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Comparison of Isolated Primary CABG in Two Successive Decades in Patients Under 40 Years of Age

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ABSTRACT

Background: Coronary artery bypass graft (CABG) surgery is rarely performed in very young patients. The purpose of our study is to compare the characteristics, treatments, in-hospital, and long-term outcomes of two groups of patients less than 40 years of age who had CABG in two successive decades: 1990-2000 and 2001-2011.

Methods: We identified 145 consecutive patients who underwent primary isolated CABG. Group 1 consisted of 78 patients operated between 1990-2000 and group 2 consisted of 67 patients operated between 2001-2011. Composite end point assessed at follow-up period involved death or recurrence of symptoms, which we defined as myocardial infarction, a need for percutaneous coronary intervention (PCI), reoperation, or congestive heart failure (CHF).

Results: Smoking and hypercholesterolemia before CABG were noted as more frequent in group 1 than in group 2: 96.1% versus 83.6%, $P = .011$; 88.5% versus 61.2%, $P = .0001$, respectively. Patients from group 2 more frequently received one graft (29.8% versus 11.5%, $P = .0059$), were operated with off-pump (41.8% versus 0%, $P < .0001$) or MIDCAB (28.4% versus 0%, $P = .0008$) techniques, and had complete arterial revascularization (58.2% versus 23.1%, $P < .0001$). Group 1 patients had a higher prevalence of composite end point (33.9% versus 17.9%, $P = .035$), with no significant difference in mortality (11.5% versus 10.4%, $P = .83$).

Conclusion: Patients operated between 1990-2000 had a higher prevalence of smoking and hypercholesterolemia and higher frequency of composite-end point during folow-up period without significant difference in mortality.

INTRODUCTION

Coronary artery disease (CAD) is mostly recognized in older and middle-age people [Nguyen 1998]. The first studies to document CAD in very young adults appeared after World War II. Yater et al [Yater 1948] found a high incidence of coronary atherosclerosis in 866 men 18 to 36 years of age. In the 450 necropsy examinations, the authors found 232 patients with nearly complete atherosclerotic occlusion of one or more coronary arteries. Enos et al revealed CAD in 77% of American soldiers killed during the Korean conflict at an average age of 22.1 years [Enos 1955]. Coronary artery bypass graft (CABG) surgery is a valuable method of therapy in patients with CAD. There is little information concerning the clinical features, treatments, and outcomes of CABG in very young patients. There have been a few series of surgical results following CABG in young adults and most of them defined young patients as less than 40 years of age [Kelly 1978; Laks 1978; French 1995; Kelly 1988; Karimi 2007]. Published studies have documented that these patients had higher prevalence of certain risk factors and that their disease was more aggressive than in the older control group [Nguyen 1998; Kelly 1988; Karimi 2007]. Unfortunatelly, previous studies have been limited to small populations or short intervals of postoperative follow-up [Laks 1978; Cohen 1986; Samuels 1996; Hurlé 2008].

The present study aims to compare the characteristics, treatments, in-hospital, and long-term outcomes of two groups of patients less than 40 years of age who underwent isolated primary CABG in two successive decades: 1990-2000 and 2001-2011.

MATERIALS AND METHODS

Between January 1990 and December 2011, 145 patients <40 years of age underwent and survived CABG at the Silesian Center for Heart Diseases in Zabrze, Poland. The age of patients ranged from 24 to 39 years with a mean of 37.5 ± 2.7 years, with 90.3% being male (n = 131). The baseline demographic and clinical characteristics of the study group are shown in Table 1. For the purpose of an analysis, patients were divided into two groups according to the decade they underwent surgery. Group 1 had CABG between 1990-2000 (78 patients) and group 2 had surgery between 2001-2011 (67 patients).

Characteristics, treatments, and in-hospital outcomes data were obtained by review of the hospital records. The preoperative variables compared between the two groups were: age, sex, class of angina CCS (Canadian Cardiovascular Society), NYHA (New York Heart Association) functional class, left ventricular ejection fraction (LVEF), history of myocardial infarction (MI), duration of angina, and risk factors of CAD.

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Table 1. Baseline Demographic and Clinical Characteristics of the Two Study Groups

	Group 1 (n = 78)	Group 2 (n = 67)	*P*
Age, y, mean ± SD	37.4 ± 2.0	37.4 ± 2.4	.88
Males (%)	73 (93.6)	58 (86.6)	.15
Smoking (%)	75 (96.1)	53 (83.6)	.011
Hypercholesterolemia (%)	69 (88.5)	41 (61.2)	.0001
Hypertension (%)	28 (35.9)	33 (49.2)	.10
Diabetes mellitus (%)	4 (5.1)	9 (13.4)	.080
Positive family history of CAD (%)	64 (82.0)	46 (68.7)	.060
Obesity (%)	19 (24.4)	18 (26.9)	.73
Duration of chest pain, months (IQR)	12 (3 - 35)	5 (2 - 12)	.020
CCS 0/I (%)	1 (1.3)	4 (6.0)	.12
CCS II (%)	23 (29.5)	26 (38.8)	.24
CCS III (%)	24 (30.8)	23 (34.3)	.65
CCS IV (%)	30 (38.5)	14 (20.9)	.022
NYHA 0/I (%)	51 (65.4)	56 (83.6)	.013
NYHA II (%)	20 (25.6)	10 (14.9)	.11
NYHA III (%)	5 (6.4)	1 (1.5)	.14
NYHA IV (%)	2 (2.6)	0 (0.0)	.19
Previous MI (%)	52 (66.7)	47 (70.1)	.54
Number of previous MI			
1 (%)	38 (48.7)	40 (59.7)	.19
2 (%)	13 (16.7)	4 (6.0)	.046
≥3 (%)	1 (1.3)	3 (4.5)	.24
Previous PCI	7 (9.0)	33 (49.2)	<.0001
Number of previous PCI			
1 (%)	7 (9.0)	26 (38.8)	<.0001
2 (%)	0 (0.0)	3 (4.5)	.059
≥3 (%)	0 (0.0)	4 (6.0)	.029
Mean preoperative LVEF	49.2 ± 9.8	50.4 ± 9.1	.47

CAD indicates coronary artery disease; IQR, interquartile range; CCS, Canadian Cardiovascular Society; NYHA, New York Heart Association; MI, myocardial infarction; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction.

Definitions of individual risk factors were as follows: cigarette smoking current or stopped <1 year; hypertension — systolic blood pressure >140 mmHg and/or diastolic >90 mmHg and/or on anti-hypertensive treatment; hypercholesterolemia — total cholesterol >200 mg/dL (5.2 mmol/L); diabetes mellitus — fasting glucose >125 mg% (7.0 mmol/L) or normal on hypoglycaemic therapy; obesity — body mass index (BMI) >30 kg/m^2; positive family history (PFH) — CAD in a first-degree relative: women <65 and men <55 years old.

Coronary angiography was conducted in all patients before surgery. Significant disease was defined as a reduction in arterial lumen diameter of at least 70%. A stenosis of 50% or more in the left main coronary artery was considered significant. During CABG, all patients received at least one of the following conduits: saphenous vein graft (SVG), left internal mammary artery (LIMA), right internal mammary artery (RIMA), and radial artery (RA) from non-dominant arm.

To make the length of follow-up period for both groups similar, the patients from group 1 were analyzed in 2004, and the patients from group 2 in 2015, giving each group at least 4 years follow-up. At follow-up, the incidence of composite end point were compared. Composite end point involved death from any cause or recurrence of symptoms defined as myocardial infarction (MI), a need for percutaneous coronary intervention (PCI), reoperation, or congestive heart failure (CHF).

Follow-up information was compiled from the case records of patients, routine mailed questionnaires, and telephone interviews with the patients themselves or with their relatives. Death was defined as death from any cause. MI was defined as an ischemic event that met the actual for that time by European Society of Cardiology criteria for myocardial infarction. Repeat revascularization was defined as additional angioplasty or CABG, performed after discharge from hospital. CHF was defined as new diagnosis of heart failure with symptoms of peripheral or pulmonary congest with or without reduced left ventricular ejection fraction. The vital status and date of death in some cases was verified by police or Ministry of Internal Affairs.

The statistical analysis included comparison of baseline, angiographic, and procedural characteristic and occurrence of composite end point during the follow-up period. Analyzed variables are expressed as numbers and percentages. Continuous variables were summarized using arithmetic mean with standard deviation (SD) for data following normal distribution or median with interquartile range (IQR) for data demonstrating non-normal distribution. Normality of the distribution was verified using the Shapiro-Wilk test. The Student t test for comparison of continuous parameters with normal distribution was performed, whereas Mann-Whitney U for parameters with non-normal distribution was used. Categorical variables were summarized using frequency tables, for both absolute numbers and percentages. The categorical variables were compared using Pearson chi-square test or Fisher exact test (if an expected number is less than 5). The composite end point, all-cause mortality, non-fatal MI, revascularization, and recently diagnosed chronic heart failure during observation period for all patients were analyzed using the Kaplan–Meier method with log-rank test. A two-sided P value ≤.05 was considered significant. The STATISTICA 10 software (StarSoft, Tulusa, Oklahoma) was used for all calculations

RESULTS

Baseline demographic, clinical, and operative characteristics of the two groups are shown in Table 1. The most common CAD risk factor before CABG in both groups was

Table 2. Operative Characteristics of the Two Study Groups

	Group 1 (n = 78)	Group 2 (n = 67)	*P*
Number of grafts			
1 (%)	9 (11.5)	20 (29.8)	.0059
2 (%)	24 (30.8)	27 (40.3)	.23
3 (%)	26 (33.3)	14 (20.9)	.095
≥4 (%)	19 (24.4)	6 (9.0)	.014
Type of operation			
CABG (%)	78 (100)	30 (44.8)	<.0001
OPCAB (%)	0 (0)	28 (41.8)	<.0001
MIDCAB (%)	0 (0)	19 (28.4)	.0008
Type of grafts			
Arterial only (%)	18 (23.1)	39 (58.2)	<.0001
Venous only (%)	7 (9.0)	0 (0)	.012
Arterial and venous (%)	53 (67.9)	28 (41.8)	.0016
Use of LIMA graft (%)	69 (88.5)	65 (97)	.052
Use of RIMA graft (%)	19 (24.4)	10 (14.9)	.16
Use of LIMA and RIMA graft (%)	17 (21.8)	9 (13.4)	.19

CABG indicates coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass grafting; MIDCAB, minimally invasive direct coronary artery bypass grafting; LIMA, left internal mammary artery; RIMA, right internal mammary artery.

smoking. Smoking and hypercholesterolemia were noted more frequently in group 1 than in group 2 96.1% versus 83.6%, *P* = .011; 88.5% versus 61.2%, *P* = .0001, respectively. Patients operated between 1990-2000 in comparison to those who had surgery between 2001-2011 had longer time from ischemic symptoms onset to CABG (12 [3-35] versus 5 [2-12] months, *P* = .02) and prevalence of unstable angina (38.5% versus 20.9%, *P* = .022). Patients in group 2 more frequently received one graft (29.8% versus 11.5%, *P* = .0059), were operated with OPCAB (41.8% versus 0%, *P* < .0001) or MIDCAB (28.4% versus 0%, *P* = .0008) techniques, and had complete arterial revascularization (58.2% versus 23.1%, *P* < .0001). Operative characteristics are outlined in Table 2.

In long-term follow-up, 9 patients from group 1 (11.5%) and 7 from group 2 (10.4%) died (Figure). There was no significant difference in mortality (P = .83). The causes of death in group 1 were: MI (3 patients), sudden cardiac death (2 patients), CHF (2 patients), and unknown reason (2 patients); in group 2: MI (2 patients), sudden cardiac death (1 patient), CHF (1 patient), pulmonary embolism (1 patient), suicide (1 patient), unknown reason (1 patient). There was no significant difference in CCS and NYHA class after surgery between the two groups, with the majority of patients being in CCS class I and NYHA class I in both groups at follow up. Group 1 patients had a higher prevalence of composite end point (33.9% versus 17.9%, *P* = .035), recurrence of symptoms (25.6% versus 7.5%, *P* = .0039), and PCI (15.4% versus 3.0%, *P* = .012) (Table 3).

Table 3. Long-Term Outcomes of the Two Study Groups

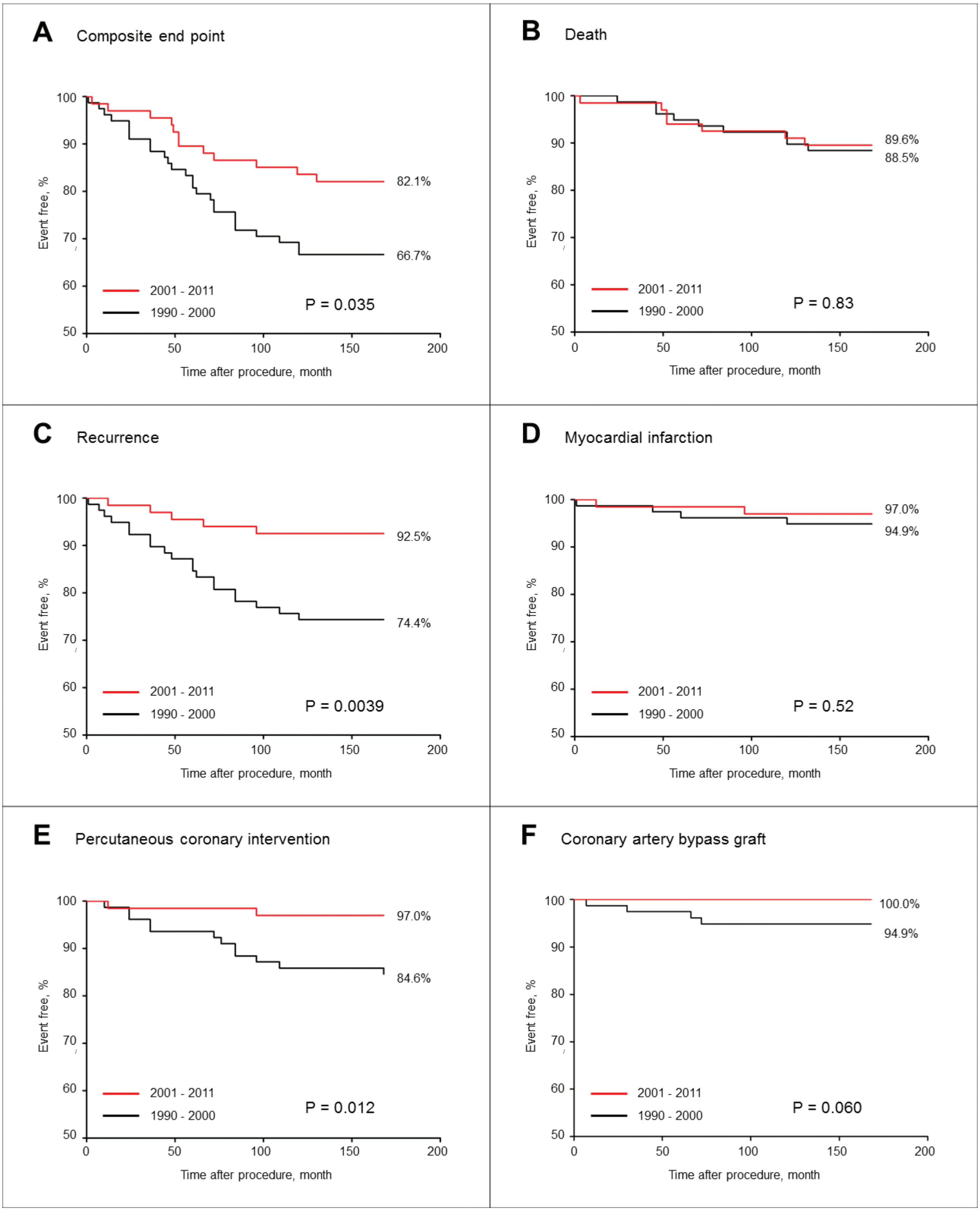
	Group 1 (n = 78)	Group 2 (n = 67)	*P*
Time of follow-up month ± SD	95.1 ± 31.1	101.0 ± 37.8	.31
Composite end point (%)	26 (33.3)	12 (17.9)	.035
Death (%)	9 (11.5)	7 (10.4)	.83
Recurrence of symptoms (%)	20 (25.6)	5 (7.5)	.0039
MI (%)	4 (5.1)	2 (3.0)	.52
PCI (%)	12 (15.4)	2 (3.0)	.012
CABG (%)	4 (5.1)	0 (0)	.06

MI indicates myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

DISCUSSION

There is a paucity of contemporary studies concerning the clinical features, treatment, and long-term outcomes of CABG in very young patients [Karimi 2007; Sajja 2005; Rohrer-Gubler 1998]. The long-term results of CABG in very young patients are often below expectations as noted by Kelly et al [Kelly 1988]. Recurrence of angina occurs in 37.5% of young and in 11% of old patients at 7.9 years after CABG. Patients less than 40 years had nearly 14 times higher reoperation rates than control older patients (16.2% versus 1.2%). In Rohrer-Gubler et al's analysis, the reintervention rate (defined as cardiac reoperation and/or PCI) was more than three times higher in the younger group than in the older control group [Rohrer-Gubler 1998].

Aggressive atherosclerosis and high reintervention rates are probably related to increased presence of coronary risk factors such as smoking, hypercholesterolemia, and PFH resulting in an increased incidence of graft occlusion and progression of disease in native arteries. Zehr et al [Zehr 1994] compared characteristic and long-term results of 2 groups of patients ≤40 years who underwent surgery between 1970-1980 and 1981-1991. The most prevalent CAD risk factor in both groups was smoking (80% versus 68%, *P* = .085), PFH (72% versus 53%, *P* = .01), and hypercholesterolemia (37% versus 52%, *P* = .065). This compares similarly to our analysis, where we found the above mentioned risk factors to occur most commonly in our patient cohort, although more frequently in the earlier decade. Common incidence of these risk factors is typical for patients who have undergone CABG at a very young age, although some varied in countries and changed over the years [Kelly 1978; Laks 1978; French 1995; Kelly 1988; Cohen 1986; Samuels 1996; Hurlé 2008; Sajja 2005; Rohrer-Gubler 1998; Zehr 1994; Ng 1997; Nataf 1992; Every 1996]. In the American studies published in the seventies and eighties, the proportion of smokers in patients under 40 years who qualified for



Rates of cardiovascular events among the study patients according to the decade they underwent surgery.

CABG ranged from 90% to 93% [Kelly 1978; Laks 1978]. A lower incidence of cigarette smoking was noted in the Swiss cohort (81.8%), and in the French population (69.6%) published in the nineties [Rohrer-Gubler 1998; Nataf 1992]. Karimi et al [Karimi 2007] noted that only 22.4% Asian patients less than 40 years old who underwent CABG at the beginning of the twenty-first century were current smokers before surgery. We have also noticed a significant decrease in the percentage of smokers in the years 2001-2011 in comparison to 1990-2000.

The second common risk factor in our analysis and the majority of other was hypercholesterolemia. Cholesterol level >200 mg/dL was noted in 88.5% patients operated in 1990-2000 and in only 61.2% who had CABG in the next decade. These data compare with other studies confirming reduction of hypercholesterolemia in the Polish population in the last years [Bandosz 2012]. In other studies, the criteria of diagnosis of hypercholesterolemia were more restrictive. Laks et al [Laks 1978] and French et al [French 1995] found cholesterol levels greater than 250 mg/dL in 64% and 65.5% of adults, respectively. Rohrer-Gubler et al noted cholesterol >300 mg/dL in 47.7% of patients operated under 40 years of age [Rohrer-Gubler 1998]. In Ng et al's analysis, 90% of patients had total cholesterol level >200 mg/dL and 37% >300 mg/dL [Ng 1997].

The incidence of PFH differs between reports. Kelly et al noted a family history of CAD in 84% of patients operated before 40 years of age [Kelly 1988]. In other studies, incidence of PFH was less frequent and recorded between 24.4% and 53.9% patients [Karimi 2007; Rohrer-Gubler 1998; Nataf 1992].

The aggressive nature of atherosclerosis in young patients undergoing CABG is confirmed by a high incidence of MI prior to surgery. In our analysis, 53.8% patients had a history of one MI, and 11.7% of two previous MIs; these numbers place our patient cohort in the middle of other analyzed studies. In Cohen et al, preoperative MI was noted in 65.8% of patients under 36 years of age who had CABG [Cohen 1986]. In the Rohrer-Gubler et al study, 65.3% of patients had MI before surgery [Rohrer-Gubler 1998]. In Hurlé et al, 45.2% of adults aged 40 years or less had previous MI before CABG [Hurlé 2008].

Sajja et al analyzed patients who had primary CABG before the age of 45 years and required reoperation in the long-term follow-up period [Sajja 2005]. The recurrence of angina was due to either graft failure or progression of disease in native vessels. The number of conduits was 2.53 per patient at primary surgery and 3.14 at reoperation. This increase suggests progression of the atherosclerosis in the native arteries. Only four patients in the earlier decade required repeat surgical revascularization. With more arterial conduits performed in the more recent decade, we feel the requirement for repeat CABG will be less, however, 20 or 30 year follow-up will be most important to analyze.

On the other hand, in spite of progress in surgical technique, pharmacology, and invasive cardiology, young patients are exposed to recurrence of symptoms and reintervention. Zehr et al, who compared long-term results of young patients who underwent surgery in the seventies and eighties, showed that introduction of PCI and arterial conduits had no significant influence on 5- and 10-year survival [Zehr 1994].

There are few contemporary data about distant results of CABG in very young adults. Hurle et al noted high incidence of major adverse events in the follow-up period in 42 patients ≤40 years who had surgical revascularization between 1989-2006 [Hurlé 2008]. Five patients died, and 13 had major cardiac non-lethal events in the mean 9.5-year follow-up period. In our analysis we did not observe a difference in mortality between the two groups, however, patients operated in the more recent decade had lower incidence of the composite end point, mostly driven by less recurrent symptoms and less need for repeat reintervention in the form of PCI.

Better long-term results of patients operated a decade later requires explanation. Patients operated between 2001-2011 had lower incidence of smoking and hypercholesterolemia and more frequently had one vessel disease, which might reflects less aggressive atherosclerosis. Moreover significant improvment in accessibility and quality of cardiological care was observed over the last 15 years in Poland [Widimsky 2010]. Interestingly, these better long-term results were not reflected in the percentage of complete arterial revascularization (only 58%); the reason complete arterial revascularization and specifically the use of RIMA was not done in a higher percentage of patients requires a short explanation. The Silesian Center of Heart Disease in Zabrze, Poland is centered in the midst of multiple coal mines; our patients not only had significant smoking history but also were coal miners, and this combination made us very wary of possible sternal complications due to postoperative pulmonary complications. Radial artery use was not popularized until the early 2000s in Poland and, due to unfamiliarity, it was not adopted as a conduit during that time.

There are some limitations in our analysis. The most important limitation is the relatively small number of patients in each group. Due to the number of included patients and low proportion of adverse cardiovascular events in the long-term observation period, advanced statistical models (i.e. multivariate analysis, propensity-matching score) were not performed.

In addition, the retrospective nature of the study and the related consequences (selection biases) make it difficult to generalize the conclusions of the present results. As a single-center study, it may not be applicable to other populations. As this study focused on patient characteristics and general outcomes in CABG in very young patients, we did not comment or analyze the surgical aspects in each patient cohort and thus cannot make any recommendations as far as the method of surgical technique (on pump versu off pump). SYNTAX score is now routinely reported at our institution and we feel that it would have been a very good adjunct in clinical decision making. We also feel that the reported percentage of total arterial revascularizations in this study does not reflect our current practice in the cardiac surgery division. We aim to revascularize using arterial conduits all left sided critically narrowed coronaries, utilizing any combination of arterial conduits. However, we are believers in the RAPS study and reserve the radial artery for a coronary with a high grade lesion [Desai 2004].

Conclusion

Patients operated between 1990-2000 had a higher prevalence of smoking and hypercholesterolemia and higher frequency of composite-end point during folow-up period without significant difference in mortality.

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