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Surgical Myocardial Revascularization versus Percutaneous Coronary Intervention with Drug-Eluting Stents in Octogenarian Patients

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ABSTRACT

Objective: Our goal was to compare the clinical outcomes of octogenarian (or older) patients who are referred for either surgical or percutaneous coronary revascularization.

Methods: We retrospectively evaluated the outcomes of all patients 80 years of age who had undergone coronary artery bypass grafting (CABG) with an internal mammary artery or had undergone a percutaneous coronary intervention (PCI) with a sirolimus-eluting stent to the left anterior descending artery in our center between May 2002 and December 2006.

Results: Of the 301 patients, 120 underwent a PCI, and 181 underwent CABG. Surgical patients had higher rates of left main disease, triple-vessel disease, peripheral vascular disease, emergent procedures, and previous myocardial infarctions (39.7% versus 3.3% [P = .001], 76.1% versus 28.3% [P = .0001], 19.6% versus 7.5% [P = .004], 15.8% versus 2.5% [P = .0001], and 35.9% versus 25% [P = .04], respectively). CABG patients had a higher early mortality rate (9.9% versus 2.5%, P = .01). There were no differences in 1- and 4-year actuarial survival rates, with rates of 90% and 68%, respectively, for the PCI group and 85% and 71% for the CABG group (P = .85). The rates of actuarial freedom from major adverse cardiac events (MACEs) at 1 and 4 years were 83% and 75%, respectively, for the PCI group, and 86% and 78% for the CABG group (P = .33). The respective rates of freedom from reintervention were 87% and 83% for the PCI group, versus 99% and 97% for the CABG group (P < .001). The 4-year rate of freedom from recurring angina was 58% for the PCI group, versus 88% for CABG patients (P < .001). Revascularization strategy was not a predictor of adverse outcome in a multivariable analysis.

Conclusion: Octogenarian CABG patients were sicker and experienced a higher rate of early mortality. The 2 strategies had similar rates of late mortality and MACEs, with fewer reinterventions and recurring angina occurring following surgery.

Dr. A. Finkelstein shares first authorship because of his contribution to the manuscript.

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INTRODUCTION

With the decline of age-adjusted death rates in Western society, life expectancy in the United States stands today at 78.1 years [Heron 2008]. Octogenarians (those 80 years of age) constitute the fastest-growing age group in the entire population, encompassing 12% of the total population of persons >60 years and increasing at a rate of 3.8% each year [UNDPI 2002].

This change in demographics has led to a higher proportion of older patients being referred for coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI). For historical and methodologic reasons, extremely elderly patients were not included in many previous studies that compared myocardial revascularization strategies.

Drug-eluting stents (DESs) have been shown to reduce the rate of restenosis and reintervention in patients who undergo PCI [Sousa 2001; Morice 2002; Sawhney 2004; Dnagas 2005], yet the concern for restenosis and the potential for late stent thrombosis [McFadden 2004; Virmani 2004] has not been eliminated and might be pronounced in the population of extremely old patients, who may need multiple PCI procedures and may not adhere appropriately to the dual antiplatelet regimen [Barat 2000].

Conversely, although the advances in CABG surgery (ie, arterial revascularization and off-pump techniques) have shown promise for improved clinical outcomes [Loop 1986; King 2000; Hannan 2007; Holzhev 2007], the major drawback of the surgical approach, its inherent invasiveness, remains a principal difficulty in treating extremely elderly and friable patients.

In this study, we sought to discover the outcomes of octogenarian patients who underwent myocardial revascularization in our center with the current surgical and interventional techniques.

MATERIALS AND METHODS

We present a registry analysis of all consecutive octogenarian (or older) patients who underwent myocardial revascularization with PCI or CABG at Tel Aviv Sourasky Medical Center between May 2002 and December 2006. All patients in the PCI group were treated with at least 1 DES (Cypher; Cordis Corporation, Warren, NJ, USA) to the left anterior descending coronary artery (LAD), with or without PCI to other coronary vessels. All patients in the surgical group (CABG only) were treated with at least 1 internal mammary artery (IMA) to the LAD. Of the 301 patients who met the inclusion criteria, 181 were in the surgical group, and 120 were in the PCI group. After institutional review board approval and individual consent form waiver, follow-up was obtained via a telephone questionnaire with the patient or his close caretaker, patients' discharge and rehospitalization files, and the national registry mortality database. The follow-up was 93.7% complete. Follow-up was complete without the actual telephone interview for 4 of the remaining 19 patients (6.3%), and no late data other than those in the national mortality database were available for the other 15 patients.

Cardiac mortality was defined as death occurring in relation to myocardial infarction (MI), cardiac arrhythmia, out-of-hospital sudden death, deteriorating congestive heart failure, and any undetermined cause of death. Major adverse cardiac events (MACEs) included occurrence of cardiac mortality, MI, or the need for repeat revascularization.

The revascularization method was determined by the treating cardiologist during or shortly after the diagnostic catheterization. In principle, there was a preference to refer patients for surgery for the following reasons: (1) complex type C lesions (calcified coronary arteries, lesion length >20 mm, torturous coronary arteries, or suspicion of a thrombus in an artery); (2), chronic total occlusion; (3) DES unavailability (in the early period of the study); and (4) multivessel disease with poor ventricular function.

In the surgical group, IMAs were dissected as skeletonized vessels and used preferentially for left-sided (LAD plus circumflex) coronary revascularization. Patients who received grafts of radial arteries were treated postoperatively with the calcium channel blocker diltiazem (90-180 mg/d, orally). Off-pump CABG patients were treated postoperatively with clopidogrel (75 mg/d for 3 months).

Overall, patients in the PCI group received aspirin (100 mg daily) before and after the procedure and clopidogrel (Plavix; Sanofi, Bridgewater, NJ, USA). A 300-mg loading dose of Plavix was administered the day before the procedure, and the patient received 75 mg daily thereafter. During the procedure, patients were treated intravenously with heparin. Patients were advised to continue with dual antiplatelet therapy (Plavix and aspirin) for at least 6 months.

Statistical Analysis

The probability (propensity score) that a patient would undergo PCI or CABG, according to the preprocedural variables (see Table 1 for all variables), was determined by using a saturated logistic regression model to take into account the different patient profiles. Because of the cohort size, we elected to use a propensity-adjustment rather than a propensity-matching technique [Blackstone 2002]. The propensity score (in logit units) was forced, as an adjustment variable, into the multivariable analysis performed. Data are expressed as the mean SD or as a proportion. The χ^2 test and 2-sample Student t tests were used to compare discrete and continuous variables, respectively. Multivariable binary

Table 1. Preprocedural Characteristics of Patients*

Characteristic	PCI	CABG	*P*
Age, y†	84 ± 3.1	82.9 ± 2.5	.003‡
Female sex, n (%)	57 (47.5)	63 (34.8)	.03
DM, n (%)	39 (32.5)	49 (27.1)	.31
DM plus insulin Rx, n (%)	4 (3.3)	7 (3.9)	.80
Obesity, n (%)	5 (4.2)	6 (3.3)	.70
Hypertension, n (%)	111 (92.5)	168 (92.8)	.92
Hyperlipidemia, n (%)	85 (70.8)	121 (66.9)	.47
COPD, n (%)	9 (7.5)	6 (3.3)	.10
CHF	37 (30.8)	54 (29.8)	.85
CRF (>1.8mg/dL creatinine), n (%)	18 (15)	24 (13.3)	.67
Old MI, n (%)	30 (25)	66 (36.5)	.037
Acute MI, n (%)	42 (35)	46 (25.4)	.07
EF < 35%, n (%)	6 (5)	10 (5.5)	.84
PVD, n (%)	9 (7.5)	35 (19.3)	.004
Prior PCI, n (%)	33 (27.5)	36 (19.9)	.12
Prior PCI to LAD, n (%)	19 (15.8)	17 (9.4)	.09
LM disease, n (%)	4 (3.3)	71 (39.2)	.000
Single-vessel disease, n (%)	41 (34.2)	6 (3.3)	.000
Double-vessel disease, n (%)	45 (37.5)	37 (20.4)	
Triple-vessel disease, n (%)	34 (28.3)	138 (76.2)	
Total coronary occlusion, n (%)	13 (10.8)	35 (19.3)	.053
IABP needed, n (%)	0 (0)	20 (11)	.000
Emergent prcedure, n (%)	3 (2.5)	27 (14.9)	.000
Prior CABG, n (%)	4 (3.3)	7 (3.9)	.81

*PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; DM indicates diabetes mellitus; Rx, resistance; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; CRF, chronic renal failure; MI, myocardial infarction; EF, ejection fraction; PVD, peripheral vascular disease; LAD, left anterior descending coronary artery; LM, left main; IABP, intra-aortic balloon pump.

†Data are expressed as the mean SD.

‡Exact day or month of birth was unavailable for some patients.

logistic regression was used to evaluate risk factors for early death. The Cox proportional hazards model was used to evaluate risk factors for survival, MACEs, return of angina, and reintervention. The odds ratio (OR) and its 95% confidence interval (CI) are given. Postoperative survival, angina-free survival, MACE-free survival, and reintervention-free survival were analyzed with the Kaplan-Meier method, and the groups were compared with the log-rank test. All analyses were performed with SPSS software (version 16; SPSS/IBM, Chicago, IL, USA).

RESULTS

Demographic and clinical preprocedural data for the 2 patient groups are summarized in Table 1. Patients in the surgical group had significantly higher rates of left main disease, previous MI, triple-vessel disease, peripheral vascular disease, emergent procedures, and need for intra-aortic balloon pump insertion. Of note is that although the mean age was 82.9 years for the CABG patients and 84.0 years for the PCI patients, the exact day or month of birth was unknown for some patients, thus limiting the ability to evaluate the exact age difference between the 2 groups. The mean follow-up time was 31.1 months (range, 1-73 months). The procedural characteristics of the 2 groups are summarized in Table 2.

Table 2. Procedural Characteristics of Patients*

Characteristic	PCI	CABG
Arterial graft to LCX, n (%)	NA	69 (38.1)
No. of vessels treated with 1 DES (%)		
1 Vessel	96 (80)	NA
2 Vessels	24 (20)	NA
DES, mean no./patient	1.48	NA
No. of vessels treated, mean no./patient	1.71	2.62
Off-pump cabg, n (%)	NA	109 (60.2)

*Percutaneous coronary intervention; CABG, coronary artery bypass grafting; LCX, left circumflex coronary artery; NA, not applicable; DES, drug-eluting stent.

The rate of early mortality was higher in the group of patients who underwent operations (9.9% versus 2.5%, $P = .013$). When redo CABG and emergent procedures were excluded from the analysis, there was still a trend favoring the PCI group, although this difference was no longer statistically significant (8.1% versus 2.7%, $P = .06$).

Rates of 1-year and 4-year actuarial survival were 90% and 68%, respectively, for the PCI group and 85% and 71% for the CABG group ($P = .85$) (see Figure 1). Rates of 1-year and 4-year actuarial freedom from MACEs were 83% and 75%, respectively, for the PCI group and 86% and 78% for the CABG group ($P = .33$) (see Figure 2). There were also no differences with respect to the occurrence of MIs and total stroke events (see Table 3).

Reintervention in the PCI patients was defined only when it was an unplanned procedure or occurred at least a few (3-6) months after the index LAD intervention. Planned non-LAD interventions were not included in the MACE analysis and were considered as part of the primary LAD revascularization procedure.

The rate of repeat revascularization was significantly higher in the PCI group (18 reinterventions in the PCI group versus 4 in the CABG group; $P < .001$) (see Figure 3). The

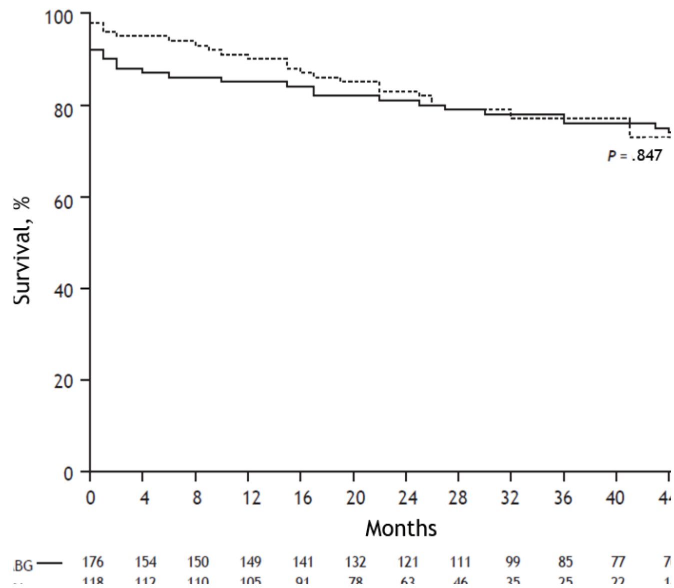

Figure 1. Kaplan-Meier actuarial survival curve: percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG). Numbers of patients are indicated below the graph.

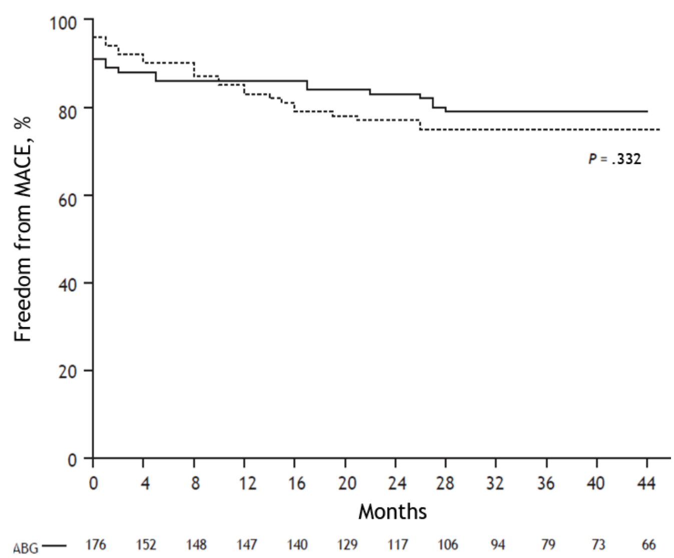

Figure 2. Kaplan-Meier actuarial survival curve for freedom from major adverse cardiac events (MACEs): percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG). Numbers of patients are indicated below the graph.

Table 3. Postprocedural Outcomes of Patients*

Outcome	PCI	CABG	*P*
Deep sternal wound infection, n (%)	NA	3 (1.7)	NA
Early CVA, n (%)	0	4 (2.2)	.10
Periprocedural MI, n (%)	5 (4.2)	3 (1.7)	.18
Need for coronary angiography, n (%)	37 (30.8)	7 (3.9)	<.001
Need for reintervention, n (%)			<.001
1 Vessel	15 (12.7)	4 (2.4)	
2 Vessels	3 (2.5)	0 (0.0)	
Late MI, n (%)	4 (3.4)	3 (1.8)	.38
Late CVA, n (%)	4 (3.4)	4 (2.4)	.60
Early death, n (%)	3 (2.5)	18 (9.9)	.01
Early death excluding redo and emergent cases, n (%)	3 (2.7)	12 (8.1)	.06
Late death, n (%)	25 (20.8)	49 (27.1)	.22
4-Year actuarial survival, %	68	71	.85
4-Year actuarial freedom from MACE, %	75	78	.33
4-Year actuarial freedom from recurring angina, %	58	88	<.001
4-Year actuarial freedom from reintervention, %	83	97	<.001

*PCI indicates percutaneous coronary intervention; CABG, coronary artery bypass surgery; NA, not applicable; CVA, cerebrovascular accident; MI, myocardial infarction; MACE, major adverse cardiac event.

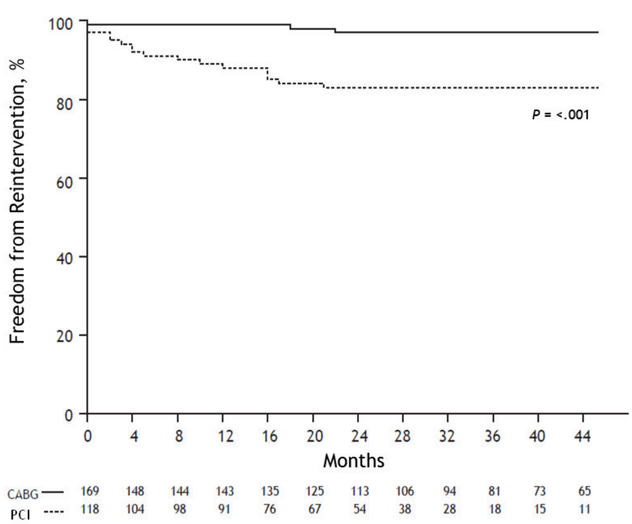

Figure 3. Kaplan-Meier actuarial survival curve for freedom from reintervention, percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG). Numbers of patients are indicated below the graph.

rates of 1-year and 4-year actuarial freedom from reintervention were 87% and 83%, respectively, for the PCI group and 99% and 97% for the CABG group ($P < .001$).

In the multivariable analysis, a low ejection fraction (EF) and redo CABG were predictors for early mortality (ORs of 5.26 [95% CI, 1.41-19.60; $P = .013$] and 5.52 [95% CI, 1.19-25.64; $P = .029$], respectively). Revascularization strategy (CABG or PCI) did not reach statistical significance, although there was a trend for CABG as a predictor for early mortality (OR, 4.69; 95% CI, 0.97-22.72; $P = .054$). When emergent and redo CABG patients were excluded from the analysis, only a low EF remained as a predictor for early mortality (OR, 7.69; 95% CI, 1.73-34.48; $P = .007$), and revascularization mode was nonsignificant ($P = .09$).

An older age, congestive heart failure, chronic renal failure, and prior CABG were predictors of long-term mortality (ORs of 1.17 [95% CI, 1.08-1.26; $P < .001$], 1.94 [95% CI, 1.19-3.15; $P = .007$], 1.96 [95% CI, 1.08-3.54; $P = .026$], and 3.067 [95% CI, 1.30-7.19; $P = .010$], respectively), whereas the presence of diabetes mellitus and a low EF were predictors for MACEs (ORs of 1.75 [95% CI, 1.03-2.98; $P = .037$] and 2.42 [95% CI, 1.08-5.43; $P = .031$], respectively). Again, revascularization mode was not found to be a predictor for an adverse outcome, although there was a trend for PCI treatment as a predictor for MACEs (OR, 1.85; 95% CI, 0.97-3.52; $P = .061$). Postprocedural outcomes for the 2 groups are summarized in Table 3.

DISCUSSION

The elderly are the fastest-growing subgroup in Western society [UNDPI 2002]. This change in demographics has led to a higher proportion of older and sicker patients that are being referred for CABG [Likosky 2008] and extensive PCIs [Urban 2006]. The feasibility and legitimacy of inclusive interventional or surgical treatment in elderly subpopulations have been evaluated in previous studies.

An analysis from the New York State angioplasty registry of 82,140 patients who had undergone angioplasty between 2000 and 2001 [Feldman 2006] included 6453 patients >80 years of age (7.85%). A multivariate analysis showed an older age to be strongly predictive of in-hospital mortality and early MACEs, in either emergent or elective procedures.

The e-Cypher registry analyzed MACE incidence in 15,157 patients and found advanced age to be an independent predictor of MACEs and in-stent thrombosis at 1 year [Feldman 2006]. In another report from the same registry [Guyon 2004], 504 octogenarians were compared with a younger cohort of patients. At the 6-month follow-up, advanced age was strongly associated with an increased mortality rate (5.2% versus 1.2%), MI (1.9% versus 0.8%), and overall MACEs (6.8% versus 2.8%). The DESIRE registry [Costa 2004] evaluated 1364 consecutive patients who were treated solely with DES, among them 116 octogenarians. After 30 months, there was an equivalent cumulative MACE rate for all patients in the different age groups; however, octogenarians had a markedly higher frequency of cardiac death. Hassani et al [2006] compared the 6-month clinical outcomes of 339 octogenarian patients who underwent a PCI incorporating DESs with 2827 younger patients and found similar rates of periprocedural death and acute MI in the 2 groups, but these investigators did find an increased rate of 6-month mortality and Q-wave MI in octogenarians presenting with an acute coronary syndrome.

From the surgical perspective, few early reports evaluated the role of cardiac surgical therapy in octogenarian patients. Not all of these reports were specific for CABG; some analyzed the outcome of revascularization procedures before the advent of arterial revascularization, off-pump techniques, and anesthesia modifications, whereas other studies had short follow-up times or small numbers of cases. Baskett et al [2005] compared the outcomes of 725 octogenarian patients who underwent CABG operations between 1996 and 2001 with those of younger patients who underwent their procedures during the same period. The octogenarians experienced a higher rate of comorbidities and were at an increased risk for death after the procedure (OR, 2.64; 95% CI, 1.95-3.57), which was attributable mainly to the higher proportion of emergent cases among the older patients. Nonetheless, octogenarians had a fair early post-CABG outcome in a recent New England cohort study, with a crude in-hospital survival rate of 98.3% for 2661 patients 80 to 84 years of age and 87.6% for patients 85 years of age [Likosky 2008].

Unfortunately, no large prospective randomized trials have compared the outcomes of CABG versus PCI in the extremely elderly population. A meta-analysis of procedural outcomes of patients older than 75 years from 6 PCI (with bare-metal stents) and 8 CABG registries from the late 1990s found a small immediate survival benefit for PCI-treated patients [Peterson 2004].

Another study by Dacey et al also found an immediate survival benefit for PCI patients not treated with DESs, with a crossover in favor of the surgical treatment after 6 months; however, there was no analysis apart from the crude mortality rate [Dacey 2007].

In this report, we have described the clinical outcomes of 301 octogenarian patients who underwent LAD revascularization with either a DES or an IMA. The surgical group was sicker, as described, and it experienced a higher periprocedural mortality rate. This finding was less evident after we excluded redo CABG procedures and the patients who needed emergent revascularization. There were no significant differences between the groups in terms of overall mortality, neurologic complications, or MACEs. The finding of more unplanned reinterventions for PCI patients is similar to the results of other comparative studies with younger cohorts of patients [Serruys 2001, 2009]. Finally, the multivariable analysis found revascularization strategy not to be a predictor of patient outcome.

These results are consistent with previous reports suggesting that octogenarian patients in need of surgical revascularization are at particular risk mostly in the perioperative period (mainly when they are already in a critical condition), whereas surgical revascularization offers a fairly good and reasonable outcome for the nonemergent octogenarian patient. Unfortunately, there seems to be a common reluctance to consider CABG in octogenarians until medical or interventional therapy options have been exhausted, at which point the patient is already a poor surgical candidate. Possibly, an approach more tolerant of surgery might improve outcomes for this patient population.

As a single-center retrospective registry analysis, the present study has all its inherent limitations. There was no predetermined referral strategy; that is, patients were referred for either treatment solely on the judgment of the interventional cardiologist. Important covariates (mainly technical), such as vessel diameter, angiographic appearance, and lesion length, were not included in the analysis. These technical parameters, which are less important in the surgical group, might affect restenosis, reoccurring angina, and reintervention in the PCI group.

Another limitation of this study is the follow-up period. Although it was relatively long compared with follow-up periods in the current literature, it may not have been sufficiently long, given the growing evidence of delayed thrombosis associated with the DES, mainly after discontinuation of antiplatelet treatment. A longer follow-up may reveal statistically significant increases in MACEs and is therefore required.

In conclusion, this retrospective analysis of octogenarian patients revealed that patients treated with CABG had higher a rate of early mortality. This finding was less evident when only nonemergent patients were analyzed. The 2 strategies had similar long-term mortality rates and numbers of MACEs, with a lower rate of reintervention and recurring angina occurring in the CABG group.

We believe that although octogenarians are indeed at higher risk for any kind of revascularization therapy, they may still benefit from both strategies. Larger prospective multicenter studies are required to determine the role of either strategy in the era of the DES.

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