Safety and feasibility of minimally invasive coronary artery bypass surgery early after drug-eluting stent implantation due to acute coronary syndrome

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ABSTRACT

Background: The evidence on performing minimally invasive coronary artery surgery early after drug-eluting stent (DES) implantation due to acute coronary syndrome (ACS) is limited.

Aim: The study aimed to determine the safety and feasibility of this approach.

Methods: This registry included 115 (78% male) patients treated from 2013 to 2018, who underwent non-left anterior descending (LAD) percutaneous coronary intervention (PCI) due to ACS with contemporary DES implantation (39% diagnosed with myocardial infarction at baseline), followed by endoscopic atraumatic coronary artery bypass (EACAB) surgery within 180 days, after temporary $P2Y_{12}$ inhibitor discontinuation. Primary composite endpoint of MACCE (major adverse cardiac and cerebrovascular events), defined as death, myocardial infarction (MI), cerebrovascular incident, and repeat revascularization was evaluated in long-term follow-up. The follow-up was collected via a telephone survey and in line with National Registry for Cardiac Surgery Procedures.

Results: The median (interquartile range [IQR]) time interval separating both procedures was 100.0 (62.0–136.0) days. Median (IQR) follow-up duration was 1338.5 (753.0–2093.0) days and was completed for all patients with regard to mortality. Eight patients (7%) died; 2 (1.7%) had a stroke; 6 (5.2%) suffered from MI, and 12 (10.4%) required repeat revascularization. Overall, the incidence of MACCE was 20 (17.4%).

Conclusions: EACAB is a safe and feasible method of LAD revascularization in patients who received DES for ACS within 180 days before surgery despite early dual antiplatelet therapy discontinuation. The adverse event rate is low and acceptable.

Key words: antiplatelet, acute coronary syndrome, EACAB, hybrid, MIDCAB

WHAT'S NEW?

The evidence on use of the surgical approach after temporary withdrawal of dual antiplatelet therapy in patients who received drug-eluting stent (DES) for acute coronary syndrome treatment is limited. In the current study, we evaluate a cohort of patients who underwent percutaneous revascularization for acute coronary syndrome and were referred for endoscopic, atraumatic coronary artery bypass grafting (EACAB) as a second stage of revascularization in a maximal time interval of 180 days. The occurence of the composite endpoint of MACCE (major adverse cardiac and cerebrovascular events), defined as death, myocardial infarction, cerebrovascular incident, and repeat revascularization was evaluated. Despite temporary withdrawal of $P2Y_{12}$ inhibitor before surgery, the long-term outcomes were satisfactory in this group, presenting a 17.4% occurrence rate of MACCE in a median follow-up of 1338.5 days (3.7 years). As such, EACAB is a safe and feasible method of revascularization in patients who received DES within 180 days before the surgery.

INTRODUCTION

The definition of hybrid coronary revascularization is not well established, but it surely addresses the initially planned strategy of performing concomitant or staged surgical and percutaneous revascularization. When considering the hybrid strategy, most studies refer to sternal-sparing surgical procedures, such as minimally invasive direct coronary artery bypass grafting (MIDCAB), endoscopic atraumatic coronary artery bypass grafting (EACAB), or totally endoscopic coronary artery bypass grafting (TECAB). Some reports consider traditional full-sternotomy OPCAB (off-pump coronary artery bypass grafting) surgery with full sternotomy as a stage of planned hybrid procedure as well. Although the definition of hybrid treatment is unclear, there is a group of patients that seems to be beyond its scope.

In many acute coronary syndrome cases (ACS), particularly myocardial infarction (MI), direct revascularization of the infarct-related artery is of the highest priority. Those patients often undergo successful percutaneous treatment. The procedure is urgent, and it is acceptable not to gather a Heart Team to treat the target lesions. Other arteries with significant stenosis need a decision on a further strategy.

If complementary left anterior descending (LAD) revascularization is required, those subjects may be referred to a cardiac surgeon for minimally invasive bypass grafting with the use of the left internal thoracic artery (LITA). In such cases, a decision to merge percutaneous and surgical procedures is made after the first stage of treatment. However, such a strategy requires temporary $P2Y_{12}$ inhibitor withdrawal, which still generates doubts regarding increased perioperative and long-term risk of adverse cardiovascular events.

Clinical guidelines underline the efficacy of coronary artery bypass grafting (CABG) as a treatment for multivessel coronary artery disease and the essential role of LITA-LAD (left internal thoracic artery-left anterior descending) bypass graft [1]. This role was the basis for the development of minimally invasive approaches, such as EACAB.

It must be noted that the classic CABG procedure has its drawbacks. Firstly, saphenous vein grafts have limited patency and may be inferior to new-generation drug-eluting stents. Furthermore, the risk of various wound complications associated with sternotomy is estimated at 0.4%–8.0% [2–4]. A minimally invasive approach may reduce morbidity, pain, scarring, and recovery time when compared to classic bypass grafting with sternotomy. The EACAB procedure with the use of endoscopic internal thoracic artery harvesting provides optimal quality and long-term patency of LITA-LAD grafts [5].

When a significant lesion is diagnosed in the LAD during percutaneous revascularization of other arteries, which are infarct-related, the proper timing of surgical LAD treatment remains a matter of debate. Some studies referring to hybrid revascularization report an interval of a few hours separating the procedures as optimal while others consider a 180-day interval acceptable [6]. However, no reports refer to hybrid revascularization of acute coronary syndrome cases. Regardless, early temporary withdrawal of the $P2Y_{12}$ inhibitor is required for the surgical stage of revascularization.

This study aimed to determine the safety and feasibility of minimally invasive coronary artery bypass surgery early after drug-eluting stent implantation due to acute coronary syndrome.

METHODS

Patients

Consecutive patients initially hospitalized in our center (Center of Cardiology and Cardiac Surgery, American Heart of Poland, Bielsko-Biała) for ACS in the years 2013––2018 were eligible for treatment and retrospective analysis if they had met several criteria based on the Heart Team assessment. First, the arterial anatomy and distribution of lesions were verified by both a cardiologist and a cardiac surgeon (LAD needed to be suitable for bypass grafting and other diseased arteries for PCI). Furthermore, patients were eligible for endoscopy-assisted CABG based on anatomy (severe obesity excludes patients) and medical course (patients with pleural adhesions, after chest radiation, and with severe respiratory disease and no option to ventilate

only one lung were excluded). Notably, in acute MI, Heart Team's assessment was not mandatory for the treatment of infarct-related artery; in those cases, Heart Team consultation following the percutaneous procedure was acceptable. Consent for surgical treatment was required at the time of the assessment by the Heart Team. Finally, the urgency of LAD revascularization was taken into consideration; we aimed to continue dual antiplatelet therapy without interruption for at least 2 months (preferably 3 months, if possible). In all other cases, different revascularization options were considered. Every case was treated individually to choose the optimal protocol for each patient.

The acceptable maximal time interval separating both procedures was 180 days. Consequently, patients who exceeded this timeframe were excluded from the analysis. Patients who underwent revascularization of LAD as an ACS-related artery or an unsuccessful attempt at LAD revascularization as a single procedure or did not receive drug-eluting stents (DES) for non-LAD revascularization were excluded. There were no further exclusion criteria, as both the number of treated vessels and device selection are highly dependent on the patient and the procedure itself.

Procedures

Percutaneous revascularization: percutaneous revascularization of the acute coronary syndrome-related artery was conducted in a hemodynamic room, urgently after admission to the cardiac department. All the patients had significant LAD stenosis based on angiography, which was evaluated by the entire Heart Team. The decision on whether to proceed with functional assessment of the LAD stenosis was based on Heart Team consultation. In the entire cohort, 22 (19.1%) patients had fractional flow reserve (FFR)/instantaneous wave-free ratio (iFR) confirming LAD stenosis.

EACAB surgery: each patient underwent EACAB surgery with the use of a thoracoscope for internal mammary harvesting and left anterolateral mini-thoracotomy for LITA-LAD anastomosis. After entering the operating room and induction of anesthesia, each patient was intubated with a double-lumen endotracheal tube. After positioning (the patient was slightly elevated on the left side with a suspension of the left arm), single right lung ventilation was initiated. The 3rd (anterior axillary line), 5th (medial axillary line), and 7th (anterior axillary line) intercostal spaces were used for port introduction. The LITA was harvested using a harmonic blade (Ethicon, Bridgewater, NJ, US) under endoscopic vision (Karl Storz, Tuttlingen, Germany). Before LITA clipping, heparin was given in a dose of 1.5 mg/kg. Target-activated clotting time (ACT) was 200–300 seconds. Left anterolateral mini-thoracotomy was made to expose the LAD. The LITA-LAD anastomosis was made using a continuous 8.0 Prolene suture during epicardial LAD stabilization (Octopus Nuvo stabilizer; Medtronic, Minneapolis, MN, US).

Procedure hospitalization

Percutaneous procedure: Blood pressure, saturation, electrocardiogram, and diuresis monitoring were conducted for 24 hours after the procedure. Dual antiplatelet therapy was initiated before the stenting procedure, and $P2Y_{12}$ antagonists were used obligatorily. Echocardiography was performed before (if possible) and after the procedure. The patient was usually discharged two or three days following an uncomplicated procedure.

Surgical procedure: No control coronary angiography was performed routinely after the percutaneous procedure. Clopidogrel or ticagrelor were withdrawn 5 or 3 days before the surgical treatment, respectively. None of the patients received prasugrel. No heparin bridging therapy was administered routinely. However, in case of need for oral anticoagulation, the patients were switched to a low-molecular-weight heparin instead of their oral medication 7 days before surgery. Aspirin treatment was not discontinued before surgery. The EACAB procedure was performed on the second day following admission to the hospital. After surgery, constant invasive blood pressure, saturation, electrocardiogram (ECG) diuresis, and drainage monitoring was conducted for 48 hours. Dual antiplatelet therapy was initiated on the first day following surgery and maintained for at least one year from the percutaneous procedure. A chest X-ray was done after surgery and after 24 hours following surgery after removal of the chest tube. Control echocardiography was performed 48 hours after the procedure and whenever it was indicated in accordance with the patient's clinical status. The patients were discharged to the rehabilitation department for rehabilitation and 30-day follow-up.

Follow-up

On their admission to the hospital, the patients gave their consent for data processing and long-term follow-up evaluation as a part of quality assessment for hospital recognition purposes. Therefore, a telephone survey database was created and analyzed to assess the outcome and primary endpoint in this group of patients. Whenever the patient was unavailable, a person authorized by the patient was contacted. In addition, the National Registry for Cardiac Surgery Procedures. was checked to obtain 100% follow-up regarding mortality.

Research ethics board consent

No formal ethical approval was necessary for the quantitative part of the study. The report was a dataset analysis, the data were readily available and did not include any interventions for the patients or participants. The patients gave their permission for data processing for clinical and scientific purposes upon their admission to the hospital.

Primary endpoints

Progression towards the composite endpoint of MACCE (major adverse cardiac and cerebrovascular events), de-

fined as death, MI, stroke, and repeat revascularization, was evaluated through both hospitalization and long-term follow-up.

Secondary endpoints

Secondary endpoints included hospitalization complications (atrial fibrillation; kidney injury which was defined in accordance with RIFLE [Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease] classification criteria as 2-fold postoperative creatine raise; fall in ejection fraction; cardiac biomarker release after surgical treatment).

Statistical analysis

The data were presented as numbers (percentages) or medians (interquartile range [IQR]). The chi-square test was used for categorical data comparison. Kaplan-Maier curves for MACCE and its components were used to determine mortality and morbidity in the long-term follow-up. The log-rank test was used to compare Kaplan-Meier estimates in subgroups. The *P*-value <0.05 was considered to be statistically significant. The data were analyzed using MedCalc v.18.5 (MedCalc Software, Ostend, Belgium).

Data availability statement

The data discussed in this article will be shared on reasonable request to the corresponding author.

RESULTS

In the years 2013–2018, there were 2364 unstable angina hospital admissions, 1841 non-ST-segment elevation MI (NSTEMI) admissions, and 998 ST-segment elevation MI (STEMI) admissions. Among those cases, 1257 unstable angina patients (53.2%), 1196 NSTEMI cases (64.9%), and 513 (51.4%) STEMI cases had significant LAD stenosis treated invasively (2966 cases). The current study reports on 3.9% of those patients.

The patient baseline characteristics were typical of a population with multivessel coronary artery disease (Table 1). All of them underwent percutaneous ACS target vessel revascularization and received drug-eluting stents. Before EACAB surgery, a median left ventricular ejection fraction was 55% (Table 2).

We did not notice any cases of MI, stroke, or death between the procedures in the analyzed group. However, two patients were hospitalized for NSTEMI while being on the list for EACAB, which caused a change in the initial strategy and their referral to other treatments whereby they were excluded from further analysis (this study addressed the safety and feasibility of EACAB surgery). Although no control coronary angiography was performed routinely between the procedures, in three cases it was done due to clinical symptoms. It confirmed significant LAD stenosis in all patients. However, the strategy remained unchanged, and those patients received surgery as planned.

During the surgical procedure, each patient received a LITA-LAD graft. Perioperatively, three patients required chest revision for bleeding. Other complications were few. They mostly included pleurocentesis and atrial fibrillation (AF) (Table 3).

Two deaths (1.7%) and two (1.7%) repeat LAD revascularization procedures were reported in the perioperative period. Seventeen patients (14.8%) were lost to long-term follow-up. In total, 8 patients (7%) died (follow-up regarding mortality is complete), 6 (5.2%) suffered from MI, repeat target vessel revascularization was performed in 12 (10.4%) cases, and 2 patients (1.7%) had a stroke (Tables 4 and 5, Figure 1). Notably, two late LAD revascularization procedures were required due to LITA-LAD graft malfunction and one due to a new stenosis distally from the graft.

Table 1. Patient characteristics

Baseline patient characteristics	n = 115
Male sex, n (%)	90 (78)
Female sex, n (%)	25 (22)
Age, years, median (IQR)	63.0 (57.0–70.0)
Acute coronary syndrome: STEMI, n (%)	23 (20)
Acute coronary syndrome: NSTEMI, n (%)	22 (19.1)
Acute coronary syndrome: unstable angina, n (%)	70 (60.9)
Percutaneous target vessel (non-LAD) revascularization for ACS, n (%)	115 (100)
More than one vessel treated, n (%)	8 (6.9)
Number of implanted drug-eluting stents, median (IQR)	1.0 (1.0–2.0)
Treated artery	
Circumflex/obtuse margin, n (%)	49 (42.6)
Right coronary artery, n (%)	68 (59.1)
Intermediate branch, n (%)	4 (3.5)
Diagonal branch, n (%)	2 (1.7)
Diabetes, n (%)	32 (27.8)
Insulin therapy, n (%)	15 (13)
Arterial hypertension, n (%)	105 (91.3)
Hypercholesterolemia, n (%)	98 (85.2)
Active smoking, n (%)	41 (35)
Asthma, n (%)	2 (1.7)
Chronic obstructive pulmonary disease, n (%)	2 (1.7)
Renal insufficiency, n (%)	5 (4.3)
History of stroke/TIA, n (%)	9 (7.8)
Atrial fibrillation, n (%)	3 (2.6)
Obesity, n (%)	25 (21.7)
BMI, kg/m^2, median (IQR)	27.78 (25.65–30.70)

Abbreviations: ACS, acute coronary syndrome; BMI, body mass index; LAD, left anterior descending; NSTEMI, non-ST-segment elevation myocardial infaction; STEMI, ST-segment elevation myocardial infarction;TIA, transient ischemic attack

Table 2. Echocardiographic parameters before EACAB

Patient characteristics	n = 115
EF, %, median (IQR)	55.0 (45.0–60.0)
LA, mm, median (IQR)	39.0 (36.0–42.0)
LV ESD, mm, median (IQR)	35.0 (30.0–38.0)
LV EDD, mm, median (IQR)	52.0 (48.0– 6.0)
PW, mm, median (IQR)	10.0 (10.0–12.0)
IVS, mm, median (IQR)	11.25 (10.0–12.0)
RV, mm, median (IQR)	26.0 (24.0–29.0)

Abbreviations: EACAB, endoscopic atraumatic coronary artery bypass grafting; EF, ejection fraction; IVS, intraventricular septum; LA, left atrium; LV EDD, left ventricular end-diastolic diameter; LV ESD, left ventricular end-systolic diameter; RV, right ventricle

Table 3. Procedural aspects of EACAB surgery

EACAB procedure, number of patients, n (%)	115 (100)
Time interval separating both stages, days, median (IQR)	100.0 (62.0–136.0)
LITA-LAD, n (%)	115 (100)
Chest revision, n (%)	3 (2.6)
Perioperative AF, n (%)	12 (10.4)
Renal injury (RIFLE classification — creatinine × 2), n (%)	4 (3.5)
PRBC transfusion, n (%)	11 (9.6)
>2 units of PRBC, n (%)	4 (3.4)
Pleurocentesis, n (%)	16 (13.9)
Perioperative EF, %, median (IQR)	50.0 (50.0–55.0)

Abbreviations: LAD, left anterior descending artery; LITA, left internal thoracic artery; PRBC, packed red blood cells; RIFLE, classification for renal failure (risk, injury, failure, loss of function, end-stage disease); other — see Table 2

Table 4. Long-term follow-up analysis

Number of patients, n (%)	115 (100)
Follow-up time, days from EACAB, median (IQR)	1338.5 (753.0–2093.0)
Follow-up completion for mortality, n (%)	115 (100)
Follow-up completion for other endpoints, n (%)	98 (85.2)
Overall MACCE (including mortality), n (%)	20 (17.4)
MACCE perioperative observation, n (%)	4 (3.5)
MACCE long-term observation, n (%)	16 (13.9)
Mortality (100% follow-up), n (%)	8 (6.9)
Mortality perioperative observation, n (%)	2 (1.7)
Mortality long-term observation, n (%)	6 (5.2)
Myocardial infarction, n (%)	6 (5.2)
Perioperative observation	0
Long-term observation, n (%)	6 (5.2)
Overall repeat revascularization in treated arteries, n (%)	12 (10.4)
Repeat revascularization, LAD, n (%)	5 (4.3)
Perioperative observation, n (%)	2 (1.7)
Long-term observation, n (%)	3 (2.6)
Repeat revascularization, non-LAD, n (%)	7 (6.1)
Perioperative observation	0
Long-term observation, n (%)	7 (6.1)
PCI in other coronary arteries, n (%)	2 (1.7)
Coronary angiography with no intervention, n (%)	6 (5.2)
Stroke, n (%)	2 (1.7)
Perioperative observation	0
Long-term observation, n (%)	2 (1.7)

Abbreviations: CCS, Canadian Cardiovascular Society grading for angina; MACCE, major adverse cardiac and cerebrovascular events (death, myocardial infarction, cerebrovascular incident and repeat target vessel revascularization); PCI, percutaneous coronary intervention; other — see Table 2

Overall primary composite endpoint of MACCE was estimated at 17.4% (Table 4, Figure 1). Six patients (5.2%) underwent coronary angiography due to suspicion of critical stenosis, but no intervention was required.

When comparing diabetic to non-diabetic cases, patients with diabetes had a significantly higher MI prevalence during the follow-up (15.6% vs. 1.2%; $P = 0.002$) (Table 5). Patients with no diagnosis of arterial hypertension (and thus limited HA-dedicated treatment) had a significantly higher incidence of MACCE during follow-up (15.2% vs. 40%; $P = 0.049$) (Table 5).

Although we did not show the impact of baseline MI on mortality following EACAB surgery or composite MACCE endpoint, a trend towards an increase of adverse events in this group was visible (Figure 2).

DISCUSSION

As evidence on using the surgical approach after temporary withdrawal of dual antiplatelet therapy in patients who received DES for ACS treatment is very limited, the current study provides reliable data on this matter and has the longest follow-up.

Despite all disadvantages of surgical treatment, in multivessel coronary disease, CABG confers a long-term survival benefit over PCI-DES because of achieving higher rates of complete revascularization [7]. This should be considered when adjusting the treatment to patients' needs. Hybrid revascularization must provide the advantages of both techniques while achieving complete revascularization.

Although reported treatment cannot be presented as a planned hybrid strategy per se, its final long-term efficacy needs to be studied in comparison to hybrid procedures. The impact of initial acute coronary syndrome and consequences of early temporary discontinuation of dual antiplatelet therapy can only be discussed when studies of planned hybrid revascularization procedures with none of those factors are taken into comparative analysis.

Adams et al. [8] reported the five-year clinical outcome for one-stage hybrid coronary revascularization — they demonstrated 91% survival, 94% freedom from angina, and 87% freedom from any form of coronary intervention, which is quite similar to our results. Other studies report 88.5% survival at 5 years and 76% at 10 years, with only 10% of patients requiring repeat revascularization [9, 10]. Our analysis confirms satisfactory outcomes and low MACCE rates. From the clinical perspective, it is important to note that the LITA-LAD procedure reduces the need for future revascularization in the non-LAD vessels while providing long-term relief from angina episodes [11].

The LITA-LAD anastomosis has been shown to be more durable than other arterial and vein grafts as well as coronary stents for treatment of LAD disease, with patency rates >90% at 5-year follow-up [2, 11, 12]. During the follow-up evaluation, we noticed only two incidents of repeat LAD revascularization due to graft failure. When internal thoracic artery (ITA) graft failure occurs, a technical error is the most common cause in the early postoperative period. In the subsequent weeks and months, localized neointimal hyperplasia may occur at the cleft between the native artery and the ITA graft at the anastomotic suture site, on the hood, and on the floor of the native LAD, which can result in localized stenosis [13, 14]. The rate of diagnosed graft failures in our report is low and acceptable.

Six incidences of MI were reported in the long-term follow-up (5.2%). Furthermore, we reported no MI perioperatively. Recent metanalysis concludes that 3.2% of patients

Table 5. Distribution of attributes in the groups defined by mortality, myocardial infarction, repeat revascularization, stroke, and composite endpoint during follow-up

	Mortality (n = 8)	Myocardial infarction (n = 6)	Repeat revascularization in treated arteries (n = 12)	Stroke (n = 2)	Composite endpoint (MACCE: death, stroke, repeat revascularization) (n = 20)
Age, years	70.0 (59.5–76.2)	65.5 (63.0–70.0)	63.0 (58.0–69.0)	65.5	64.0 (58.5–70.2)
Diabetes mellitus (32 patients at baseline)	4 (50%)	5 (83.3%)	2 (16.7%)	0	8 (40%)
Subgroup analysis:	Diabetic vs. non-diabetic[a]: 4/32 (12.5%) vs. 4/83 (4.8%) $P = 0.15$	Diabetic vs. non-diabetic[a]: 5/32 (15.6%) vs. 1/83 (1.2%) $P = 0.002$	Diabetic vs. non-diabetic[a]: 2/32 (6.25%) vs. 10/83 (12%) $P = 0.36$	Diabetic vs. non-diabetic[a]: 0/32 vs. 2/83 (2.4%) $P = 0.39$	Diabetic vs. non-diabetic[a]: 8/32 (25%) vs. 12/83 (14.5%) $P = 0.18$
AH (105 patients at baseline)	6 (75%)	5 (83.3%)	10 (83.3%)	2 (100%)	16 (80%)
Subgroup analysis:	AH vs. non-AH[a]: 6/105 (5.7%) vs. 2/10 (20%) $P = 0.09$	AH vs. non-AH[a]: 5/105 (4.8%) vs. 1/10 (10%) $P = 0.48$	AH vs. non-AH[a]: 10/105 (9.5%) vs. 2/10 (20%) $P = 0.30$	AH vs. non-AH[a]: 2/105 (1.9%) vs. 0/10 $P = 0.66$	AH vs. non-AH[a]: 16/105 (15.2%) vs. 4/10 (40%) $P = 0.049$
Active smoking (41 patients at baseline)	3 (37.5%)	2 (33.3%)	5 (41.7%)	0	8 (40%)
Subgroup analysis:	Smokers vs. no-smokers[a]: 3/41 (7.3%) vs. 5/74 (6.7%) $P = 0.91$	Smokers vs. no-smokers[a]: 2/41 (4.9%) vs. 4/74 (5.4%) $P = 0.90$	Smokers vs. no-smokers[a]: 5/41 (12.2%) vs. 7/74 (9.5%) $P = 0.65$	Smokers vs. no-smokers[a]: 0/41 vs. 2/74 (2.7%) $P = 0.29$	Smokers vs. no-smokers[a]: 8/41 (19.5%) vs. 12/74 (16.2%) $P = 0.56$
Male sex (90 patients at baseline)	5 (62.5%)	4 (66.7%)	10 (83.3%)	1 (50%)	16 (80%)
Subgroup analysis:	Male vs. female[a]: 5/90 (5.6%) vs. 3/25 (12%) $P = 0.26$	Male vs. female[a]: 4/90 (4.4%) vs. 2/25 (8%) $P = 0.48$	Male vs. female[a]: 10/90 (11.1%) vs. 2/25 (8%) $P = 0.65$	Male vs. female[a]: 1/90 (1.1%) vs. 1/25 (4%) $P = 0.33$	Male vs. female[a]: 16/90 (17.8%) vs. 4/25 (16%) $P = 0.84$
Obesity (25 patients at baseline)	3 (37.5%)	3 (50%)	2 (16.7%)	0	5 (25%)
Subgroup analysis:	Obese vs. non-obese[a]: 3 /25 (12%) vs. 5/90 (5.6%) $P = 0.26$	Obese vs. non-obese[a]: 3/25 (12%) vs. 3/90 (3.3%) $P = 0.09$	Obese vs. non-obese[a]: 2/25 (8%) vs. 10/90 (11.1%) $P = 0.65$	Obese vs. non-obese[a]: 0/25 vs. 2/90 (2.2%) $P = 0.45$	Obese vs. non-obese[a]: 5/25 (20%) vs. 15/90 (16.7%) $P = 0.70$

Data are presented as numbers (percentage) and medians (interquartile range). [a]χ^2 test

Abbreviations: AH, arterial hypertension; other — see Table 4

treated with hybrid coronary revascularization (HCR) suffered from MI compared with 2.6% of patients undergoing CABG, with no statistical significance [15]. The low rate of MI may be a result of not only the revascularization strategy but also adequate timing of both procedures.

From the obtained follow-up, 12 patients required urgent repeat target vessel revascularization; 7 (6.1%) of them were in DES-treated arteries. This result is satisfactory, but further observation may be crucial, as some studies report 21% DES-treated vessel failure at 5-year follow-up [12]. As mentioned previously, some cases of restenosis may remain undiagnosed, as angina may not be present due to patent LITA-LAD anastomosis [11].

We diagnosed no stroke in the perioperative period and two cases of stroke during the follow-up. A low incidence of cerebrovascular episodes is considered a significant advantage of the minimally invasive approach, as cardiopulmonary bypass and aortic manipulation during CABG create a direct danger and may cause stroke. In a recently published analysis, the incidence of cerebrovascular events in the HCR group was 0.9% compared with 1.4% in CABG patients [15]. In general, the risk of stroke after CABG varies across studies ranging from 0.0 % to 5.2 %, depending on study design, patient risk profile, operative techniques, and the length of study follow-up [16, 17]. A cerebrovascular incident following CABG remains one of the most devastating complications after CABG surgery, entailing permanent disability and a 3–6 fold increase in the risk of death with a case-fatality rate of up to 20% [18–19].

Kidney injury and failure following coronary artery bypass grafting are concerning. The injury following the surgery is the second most common cause of acute kidney injury (AKI) in the intensive care setting (after sepsis) and is associated with increased morbidity and mortality [20]. It must be noted that the mortality rate (hospital discharge or 30-day mortality) is between 3.8% and 54.4% in patients who develop the injury and increases progressively with the degree of renal impairment. The 3.5% rate of kidney

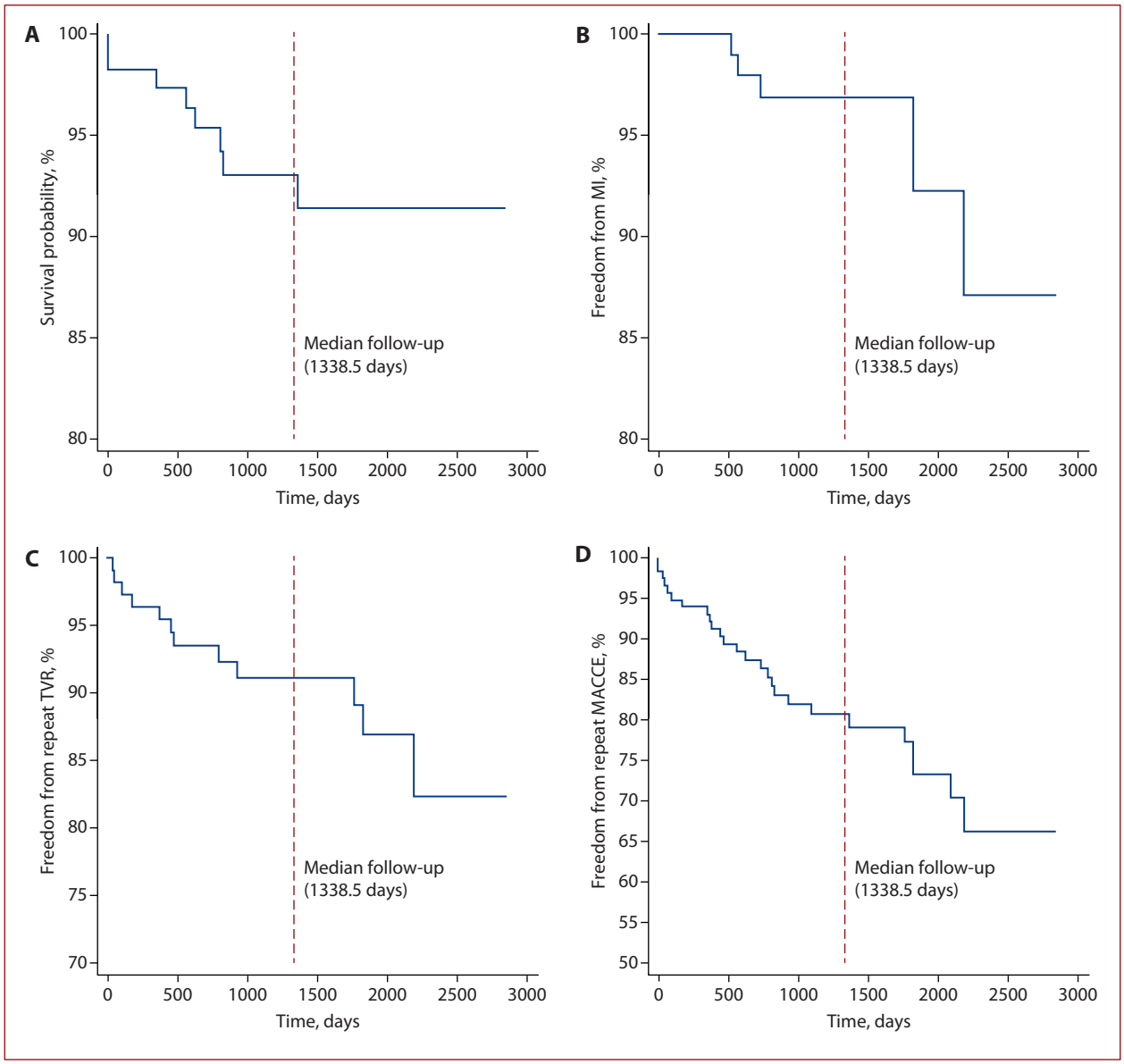

Figure 1. Kaplan-Meier curves for mortality (**A**), freedom from myocardial infarction (**B**), freedom from repeat revascularization (**C**), and freedom from MACCE **(D)** following EACAB surgery

Abbreviations: EACAB, endoscopic atraumatic coronary artery bypass grafting; MACCE, major adverse cardiac and cerebrovascular incidents (death, myocardial infarction, stroke, repeat revascularization); PCI, percutaneous coronary intervention

injury in the perioperative period is low and acceptable. However, some reports indicate that renal failure following a hybrid procedure is estimated at 1.7%, compared with 2.6% in the CABG groups [15].

Atrial fibrillation is a very common complication after surgical procedures. There are multiple concepts for pathogenesis, but no clear evidence regarding triggers for arrhythmia onset. Nonetheless, it worsens the postoperative state and prognosis and increases considerably the length of intensive care unit (ICU) stay and hospitalization as well as hospital costs [21, 22]. Seven studies examined the incidence of postoperative AF in the HCR group, and the incidence of fibrillation was 17%, compared with 19.2% in the CABG group [15]. We report an even lower number of AF occurrences in the perioperative period, which according to most reports, makes this method superior to CABG in this context.

It has been reported that 22.8% of HCR patients receive blood transfusion [15]. Our results are encouraging, as only 9.2% received blood products. However, this may be the result of the time interval separating both surgical and percutaneous procedures, which could reach 180 days. Narrowing the time interval would probably increase the rate of transfusion, as coronary angiography with angioplasty may lower the blood parameters.

In a recent randomized trial comparing CABG, hybrid coronary revascularization, and multivessel percutaneous intervention, residual myocardial ischemia and MACCE were similar at 12 months [23]. Notably, more than one-half of the patients had prior MI (55.5%). The HCR patients had

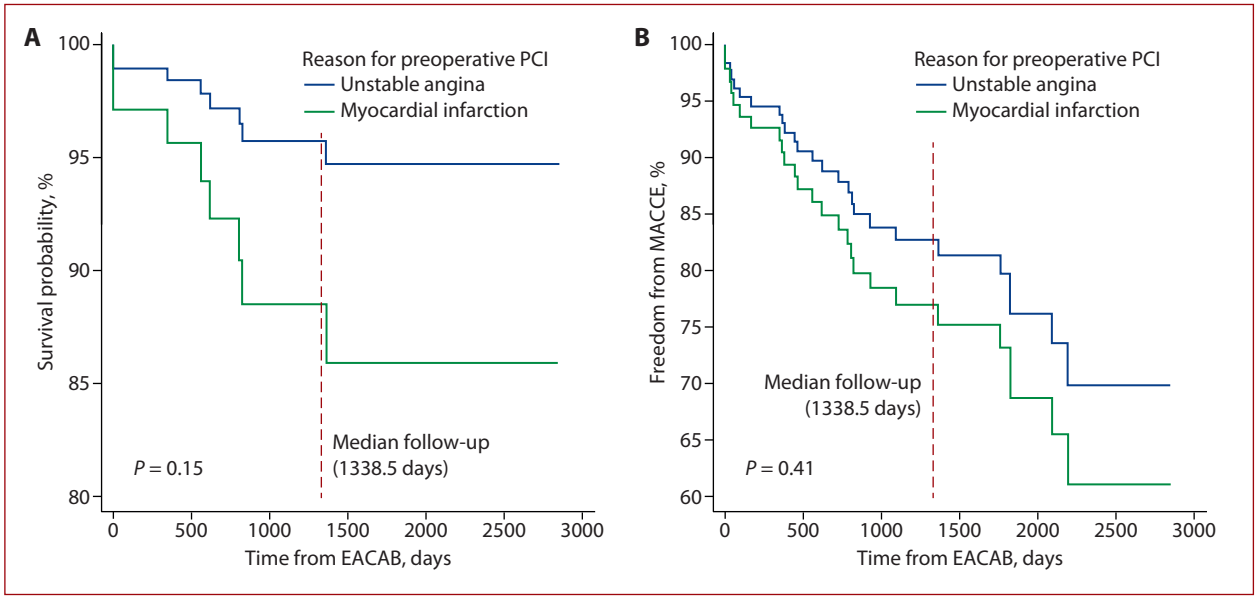

Figure 2. Kaplan-Meier curves for mortality (**A**) and freedom from MACCE (**B**) with relation to preoperative acute coronary syndrome. The *P*-values are for the log-rank test

Abbreviations: see Figure 1, Table 4

PCI within 3 days (in most cases at 24–48 hours) after undergoing minimally invasive direct coronary artery bypass (MIDCAB) LITA-LAD. The advantage of that protocol was assessing the early LITA-LAD patency. The coronary angiogram showed LITA thrombotic occlusion in 1 case (2.1%). Angiographic control at 12 months demonstrated 9 saphenous vein grafts (SVGs) and 1 LITA stenosis/occlusion in the CABG group (10/49, 20.4%), 3 LITA stenoses/occlusions and 1 in-segment restenosis in the HCR group (4/49, 8.2%). A long-term follow-up is expected. The protocol for mandatory angiography provides some reasonable results regarding graft patency. However, invasiveness of the procedure must be taken into consideration. Our follow-up protocol did not assume routine angiography in asymptomatic patients.

The MERGING clinical trial provided late clinical outcomes of myocardial hybrid revascularization versus coronary artery bypass grafting for a three-vessel coronary artery disease [24]. The percutaneous phase was performed 48–72 hours after withdrawal of the chest tubes and administering a loading dose of clopidogrel (600 mg). The 2-year rate of major cardiovascular events defined as death, MI, stroke, or repeat revascularization was evaluated. However, the authors noted that hybrid coronary revascularization was associated with increased rates of MACCE during 2 years of clinical follow-up while the control group treated with conventional surgery presented with low complication rates during the same period. The adverse events included mainly unplanned revascularization, whose rates increased over time in both groups, reaching 14.5% vs. 5.9% in the hybrid and the CABG groups, respectively. The authors point out that the patients underwent two invasive procedures either simultaneously or within days. Also, iodine contrast and antithrombotic medications (for the PCI step) were used in proximity to major surgery (the CABG step) so the minimally invasive nature of PCI is virtually canceled by the surgical procedure. In this matter, our study reports quite a different perspective, assuming that a longer interval between both procedures may not necessarily worsen the outcomes. As restenosis can result from several mechanisms including inflammation and oxidative stress [25], the beneficial effect of separating both procedures may be hypothesized. Those factors are present in on-pump as well as off-pump surgical procedures [26].

Study limitations

This study has its drawbacks: it was a single-center, retrospective analysis with no control group. Furthermore, although follow-up regarding mortality was complete, only 85.2% of follow-up data regarding MI, stroke, and repeat revascularization were available. Coronary angiography was not performed routinely in patients with no symptoms.

CONCLUSIONS

EACAB is safe and a feasible method of LAD revascularization in patients who received DES for ACS within 180 days before surgery, despite early dual antiplatelet therapy discontinuation. The adverse events rate in the long-term follow-up was low and acceptable.

Article information

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