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Impact of Early Coronary Artery Bypass Graft in an Unselected Acute Coronary Syndrome Patient Population

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Background—Performance of coronary artery bypass graft (CABG) during an acute coronary syndrome (ACS) is mainly used in high-risk patients. Although potentially life-saving, patients undergoing early CABG are traditionally associated with a worse outcome than those not requiring CABG. Is this really true in an unselected ACS population? The aim of this study was to evaluate, in an ACS population, if the performance of CABG during the index hospitalization influences in-hospital outcome.

Methods and Results—Retrospective analysis of a nationwide database of 12 988 ACS patients admitted since 2002. Of those, 267 patients underwent CABG during the index hospitalization (group A) and 12 721 did not (group B). Group B patients were further divided in 2 subgroups: those submitted to percutaneous coronary interventions (PCI) (group B_1; n=3948) during the index hospitalization and those not submitted to mechanical revascularization (group B_2; n =8773). Patients from group A more frequently had diabetes, hypercholesterolemia, hypertension, and previous angina; they were also more often on cardiovascular medication before admission. Patients that underwent CABG were more often in Killip class IV at admission (4.8% versus 1.4% versus 2.0%); they also received more nitrates and catecholamines. Left ventricular function was better in group B_1. Group A patients were more often on mechanical ventilation and intra-aortic pump and they had more in-hospital complications (31.1% versus 18.7% versus 17.3%), namely recurrent angina, re-infarction, and mechanical complications. They had a more severe coronary anatomy and the culprit lesion was more frequently on the left main (7.7% versus 0.5% versus 2.2%). However, their in-hospital mortality was significantly lower (1.1% versus 2.2% versus 6.8%; $P<0.001$). Multivariate analysis showed that performance of early CABG was an independent predictor of lower mortality (odds ratio of 0.12), as were the use of low-molecular-weight heparins, beta-blockers, and angiotensin-converting enzyme inhibitors.

Conclusions—In unselected patients admitted for ACS, performance of early CABG, despite being performed in higher-risk patients, is associated with very low in-hospital mortality, even when compared with the mortality of lower-risk population not submitted to early CABG. Therefore, early performance of this procedure should be considered more often in eligible patients. **(*Circulation*. 2006;114[suppl I]:I-467–I-472.)**

Key Words: acute coronary syndromes ■ coronary artery bypass graft ■ prognosis

Acute coronary syndromes (ACS) are important causes of death and morbidity among coronary artery disease patients. In recent years, treatment of ACS patients was significantly improved, leading to the decrease of in-hospital and long-term mortality.[1–4] In many patients with ACS in whom coronary artery bypass graft (CABG) is indicated, the decision is to postpone it for a few days, so that the ACS can be "cooled" and the surgery performed with lower risk for the patient. This common practice leads to the fact that CABG in the first few days after an ACS is mainly used to treat life-threatening situations, like mechanical complications or severe left main coronary artery disease.[5] However, a question remains largely unanswered: what is the impact of early CABG in the in-hospital outcome in an unselected "real world" ACS population?

Methods and Results

The Portuguese Registry on ACS is a prospective and observational registry, started in 2002. All the Portuguese cardiology departments were invited to participate; 44 accepted (see appendix A).

Four centers were teaching hospitals, 12 were specialty hospitals, and 28 were community hospitals; 16 were considered large and 28 were small hospitals. All of them were in urban areas, with 31 in high-density and 13 in low-density areas; 22 centers had on-site cath labs and 8 had on-site cardiac surgery departments.

Inclusion Criteria

All ACS patients were admitted between January 2002 and December 2004 and their records were available in the Portuguese ACS registry database.

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TABLE 1. Comparison of Demographic Data, Main Coronary Artery Disease Risk Factors, and Previous Medication in the 3 Groups

Parameters/Groups	Group A (Early CABG) n=267	Group B_1 (Early PCI) n=3948	Group B_2 (No Mechanical Revascularization) n=8773	*P*
Male (%)	72.8	75.5	66.5	<0.05
Mean age (years)	67 (59–74)	63 (53–72)	70 (59–78)	<0.05
Mean BMI (kg/m^2)	27 (24–29)	27 (24–29)	27 (24–29)	n.s.
Diabetes (%)	32.2	22.7	28.0	<0.05
Hypertension (%)	63.3	56.4	61.1	<0.05
Hypercholesterolemia (%)	51.3	47.3	41.0	<0.05
Smoking habits (%)	22.8	35.3	20.3	<0.05
Aspirin (%)	32.6	20.2	24.4	<0.05
Beta-blockers (%)	22.5	15.1	15.4	<0.05
ACE inhibitors (%)	27.7	18.6	24.6	n.s.
Statins (%)	24.0	16.9	18.4	<0.05

ACE indicates angiotensin-converting enzyme, BMI, body mass index.

Statistical Analysis

Continuous variables are presented as mean and interquartile intervals (percentiles 25 and 75) and were evaluated with analysis of variance test or Student *t* test. Categorical variables were compared using χ^2 test.

Statement of Responsibility

The authors had full access to the data and take full responsibility for their integrity. All authors have read and agree to the manuscript as written.

Definition of Study Groups

A total of 12 988 registries were received. Patients were divided in 2 groups, according to the performance (group A; n=267) or not (group B; n =12 721) of CABG during the index hospital admission for ACS. Group B patients were then divided in 2 subgroups: those submitted to percutaneous coronary interventions (PCI) (group B_1; n=3948) during the index hospitalization and those not submitted to mechanical revascularization (Group B_2; n=8773).

Diagnosis and Baseline Population Characteristics

Table 1 shows the 3 groups' general characteristics regarding demographic data, risk factors, and previous cardiovascular medication.

Male gender was more prevalent in group B_1, whereas B_2 patients were older. No significant differences were found regarding body mass index (BMI).

Diabetes, hypercholesterolemia, hypertension, and previous angina were more prevalent in group A, resulting in higher use of previous cardiovascular medication in this group (see Table 1).

Regarding angina characteristics, in group A 75.7% had chest pain for >20 minutes, 53.6% had chest pain at hospital admission, and 47.9% had >1 angina episode in the last 24 hours; in groups B_1 and B_2, there were more cases of prolonged chest pain (84.5% and 79.3%%; $P<0.05$) and less prehospital angina recurrence (34.6% and 27.8%; $P<0.05$), whereas angina at admission was higher in B_1 patients (61.3%; $P<0.05$). Killip class IV on admission was more frequent in group A patients (4.8% versus 1.4% versus 2.0%;

TABLE 2. Comparison of In-Hospital Medication in the 3 Groups

Parameters/Groups	Group A (Early CABG) n=267	Group B_1 (Early PCI) n=3948	Group B_2 (No Mechanical Revascularization) n=8773	*P*
Aspirin (%)	97.3	98.9	96.3	<0.05
Clopidogrel (%)	35.9	87.7	26.1	<0.05
LMWH (%)	84.7	78.4	89.6	<0.05
GP IIb/IIIa inhib (%)	26.0	53.1	16.2	<0.05
Nitrates (%)	95.5	86.2	86.8	<0.05
Beta-blockers (%)	75.9	79.9	77.2	<0.05
ACE inhibitors (%)	75.9	72.9	69.4	<0.05
CCBs (%)	17.2	10.8	17.5	<0.05
Statins (%)	86.2	89.5	75.8	<0.05
Chatecolamines (%)	19.2	5.1	7.4	<0.05

ACE indicates angiotensin-converting enzyme; CCBs, calcium channel blockers; LMWH, low-molecular weight heparins; GP IIb/IIIa Inib, glycoprotein IIb/IIIa inhibitors.

TABLE 3. Comparison of Left Ventricular Function in the 3 Groups

Parameters/Groups	Group A (Early CABG) n=267	Group B_1 (Early PCI) n=3948	Group B_2 (No Mechanical Revascularization) n=8773	*P*
Normal LV function (%)	53.9	64.0	53.2	<0.05
Mild to moderate dysfunction (%)	35.5	31.0	33.7	<0.05
Severe LV dysfunction (%)	10.6	5.0	13.1	<0.05

P<0.05), whereas Killip class I was less frequent (73.9% versus 89.0% versus 75.5%; *P*<0.05).

Both cardiac troponins (69.3% versus 83% versus 81.6%; *P*<0.05) and creatin kinase–MB fraction (CK-MB) (55.8% versus 71.4% versus 68.8%; *P*<0.05) were less frequently elevated in group A.

Pharmacological Therapy During Hospital Stay

Group A received more nitrates, angiotensin-converting enzyme inhibitors, and catecholamines, whereas group B_1 received more clopidogrel, aspirin, glycoprotein IIb/IIIa inhibitors, beta-blockers, and statins, and group B_2 received more low-molecular-weight heparins and calcium channel blockers (Table 2).

Left Ventricular Function Evaluation and Maximal Killip Class

Echocardiography was the method most often used to evaluate left ventricular function, which was better in patients treated with early PCI (Table 3).

Group A patients reached more often a Killip class IV during hospital stay (12.9% versus 5.0% versus 6.6%; *P*<0.05).

Use of Invasive Procedures During Hospital Stay

Group A required mechanical ventilation, intra-aortic balloon pump, and provisional or permanent pacemakers more often (Table 4).

Use of Coronary Angiography, Surgical, and Nonsurgical Revascularization Procedures

Besides all group A and B_1 patients, 32.8% of group B_2 patients were also submitted to coronary angiography during hospital stay. Coronary anatomy was more severely diseased in group A, with more significant stenosis in the left main (36.3% versus 1.5% versus 2.8%; *P*<0.05), left anterior descending (84.6% versus 65.7% versus 21.3%; *P*<0.05), left circumflex (68.5% versus 43.8% versus 17.4%; *P*<0.05), and right coronary (67.0% versus 52.0% versus 17.7%; *P*<0.05) arteries. Group A also had higher incidence of 2- and 3-vessel disease.

Elective coronary angiography for risk stratification was the main reason to perform the examination in all groups; urgent coronary angiography was more frequent in group A, whereas coronary angiography in context of an acute STEMI was more frequent in B_1, and after a positive stress test in B_2 (Table 5). Primary or non-primary PCI was performed in 7.9% of group A patients. Time interval between ACS and main intervention (CABG or PCI) was 9.1±11.3 days after admission in group A and 3.7±4.9 days in B_1 (*P*<0.05).

Complications

Recurrent angina (the most frequent in-hospital complication), re-infarction, major hemorrhage (including intracranial bleeding), and mechanical and overall complications were more frequent in group A.

However, patients submitted to early CABG had an in-hospital mortality significantly lower than those submitted to early PCI or not submitted to early mechanical revascularization (1.1% versus 2.2% versus 6.8%; *P*<0.05) (Table 6).

Pharmacological Therapy at Discharge

Group A patients received more nitrates, but less aspirin and beta-blockers, whereas group B_1 received more clopidogrel and statins and group B_2 received more calcium channel blockers (Table 7).

Multivariate and Subgroup Analysis

Multivariate analysis showed that performance of early CABG (but not early PCI) was an independent predictor of lower mortality (odds ratio, 0.12), as were low-molecular-weight heparins, beta-blockers, and angiotensin-converting enzyme inhibitors (Table 8).

Heterogeneity of the population not submitted to early mechanical revascularization (group B_2) led to a comparison between patients that did (n=5813) and did not (n=7175) undergo coronary angiography during their index ACS hospitalization. Patients not submitted to coronary angiography

TABLE 4. Comparison of Invasive Procedures Used in the 3 Groups

Parameters/Groups	Group A (Early CABG) n=267	Group B_1 (Early PCI) n=3948	Group B_2 (No Mechanical Revascularization) n=8773	*P*
Swan-Ganz catheter (%)	0.4	0.3	0.1	NS
Mechanical ventilation (%)	16.5	2.3	2.2	<0.05
IABP (%)	11.2	1.3	0.2	<0.05
Pacemaker (%)	3.0	2.6	1.9	<0.05

IABP indicates intra-aortic balloon pump.

TABLE 5. Comparison of the Use of Coronary Angiography and Reason for Its Use in the 3 Groups

Parameters/Groups	Group A (Early CABG) n=267	Group B_1 (Early PCI) n=3948	Group B_2 (No Mechanical Revascularization) n=8773	*P*
Patients studied (%)	100	100	32.8%	—
Primary coronary angiography (%)	11.8	29.1	5.0	<0.05
Rescue coronary angiography (%)	1.8	3.6	0.7	NS
Urgent coronary angiography (%)	38.6	23.1	23.1	<0.05
Elective coronary angiography (%)	43.2	37.2	56.1	NS
Post-stress test coronary angiography (%)	4.5	6.9	15.2	<0.05

were less often male and had more previous diabetes, myocardial infarction, and cardiovascular medication. During hospitalization, they received fewer drugs recommended by guidelines, and their left ventricular function was worse (data not shown). They showed a trend toward lower in-hospital complications rate (67.5% versus 69.4%; *P*=not significant), but their in-hospital mortality was significantly higher (9.1% versus 2.1%). Multivariate analysis showed that performance of coronary angiography was an independent predictor of low in-hospital mortality (odds ratio, 0.27).

Another subgroup analysis was performed, considering 3 patient groups, within the population submitted to early coronary angiography (early CABG, early PCI, and nonrevascularized): CABG patients had the lowest in-hospital mortality (1.1%), followed by nonrevascularized patients (1.9%) and those submitted to PCI (2.2%; *P*=not significant, except CABG versus PCI). Multivariate analysis showed that, even in this subpopulation of patients submitted to coronary angiography, early CABG (unlike early PCI) was an independent predictor of good in-hospital prognosis (odds ratio, 0.27).

Discussion

During past decade, a "revolution" in ACS diagnosis and treatment has occurred. Cardiac troponins made the diagnosis more accurate, leading to a redefinition of acute myocardial infarction.[6] Coronary angiography and PCI became more widely available and more often used with better results, partially because of recent therapeutic advances like drug-eluting stents, clopidogrel, and glycoprotein IIb/IIIa inhibitors.[1–4] Results of several clinical trials led to a shift from more conservative approaches to being more invasive early in the ACS natural history.[7]

All these advances led to a progressive decrease in the use of CABG early in the history of ACS patients,[8] being used primarily in certain ACS complications and in patients with severe left main disease.

However, a question remained largely unanswered: what is the impact of early CABG in an unselected ACS population?

Some authors have studied the impact of the type of urgent CABG performed in the outcome of these patients. Ochi et al reported that off-pump surgery is feasible and safe in this set of patients,[9] partially contradicting previously reports stating that this surgical technique, although feasible, was associated to significant morbidity and mortality.[10]

The CRUSADE investigators[11] clearly showed than an early invasive strategy (involving early angiography, usually followed by PCI or CABG) is the best in ACS, even in an unselected population. This result is in line with a recently published substudy of the GUSTO IV-ACS trial, which also compared ACS patients submitted or not to early revascularization (PCI or CABG).[12]

However, our study goes beyond these results, because it shows that the performance of early CABG can be associated to improved in-hospital mortality, even when the comparator is a group of patients where 54.3% underwent coronary angiography and 31.7% received early PCI. Regarding morbidity, the situation is opposite: patients who underwent urgent CABG had higher morbidity. However, this may reflect the fact that this is an high-risk population, in which the rate of nonfatal events is usually higher; however, most of this events occurred before surgery and may have weighed on

TABLE 6. Comparison of Main In-Hospital Complications in the 3 Groups

Parameters/Groups	Group A (Early CABG) n=267	Group B_1 (Early PCI) n=3948	Group B_2 (No Mechanical Revascularization) n=8773	*P*
Recurrent angina (%)	17.6	9.0	5.9	<0.05
Re-infarction (%)	3.4	2.7	1.3	<0.05
Major bleeding (%)	9.4	1.4	1.2	<0.05
Mechanical complication (%)	4.9	0.9	1.4	<0.05
Second/third AV block (%)	3.0	3.2	3.3	NS
VF(%)	2.2	3.0	1.9	<0.05
Death(%)	1.1	2.2	6.8	<0.05
Total (%)	31.1	18.7	17.3	<0.05

TABLE 7. Comparison of Main Drug Classes Used at Discharge in the 3 Groups

Parameters/ Groups	Group A (Early CABG) n=267	Group B_1 (Early PCI) n=3948	Group B_2 (No Mechanical Revascularization) n=8773	*P*
Aspirin (%)	88.0	98.0	90.7	<0.05
Clopidogrel (%)	20.3	93.8	18.9	<0.05
Nitrates (%)	75.5	49.6	65.6	<0.05
Beta-blockers (%)	62.2	77.8	65.0	<0.05
ACE inhibitors (%)	68.2	68.6	67.6	NS
CCBs (%)	13.4	9.0	18.8	<0.05
Statins (%)	84.5	92.6	79.2	<0.05

the decision to undergo early CABG (that is, this high morbidity was often the cause of early CABG and not caused by early CABG).

Recently published results of a EuroHeart Survey on Acute Coronary Syndromes substudy[13] also shows a trend toward lower in-hospital mortality in the subset of patients treated with CABG, leading the authors to conclude that "CABG remains an effective and safe means to achieve revascularization among ACS patients in current clinical practice".

However, a recent study by Thielmann et al shows that, even within ACS patients undergoing urgent CABG, it is possible to stratify them regarding mortality, using simple markers, like preoperative troponin I.[14]

In our study, gender did not independently influence the decision to undergo urgent CABG, unlike the reports in a substudy of the CURE trial.[15] Unlike results of the GRACE investigators,[16] and although in our study patients submitted to early CABG had an higher morbidity rate, CABG did not increased the nonhemorrhagic stoke rate.

Although the 6-month follow-up data in our registry are currently available only for ≈30% of the patient population (3515 patients), mortality remains lower in the group submitted to CABG (2.6% versus 3.1% versus 8.6%; $P<0.05$). These preliminary results of the CABG "arm" of our registry are in line with those reported by the SoS investigators regarding a 1-year composite endpoint of death or myocardial infarction in a ACS population.[17]

The 2 subgroup analyses performed reinforce the results from the main study and strengthen the idea that, in eligible ACS patients, early CABG should be performed to improve their in-hospital outcome.

TABLE 8. Main Results From Multivariate Analysis

Parameters	Odds Ratio	95% CI
Early CABG	0.12	0.014–0.502
LMWH	0.514	0.305–0.867
Beta-blockers	0.374	0.251–0.558
ACE inhibitors	0.581	0.386–0.877

Parameters included: gender, age, body mass index, CAD risk factors, previous cardiovascular therapy, systolic and diastolic blood pressure at admission, heart rate and Killip class at admission, medication during hospital stay, significant coronary lesions, performance of early coronary angiography, PCI and CABG. LMWH indicates low-molecular weight heparins; ACE, angiotensin.

Limitations

Although all the participating centers were asked to include in the registry all their ACS patients, it was not possible to confirm if that was achieved. Because of its characteristics, it is not possible to determine the number and clinical features of patients who were admitted during the timeframe analyzed, but whose ACS was not diagnosed. Data from the prespecified 6-month follow-up is not available for all ACS patients, so a full and definitive analysis of those data at the moment is not possible.

Conclusions

This large dataset from a nationwide prospective registry, including both small peripheral hospitals and large reference and university hospitals, represents a "real world" cardiology practice regarding ACS patients.

In this patient population, performance of CABG during the index hospitalization for ACS seems to represent a short-term mortality benefit. This is particularly relevant, because this group of patients had a worse risk factor profile, more coronary lesions, higher maximal Killip class, and increased in-hospital morbidity.

Therefore, we conclude that early CABG should be considered more often in eligible ACS patients.

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Disclosures

None.

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