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Excellent Results of Contemporary Coronary Artery Bypass Grafting with Systematic Application of Modern Perioperative Strategies

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ABSTRACT

Background. The patient population referred for coronary artery bypass grafting (CABG) has become more challenging. The surgical population is aging and patients present with significant preoperative comorbidities. This worsening risk profile has led to the development of operative techniques (off-pump CABG) and perioperative measures (epi-aortic scanning, intensive insulin therapy) to preserve the quality of care following CABG. The aim of this study was to determine the outcome of contemporary CABG following the implementation of the above measures in our practice.

Methods. We retrospectively analyzed prospectively collected data of 2725 patients undergoing CABG between 01/1998 and 12/2005 (mean age, 65 ± 11 years; 843 [31%] female; mean ejection fraction, 45% ± 14%). Outcome measures included hospital mortality, postoperative complications, and long-term survival and independent predictors of outcome. Subgroup analyses were performed for 2 study periods (1998-2002 versus 2003-2005) where the above measures were implemented and for patients undergoing conventional versus off-pump CABG.

Results. When comparing the 2 study periods, we observed a substantial worsening of the risk profile with an increased EuroSCORE predicted mortality from 6.4% ± 6.8% to 7.0% ± 7.8% ($P = .028$). During the same period, operative mortality decreased from 2.4% to 0.7% ($P < .001$). This reduction in mortality was also observed in diabetic patients (3.1% versus 1.0%, $P = .021$) and those with low ejection fraction (4% versus 2.6%, P = not significant). Off-pump procedures were performed with an increasing frequency in high-risk patients in whom we obtained excellent results. Finally, we observed a reduction of postoperative complications including respiratory failure ($P = .013$), gastrointestinal complications ($P = .017$), and stroke ($P = .094$). Independent predictors of mortality included renal failure (OR = 5.7), peripheral vascular disease (OR = 2.9), intra-aortic balloon pump (OR = 4.8), reoperation (OR = 3.3), and hypertension (OR = 2.3).

Conclusion. Despite a worsening case mix, contemporary CABG can be performed with excellent results (operative mortality <1%). Off-pump CABG performed in very high-risk patients obtains results similar to those of the general CABG population. Diabetes and ejection fraction were not independent predictors of early outcome. In our experience, these excellent outcomes were achieved by adopting an operative approach using modern perioperative management (epi-aortic scanning, intensive insulin therapy) and surgical techniques (off-pump CABG) based on individual patients.

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INTRODUCTION

During the last decade, with the broader application of percutaneous coronary intervention (PCI) and the use of drug-eluting stents, the indications for surgical revascularization have significantly changed. Currently, coronary artery bypass grafting (CABG) remains the method of choice in patients with left main disease, multivessel disease (particularly in diabetic patients or those with left ventricular dysfunction), and in the event of PCI failure and in-stent restenosis. During the same period, the patient population referred for CABG has become more challenging. A growing number of patients present with multiple preoperative risk factors including advanced age, type II diabetes, diffuse atherosclerotic disease involving the ascending aorta, and associated comorbidities such as renal failure or previous stroke. This worsening in the preoperative patient profile has led to the development of new operative techniques and perioperative measures in order to preserve the quality of care in our patients. Some of these advances include epi-aortic scanning prior to aortic manipulation and cannulation, off-pump CABG, and tight perioperative glycemic control.

In this study, we sought to determine the outcome of CABG in a contemporary cohort of patients with an emphasis on 2 study periods (1998-2002 versus 2003-2005) when some of these modern perioperative measures were introduced in our daily practice.

MATERIAL AND METHODS

Study Population

From January 1998 to December 2005, a total of 2725 patients underwent isolated CABG at the Mount Sinai Medical Center. Patients with previous cardiac operations or emergent procedures were included in this analysis. Patients admitted in cardiogenic shock undergoing a salvage procedure were excluded. Patients with concomitant valvular heart disease and left ventricular aneurysm requiring surgical left ventricular remodeling were also excluded.

The protocol was approved by our local Institutional Review Board, and is compliant with the Health Insurance Portability and Accountability Act (HIPAA) regulations and the ethical guidelines of the 1975 declaration of Helsinki. The approval included a waiver of informed consent.

Data Collection and Outcome Analysis

Preoperative, intraoperative, and postoperative data were prospectively collected using the New York State Department of Health (NYSDH, State Cardiac Advisory Committee) registry. The NYSDH data registry represents a mandatory verified peer-reviewed data collection system, coding and recording data in a strictly supervised and widely reported fashion. The medical chart of patients was reviewed to obtain further information when required. Variables used in this study are shown in Table 1.

The logistic EuroSCORE was used for risk stratification [Nashef 1999]. The EuroSCORE is a risk stratification system based on multiple preoperative risk factors to predict operative mortality. Patients were divided into 4 subgroups determined by their predicted mortality as follows: low risk (<3%), moderate risk (3%-8.9%), high risk (9%-25%), and very high risk (>25%).

Outcome measures for this study included hospital mortality, major postoperative complications (postoperative stroke, respiratory failure, renal failure, deep sternal wound infection, bleeding requiring reoperation, unplanned reoperation, gastrointestinal complications), length of hospital stay, and late survival. Hospital mortality was defined as death following the procedure before patient discharge regardless of the duration of hospitalization. Patients who died after discharge from hospital but within 30 days following the procedure were also considered as hospital deaths. Stroke was defined as a new permanent neurological event occurring perioperatively or postoperatively. Respiratory failure was defined as prolonged ventilator therapy (>72 hours) or need for reintubation or tracheostomy. Renal failure was defined as creatinine >2.5 mg/dL for more than 7 postoperative days or the need for dialysis. Follow-up information was obtained by cross matching a patient's social security number with the web-based social security death index website.

Table 1. Variables Included in the Statistical Analysis and Their Definitions

Preoperative variables
Age
Gender
Weight, kg
Height, cm
Body mass index, kg/m^2
Diabetes mellitus requiring medication
Hypertension
Preoperative renal failure (creatinine >2.5 mg/dL or dialysis)
Prior cerebrovascular accident
Peripheral vascular disease
Chronic obstructive pulmonary disease
Hepatic failure (liver disease and bilirubin >2 mg/dL and albumin <3.5 g/dL)
Prior myocardial infarction
Prior heart operation
Congestive heart failure (New York Heart Association class III and IV)
Ejection fraction, %
Urgent operation (requiring operation during current hospitalization)
Emergent operation (refractory unrelenting cardiac compromise requiring emergency operation)
Unstable (patient requires pharmacologic or mechanical support to maintain blood pressure or output)
Cardiogenic shock (acute hypotension or low cardiac index despite support)
Intraoperative variables
Type of procedure
Cardiopulmonary bypass time
Cross-clamp time
Use of internal mammary artery
Postoperative variables
Hospital mortality (death during same admission or within 30 day after surgery when discharged)
Renal failure (creatinine >2.5 mg/dL more than 7 days or dialysis)
Respiratory failure (prolonged ventilator therapy >72 h, reintubation or tracheostomy)
Stroke (new permanent neurological event)
Postoperative myocardial infarction
Unplanned reoperation
Gastrointestinal complication
Bleeding requiring re-exploration
Length of hospital stay

SURGICAL TECHNIQUES AND PERIOPERATIVE MANAGEMENT

Surgical Techniques

A small skin incision and a full sternotomy were performed in all patients (n = 2725). Bypass conduits were harvested first. The left internal mammary artery was harvested as a pediculated graft and the right internal mammary artery as a skeletonized graft in most instances. The greater saphenous vein was harvested using minimally invasive endoscopic techniques. Myocardial revascularization was performed with or without cardiopulmonary bypass (CPB) (conventional CABG versus off-pump CABG).

Conventional CABG (n = 2316, 85%)

After systemic heparinization (goal activated coagulation time ≥ 480 seconds), CPB was instituted between the

ascending aorta and the right atrium using a 2-stage cannula. During CPB, a minimum flow of 2.2 L/min per m^2 and a perfusion pressure of >60 mmHg were maintained in all patients. Following aortic cross clamping and cardioplegic arrest, distal anastomoses were performed first followed by proximal anastomoses using the single cross-clamp technique [Aranki 1994]. Aortic cross clamp was released hereafter and the patients were weaned from CPB after a short reperfusion. After the completion of CPB, protamine was given based on the heparin level.

Off-Pump CABG (n = 409, 15%)

Off-pump CABG was performed based on the surgeon's preferences. This technique, however, was favored particularly in patients with significant comorbidities such as atherosclerotic disease of the ascending aorta, chronic obstructive pulmonary disease (COPD) or renal dysfunction. Coronary stabilizer and cardiac positioning devices were used to access the coronary arteries under beating heart conditions. Intracoronary shunts were used to prevent prolonged myocardial ischemia while distal anastomoses were created. Following the completion of the procedure, protamine was administered based on the heparin level.

Since 2003, measures that have been implemented in our practice include:

- Epi-aortic ultrasonography to detect any atherosclerotic lesions prior to manipulation or cannulation of the ascending aorta [Wareing 1993]. The surgical strategy was defined according to the presence or absence of calcification in the ascending aorta and its extent. In the presence of localized atherosclerotic disease, two approaches were selected based on surgeons preference: (1) off-pump CABG; (2) identification of a disease-free segment of the aorta for aortic cannulation and cross clamping followed by conventional CABG. In the presence of extensive aortic calcifications, off-pump CABG was the procedure of choice.
- Systematic use of high-potassium cold blood cardioplegic solution in an antegrade or antegrade/retrograde fashion for myocardial protection [Filsoufi 2004]. In selected patients, particularly in those with acute myocardial infarction, cardiogenic shock, and/or severe left ventricular dysfunction, a solution of antegrade warm blood was administered before removal of the aortic cross clamp ("hot-shot" solution) [Filsoufi 2004]. Prior to this period, depending on the surgeon's preference, myocardial protection was achieved either by administration of cold blood cardioplegia or crystalloid "Centigrade Cardioplegia" [Lansman 1993].
- Use of an intensive insulin therapy (IIT) protocol with a target glucose level of 80 to 110 mg/dL for both diabetic and nondiabetic patients. An intravenous insulin infusion was started intraoperatively and continued postoperatively in the intensive care unit. The IIT protocol consisted of a physician-driven individualized protocol. The IIT protocol was transitioned to subcutaneous insulin therapy, oral antidiabetic therapy, or discontinued after 48 hours. Diabetic patients were followed by the endocrinologist on a daily basis until hospital discharge.

Postoperatively, in the absence of bleeding (chest-tube output > 100 mL/hour) antiplatelet therapy was initiated on the first night following surgery. Aspirin 325 mg was used in patients who underwent conventional CABG, whereas aspirin 81 mg in combination with clopidogrel 75 mg was used in the off-pump group.

Statistical Analyses

Data was first analyzed in regard to the overall study period from 1998 to 2005. Subgroup analysis was then performed comparing the two study periods (1998-2002 and 2003-2005). Normally distributed continuous variables are presented as mean ± standard deviation (SD) and otherwise as median and interquartile range (IQR). Categorical variables are shown as the percentage of the sample. The χ^2 test was used to evaluate potential confounders of the relationship between CABG and hospital mortality and morbidities when comparing the two subgroups determined by the study period. Stepwise multivariate logistic regression was then performed to assess the influence of each variable included in the analysis as an independent risk factor for hospital mortality in patients undergoing CABG [Hosmer 2000]. A P value <.05 was considered significant for all statistical methods. Long-term survival was analyzed using Kaplan-Meier survival curves. Differences in patient characteristics were controlled by Cox proportional hazard analysis. The statistical analyses were performed with the use of SPSS 15 (SPSS, Chicago, IL, USA).

RESULTS

Patient Demographics

A total of 2725 adult patients were included in this study. Patient demographics and risk profile are shown in Table 2. For patients with a history of myocardial infarction, the time interval between diagnosis and surgical revascularization was as follows: ≤24 hours, n = 45 (4%); 1-3 days, n = 141 (10%); ≥4 days, n = 1180 (86%).

Patient Demographics According to the Study Period

There were significant differences in terms of patient characteristics and preoperative variables when comparing the two study periods. Patients who underwent CABG during the second study period (2003-2005) presented more likely with hypertension ($P = .013$), diabetes mellitus ($P = .001$) and obesity ($P = .019$) and showed an increased rate of preoperative stroke ($P = .003$). In this group of patients, we also observed an increased prevalence of markers of operative mortality risk such as emergent surgery ($P < .001$) and an increased mean predicted EuroSCORE ($P = .028$). On the other hand, there were more patients with congestive heart failure ($P = .029$), previous myocardial infarction ($P = .001$), and decreased ejection fraction ($P = .001$) during the first period of the study.

Patient Demographics According to the Procedure

The patient profile was different when patients undergoing conventional CABG were compared to the off-pump population (Table 3). Off-pump patients were older ($P = .001$), more likely to be female ($P = .008$), and as expected presented with

Table 2. Patient Demographics and Risk Factors According to the Study Period*

	Coronary Artery Bypass Grafting, n = 2725 (%)	1998-2002, n = 1862 (%)	2003-2005, n = 863 (%)	P
Age, y	65 ± 11	65 ± 11	65 ± 10	ns
Gender, female	843 (31)	567 (30)	276 (32)	ns
Body mass index, kg/m^2	27 ± 7	27 ± 5	28 ± 12	.001
Congestive heart failure	477 (17)	343 (18)	134 (15)	.029
Previous myocardial infarction	1366 (50)	997 (53)	369 (43)	.001
Previous cerebrovascular accident	210 (8)	125 (7)	85 (10)	.003
Peripheral vascular disease	360 (13)	258 (14)	102 (12)	ns
Chronic obstructive pulmonary disease	175 (6)	123 (7)	52 (6)	ns
Renal failure or dialysis	129 (5)	88 (5)	41 (5)	ns
Diabetes mellitus	1085 (40)	701 (38)	384 (44)	.001
Hypertension	2146 (78)	1452 (78)	694 (80)	ns
Aortic calcification-atherosclerosis	139 (5)	102 (5)	37 (4)	ns
Previous cardiac operation	98 (4)	65 (3)	33 (4)	ns
Previous percutaneous transluminal coronary angioplasty	559 (21)	357 (19)	202 (23)	.007
Coronary artery disease				
1 Vessel	112 (4)	76 (4)	36 (4)	ns
2 Vessel	466 (17)	299 (16)	167 (19)	.001
3 Vessel	2147 (79)	1487 (80)	660 (77)	.001
Ejection fraction, %	45 ± 14	44 ± 13	48 ± 13	.001
≤ 30	495 (18)	379 (20)	116 (13)	.001
31-50	1373 (50)	988 (53)	385 (45)	.001
Emergent surgery	125 (5)	66 (3)	59 (7)	.001
EuroSCORE, %	6.6 ± 7.1	6.4 ± 6.8	7 ± 7.8	.028
Low, <3	1012 (37)	697 (37)	315 (37)	ns
Moderate, 3-9	1145 (42)	793(43)	352 (41)	ns
High, 9-25	474 (17)	319 (17)	155 (18)	ns
Very high, >25	94 (4)	53 (3)	41 (5)	.009

*ns indicates not significant.

risk factors such as COPD ($P < .001$), renal failure ($P = .04$), and diabetes ($P = .001$). Finally, the predicted mortality by EuroSCORE was significantly higher in off-pump patients compared to those who underwent conventional CABG (7.8% ± 8.2% versus 6.4% ± 6.9%, $P < .001$).

Operative Characteristics

Eighty-five percent (n = 2316) of procedures were performed utilizing CPB. The remaining 15% (n = 409) of procedures were performed off-pump. The number of off-pump procedures increased during the second period (13% versus 20%, $P < .001$). The mean number of grafts were 3.3 ± 1.3 and 3.3 ± 1.1 during the first and the second period, respectively (P = not significant). Patients who underwent off-pump CABG received significantly less grafts compared to conventional CABG patients (2.6 ± 1.1 versus 3.5 ± 1.1, $P < .001$). The use of internal mammary artery (left-sided or bilateral) increased significantly during the second period of the study (81% versus 95%, $P < .001$). In patients who underwent conventional CABG, mean CPB and aortic cross-clamp time were 103 ± 54 minutes and 83 ± 50 minutes, respectively (Table 4).

Mortality and Predictors

The overall hospital mortality among our study population was 1.8% (n = 50). When comparing the two study periods, the mortality rate decreased from 2.4% to 0.7% ($P = .001$) (Figure 1). This reduction of operative mortality was

Table 3. Patient Demographics and Risk Factors According to the Procedure*

	On-Pump, n = 2316 (%)	Off-Pump, n = 409 (%)	P
Age, y	65 ± 11	67 ± 10	.001
Gender, female	695 (30)	148 (36)	.008
Body mass index, kg/m^2	27 ± 5	28 ± 15	ns
Congestive heart failure	403 (17)	74 (18)	ns
Previous myocardial infarction	1174 (51)	192 (47)	ns
Previous cerebrovascular accident	171 (7)	39 (10)	ns
Peripheral vascular disease	297 (13)	63 (15)	ns
Chronic obstructive pulmonary disease	132 (6)	43 (10)	<.001
Renal failure or dialysis	102 (4)	27 (7)	.04
Diabetes mellitus	701 (38)	384 (44)	.001
Hypertension	1820 (79)	326 (80)	ns
Aortic calcification-atherosclerosis	115 (5)	24 (6)	ns
Previous cardiac operation	73 (3)	25 (6)	.004
Previous percutaneous transluminal coronary angioplasty	464 (20)	95 (23)	.028
Coronary artery disease			.03
1 Vessel	85 (4)	27 (7)	
2 Vessel	378 (17)	88 (21)	
3 Vessel	1853 (79)	294 (72)	
Ejection fraction, %	45 ± 14	45 ± 13	ns
≤ 30	424 (18)	71 (17)	ns
31-50	1156 (50)	217 (53)	ns
Emergent surgery	112 (5)	13 (37)	ns
EuroSCORE, %	6.4 ± 6.9	7.8 ± 8.2	<.001
Low, <3	882 (38)	130 (31)	.011
Moderate, 3-9	983 (42)	162 (40)	ns
High, 9-25	380 (16)	94 (23)	<.001
Very high, >25	71 (3)	23 (6)	<.001

*ns indicates not significant

Table 4. Perioperative Variables*

Operative Variables	Coronary Artery Bypass Grafting, n = 2725	1998-2002, n = 1862	2003-2005, n = 863	P
Off-pump procedures (%)	409 (15)	239 (13)	170 (20)	<.001
Number of grafts, mean ± SD	3.3 ± 1.2	3.3 ± 1.3	3.3 ± 1.1	ns
Use of left mammary artery (%)	2038 (75)	1323 (71)	715 (83)	<.001
Use of bilateral mammary arteries (%)	292 (11)	188 (10)	104 (12)	ns
Cardiopulmonary bypass time, min	103 ± 54	103 ± 51	103 ± 59	ns
Aortic cross-clamp time, min	83 ± 50	83 ± 43	83 ± 60	ns

*ns indicates not significant.

observed while the mean predicted mortality by EuroSCORE increased from 6.4% ± 6.8% to 7.0% ± 7.8% ($P < .001$). This improvement of surgical outcome was also confirmed in subgroup analysis. In diabetic patients, the mortality decreased from 3.1% to 1% ($P = .021$). Similarly, in patients with severely depressed left ventricular function (ejection fraction ±30%), the hospital mortality decreased from 4% to 2.6%; however, this difference did not reach statistical significance. Table 5 summarizes mortality and morbidities according to the study period.

When analyzing operative mortality according to the procedure, it was 2% in the off-pump CABG group compared to 1.8% in conventional CABG patients (P = not significant) (Table 6). It is important to emphasize that off-pump patients were older and presented more risk factors than the conventional CABG population with a predicted mortality by EuroSCORE of 7.8% ± 8.2% compared to 6.4% ± 6.9% ($P < .001$).

We also performed a subgroup analysis according to the time interval between the occurrence of myocardial infarction and CABG. In patients with a history of myocardial infarction, overall mortality was 2.3% and was not significantly different compared to the mortality of CABG without prior infarction (1.4%). The highest mortality in this subgroup was observed in patients who underwent CABG within 24 hours following myocardial infarction (13.3%) compared to those who underwent surgery after 1 to 3 days (1.4%) or later (1.9%) (Figure 2).

Table 7 shows risk factors for in-hospital mortality among the overall study population in univariate and multivariate analysis. Multivariate regression analysis revealed renal failure (OR = 5.7), peripheral vascular disease (OR = 2.9), preoperative intra-aortic balloon pump (OR = 4.8), reoperation (OR = 3.3), and hypertension (OR = 2.3) as independent predictors of hospital mortality. Interestingly, diabetes and severely depressed left ventricular function were not found to be predictors of hospital mortality.

Morbidities

Postoperative morbidities are summarized in Table 5. During the second study period, we observed a significantly lower rate of postoperative respiratory failure ($P = .013$) and gastrointestinal complications ($P = .017$) in univariate analysis compared to the first period. The rate of other major complications was decreased but did not reach statistical significance.

When patients who underwent off-pump procedures were compared to the conventional CABG group, it appeared that off-pump patients had no perioperative myocardial infarctions (1% in the conventional CABG group, $P = .033$) (Table 6).

The median length of stay in hospital was 6 days (IQR: 5-9 days) and similar when comparing the two study periods (Table 5). The length of stay did not differ when comparing off-pump and conventional CABG patients.

Follow-up Data

The mean follow-up time of surviving patients was 4.2 ± 2.5 years. Assessment of long-term survival was completed for 2648 patients. Follow-up data were not available for 1% of patients (n = 27). These included mainly patients from abroad without a social security number. One-, 3-, and 5-year survival was 95.1% ± 0.4%, 91.1% ± 0.6%, and 84.5% ± 0.8%, respectively. The survival rate significantly decreased following risk stratification using EuroSCORE predicting model ($P = .001$) (Figure 3). Patients with a very high risk had a 5-year survival of only 57.7% ± 6.4% compared to 68.5% ± 2.6% (high risk), 84.9% ± 1.2% (moderate risk), and 93.6% ± 1.0% (low risk) ($P < .001$).

DISCUSSION

Mortality and Morbidity following CABG

The intense focus on operative outcome following CABG has been motivated partly by steady improvements in the results and applicability of PCI and also by the wider availability of

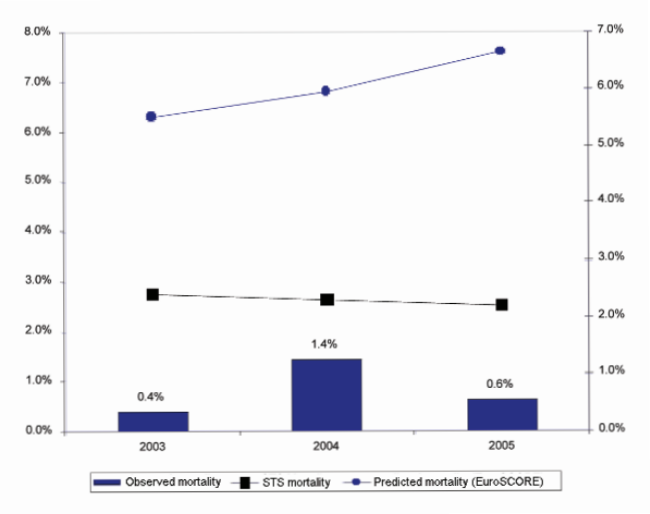

Figure 1. Mortality compared to STS database and EuroSCORE.

Table 5. Mortality and Morbidities According to the Study Period*

Postoperative Outcome	Coronary Artery Bypass Grafting, n = 2725 (%)	1998-2002, n = 1862 (%)	2003-2005, n = 863 (%)	P
In-hospital mortality	50 (1.8)	44 (2.4)	6 (0.7)	.001
Postoperative stroke	46 (2)	36 (2)	10 (1)	ns
Postoperative myocardial infarction	21 (1)	18 (1)	3 (0.3)	ns
Postoperative renal failure-dialysis	22 (1)	12 (1)	10 (1)	ns
Respiratory failure	154 (6)	118 (6)	36 (4)	.013
Deep sternal wound infection	37 (1)	28 (2)	9 (1)	ns
Postoperative systemic infection	40 (1)	31 (2)	9 (1)	ns
Re-exploration for bleeding	52 (2)	37 (2)	15 (2)	ns
Gastrointestinal complications	26 (1)	23 (1)	3 (0.3)	.017
Length of stay	6 (IQR 5-9)	6 (IQR 6-9)	6 (IQR 5-8)	ns

*ns indicates not significant.

accurate, risk-stratified, surgeon-specific unit and national outcome data. Analysis of national figures for the US reveals that during the last decade, the annual mortality among patients undergoing CABG decreased from 3.2% in 1996 to 2.2% in 2005 [2006], despite an increase in the proportion of patients presenting with multiple preoperative morbidities [Ferguson 2002].

This changing patient profile was reflected in our study, where an increase in mean EuroSCORE from 6.4% to 7.7% ($P < .01$) was observed over the study period. Operative mortality, on the other hand, fell from 2.4% to 0.7% ($P < .001$) during the same time frame. This may be due to incremental changes in surgical strategy, such as application of off-pump CABG in very high risk patients and improvements in perioperative management during the second period (epi-aortic scanning, systematic use of high-potassium cold blood cardioplegic solution for myocardial protection, and IIT).

Epi-aortic scanning is a safe, fast, and precise method for detection of atherosclerotic disease of the ascending aorta. It has been suggested that scanning the ascending thoracic aorta is a useful adjunct to detect and localize atherosclerotic disease in order to refine operative strategies to prevent thromboembolic complications such as stroke [van der Linden 2001; Filsoufi 2002].

Stroke is one of the most devastating complications following cardiac surgery, with a significant impact on survival and quality of life. Bucerius et al studied 16,184 patients who were operated on between 1996 and 2001 and reported an incidence of stroke of 3.8% for on-pump CABG [Bucerius 2003]. This data was confirmed in a recent report presented by McKhann et al, who analyzed patients who underwent cardiac surgery at the Johns Hopkins University between 2001 and 2004 and observed a stroke rate of 4.1% following CABG [McKhann 2006]. This complication was associated with an increased hospital mortality and prolonged length of stay in the intensive care unit and in hospital.

The main etiology for the occurrence of perioperative stroke is thromboembolic due to calcifications of the ascending aorta and the aortic arch. Van der Linden et al, who evaluated the ascending aorta of 921 consecutive patients undergoing cardiac surgery using epi-aortic ultrasound prior to aortic manipulation or cannulation reported that as many as 26% of patients had atherosclerosis of the aorta and in 44% of them in more than one segment [van der Linden 2001]. In their series, the incidence of stroke was 8.7% in patients with atherosclerotic disease of the aorta compared to 1.8% in patients without ($P < .0001$). The authors identified the presence of aortic calcifications as the most important predictor of perioperative stroke. In our study, the rate of stroke was as low as 1.2% during the second period. Interestingly, with systematic application of epi-aortic scanning and a tailored surgical strategy (off-pump CABG or conventional CABG using a disease-free segment of the aorta) in patients with ascending aorta calcifications, we did not observe any case of stroke in these patients. Similar to the reduced stroke rate, the rate of gastrointestinal complications, particularly ischemic bowel disease, decreased during our study (1.2% in 1998-2002; 0.3% in 2003-2005; $P = .017$). This decrease is probably multifactorial, but might be partly related to a reduced rate of thromboembolic events, achieved by the implementation of epi-aortic scanning.

Another major factor has been the improvement of myocardial protection during the study. This has probably led to an improvement of results in patients with severely depressed left ventricular function. Patients with an ejection fraction ≤30% undergoing CABG have been shown to

Table 6. Mortality and Morbidities According to the Procedure*

Postoperative Outcome	On-Pump, n = 2316 (%)	Off-Pump, n = 409 (%)	P
In-hospital mortality	42 (1.8)	8 (2.0)	ns
Postoperative stroke	41 (2)	5 (1)	ns
Postoperative myocardial infarction	21 (1)	0 (0.0)	.033
Postoperative renal failure-dialysis	17 (1)	5 (1)	ns
Respiratory failure	131 (6)	23 (6)	ns
Deep sternal wound infection	28 (1)	9 (2)	ns
Postoperative systemic infection	31 (1)	9 (2)	ns
Re-exploration for bleeding	47 (2)	5 (1)	ns
Gastrointestinal complications	20 (1)	6 (2)	.017
Length of stay	6 (IQR 5-9)	6 (IQR 4-9)	ns

*ns indicates not significant.

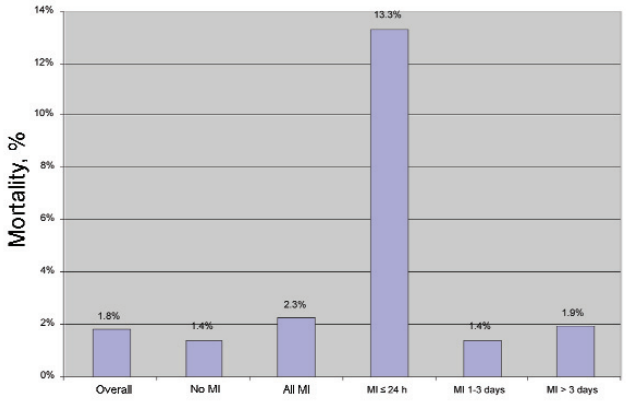

Figure 2. Impact of myocardial infarction (MI) on operative mortality following coronary artery bypass grafting.

have higher operative mortality compared to patients with an ejection fraction >30%. In the 1990s, the majority of series of low ejection fraction patients undergoing CABG reported early mortalities between 5% and 15%[Christakis 1992; Argenziano 1999] The observed mortality in patients with low ejection fraction, however, decreased during recent years. An analysis from the New York State Cardiac Surgery Registry among patients who underwent CABG between 1997 and 1999 reported 6.5% and 4.1% in-hospital mortality in patients with an ejection fraction <20% and between 21% and 30%, respectively [Topkara 2005]. Our results reflect this steady improvement in mortality seen in the literature, particularly during the second period of our study, where we observed a mortality of 2.6% in this population.

Similarly, the rate of respiratory failure was reduced by a third, from 6% (n = 118) to 4% (n = 36) ($P = .013$). Several studies have shown that depressed left ventricular function is the strongest predictor of respiratory failure following cardiac surgery. The improvement of myocardial protection and the overall results in patients with depressed left ventricular function may have played a major role in the reduction of this complication during the recent era.

Finally, the implementation of an IIT in diabetic and nondiabetic patients might have contributed in reducing operative mortality. Previous studies have demonstrated the positive impact of IIT in diabetic patients undergoing CABG [Furnary 2003]. Furnary et al have reported that maintaining the glucose level in the range of 100 to 150 mg/dL decreased mortality in their study group (2.5% versus 5.3%, $P < .001$). These authors were able to show that this treatment strategy was an independent predictor of improved outcome following CABG [Furnary 2003; Gao 2003]. The positive impact of this IIT on diabetic patients was reflected by our observation that the mortality among diabetic patients decreased during the second study period from 3.1% to 1.0% ($P = .021$). Future studies are, however, required to further determine the impact of IIT on operative outcome in both diabetic and non-diabetic patients undergoing CABG.

Off-Pump CABG

We employed a strategy of using off-pump surgery in patients who are likely to gain a clear benefit from avoiding CPB, such as patients with heavily calcified or atheromatous aortas, renal failure, COPD, and advanced age [van der Linden 2001]. As a result, the mean EuroSCORE was significantly higher in the off-pump CABG group (6.4% versus 7.8%, $P < .001$). Despite this worsening case mix, there was no significant difference in mortality or stroke between patients undergoing off-pump or on-pump surgery. Furthermore, the incidence of postoperative myocardial infarction was zero in this patient population, confirming previous reports with respect to the avoidance of irreversible myocardial damage [Selvanayagam 2004]. Our findings suggest that this selective approach to off-pump surgery was appropriate and is beneficial, particularly in high-risk patients undergoing CABG.

Limitations

Despite the fact that data were collected prospectively, this is a retrospective observational study and conclusions are necessarily limited in their application. Clinical outcomes focused on postoperative morbidity and mortality with no information on late complications, quality of life, cause of death, or cost-analysis. The main limitation is that several changes occurred in our practice; therefore, it is difficult to analyze the individual impact of each factor on operative

Table 7. Predictors of Mortality in Patients Undergoing Coronary Artery Bypass Grafting

	Univariate			Multivariate		
	OR	95% CI	*P*	OR	95% CI	*P*
Female gender	1.71	(0.98-3.00)	.06	1.71	(0.95-3.09)	.076
Age > 70 years	0.88	(0.44-1.77)	.725	0.78	(0.37-1.64)	.521
Body mass index >30	1.26	(0.68-2.35)	.46	1.30	(0.67-2.50)	.435
Ejection fraction <30%	2.51	(1.40-4.49)	.002	1.43	(0.72-2.86)	.311
Previous myocardial infarction	1.57	(0.89-2.77)	.117	1.13	(0.60-2.11)	.707
Congestive heart failure	2.63	(1.47-4.72)	.001	1.35	(0.67-2.74)	.398
Hemodynamic instability	6.24	(2.13-18.23)	.001	2.37	(0.69-8.18)	.173
Intra-aortic balloon placement	5.16	(2.36-11.29)	<.001	4.81	(2.00-11.56)	<.001
Reoperation	3.02	(1.17-7.77)	.022	3.31	(1.23-8.86)	.017
Diabetes mellitus	1.59	(0.91-2.76)	.103	1.12	(0.61-2.06)	.704
Peripheral vascular disease	3.84	(2.14-6.89)	<.001	2.89	(1.56-5.34)	.001
Previous stroke	1.02	(0.36-2.86)	.971	.74	(0.25-2.17)	.583
Hypertension	2.66	(1.33-5.34)	.006	2.29	(1.13-4.65)	.022
Renal failure	6.67	(3.40-13.06)	<.001	5.71	(2.80-11.67)	<.001
Chronic obstructive pulmonary disease	0.59	(0.14-2.45)	.467	0.45	(0.10-1.95)	.288

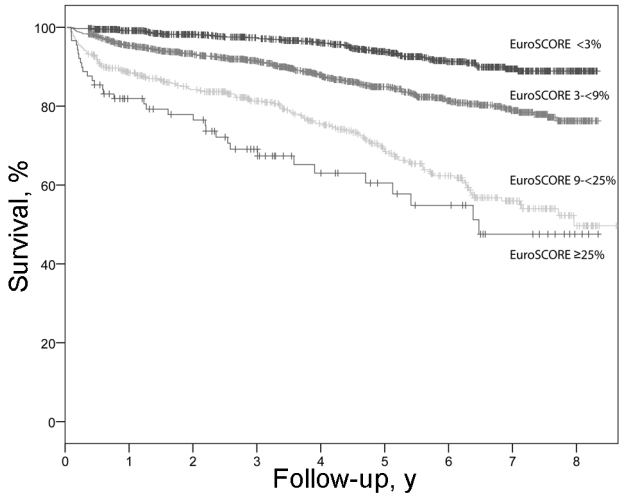

Figure 3. Survival following coronary artery bypass grafting stratified by EuroSCORE-predicted mortality.

outcome. The study, however, provides useful information with respect to the potential benefit of modern perioperative management and surgical techniques such as off-pump surgery in high-risk patients.

During the last decade, the profile of patients referred for cardiac surgery has worsened as shown by an increased predicted mortality by EuroSCORE. Surgical outcomes have, however, steadily improved and currently CABG can be performed with an operative mortality of <1%. In our experience, this improvement of surgical outcome is multifactorial and related to a tailored approach using modern perioperative management (epi-aortic scanning, ITT) and surgical techniques (off-pump CABG) based on individual patients.

REFERENCES

Aranki SF, Rizzo RJ, Adams DH, et al. 1994. Single-clamp technique: an important adjunct to myocardial and cerebral protection in coronary operations. Ann Thorac Surg 58:296-302; discussion 303.

Argenziano M, Spotnitz HM, Whang W, et al. 1999. Risk stratification for coronary bypass surgery in patients with left ventricular dysfunction: analysis of the coronary artery bypass grafting patch trial database. Circulation 100(19 suppl):II119-24.

Bucerius J, Gummert JF, Borger MA, et al. 2003. Stroke after cardiac surgery: a risk factor analysis of 16,184 consecutive adult patients. Ann Thorac Surg 75:472-8.

Christakis GT, Weisel RD, Fremes SE, et al. 1992. Coronary artery bypass grafting in patients with poor ventricular function. Cardiovascular Surgeons of the University of Toronto. J Thorac Cardiovasc Surg 103:1083-91; discussion 1091-2.

Executive Summary STS Spring 2006 Report: The Society of Thoracic Surgery; 2006.

Ferguson TB Jr., Hammill BG, Peterson ED, et al. 2002. A decade of change—risk profiles and outcomes for isolated coronary artery bypass grafting procedures, 1990-1999: a report from the STS National Database Committee and the Duke Clinical Research Institute. Society of Thoracic Surgeons. Ann Thorac Surg 73:480-9; discussion 489-90.

Filsoufi F, Adams DH. 2002. Surgical approaches to coronary artery disease. Curr Treat Options Cardiovasc Med 4:55-63.

Filsoufi F, Adams DH. 2004. Conventional CABG. In: Yang SC, Cameron DE, ed. *Current Therapy in Thoracic and Cardiovascular Surgery*. Mosby; 655-8.

Furnary AP, Gao G, Grunkemeier GL, et al. 2003. Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. J Thorac Cardiovasc Surg 125:1007-21.

Hosmer DW, Lemeshow S. 2000. *Applied Logistic Regression*. 2nd ed. Wiley; New York, NY.

Lansman SL, Cohen M, Galla JD, et al. 1993. Coronary bypass with ejection fraction of 0.20 or less using centigrade cardioplegia: long-term follow-up. Ann Thorac Surg 56:480-5; discussion 5-6.

McKhann GM, Grega MA, Borowicz LM, Jr, et al. 2006. Stroke and encephalopathy after cardiac surgery: an update. Stroke Feb; 37(2):562-71.

Nashef SA, Roques F, Michel P, et al. 1999. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 16(1):9-13.

Selvanayagam JB, Petersen SE, Francis JM, et al. 2004. Effects of off-pump versus on-pump coronary surgery on reversible and irreversible myocardial injury: a randomized trial using cardiovascular magnetic resonance imaging and biochemical markers. Circulation; 109:345-350.

Topkara VK, Cheema FH, Kesavaramanujam S, et al. 2005. Coronary artery bypass grafting in patients with low ejection fraction. Circulation 112(9 suppl):I344-50.

van der Linden J, Hadjinikolaou L, Bergman P, et al. 2001. Postoperative stroke in cardiac surgery is related to the location and extent of atherosclerotic disease in the ascending aorta. J Am Coll Cardiol 38(1):131-5.

Wareing TH, Davila-Roman VG, Daily BB, et al. 1993. Strategy for the reduction of stroke incidence in cardiac surgical patients. Ann Thorac Surg 55(6):1400-7; discussion 7-8.