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# Coronary Artery Disease in Young Adults: Who Needs Surgical Revascularization? A Retrospective Cohort Study

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## ABSTRACT

**Background:** Coronary artery disease (CAD) is a major cause of death and disability in developed countries. Despite the fact that prevalence accrues with age, an increasing number of young patients suffering from CAD is being observed worldwide. The aim of this study is to describe the population of young adults suffering from CAD and requiring coronary artery bypass grafting (CABG), and to assess early outcomes after the procedure.

**Methods:** A retrospective cohort study analyzed 190 consecutive patients aged ≤50 years old that underwent CABG between 2010 and 2014. Baseline characteristics and operative data were presented in the study. Postoperative complications, such as major adverse cardiac and cardiovascular events (MACCE), prolonged mechanical ventilation (>72 hours), bleeding requiring reexploration, sternal dehiscence, and others were assessed.

**Results:** A population comprising mostly overweight or obese males with a mean age of 46 ± 4.1 years was analyzed. Patients suffered mostly from three-vessel disease (81%), hypertension (74.7%), and had previous history of myocardial infarction (MI) (60%). The majority of patients had normal left ventricle ejection fraction (LVEF) (83.1%). 22.6% of cases were emergent procedures. Perioperative mortality was low (1%) and overall MACCE rate stood at 2.6%. Emergent surgery was associated with a higher incidence of postoperative complications ($P = .007$). The number of diseased vessels, LVEF, and CCS/NYHA class-on-admission was not associated with a higher incidence of postoperative complications ($P > .05$ for all).

**Conclusion:** CAD in young patients remains an issue described insufficiently in the literature. Among our study cohort of younger patients undergoing CABG, the majority of the patients had multivessel disease and were slightly symptomatic with normal LVEF. Although the postoperative complication rate was low, the percentage of emergent surgeries was alarmingly high in this population. Consistent with the literature, we highlight the importance of CAD screening in the young population to detect subclinical disease, which might be treated therapeutically or operated electively.

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## INTRODUCTION

Coronary artery disease (CAD) is a major cause of death and disability in developed countries. Although the prevalence accrues with age, an increasing number of young patients suffering from CAD is being observed worldwide. When the disease affects professionally active individuals, it may have a devastating effect on both the patient and their family. Although the CAD mortality rates have declined over the last few decades, CAD is still responsible for approximately one-third of all deaths in the population over 35 years old [Nichols 2014]. Moreover, the lowering CAD mortality rates have not been uniformly observed in younger age groups or in females [Rubin 2012].

The prevalence of CAD in young patients is difficult to establish as a majority of cases remain subclinical [Alkhawam 2015]. A study showed that 20% of 30- to 34-year-old men and 8% of 30- to 34-year-old women with no prior history of angina had advanced lesions in coronary arteries when analyzed for microscopic qualities in the autopsy [McGill 2000].

Despite already existing lesions, the majority of patients remain asymptomatic for many years. As studies show, acute coronary syndrome (ACS), especially ST-elevation myocardial infarction (STEMI), is commonly the first clinical manifestation of CAD in young age groups. The angiographic findings of these individuals most frequently present with a complex lesion in a single vessel caused by plaque rupture, and require primary percutaneous coronary intervention (PCI) [Fournier 1996; Chen 1995; Klein 1987]. Other young patients suffer from multiple vessel disease and need to be treated with surgical revascularization. Currently, there is limited data regarding specificity of surgical revascularization for CAD in the younger age groups and their prognosis.

The aim of this study is to illustrate the population of young adults suffering from CAD and requiring coronary artery bypass grafting (CABG), and to assess short-term outcomes after the procedure.

## MATERIALS AND METHODS

In a retrospective cohort study, we analyzed 190 consecutive patients aged ≤50 years old who underwent CABG surgery between 2010 and 2014 in the Department of Cardiovascular Surgery and Transplantology, John Paul II Hospital, Krakow, Poland. All patients in the analysis were qualified for surgical revascularization according to the European Society of Cardiology (ESC) guidelines [Taggart 2011; Authors/Task Force Members 2014].

On-pump CABG procedures were performed with placement of arterial grafts (left internal mammary artery [LIMA], right internal mammary artery [RIMA], and radial artery [RA]), venous grafts (saphenous vein graft [SVG]), or both. Arterial and venous grafts were used based on indications defined by our institution's protocol and surgeon's preferences. General anesthesia was carried out using propofol as a hypnotic, sufentanyl as an analgesic, and non-depolarizing muscle relaxant. Heparinization was achieved before starting cardiopulmonary bypass (CPB) and subsequently reversed with protamine. Our institution's standard protocol includes heparin 3 mg/kg and protamine 1:1. Blood or crystalloid cardioplegia was used for all cases. Distal and proximal anastomoses were attached with continues running sutures, using non-absorbable Prolene.

When suitable, off-pump surgery was performed. Preoperative care and anesthesia were carried out following the same protocols. Distal anastomoses were performed as during on-pump procedure with or without tissue stabilizers.

All surgeries were performed via median sternotomy.

Postoperative complications were assessed as follows:

(1) Major adverse cardiac and cerebrovascular events (MACCE), defined as any postoperative MI, death from cardiac causes and acute stroke; (2) low cardiac output syndrome (LCOS) without elevated cardiac enzymes; (3) death from non-cardiac causes; (4) multiple organ dysfunction syndrome (MODS); (5) acute kidney injury (AKI); (6) prolonged mechanical ventilation (>72 hours); (7) sternal dehiscence; (8) excessive bleeding requiring reexploration.

Requirement for blood product transfusion was evaluated separately.

Ethics approval was obtained from the Bioethics Committee, Jagiellonian University Medical College - KBET/124/B/2014. Research analyzed medical documentation and did not require patient consent.

### *Statistical Analysis*

Statistical analysis was performed using STATISTICA software, version 10.0. In order to confirm a normal distribution of continuous variables, the Shapiro-Wilk test was used. Results were presented based on the parameters of descriptive statistics, including mean values and standard deviations, or median values and quartiles, as appropriate. Categorical variables were presented as percentages. Continues variables were compared using Student t test and categorical variables using Pearson chi-square test. Univariate logistic regression analysis was performed to determine the influence of commonly described risk factors on complications occurrence in the study cohort. *P* value less than .05 were considered significant.

Table 1. Baseline Patient Characteristics*

| | |
|---|---|
| Age, years | 46 (±4.1) |
| Male sex, n (%) | 170 (89.5) |
| BMI, kg/m$^2$ | 28.2 (±4.2) |
| Normal weight, n (%) | 53 (27.9) |
| Underweight, n (%) | 2 (1) |
| Overweight, n (%) | 75 (39.5) |
| Obese, n (%) | 60 (31.6) |
| Diabetes, n (%) | 34 (17.9) |
| Hypertension, n (%) | 142 (74.4) |
| Hyperlipidemia, n (%) | 49 (25.8) |
| CCS class 0, n (%) | 2 (1) |
| CCS class I, n (%) | 20 (10.5) |
| CCS class II, n (%) | 79 (41.6) |
| CCS class III, n (%) | 67 (35.3) |
| CCS class IV, n (%) | 22 (11.6) |
| Single-vessel disease, n (%) | 36 (19) |
| Two-vessel disease, n (%) | 39 (20.5) |
| Three-vessel disease, n (%) | 115 (60.5) |
| LM disease, n (%) | 62 (32.6) |
| LVEF, % | 51.6 (±11.1) |
| LVEF ≤ 40%, n (%) | 32 (16.9) |
| Previous MI, n (%) | 114 (60) |
| Previous PCI, n (%) | 56 (29.5) |

*Data shown as mean ± SD or as median (IQR), or number (percentage). BMI indicates body mass index; CCS, Canadian Cardiovascular Society; LM, left main; LVEF, left ventricle ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention.

## RESULTS

Analyzed population comprised mostly overweight or obese (71.1% patients with BMI > 25kg/m$^2$) males (89.5%) with a mean age of 46 ± 4.1 years. On admission, most patients presented without acute symptoms (77.4% cases operated electively) and had slightly exacerbated chronic symptoms (53.1% patients in CCS class II or less). 81% of the individuals had multivessel disease (two- and three-vessel disease 20.5% and 60.5% respectively). 60% of the population had a history of previous MI and 29.5% underwent previous PCI. 74.7% of the patients suffered from accompanying hypertension and 16.9% had impaired left ventricle ejection fraction (LVEF ≤ 40%) (Table 1).

In the study cohort, medical history of hypertension, diabetes, hyperlipidemia, and BMI > 25kg/m$^2$ was not associated with the number of diseased vessels, previous MI, or previous

Table 2. Intraoperative Data*

| | |
|---|---|
| Elective surgery, n (%) | 147 (77.4) |
| Emergent surgery, n (%) | 43 (22.6) |
| On-pump surgery, n (%) | 181 (95.3) |
| Off-pump surgery, n (%) | 9 (4.7) |
| Surgery time, min | 240 (180-275) |
| Aortic cross-clamp time, min | 45 (34-58) |
| 1 bypass graft, n (%) | 31 (16.3) |
| 2 bypass grafts, n (%) | 79 (41.6) |
| 3 bypass grafts, n (%) | 68 (36.3) |
| 4 bypass grafts, n (%) | 11 (5.8) |
| 5 bypass grafts, n (%) | 1 (0.5) |
| LIMA graft, n (%) | 178 (93.7) |
| SVG graft, n (%) | 140 (77.4) |
| RIMA graft, n (%) | 31 (16.3) |
| RA graft, n (%) | 9 (4.7) |

*Data shown as mean ± SD or as median (IQR), or number (percentage). LIMA indicates left internal mammary artery; SVG, saphenous vein graft; RIMA, right internal mammary artery; RA, radial artery.

Table 3. Postoperative Complications*

| | |
|---|---|
| MACCE, n (%) | 5 (2.6) |
| Death, n (%) | 2 (1) |
| Postoperative MI, n (%) | 2 (1) |
| Acute stroke, n (%) | 1 (0.5) |
| LCOS without elevated cardiac enzymes, n (%) | 2 (1) |
| Prolonged mechanical ventilation, n (%) | 2 (1) |
| AKI, n (%) | 0 (0) |
| MODS, n (%) | 0 (0) |
| Sternal dehiscence, n (%) | 4 (2.1) |
| Reexploration for bleeding, n (%) | 6 (3.1) |
| Any postoperative complication, n (%) | 19 (10) |
| Any blood products transfusion, n (%) | 94 (49.5) |
| PRBC transfusion, n (%) | 67 (35.3) |
| FFP transfusion, n (%) | 58 (30.5) |
| PLT transfusion, n (%) | 36 (19) |
| Single-vessel disease, n (%) | 36 (19) |
| Two-vessel disease, n (%) | 39 (20.5) |
| Three-vessel disease, n (%) | 115 (60.5) |
| LM disease, n (%) | 62 (32.6) |
| LVEF, % | 51.6 (±11.1) |
| LVEF ≤ 40%, n (%) | 32 (16.9) |
| Previous MI, n (%) | 114 (60) |
| Previous PCI, n (%) | 56 (29.5) |

*Any postoperative complication – excluding blood products transfusions. MACCE indicates major adverse cardiac and cerebrovascular event; MI, myocardial infarction; LCOS, low cardiac output syndrome; AKI, acute kidney injury; MODS, multiple organ dysfunction syndrome; PRBC, packed red blood cells; FFP, fresh frozen plasma; PLT, platelets.

PCI ($P > .05$ for all). Moreover, chronic intensity of symptoms, defined as CCS and NYHA class, was not associated with the number of diseased vessels, previous MI, or previous PCI ($P > .05$). The number of diseased vessels did not correlate with LVEF on admission ($P > .05$).

Most procedures were performed electively (77.4%) with usage of CPB and placement of 2 bypass grafts. The LIMA graft was used in nearly all cases (93.7%). Median procedure time and aortic cross-clamp time were 240 and 46 minutes respectively (Table 2). The number of diseased vessels and BMI were the only factors that prolonged procedure time with statistical significance ($P = .001$ and $P = .001$, respectively).

Postoperative MACCE occurred in 5 cases (2.6%), and 2 patients (1%) died before discharge. Two patients (1%) suffered from LCOS without elevated cardiac enzymes. Eventful recovery was observed in 19 cases (10%). Nearly half of patients required blood products transfusions (49.5%). Packed red blood cells (PRBC) and fresh frozen plasma (FFP) were more commonly used than platelet (PLT) transfusions (35.3%, 30.5%, and 19%, respectively). Four patients (2.1%) suffered from postoperative sternal dehiscence, where one case was due to deep wound infection. Two underwent the procedure with both LIMA and RIMA grafts and the other 2 were operated with implantation of LIMA and SVG grafts. Six patients (3.1%) required reexploration for bleeding, where 2 of them underwent the procedure with both LIMA and RIMA grafts and the other 4 with LIMA and SVG grafts (Table 3).

Emergent procedures were performed in 22.6% of cases, whereas the rate of emergent CABG procedures performed at our institution from 2010 to 2014 in patients over 50 years old stood at 18.7%. Emergent surgery was the only risk factor associated with higher incidence of postoperative complications ($P = .007$; OR, 3.63; 95% CI, 1.37-9.62). The number of diseased vessels, CCS and NYHA class, LVEF on admission, history of MI and PCI, age, and comorbidities did not influence the incidence of postoperative complications ($P > .05$ for all).

## DISCUSSION

Age remains an undisputed and not modifiable risk factor for cardiovascular disease. Unfortunately, there is an increasing number of young individuals suffering from CAD worldwide. According to guidelines for cardiovascular prevention, screening for risk factors for CAD should be started in males over 40 years old and females over 50 years old. For individuals suffering from hyperlipidemia or diabetes, risk of CAD should be assessed when over 45 years old, and for patients with hypertension or obesity with no age references [Perk 2012]. Concerning atherosclerosis prevention, the ongoing

ECAD trial investigates even younger individuals: males over 35 and females over 45 years old [Domanski 2015].

Prevalence of risk factors for early onset of CAD (hypertension, diabetes, hyperlipidemia, and obesity) was high and expected in the study group [Rubin 2012; Maroszyńska-Dmoch 2016; Maroszyńska-Dmoch 2014]. However, they were associated with neither the number of diseased vessels nor the history of MI or PCI and therefore were not a predictor of the severity of the disease in the study cohort. More than half of the individuals analyzed in this study had previous MI, and nearly one third of them were previously treated with PCI. Despite that, most of the study group was slightly symptomatic or asymptomatic (CCS class II or less) with normal LV function, but still suffered from multiple vessel disease. Moreover, there was no statistical significance in the association between the CCS or NYHA class and the number of diseased vessels. As there was no correlation between the number of affected coronary arteries and LVEF, physiologic compensation may allow the younger age group to be only slightly symptomatic or even asymptomatic, despite ongoing disease.

Young patients suffering from CAD are difficult to diagnose. Concerning age, CAD may not be the first on the list for differential diagnosis. The stress test, which is a diagnostic method of choice, may not be distinguishing due to the lack of symptoms, normal LV function, and slightly exacerbated comorbidities. On the other hand, angiography will be considered only for patients with CCS/NYHA class greater than or equal to III. Even then, due to young age, it would not be recommended for routine testing, as the probability of CAD will be low [Budaj 2015]. However, this population is increasing and often requires revascularization. The stratification of risk and exacerbation of disease remains an important question to predict outcome in younger age groups based on risk factors and their genetic predisposition.

New ESC guidelines for CAD prevention are expected in 2016.

Neither PCI nor CABG alone can provide a solution for the entire spectrum of young CAD patients. CABG procedure is recommended for patients suffering from left main or proximal LAD stenosis, especially with accompanying two- or three-vessel disease [Authors/Task Force Members 2014].

Most of our patients required an on-pump surgery. The rate of off-pump procedures was low (4.8%), but similar to the rates observed in other cardiac surgery centers in Poland.

Aside from the number of affected vessels, surgery time was higher only in obese males. Prolonged time is considered to be associated with the fact that those patients required more bypass grafts and more precise hemostasis.

Usually, first symptoms of stable angina occur in males older than 40 years old and females older than 50 years old. However, in young patients, ACS is often the first clinical presentation of the disease [Budaj 2015]. Studies analyzing STEMI patients showed that compared to the older population, a higher proportion of young adults deny previous experience of angina [Doughty 2002]. Emergent procedures due to ACS that required surgical revascularization were performed more frequently than observed in individuals over 50 years old. Emergent surgery is a well described risk factor for poor outcome after adult cardiac procedures, as it contributes to a greater risk of postoperative bleeding, prolonged mechanical ventilation, and prolonged hospital stay [Ding 2015; Fukui 2013; Deutsch 2016]. In this study, emergent procedure was the only factor that was associated with postoperative complications. In young patients, in comparison to the older population, ACS may carry a greater risk as a result of insufficiently developed collateral circulation. Since the rate of postoperative complications was low and young individuals tend to have good outcomes after cardiac procedures, this brings forth the question whether the incidence rate could be even lower if the surgeries were performed electively, considering the fact that there were no differences in complications occurrence in relation with the number of diseased vessels, on admission LVEF, or previous history of MI or PCI.

Performing CABG procedure in young patients is also associated with the issue of graft patency. It has been well documented that in long-term follow up, arterial grafts remain superior in patency over venous [Barner 1985; Calafiore 1994]. Therefore, arterial grafts were preferable in our study group and LIMA:LAD was the most commonly performed. However, supplying a patient with three-vessel disease with three arterial grafts, especially during an emergent procedure, may be impossible to accomplish.

### *Conclusion*

CAD proved to be a major threat to people's health in wealthy states. However, in young patients, it remains an issue described insufficiently in the literature. This study is the first to illustrate the Polish population of young adults suffering from CAD and undergoing CABG, and the short-term outcomes after the procedure.

Although the postoperative complication rate was low, the percentage of emergent surgeries was alarmingly high in this population. Despite the fact that young patients tend to have better outcomes after cardiac procedures, the actual risk may be greater than expected due to high incidence of emergent surgeries.

The majority of patients in the study cohort had multivessel disease and were slightly symptomatic with normal left ventricle function, and therefore remained undiagnosed despite being at high risk of ACS. The affected population had commonly described risk factors for early onset of CAD, such as male sex, hypertension, and overweight or obesity. In congruence with the literature, we highlight the importance of screening for CAD in young age groups to detect subclinical disease, which might be treated pharmacologically, percutaneously, or operated electively. Further studies are essential to develop risk models and reference limits for screening tests, and to assess treatment concerns for young adults.

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