strategy to be selected in a particular patient depends on the perceived risk of progression to myocardial infarction or death. All patients presenting with NSTE-ACS were stratified to their individual risk, using the established independent predictors like: (A) markers of thrombotic risk, such as recurrence of chest pain, ECG-changes, or elevated levels of cardiac markers for myocardial damage and severity of coronary artery disease, and (B) risk-factors and comorbidities, such as age, history of previous MI, left ventricular function, renal dysfunction, etc [15-17].

Preoperative management

Patients presenting NSTE-ACS were treated preoperatively on the evidence of clinical trials or meta-analyses with: (1) hemodynamic monitoring; (2) adjunctive pharmacological therapeutic measures, using beta-blockers, nitrates, low-molecular-weight or intravenous heparin, and finally ADP receptor antagonists, such as ticlopidine and clopidogrel resulting in inhibition of platelet aggregation in patients with NSTE-ACS; (3) the optimal timing of CABG surgery, which depends on the preoperative dynamics of acute myocardial injury and (4) the evaluation of the prophylactic use of preoperative IABP treatment, especially in high-risk patients due to (a) impaired left ventricular ejection fraction, (b) preoperative hemodynamic instability with necessity of inotropic support, (c) unstable angina at the time of operation despite intravenous nitroglycerin and heparin, and (d) filiform left mainstem disease or left main equivalent or severe three-vessel disease.

Surgical management

Standard anesthetic and monitoring techniques were used in all patients. Internal thoracic artery, radial artery, and saphenous vein grafts were used as graft conduits. Heparin was administered in order to achieve an activated coagulation time above 400 s. Standard cardiopulmonary bypass (CPB) technique was used with ascending aortic and two-stage venous cannulation. During CPB, moderate hemodilution with a hematocrit level between 20% and 25% using mild systemic hypothermia (>32°C) was maintained. A maximum of myocardial protection was achieved using simultaneous antegrade and retrograde cristalloid cardioplegic arrest (Bretschneider) with additional topical cooling, and single aortic cross clamping for all distal anastomosis. In addition, cardioplegia was administered through the distal grafts until aortic unclamping if necessary. Depending on the severity of coronary artery disease and the resultant estimated extent of acute myocardial injury, the C-1-esterase inhibitor (Berinert) was administered intravenously 5 minutes before reperfusion. Reperfusion was performed using a modified protocol with aortic systolic blood pressure <50 mmHg at aortic unclamping for the first 3 minutes of reperfusion. Proximal graft anastomoses to the aorta were performed with partial occlusion of the ascending aorta. IABP support was applied intra- and postoperatively according to the morphology of coronary arteries, necessity of inotropic support and/or hemodynamic difficulties during CPB weaning time or in the early postoperative course.

Postoperative management

Postoperative management for high-risk CABG patients was standardized. Patients were monitored with respect to arterial pressure, pulmonary pressure, central venous pressure. A 12-lead ECG as well as the serum biomarkers for myocardial damage, such as cardiac troponin I, myoglobin, and creatin kinase were determined immediately after arrival on the intensive care unit and at 6, 12 and 24 hours postoperatively and once a day thereafter. A medication of 500 mg acetylsalicylic acid was administered intravenously within the first 6 hours after surgery in the absence of significant bleeding.

Statistical analysis

Data are reported as mean ±SD and categorical variables by their percentage. For all categorical variables the odds ratios (OR) and 95% confidence intervals (CI) were calculated. Comparisons of categorical variables between the groups were performed by Pearson's Chi-square test, since expected frequencies <5 occurred all P values were calculated exactly. Comparisons of continuous variables between groups were analyzed by students t-test. Univariate and multivariate logistic regression analyses were performed to identify preoperative independent predictors for in-hospital mortality. All preoperative predictor variables that were identified as significant at a two-tailed nominal P value of less than 0.10 in univariate regression analysis were then entered into a multivariate logistic regression analysis model. Receiver operating curve (ROC) analyses were applied to determine optimal cut-off values of cTnI and to evaluate the predictive power for in-hospital mortality. A P value less than 0.05 was considered to indicate statistical significance. All statistical analyses between groups were performed using the SPSS software package (SPSS Inc., Chicago, IL, USA).

Results

The demographics and baseline data of the two groups are summarized in *Tab. 1*. Preoperative baseline characteristics and demographics of the patients were comparable with the contemporary coronary surgery patient profile. A preoperative significant difference between the groups could be observed in terms of age, smoking history, previous myocardial infarction, symptoms of angina, left mainstem disease, left ventricular ejection fraction as well as the preoperative cTnI serum level (*Fig. 2A*) and CK activity. The preoperative cTnI serum level was likewise significantly different according to the survival

Table 1. Baseline characteristics

	Group 1 N-ACS (n=3124)	Group 2 NSTE-ACS (n=386)	P value	
Demographics				
Age, y	66±9	67±9	0.01	
Gender, female	635 (20)	95 (25)	0.11	
Body weight, kg	81 ± 14	82±16	0.44	
Cardiovascular risk factors				
Diabetes mellitus	941 (30)	122 (30)	0.72	
Hypertension	2588 (83)	333 (86)	0.15	
Hyperlipidemia	2525 (81)	295 (76)	0.09	
Family history	1409 (45)	178 (45)	0.82	
Smoking history	1902 (61)	199 (62)	0.004	
Comorbidities				
History of stroke	221 (7)	22 (6)	0.77	
COPD	497 (16)	70 (16)	0.18	
PVD	472 (15)	54 (15)	0.62	
Renal disease*	436 (14)	51 (13)	0.92	
Dialysis	65 (2)	7 (2)	0.59	
Cardiac history				
Previous MI**	1028 (33)	189 (43)	< 0.0001	
Previous PCI	625 (20)	66 (17)	0.18	
CCS III-IV	1839 (59)	268 (66)	0.0001	
Extent of CAD				
Left-mainstem disease	782 (25)	123 (32)	0.02	
One-vessel disease	90 (3)	11 (4)	0.06	
Two-vessel disease	472 (15)	57 (14)	0.44	
Three-vessel disease	2595 (83)	318 (82)	0.97	
LV function				
LV-EF, %	60 ± 15	56±15	< 0.0001	
Preoperative serum marker				
cTnI, ng/mL	0.03 ± 0.04	2.4 ± 7.6	< 0.0001	
CK, IU/L	55 ± 63	85±120	< 0.0001	

Data are presented as mean \pm SD or number (%); COPD – Chronic obstructive pulmonary disease; PVD – Peripheral vascular disease; MI – Myocardial infarction; PCI – Percutaneous coronary intervention; CCS – Canadian Cardiovascular Society; CAD – Coronary artery disease; LV – Left ventricle; EF – Ejection fraction; * – Serum Creatinine >0.2 µmol/l; ** – >7 days

staus of the entire study cohort (Fig. 2B). As demonstrated in Tab. 2 the intraoperative data did not differ between the groups, except the amount of cardioplegia to be used, which was slightly but significantly more in group 2 compared to group 1 (P=0.01). The aortic cross clamping time and the cardiopulmonary bypass time tended to be longer in group 2. The number of graft conduits per patient did not differ between the groups and the percentage of internal mammary artery grafts to be used was also not different. The intraoperative mean graft flow, as measured by Doppler flowmetry, did also not differ between the groups. According to the postoperative data, as shown in Tab. 2 and Fig. 1, a significant difference in the necessity for intraoperative and postoperative intraaortic balloon pump (IABP) support between the groups (P<0.001) accompanied by a significantly prolonged postoperative ventilation time (P<0.001) and a longer ICU stay (P<0.001) could be observed. Among the 3124 patients with N-ACS of group 1, 47 (1.5%) died *Figure 1.* Preoperative, intraoperative and postoperative use of intraaortic ballon counterpulsation support in CABG patients with NACS versus NSTE-ACS (P<0.001)

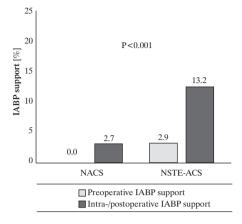


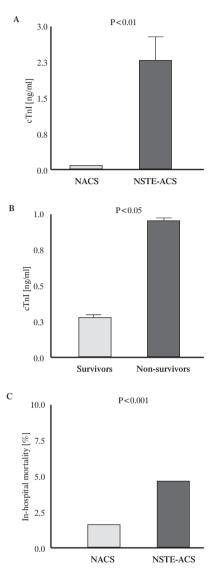
Table 2. Intra- and postoperative characteristics

	Group 1 N-ACS (n=3124)	Group 2 NSTE-ACS (n=386)	OR (95% CI)	P value	
Intraoperative data					
ACC time, min	68 ± 23	72 ± 23	-	0.19	
CPB time, min	106 ± 39	110 ± 33	-	0.21	
Cardioplegia, mL	1516 ± 473	1579 ± 445	-	0.01	
Reperfusion time, min	31±16	34 ± 14	-	0.11	
Grafts per patient, n	3.0 ± 0.8	3.0 ± 0.8	-	0.30	
Postoperative data					
Ventilation time, h	8 (7-11)	8 (7-13)	-	< 0.001	
IABP support	84 (2.7)	51 (13)	5.5(3.8-8.1)	< 0.001	
ICU stay, d	1 (1-2)	1 (1-4)	-	< 0.001	
Hospital stay, d	8 (6-12)	8 (6-12)	-	0.21	
Major adverse events					
Death in hospital	47 (1.5)	16 (4.2)	2.8(1.5-5.2)	< 0.001	
LCOS	48 (1.5)	22 (5.7)	3.9(2.2-6.7)	< 0.001	
PMI	171 (5.5)	44 (11.5)	2.2(1.5-3.2)	< 0.001	
Stroke	62 (2.0)	6 (1.6)	0.8(0.3-1.9)	0.56	
Other complications					
Major bleeding	110 (3.5)	11 (2.8)	0.8(0.4-1.6)	0.50	
Rethoracotomy	88 (2.8)	16 (4.1)	1.5(0.8-2.6)	0.15	
Arrhythmia	410 (13)	78 (20)	1.7(1.3-2.1)	< 0.001	
Renal failure (dialysis)	172 (5.5)	62 (16)	3.3(2.4-4.5)	< 0.001	

Data are presented as mean \pm SD, median (25% – 75% Interquartile) or number (%); ACC – Aortic cross-clamp; CPB – Cardiopulmonary bypass; IABP – Intraaortic ballon counterpulsation; ICU – Intensive care unit; LOS – Low cardiac output syndrome; PMI – Perioperative myocardial infarction; OR – odds ratio and 95% confidence interval between group 1 and 2

in the postoperative course within 30 days or within the same time of hospital stay, whereas 16 (4.2%) deaths occurred among 386 patients with NSTE-ACS in group 2 (P<0.001; *Fig. 2C*). The difference of in-hospital mortality was accompanied by a significant difference in the appearence of postoperative low cardiac output syndrome (P<0.001) and the incidence of perioperative myocardial infarction (P<0.001). The incidence

Figure 2. (A) Preoperative serum cTnI levels in patients with NACS versus NSTE-ACS (P<0.01). (B) Prognostic value of pre-CABG cTnI serum levels: survival status of the entire study cohort according to pre-CABG cTnI levels (P<0.05). (C) In-hospital mortality in CABG patients with NACS versus NSTE-ACS (P<0.001)



of postoperative stroke was not significantly different. Other postoperative complications and adverse events like major bleeding (>200 ml/h first 6 h) and all causes of rethoracotomy were not different between the groups. The occurrence of newonset arrhythmia (P<0.001) and the incidence of postoperative renal failure requiring temporary veno-venous hemofiltration or hemodialysis was significantly different between the two groups (P<0.001).

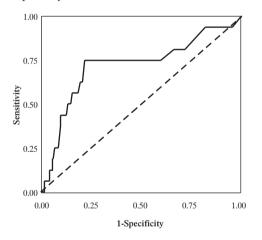
Univariate and multivariate logistic regression analyses identified a number of risk factors and preoperative variables like age, peripheral vascular disease, previous PCI, angina class and preoperative cTnI serum level to be related with in-hospital mortality. These independent predictors of death are detailed in *Tab. 4.* In this regard, the preoperative cTnI serum level

	Univariate Regression Analysis		Multivariate Regeression Analysis	
	Odds Ratio [95% CI]	P Value	Odds Ratio [95% CI]	P Value
Age	1.1 (1.0-1.1)	< 0.001	1.1 (1.0-1.1)	0.02
Gender	2.1 (1.1-4.1)	0.02	1.3 (0.6-2.8)	0.46
Obesity	0.9 (0.5-1.7)	0.80		_
Smoking	0.4 (0.2-0.8)	0.01	0.6 (0.3-1.2)	0.17
Diabetes mellitus	1.9 (1.0-3.5)	0.05	1.3 (0.7-2.7)	0.44
Hypertension	3.8 (0.9-15.9)	0.07	2.1 (0.5-8.9)	0.33
Hyperlipidemia	1.8 (0.7-4.5)	0.24		_
Renal disease	1.0 (0.3-2.8)	0.96		_
COPD	1.5 (0.7-3.2)	0.29		_
PVD	2.6 (1.3-5.2)	0.01	2.5 (1.2-5.2)	0.01
Previous MI	1.5 (0.8-2.9)	0.19		_
Previous PCI	2.4 (1.2-4.7)	0.01	2.7 (1.3-5.6)	0.01
Angina Class III-IV	5.5 (2.0-15.5)	0.01	3.5 (1.2-10.2)	0.02
Left-mainstem disease	1.0 (0.5-2.0)	0.91		_
LV-EF (%)	0.98 (0.96-1.0)	0.12		_
CK (IU/L)	1.0 (0.99-1.0)	0.62	_	_
cTnI (ng/mL)	1.1 (1.0-1.1)	< 0.0001	1.1 (1.0-1.1)	< 0.001

Table 4. Univariate and multivariate logistic regression analysis of variables between groups 1 and 2

* - All cause of death; CI - Confidence interval

Figure 3. ROC curve analysis demonstrating the discriminatory power of preoperative cTnI levels for in-hospital mortality. The optimal per-CABG cTnI serum level was found with 1.5 ng/ml with an area under curve of 0.72 ± 0.08 , a sensitivity of 75.0% and a specificity of 78.5%



was found to be the strongest independent risk factor for death (P<0.0001). The discriminative power of the preoperative cTnI serum level for in-hospital mortality by using a receiver operating characteristic (ROC) curve analysis revealed an optimal cTnI cut-off value of 1.5 ng/ml, with an area under curve of 0.72 ± 0.08 , a sensitivity of 75.0% and a specificity of 78.5% (*Fig. 3*).

Discussion

Our findings in the present study suggest that in a surgical population of patients undergoing CABG, the existence of pre-

operative non-ST-elevation ACS is associated with a significantly higher mortality within 30 days and a higher incidence of major adverse cardiac events, such as perioperative myocardial infarction or low cardiac output syndrome. Moreover, the present study could clearly demonstrate, that increased mortality rates after CABG due to NSTE-ACS are significantly associated with several independent preoperative predictors, most notably, with the degree of preoperative cTnI serum elevation. Furthermore, the present study suggest that the surgical revascularization with the concomitant perioperative management strategies is safe and effective in the clinical course of patients presenting NSTE-ACS. At our institution, the average mortality rate was 4.2% during hospital stay or within 30 days for CABG patients with NSTE-ASC, which was significantly higher compared to CABG patients without ACS during the same interval. This overall hospital mortality rate is well in the range of actual data of the current literature [11].

Multiple studies have shown that patients undergoing coronary artery bypass grafting who present acute myocardial infarction with ST-segment elevations on the electrocardiogram have an clearly increased risk of suffering death in hospital. It has been clearly shown that emergency revasculratzation of patients with an acute transmural myocardial infarction have an increased adverse prognosis in the setting of percutaneous coronary intervention [5,18] as well as in patients following emergency CABG [6,7]. However, the occurences and reasons for higher adverse prognosis and increased mortality rates in patients with non-ST-elevation ACS (NSTE-ACS) associated with 'minor myocardial damage' resulting in minor elevations of cardiac troponins are not fully understood. In the setting of ACS, elevations of cardiac troponins were found to be associated with multivessel disease, complex coronary lesions with unstable and ruptured plaques, distal coronary microembolization of platelet microaggregates and plaque debris [19,20] as well as abnormal microvascular myocardial perfusion [5], which might be an alternative or contributory cause of elevations of cardiac troponins. In several recent studies, it has been shown that patients with unstable CAD and elevated cardiac troponins had more widespread CAD than those without elevated cardiac troponins and had more often complex coronary lesions and visible thrombus in the culprit vessel [21,22]. It has also been demonstrated, that minor elevations of cardiac troponins and thus, a 'minor myocardial damage', is present in approximately 30% of patients with rest angina and negative CK/CK-MB values [23].

According to risk stratification among patients with NSTE-ACS, there is an increased risk of death within 6 weeks in those with elevated serum levels of cardiac troponins and the risk of death continues to increase as the cardiac troponin serum level increases [8,10]. Reversible ST-segment depression is associated with an increase by a factor of 3-6 in the likelihood of death, myocardial infarction, ischemia at rest, or provocable ischemia during a test to stratify risk. Although the conditions of the majority of patients with unstable angina will stabilize with effective antiischemic medications, approximately 50-60% of such patients will require revascularization treatment because of the "unresponsiveness" of medical therapy [12]. High-risk patients are those who have had angina at rest, prolonged angina, or persistent angina with positive serum levels of cardiac troponins or dynamic ST-segment changes or hemodynamic instability, and these patients urgently require invasive diagnostic evaluation and subsequent revascularization treatment. In accordance to the present guidelines of the ACC/AHA, patients with NSTE-ACS require, first of all, an aggressive medical treatment in order to stabilize and control the symptoms if possible. Medical therapy should be adjusted rapidly to relieve manifestations of ischemia and should include antiplatelet therapy (aspirin, or ticlopidine or clopidogrel if aspirin is contraindicated), antithrombotic therapy (unfractionated heparin or lowmolecular-weight heparin), beta-blockers, nitrates, and possibly calcium-channel blockers. Early administration of glycoprotein IIb/IIIa inhibitors may be particularly important, especially in high-risk patients with positive troponin tests or those in whom implantation of coronary stents is anticipated [8-10]. However, even in patients with NSTE-ACS were surgical revascularization is indicated, a recently published randomized trial have demonstrated that the benefit (freedom from cardiovascular death, MI, stroke) of administering clopidogrel early on admission appear to outweight the risk of life-threatening bleeding in patients with NSTE-ACS following CABG [24].

Surgical myocardial revascularization with CABG for patients with unstable angina and left main stem stenosis or equivalent with evidence of myocardial ischemia, or with triple vessel disease and impaired left ventricular function, improves prognosis and has, so far, a clear indication based on the obstructive coronary artery lesion; all of them considered of high-risk according to the ACC/AHA guidelines [8-10]. The perioperative treatment strategies of NSTE-ACS patients undergoing CABG are basically based on numerous suggestions and recommendations that have been made to reduce the risk for CABG surgery in patients with AMI 'in general', including better selection and optimal timing of surgery [7], adjunctive pharmacological therapy [25], and accurately timed IABP support [26].

The benefical effects of preoperative IABP treatment on outcome in high-risk patients have been clearly demonstrated in several non-randomized and randomized trials. Even in patients undergoing CABG with preoperative evidence of myocardial ischemia and/or preoperative hemodynamic instability, there is strong evidence of the benefical effect for preoperative and intraoperative use of the IABP [26-28].

The optimal timing of surgical revascularization in patients with AMI has been described in several previous studies. It has been shown that hospital mortality decreases with increasing time interval between CABG and AMI [7,29]. However, no data are currently available according to the optimal timing of CABG in patients with NSTE-ACS. At our institution, the timing for surgery of patients with NSTE-ACS was depending on the severity of symptoms and the level and/or kinetic of preoperative cTnI value indicating ongoing myocardial ischemia despite maximal non-surgical therapy on the one hand, and the complexity and severity of the coronary artery lesions on the other hand.

In terms of using the optimal myocardial protection during CABG, the type of cardioplegia (blood versus cristalloid, warm versus cold) has been the subject of numerous experimental and clinical studies, but this issue still remains controversial [30-32]. The benefical effect with optimal delivery of the cardioplegic solution by the use of simultaneous antegrade/retrograde cardioplegia and additional administration through the distal grafts, however, have been clearly demonstrated [33-35].

The adjunctive pharmacological therapy and thus, the optimal cardiac protection during AMI and/or myocardial injury due to ischemia/reperfusion is still a challenging field of cardiovascular research since numerous treatment options have been investigated so far to reduce myocardial infact size. Intravenous beta-blockers administered in the early hours of infarction were clearly shown to be of benefit [36]. Intravenous adenosine appeared promising for AMIs and myocardial protection during CABG, as did C1-esterase inhibitors and cariporide in some studies [37-40]. However, the majority of other medications were studied with negative or marginal results. Moreover, no data are currently available according to the optimal adjunctive pharmacological therapy of patients undergoing CABG with NSTE-ACS.

Conclusions

The present study demonstrates a significantly higher risk for patients with NSTE-ACS undergoing surgical revascularization compared to patients with N-ACS with significantly increased in-hospital morbidity and mortality rates. Multivariate logistic regression analysis revealed the preoperative cardiac troponin I level as the most strongest independent predictor of death in-hospital. Therefore, a more precise patient's risk assessment and a tailored perioperative management strategy may improve patients outcome.

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References

1. Adams III JE, Bodor GS, Dávila-Román VG, Delmez JA, Apple FS, Ladenson JH, Jaffe AS. Cardiac troponin I: A marker with high specificity for cardiac injury. Circulation, 1993; 88: 101-6.

2. Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined – a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. JACC, 2000; 36: 959-69.

3. Antman EM, Tanasijevic MJ, Thompson B, Schactman M, McCabe CH, Cannon CP, Fischer GA, Fung AY, Thompson C, Wybenga D, Braunwald E. Cardiac-specific troponin i levels to predict the risk of mortality in patients with acute coronary syndromes. The New England Journal of Medicine, 1996; 335: 1342-9.

4. Matetzky S, Sharir T, Domingo M, Noc M, Chyu K-Y, Kaul S, Eigler N, Shah PK, Cercek B. Elevated troponin I level on admission is associated with adverse outcome of primary angioplasty in acute myocardial infartion. Circulation, 2000; 102: 1611-6.

5. Giannitsis E, Muller-Bardorff M, Lehrke S, Wiegand U, Tolg R, Weidtmann B, Hartmann F, Richardt G, Katus HA. Admission troponin T level predicts clinical outcomes, TIMI flow, and myocardial tissue perfusion after primary percutaneous intervention for acute ST-segment elevation myocardial infarction. Circulation, 2001; 104: 630-5.

 Albes JM, Gross M, Franke U, Wippermann J, Cohnert TU, Vollandt R, Wahlers T. Revascularization during acute myocardial infarction: risks and benefits revisited. The Annals of Thoracic Surgery, 2002; 74: 102-8.

7. Lee DC, Oz MC, Weinberg AD, Ting W. Appropriate timing of surgical intervention after transmural acute myocardial infarction. The Journal of Thoracic and Cardiovascular Surgery, 2003; 125: 115-20.

8. Bertrand ME, Simoons ML, Fox KAA, Wallentin LC, Hamm CW, McFadden E, De Feyter PJ, Specchia G, Ruzyllo W. Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European Heart Journal, 2002; 23: 1809-40.

9. Eagle KA, Guyton RA, Davidoff R, Edwards FH, Ewy GA, Gardner TJ, Hart JC, Herrmann HC, Hillis LD, Hutter AM Jr., Lytle BW, Marlow RA, Nugent WC, Orszulak TA, Antman EM, Smith SC Jr., Alpert JS, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Gregoratos G, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK, Ornato JP. ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery: Summary Article: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). Circulation, 2004; 110: 1168-76.

10. Hamm C. Guidelines: acute coronary syndrome (ACS). 1: ACS without persistent ST segment elevations. Z Kardiol, 2004; 93: 72-90.

11. Louagie YAG, Jamart J, Buche M, Eucher PM, Schoevaerdts D, Collard E, Gonzalez M, Marchandise B, Schoevaerdts JC. Operation for unstable angina pectoris: factors influencing adverse in-hospital outcome. The Annals of Thoracic Surgery, 1995; 59: 1141-9.

12. Solodky A, Behar S, Boyko V, Battler A, Hasdai D. The outcome of coronary artery bypass grafting surgery among patients hospitalized with acute coronary syndrome: the Euro Heart Survey of acute coronary syndrome experience. Cardiology, 2005; 103: 44-7.

13. Vahl CF, Tochtermann U, Gams E, Hagl S. Efficiency of a computer network in the administrative and medical field of cardiac surgery. Concept of and experience with a departmental system. European Journal of Cardio-Thoracic Surgery, 1990; 4: 632-8.

14. Thielmann M, Massoudy P, Marggraf G, Kamler K, Herold U, Piotrowski J, Schmermund A, Erbel R, Jakob H. Diagnostic discrimination between early graft failure and non-graft related perioperative myocardial infarction with cardiac troponin I following coronary artery bypass surgery. Circulation, 2003; 108 (Suppl. S): 391-2.

15. Parsonnet V, Dean D, Bernstein AD. A method of uniform stratification of risk for evaluating the results of surgery in acquired adult heart disease. Circulation, 1989; 79 (Suppl. I): 3-12.

16. Higgins TL, Estafanous FG, Loop FD, Beck GJ, Blum JM,

Paranandi L. Stratification of morbidity and mortality outcome by preoperative risk factors in coronary artery bypass patients. A clinical severity score. JAMA, 1992; 267: 2344-8.

17. Nashef SAM, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). European Journal of Cardio-Thoracic Surgery, 1999; 16: 9-13.

18. Opfermann UT, Peivandi AA, Dahm M, Hilgenstock H, Hafner G, Loos A, Oelert H. Postoperative patterns and kinetics of cTnI, cTnT, CK-MB-activity and CK-activity after aortic valve replacement. Swiss Med Wkly, 2001; 131: 550-5.

19. Topol EJ, Yadav JS. Recognition of the Importance of embolization in atherosclerotic vascular disease. Circulation, 2000; 101: 570-80.

20. Heusch G, Schulz R, Haude M, Erbel R. Coronary microembolization. Journal of Molecular and Cellular Cardiology, 2004; 37: 23-31.

21. Jurlander B, Farhi ER, John J, Keany CM, Balu D, Grande P, Ellis AK. Coronary angiographic findings and troponin t in patients with unstable angina pectoris*1. The American Journal of Cardiology, 2000; 85: 810-4.

22. Lindahl B, Diderholm E, Lagerqvist B, Venge P, Wallentin L. Mechanisms behind the prognostic value of troponin T in unstable coronary artery disease: a FRISC II substudy. Journal of the American College of Cardiology, 2001; 38: 979-86.

23. Katus HA, Remppis A, Neumann FJ, Scheffold T, Diederich KW, Vinar G, Noe A, Matern G, Kuebler W. Diagnostic efficiency of troponin T measurements in acute myocardial infarction. Circulation, 1991; 83: 902-12.

24. Fox KAA, Mehta SR, Peters R, Zhao F, Lakkis N, Gersh BJ, Yusuf S. Benefits and risks of the combination of clopidogrel and aspirin in patients undergoing surgical revascularization for non-stelevation acute coronary syndrome: the clopidogrel in unstable angina to prevent recurrent ischemic events (CURE) trial. Circulation, 2004; 110: 1202-8.

25. Kloner RA, Rezkalla SH. Cardiac protection during acute myocardial infarction: Where do we stand in 2004? Journal of the American College of Cardiology, 2004; 44: 276-86.

26. Christenson JT, Simonet F, Badel P, Schmuziger M. Optimal timing of preoperative intraaortic balloon pump support in high-risk coronary patients. The Annals of Thoracic Surgery, 1999; 68: 934-9.

27. Cohen M, Urban P, Christenson JT, Joseph DL, Freedman RJ Jr., Miller MF, Ohman EM, Reddy RC, Stone GW, Ferguson JJ, III, on behalf of the Benchmark Registry collaborators. Intra-aortic balloon counterpulsation in US and non-US centres: results of the Benchmark(R) Registry. European Heart Journal, 2003; 24: 1763-70.

28. Stone GW, Ohman EM, Miller MF, Joseph DL, Christenson JT, Cohen M, Urban PM, Reddy RC, Freedman RJ, Staman KL. Contemporary utilization and outcomes of intra-aortic balloon counterpulsation in acute myocardial infarction*1: The Benchmark Registry. Journal of the American College of Cardiology, 2003; 41: 1940-5.

29. Lee DC, Oz MC, Weinberg AD, Lin SX, Ting W. Optimal timing of revascularization: transmural versus nontransmural acute myocardial infarction. The Annals of Thoracic Surgery, 2001; 71: 1198-204.

30. Elvenes OP, Korvald C, Myklebust R, Sorlie D. Warm retrograde blood cardioplegia saves more ischemic myocardium but may cause a functional impairment compared to cold crystalloid. European Journal of Cardio-Thoracic Surgery, 2002; 22: 402-9.

31. Kamlot A, Bellows SD, Simkhovich BZ, Hale SL, Aoki A, Kloner RA, Kay GL. Is Warm retrograde blood cardioplegia better than cold for myocardial protection? The Annals of Thoracic Surgery, 1997; 63: 98-104.

32. Pichon H, Chocron S, Alwan K, Toubin G, Kaili D, Falcoz P, Latini L, Clement F, Viel J, Etievent JP. Crystalloid versus cold blood cardioplegia and cardiac troponin I release. Circulation, 1997; 96: 316-20.

33. Tian G, Shen J, Sun J, Xiang B, Oriaku GI, Zhezong L, Scarth G, Somorjai R, Saunders JK, Salerno TA, Deslauriers R. Does simultaneous antegrade/retrograde cardioplegia improve myocardial perfusion in the areas at risk? A magnetic resonance perfusion imaging study in isolated pig hearts. The Journal of Thoracic and Cardiovascular Surgery, 1998; 115: 913-24.

34. Tian G, Dai G, Xiang B, Sun J, Lindsay WG, Deslauriers R. Effect on myocardial perfusion of simultaneous delivery of cardioplegic solution through a single coronary artery and the coronary sinus*1. Journal of Thoracic and Cardiovascular Surgery, 2001; 122: 1004-10.

35. Gundry SR, Razzouk AJ, Vigesaa RE, Wang N, Bailey LL. Optimal delivery of cardioplegic solution for "redo" operations. The Journal of Thoracic and Cardiovascular Surgery, 1992; 103: 896-901.

36. Beta-Blocker Heart Attack Research Group. A randomized trial of propanolol in patients with acute myocardial infarction. I. Mortality results. JAMA: The Journal of the American Medical Association, 1982; 247: 1707-14.

37. Horstick G, Berg O, Heimann A, Gotze O, Loos M, Hafner G, Bierbach B, Petersen S, Bhakdi S, Darius H, Horstick M, Meyer J, Kempski O. Application of C1-esterase inhibitor during reperfusion of ischemic myocardium: dose-related beneficial versus detrimental effects. Circulation, 2001; 104: 3125-31.

38. Horstick G. C1-esterase inhibitor in ischemia and reperfusion. Immunobiology, 2002; 205: 552-62.

39. Bauernschmitt R, Bohrer H, Hagl S. Rescue therapy with C1-esterase inhibitor concentrate after emergency coronary surgery for failed PTCA. Intensive Care Med, 1998; 24: 635-8.

40. Boyce SW, Bartels C, Bolli R, Chaitman B, Chen JC, Chi E, Jessel A, Kereiakes D, Knight J, Thulin L. Impact of sodium-hydrogen exchange inhibition by cariporide on death or myocardial infarction in high-risk CABG surgery patients: results of the CABG surgery cohort of the GUARDIAN study*1. Journal of Thoracic and Cardiovascular Surgery, 2003; 126: 420-7.