



Off-pump coronary artery bypass grafting versus optimal medical therapy alone: effectiveness of incomplete revascularization in high risk patients

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Abstract

Background Geriatric patients with multivessel coronary artery disease (CAD) are a challenging group to treat; these cases elicit discussion within heart teams regarding the actual benefit of undertaking major surgery on these patients and often lead to abandon the surgical option. Percutaneous procedures represent an important option, but coronary anatomy may be unfavorable. Off-pump coronary artery bypass (OPCAB) provides good quality graft on left anterior descending (LAD) without exposing the patient to cardiopulmonary bypass, and might be the ideal choice in patients with multiple comorbidities, not eligible to percutaneous or on-pump procedures. The objective of this study was to compare survival during a mid-term follow-up in high-risk patients with no percutaneous alternative, either treated with OPCAB or discharged in medical therapy. **Methods** We retrospectively evaluated from June 2008 to June 2013, 83 high-risk patients with multivessel CAD were included: 42 were treated with incomplete off-pump revascularization using left internal mammary artery (LIMA) on LAD; 41 were discharged in optimal medical therapy (OMT), having refused surgery. Follow-up ended in March 2015, with a telephonic interview. Primary endpoint was survival from all-cause mortality; secondary endpoints were survival from cardiac-related mortality and freedom from non-fatal major adverse cardiac events (MACEs). **Results** During follow up, 11 deaths in OPCAB group and 27 deaths in OMT group occurred. Death was due to cardiac factors in 6 and 15 patients, respectively. MACEs were observed in 6 patients in OPCAB group and in 4 patients in OMT group. With regards to survival from all-cause mortality, patients who underwent OPCAB survived more than those discharged in OMT (Log Rank < 0.001), and OMT group carries a propensity score-adjusted hazard ratio of 3.862 ($P < 0.001$). With regards to survival from cardiac-related events, patients who underwent OPCAB survived more than those discharged in OMT (Log Rank = 0.002), and OMT group carries a propensity score-adjusted hazard ratio of 3.663 ($P = 0.010$). There is no statistically significant difference concerning freedom from MACEs (Log Rank = 0.273). **Conclusions** For high-risk patients with multivessel CAD, not eligible to on-pump complete revascularization surgery or percutaneous procedures, incomplete revascularization with OPCAB LIMA-on-LAD offers benefits in survival when compared to OMT alone.

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1 Introduction

A great number of trials investigated different techniques of surgical myocardial revascularization, and showed benefit or non-inferiority of off-pump coronary artery bypass (OPCAB) when compared to on-pump coronary artery by-

pass.^[1–4] Most of those trials included a mixed population with different risk factors; retrospective analysis was fundamental to demonstrate a benefit for OPCAB in patients with multiple risk factors. However, there is not a common definition for “high-risk” for patients with coronary artery disease (CAD), similarly to the definition of a “geriatric patient”. In fact, those definitions cannot rely only on demographic approaches, but comorbidities and functional impairments should be considered. Therefore results of clinical trials in aged populations with strict inclusion criteria, which depend exclusively on age, are difficult to be interpreted and reproduced in current clinical practice.

Complete myocardial revascularization is considered su-

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perior to incomplete revascularization, providing a better recovery of ventricular function and protection against adverse events, which turns into a better long-term survival and a reduced rate of re-intervention.^[5,6] However, complete myocardial revascularization is associated with a longer duration of surgery with increase in procedural risks, and this might be not ideal in patients with multiple comorbidities. Therefore a tailored revascularization plan depending on pre-operative conditions has been advocated as a desirable strategy when approaching high-risk patients such as the geriatric population,^[7] in this context the term “reasonable incomplete revascularization” is generally accepted.^[8] In fact, pursuing a complete myocardial revascularization in patients with multiple comorbidities may be harmful.^[9] In this extent, incomplete myocardial revascularization could be the ideal treatment for high-risk patients, because is associated with less procedural risks and similar short-term prognosis in comparison to conventional surgery.^[10] Incomplete myocardial revascularization can be achieved using OPCAB technique, with an additional reduction of procedural adverse events when compared to on-pump techniques.^[2] Revascularization of left anterior descending (LAD) has been shown to be the most important prognostic factor in CAD,^[11,12] and this grafting can be accomplished using OPCAB without interfering with graft quality.^[3,13–15] OPCAB is currently an accepted alternative to on-pump revascularization especially in patients with low ejection fraction,^[16] or in patients with advanced age,^[17] even in case of multivessel disease.^[1,4,18,19] Purpose of this study was to compare survival in high-risk patients with multivessel CAD, treated with incomplete off-pump surgical myocardial revascularization or discharged in optimal medical therapy.

2 Methods

This retrospective study compares OPCAB with optimal medical therapy (OMT) in high-risk patients with multivessel CAD and multiple comorbidities, not eligible to both on-pump revascularization and percutaneous procedures. The group of patients undergoing OPCAB received an incomplete myocardial revascularization using left internal mammary artery (LIMA) on LAD without cardiopulmonary bypass. The other group is constituted of patients with similar pre-operative characteristics that refused the operation due to personal decision, and were discharged in good clinical conditions with indication to OMT to control ischemia-related symptoms according to the guidelines for ischemic heart disease.^[20,21] It is important to discuss the available options with patients who are candidates for sur-

gical procedures, and “pro et contra” should be carefully weighted when discussing any treatment option. In our study, the off-pump LIMA-on-LAD surgical grafting was proposed to any patient, and those who refused surgery were discharged in OMT. After heart team evaluation, the surgical option was proposed to each patient since the revascularization of LAD is prognostically favorable in patients with CAD, through controlling ischemia-related symptoms, preventing adverse cardiac events and ameliorating the functional mitral regurgitation grade.^[11,12] We considered that is ethically unacceptable to randomize patients between these two opposite alternatives, because patient’s decision is central and cannot be replaced by a mere randomization process. Thus, the retrospective design appeared to be the only ethically acceptable way to conduct this study, and statistical analysis using propensity score was used to adjust results for potential confounders, thus allowing have a quasi-randomized clinical trial.

Our study involved “high-risk” patients with coronary anatomy unfavorable to percutaneous coronary intervention and not eligible for any other way of revascularization because of their comorbidity profile. Patients were included in our study in case of both EuroSCORE II > 6% and presence of at least one risk factors discussed in Table 1, as previously described.^[1,9,22–24] Patients with multivessel CAD who received OPCAB for procedural or anatomical reasons were not considered in our study. Inclusion and exclusion criteria are listed in Table 1.

Primary endpoint was the evaluation of survival from all-cause mortality. Secondary endpoints were the evaluation of freedom from non-fatal major adverse cardiac events (MACEs), defined as non-fatal cardiac arrest, acute coronary syndrome, congestive heart failure and arrhythmia requiring hospitalization, and survival from cardiac-related mortality during a mid-term follow up.

From June 2008 to June 2013, 83 patients were retrospectively included in our study held in Università Campus Bio-Medico di Roma (Rome, Italy); 42 patients underwent OPCAB with LIMA to LAD and were discharged in OMT (group 1, OPCAB group, $n = 42$) and 41 patients were directly discharged in OMT (group 2, OMT group, $n = 41$). Surgical option was proposed to all patients and discharge in OMT was performed if patients refused surgery, as previously discussed; informed consent to surgical procedure was obtained from every patient. Patients received a complete and multidisciplinary clinical evaluation, and underwent blood tests, electrocardiography, chest X-rays, echocardiogram, epiaortic Doppler-ultrasound and coronary angiography. Patients were followed at our Center every 6 months from discharge, or earlier if clinically indicated.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria	
Multivessel coronary artery disease with left anterior descending involvement	
Coronary anatomy unfavorable to percutaneous coronary intervention	
EuroSCORE II > 6%	
At least one of the following risk factors	
Advanced age (> 80 years old)	
Obesity (body mass index > 30 kg/m ²)	
Carotid artery disease (stenosis of the internal carotid artery > 65%)	
Chronic renal failure stage III-B (creatinine clearance < 40 mL/min)	
Neurological risk, defined as one of the following	
Recent stroke (less than 90 days before admission)	
Cortical vascular ischemic disease	
Hematological risk, defined as one of the following	
Hemoglobin < 10 g/dL	
Platelet count < 100,000 / μ L	
Cardiologic risk, defined as one of the following	
Ejection fraction < 30%	
Ejection fraction < 40% associated with moderate mitral regurgitation	
Dyspnea and chest pain at rest	
Exclusion criteria	
Patients who underwent off-pump surgery for technical reasons	
Porcelain aorta or severe atherosclerotic disease	
Patients undergoing redo cardiac surgery	
Patients who underwent off-pump surgery for anatomical reasons	
Epicardic arteries with a diameter less than 1 mm	
Absence of conduits to perform aorta-coronary graft	

Patients were all discharged in antiplatelet therapy with aspirin, associated with a maximum tolerate nitrate and anti-hypertensive therapy with angiotensin converting enzyme inhibitor or, if not tolerated, angiotensin receptor antagonist. Beta-blocker therapy was provided to any patient, and in case of contra-indication it was replaced with cardioselective calcium channel antagonists. OMT was defined according to ESC guidelines,^[20,21] and therapy was optimized for each patient during the outpatient visit. This study was performed essentially before the advent of the extensive use of P2Y12 inhibitors; for this reason this class of drugs was not listed as optimal therapy in the enumeration of medications, and patients taking P2Y12 inhibitors were not included in the study. Underlying domiciliary therapy was continued.

Follow up was concluded in March 2015, with a telephonic interview with the patients or one of his relatives. In OPCAB group, follow up extended up to 78.5 months, whereas in OMT group maximum follow up was 87.1 months.

OPCAB was performed under general anesthesia, full median sternotomy, with an epicardic stabilizer (Octopus Tissue Stabilizers, Medtronic), using the common surgical procedure. Bypass was performed using the skeletonized LIMA on LAD. Patients were extubated after a mean time of 4 h after surgery, and 12 patients (28.6%) required blood products. Intensive Care Unit stay was 1.45 ± 1.14 days. Patients were discharged in good clinical conditions 6.07 ± 2.07 days after surgery. No operative mortality was reported, and relevant post-operative complications were not observed.

Results were considered statistically significant in case of a *P* value less than 0.05. Binary variables were analyzed using Fisher’s test considering the small amount of patients in each group. The comparison between mean values was performed with Student *t*-test or Mann-Whitney test for independent samples, according to D’Agostino-Pearson test for Normal distribution. Multiple comparisons in tables were performed using Chi-square test. Causes of death were classified as cardiac or non-cardiac depending on the medical records documentation, and deaths of unknown causes were considered as cardiac. Survival and freedom from MACEs were evaluated from raw data using Kaplan-Meier plots, and significance was studied with Log Rank (Mantel-Cox) using Chi-square test. Cox regression was performed using “enter” method, and group effect was evaluated before and after propensity score adjustment with logit model. Variables included in propensity score consisted in the inclusion criteria were listed in Table 1. Results are shown in text and tables as absolute values, or as mean \pm SD or 95% CI as appropriate. Statistical analysis was performed using IBM SPSS Statistics (IBM Corp 21.0, Armonk, New York; 2012) and STATA Statistics/Data Analysis (StataCorp 13.0, College Station, Texas; 2013).

3 Results

Mean age was comparable between the two groups: 77.9 ± 4.1 years in OPCAB group and 80.1 ± 4.8 years in OMT group (*P* = 0.160). A summary of the findings obtained at pre-operative evaluation is shown in Table 2.

Blood tests on admission were comparable in both groups. Clinical presentation on admission was similar with the majority of the patients exhibiting signs of moderate or severe congestive heart failure, and few patients presenting with chest pain at rest. In OPCAB and OMT group, respectively, 12 and 13 patients presented with dyspnea class New York Heart Association (NYHA) II, 23 and 24 patients with class NYHA III, 7 and 4 patients with class NYHA IV, 7 and 4 patients had pain at rest. Statistical analysis shows no

Table 2. Pre-operative evaluation.

	OPCAB group (n = 42)	OMT group (n = 41)	P value
Female	14	16	1.000
Age, yrs	77.9 ± 4.1	80.1 ± 4.8	0.160
Familiarity for cardiovascular diseases	29	22	0.180
Hypertension	42	40	0.494
Dyslipidemia	35	34	1.000
Insulin dependent diabetes mellitus	20	16	0.509
Smokers or past smokers	29	25	0.495
BMI, kg/m ²	27.1 (25.9–28.3)	27.1 (25.5–28.6)	0.771
Chronic obstructive pulmonary disease	18	21	0.512
Permanent atrial fibrillation	6	9	0.405
Previous myocardial infarction	15	16	0.822
Recent myocardial infarction	19	13	0.261
STEMI	7	4	
NSTEMI	12	9	
Stable angina	16	13	0.647
Unstable angina	15	11	0.479
Previous stroke	9	11	0.615
Previous coronary stent implantation	14	11	0.634
Ejection fraction (%)	42.8% (40.4%–45.3%)	41.5% (39.2%–43.8%)	0.253
Creatinine clearance, mL/min	60.4 (54.9–65.9)	54.7 (48.9–60.4)	0.099
Carotid artery disease	15	11	0.479

BMI, ejection fraction and creatinine clearance are presented as median (95% CI), age is presented as mean ± SD, and others are presented as *n*. BMI: body mass index; OMT: optimal medical therapy; OPCAB: off-pump coronary artery bypass; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction.

differences in clinical presentation between the two groups ($\chi^2 = 0.868$, $P = 0.648$).

Echocardiographic evaluation showed no differences in the incidence of severe left ventricular dysfunction, defined as an ejection fraction less than 30% (10 patients in OPCAB and 10 patients in OMT group). Associated valvular diseases were moderate aortic regurgitation (three patients in OPCAB, one in OMT), moderate tricuspid regurgitation (four patients in OPCAB, nine in OMT) and moderate aortic stenosis (three patients in OMT). Also, there were five patients in the OPCAB group with a pre-operative moderate-severe mitral regurgitation (at transesophageal intra-operative examination, two of these were severe and three were moderate). In the OMT group, one patient had a severe mi-

tral regurgitation, while nine patients had a moderate mitral regurgitation. Patients with severe ischemic mitral regurgitation did not undergo mitral valve repair because of the need of cardiopulmonary bypass to perform this procedure, and the risk of a combined procedure exceeded any benefit for the patient. Patients with valvular heart disease received the same treatment of other patients.

Involvement of LAD at coronary angiography was always present, and the coronary anatomy of the cohort is shown in Table 3. Differences in diseased coronary vessels and in clustered SYNTAX score failed to reach statistical significance ($P = 0.418$ and 0.595 , respectively).

After interventional cardiologist evaluation, in any case those patients were not eligible to percutaneous coronary intervention because they suffered from intra-stent re-stenosis on proximal LAD, disease in proximal LAD associated with an early diagonal branch, tortuous LAD, or diffuse multivessel disease.

Six patients underwent OPCAB urgently, because of unstable clinical presentation (ingravescent angina in four patients and extreme worsening of dyspnea in two patients). In those patients, however, there were not procedural differences.

The estimated risk mortality in OPCAB and OMT groups using EuroSCORE II were 7.46 (95% CI: 6.86–8.06) and 7.40 (95% CI: 6.81–8.00), respectively ($P = 0.716$). No differences were observed in the cumulative number of inclusion criteria in both groups ($\chi^2 = 3.128$, $P = 0.537$).

Considering all-cause mortality, there had been 11 deaths (26.2%) in OPCAB group and 27 deaths (65.8%) in OMT group during follow up. Death was due to cardiac factors in

Table 3. Coronary angiography: anatomy, diseased vessels and SYNTAX score.

	OPCAB group (n = 42)	OMT group (n = 41)
Right dominance	38 (90.5%)	36 (87.8%)
Disease of LAD	42 (100.0%)	41 (100.0%)
Two-vessels disease	24 (57.1%)	19 (46.3%)
LAD + RCA	17 (40.5%)	11 (26.8%)
LAD + LCX	7 (16.7%)	8 (19.5%)
Three-vessels disease	18 (42.9%)	22 (53.7%)
LAD + LCX + RCA		
SYNTAX score ≤ 22	15 (35.7%)	12 (29.3%)
SYNTAX score 23–32	22 (52.3%)	21 (51.2%)
SYNTAX score ≥ 33	5 (11.9%)	8 (19.5%)
Completeness of revascularization	42.7%	-

Data are presented as *n* (%) unless other indicated. LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery.

6 and 15 patients, respectively. Other causes of death included septic shock after acute limb ischemia, poor mobility due to musculoskeletal disorders, end-stage kidney disease, neoplasms, stroke and respiratory failure. Using a Kaplan-Meier analysis, there is a statistically significant difference with regards to survival from all-cause mortality, with the group of patients who underwent OPCAB showing better survival than those discharged in OMT (Chi-square = 19.432, Log Rank < 0.001) (Figure 1A). Mean survivals were 62.7 months (95% CI: 55.3–70.0) in OPCAB group and 35.6 months (95% CI: 25.0–46.1) in OMT group. Cox regression analysis showed that treatment selection had a significant impact on survival from all-cause mortality. OPCAB was associated with a raw hazard ratio (HR) of 0.229, while OMT carried an HR of 4.375 ($P < 0.001$). After propensity score adjustment, OPCAB was associated to an HR of 0.259, and OMT group showed an HR of 3.862 ($P < 0.001$). Results are summarized in Table 4. Considering survival probabilities at the end of the study and the complete follow up, reverse power analysis showed for our cohort a type 2 error probability of 0.065, which describes a statistical power of 93.5%, and a between-group effect size of 0.283, considered as HR. Observed survival rates were 73.8% in OPCAB group and 34.2% in OMT group.

We observed six MACEs in OPCAB group and four MACEs in OMT group. In OPCAB group, three patients complicated with acute congestive heart failure and three patients had a subsequent acute coronary syndrome, after a mean time of 34.6 months. In OMT group, after a mean time of 27.0 months, two patients had a ventricular arrhythmia, one patient required hospitalization for acute heart failure and one patient had an acute coronary syndrome. Acute coronary syndromes during follow up were treated without percutaneous or surgical procedures due to unfavorable coronary anatomy. Also, three patients in OMT

group underwent an elective automated implantable cardioverter-defibrillator implantation for secondary prevention of sudden cardiac death, with an average timing of implant of 1.98 months from discharge;^[20,21,25] authors acknowledge that cardioverter-defibrillator implantation might be considered as a confounding factor, but plotting the results in a Kaplan-Meier curve, there is no statistically significant difference in the two groups with regards to freedom from MACEs ($\chi^2 = 1.201$, Log Rank = 0.273) (Figure 1B).

During follow up, 6 and 15 deaths for cardiac events were observed in OPCAB and OMT group, respectively. In OPCAB group, death was due to acute congestive heart failure in five patients and acute coronary syndrome in one patient. In OMT group, death was due to ventricular malignant arrhythmia in 10 patients, acute coronary syndrome in four patients, and acute congestive heart failure in one patient. Using a Kaplan-Meier analysis, statistically significant difference with regards to survival from cardiac-related mortality was found between the two populations with the OPCAB patients showing better survival than those discharged in OMT ($\chi^2 = 9.492$, Log Rank = 0.002) (Figure 1C). Mean survivals were 68.9 months (95% CI: 62.1–75.6) in OPCAB group and 53.1 months (95% CI: 40.3–66.1) in OMT group. Cox regression analysis showed that treatment selection had a significant impact on survival from cardiac-related mortality. OPCAB was associated with a raw HR of 0.247, while OMT showed an HR of 4.049 ($P = 0.004$). After propensity score adjustment, OPCAB carried an HR of 0.273, and OMT was associated with an HR of 3.663 ($P = 0.010$) (Table 4).

4 Discussion

Beside the caveat of the small sample size, the results of this study is shedding light on the management of a class of

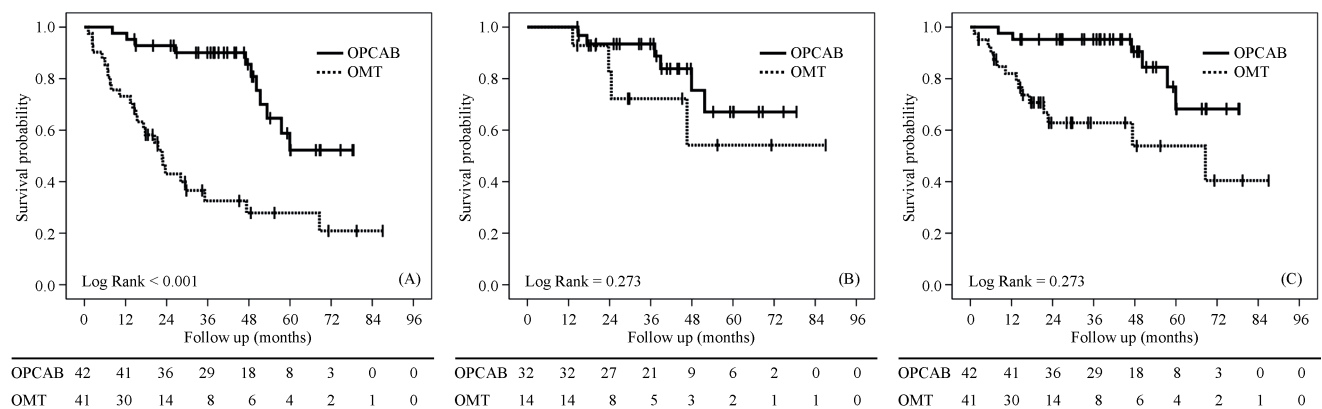


Figure 1. Kaplan-Meier plot. (A): survival from all-cause mortality; (B): freedom from non-fatal MACEs; and (C): survival from cardiac-related mortality. Patient numbers at risk for each time point are shown below the figure for each group. OMT: optimal medical therapy group; OPCAB: off-pump coronary artery bypass group; MACEs: major adverse cardiac events.

Table 4. Cox regression: hazard ratios.

	OPCAB		OMT		P value	
	Raw	After PS adjustment	Raw	After PS adjustment	Raw	After PS adjustment
Overall mortality	0.229 (0.112–0.465)	0.259 (0.125–0.538)	4.375 (2.148–8.911)	3.862 (1.858–8.025)	< 0.001	< 0.001
Cardiac related mortality	0.247 (0.094–0.643)	0.273 (0.102–0.734)	4.049 (1.553–10.638)	3.663 (1.362–9.804)	0.004	0.010

Data are presented as HR (95% confidence interval). OMT: optimal medical therapy; OPCAB: Off-pump coronary artery bypass; PS: propensity score.

patients which usually fall in a “grey zone” during heart teams and multidisciplinary team discussion. This group is constituted by patients which are not considered eligible for conventional surgery because of their status or comorbidities, and in which the risk of the procedure might outweigh the actual benefit achievable from the operation. If a non-invasive revascularization option is not available or possible, these patients are normally treated pharmacologically with an optimal medical regimen and the surgical option is abandoned given the high mortality risk arising from prolonged cardiopulmonary bypass time and intra-procedural complications. Data from national registries show that OPCAB is performed worldwide, even if with differences across countries: it represents about the 15% of the isolated myocardial revascularization procedures in United States, 19% in United Kingdom (National Adult Cardiac Surgery Audit, Annual Report 2010–2011), but more than 45% in Japan (CREDO-Kyoto Registry) and the 95% in India (Adheet Gogate, HASA 2013 Conference). Myocardial revascularization without cardiopulmonary bypass is increasingly demonstrating its feasibility and non-inferiority in comparison to conventional surgery using cardiopulmonary bypass,^[1–4] and in some trials OPCAB technique was associated with a reduced overall mortality and a lower incidence of MACEs.^[22,24] In our series, despite a small size of the study cohort, operative mortality was null.

Avoiding risks associated with cardiopulmonary bypass and aortic clamping, “beating-heart” revascularization can be considered much safer than conventional surgical revascularization and might be attractive in geriatric patients, since they have high operative risk due to comorbidities, most notably chronic kidney disease. In addition, in patients with high operative risk, the concept of revascularization strategies minimizing the number of graft to be performed, which it is increasingly accepted in the literature.^[8] A so called “reasonable incomplete revascularization”, which guarantees a high-quality graft on LAD reperfusing the majority of the myocardium, could be considered a suitable option when balancing with the clinical condition, ventricular function and comorbidities. The advantage offered by the reduction of operative time might be precious and acquire an important significance and impact on surgical outcome and survival. Combination of incomplete revasculari-

zation and off-pump technique would therefore carry an additional advantage in this context. Clinical trials comparing OPCAB and OMT in high-risk patients with multivessel CAD and considering survival and freedom from MACEs are not currently available in the literature. We reviewed literature to define criteria pertinent to a high-risk group and we included patients retrospectively without selection bias as OPCAB was the only alternative to OMT. In our study, OPCAB on LAD was able to produce survival benefit when compared to OMT in a high-risk population normally considered not suitable or at extreme risk for conventional surgery. We might reliably speculate that the single LIMA-to-LAD anastomosis is able to provide perfusion to the greatest portion of myocardium protecting the heart from adverse left ventricular remodeling or arrhythmic events, which have been the major cause of death in the OMT group.

Considering the most recent epidemiological data, it appears that patients with multivessel CAD are becoming older with a greater number of comorbidities,^[26] and these might act as risk factors which increase the surgical expected mortality. A rapid and relatively effective surgical strategy might be considered in this context, as producing a survival advantage with a relatively low procedure-related risk. The results of this study might be paradoxically read in similitude to the option of transcatheter aortic valve implantation (TAVI), as an off-pump alternative for aortic valve replacement in high-risk population. OPCAB can be considered as a TAVI-like alternative for patients with ischemic heart disease who are either unable or at too high risk to undergo conventional surgical revascularization, providing better results than medical therapy alone.

Authors acknowledge some limitations of this study. The size of our cohort is small, which is due to the characteristics of our patients, who are in the frontiers of surgical indication: it remains difficult to find patients with CAD not eligible to percutaneous procedures or with comorbidities that do not allow surgery using cardiopulmonary bypass. Authors are aware of the fact that this is a retrospective study and therefore results could depend on patients’ selection. However, a real randomization to “treatment or discharge” was ethically unacceptable, since patient’s decisions are a fundamental part of clinical practice and must be

respected. Surgical procedure was proposed to any patient; those who refused surgery were discharged in medical therapy alone and placed in the OMT group. Thus, our study is retrospective since no randomization to OPCAB or OMT treatment was ethically acceptable. However, the propensity score analysis might have minimized the statistical bias and the finding of a non-significant difference in the main outcomes calculated before and after propensity score adjustment might allow to reliably speculate that patient selection in this study was unbiased and the two populations were actually comparable. Secondly, there are no objective criteria characterizing the “high-risk condition”, because our inclusion criteria, even if supported and extrapolated by the literature, are established without using parameters of an accepted score system. After literature review, we tried to extrapolate a shared definition for high-risk patient, which takes into account both a score system and the existing comorbidities. Additionally, the implantation of cardioverter-defibrillator in the non-surgical group, even if occurred in only three patients, might have given a survival advantage to the OMT population. However, despite this, survival benefit was still in favor of the surgical option. Finally, quality of life measures are not available due to the retrospective design of the study. In this study, we have not considered patients who underwent minimally invasive direct coronary artery bypass, or patients receiving planned staged hybrid procedures; it would be interesting to evaluate similar patients treated with those alternative procedures over a similar follow up period.

We might conclude that, although with limits of the statistical analysis utilized and the volume of population evaluated, mid-term survival of patients who underwent OPCAB was better than patients who were discharged in medical therapy alone, considering both survival from all-cause mortality and cardiac-related mortality.

Geriatric patients affected by multivessel CAD are exposed to the risk of developing an acute coronary syndrome and death, and need a rapid evaluation for potential surgical option. Sometimes the risk inherent the procedure outnumbers the actual achievable benefit and the surgical option tends to be abandoned. Off-pump coronary artery bypass carries a lower risk in respect to the classic on pump approach as circumvents the complications related to cardiopulmonary bypass and does not imply cardioplegic arrest. In expert hands, this type of operation may therefore represent a very attractive alternative in these high-risk conditions. We truly believe the results of this study might prompt the discussion during multidisciplinary teams and heart teams meeting towards the evaluation of beating heart single vessel surgery in every case presenting with elevated operative

risk, contra-indication to perform percutaneous coronary intervention, and a critical multivessel disease with LAD involvement.

References

- 1 Puskas JD, Williams WH, Duke PG, *et al.* Off-pump coronary artery bypass grafting provides complete revascularization with reduced myocardial injury, transfusion requirements, and length of stay: a prospective randomized comparison of two hundred unselected patients undergoing off-pump versus conventional coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2003; 125: 797–808.
- 2 Straka Z, Widimsky P, Jirasek K, *et al.* Off-pump versus on-pump coronary surgery: final results from a prospective randomized study PRAGUE-4. *Ann Thorac Surg* 2004; 77: 789–793.
- 3 Brown JM, Poston RS, Gammie JS, *et al.* Off-pump versus on-pump coronary artery bypass grafting in consecutive patients: decision-making algorithm and outcomes. *Ann Thorac Surg* 2006; 81: 555–561; discussion 561.
- 4 Hannan EL, Wu C, Smith CR, *et al.* Off-pump versus on-pump coronary artery bypass graft surgery: differences in short-term outcomes and in long-term mortality and need for subsequent revascularization. *Circulation* 2007; 116: 1145–1152.
- 5 Takagi H, Watanabe T, Mizuno Y, *et al.* A meta-analysis of adjusted risk estimates for survival from observational studies of complete versus incomplete revascularization in patients with multivessel disease undergoing coronary artery bypass grafting. *Interact Cardiovasc Thorac Surg* 2014; 18: 679–682.
- 6 Sandoval Y, Brilakis ES, Canoniero M, *et al.* Complete versus incomplete coronary revascularization of patients with multivessel coronary artery disease. *Curr Treat Options Cardiovasc Med* 2015; 17: 366.
- 7 Kleisli T, Cheng W, Jacobs MJ, *et al.* In the current era, complete revascularization improves survival after coronary artery bypass surgery. *J Thorac Cardiovasc Surg* 2005; 129: 1283–1291.
- 8 Dauerman HL. Reasonable incomplete revascularization. *Circulation* 2011; 123: 2337–2340.
- 9 Barandon L, Richebe P, Munos E, *et al.* Off-pump coronary artery bypass surgery in very high-risk patients: adjustment and preliminary results. *Interact Cardiovasc Thorac Surg* 2008; 7: 789–793.
- 10 Guerra M, Miranda JA, Ponce P, *et al.* Impact of isolated bypass grafting of the left internal thoracic artery to the left anterior descending coronary artery in high-risk patients with three-vessel coronary artery disease. *Rev Port Cardiol* 2008; 27: 1239–1247.
- 11 Yusuf S, Zucker D, Peduzzi P, *et al.* Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet* 1994; 344: 563–570.
- 12 Hannan EL, Racz MJ, McCallister BD, *et al.* A comparison of

- three-year survival after coronary artery bypass graft surgery and percutaneous transluminal coronary angioplasty. *J Am Coll Cardiol* 1999; 33: 63–72.
- 13 Puskas JD, Williams WH, Mahoney EM, et al. Off-pump vs conventional coronary artery bypass grafting: early and 1-year graft patency, cost, and quality-of-life outcomes: a randomized trial. *JAMA* 2004; 291: 1841–1849.
- 14 El-Hamamsy I, Cartier R, Demers P, et al. Long-term results after systematic off-pump coronary artery bypass graft surgery in 1000 consecutive patients. *Circulation* 2006; 114: I486–I491.
- 15 Puskas JD, Williams WH, O'Donnell R, et al. Off-pump and on-pump coronary artery bypass grafting are associated with similar graft patency, myocardial ischemia, and freedom from reintervention: long-term follow-up of a randomized trial. *Ann Thorac Surg* 2011; 91: 1836–1842; discussion 1842–1833.
- 16 Keeling WB, Williams ML, Slaughter MS, et al. Off-pump and on-pump coronary revascularization in patients with low ejection fraction: a report from the society of thoracic surgeons national database. *Ann Thorac Surg* 2013; 96: 83–88; discussion 88–89.
- 17 Lee DC, Ramirez SA, Bacchetta M, et al. Off-pump versus on-pump coronary artery bypass grafting in octogenarians: comparison of short-term outcomes and long-term survival. *Cardiology* 2013; 125: 164–169.
- 18 Racz MJ, Hannan EL, Isom OW, et al. A comparison of short- and long-term outcomes after off-pump and on-pump coronary artery bypass graft surgery with sternotomy. *J Am Coll Cardiol* 2004; 43: 557–564.
- 19 Puskas JD, Edwards FH, Pappas PA, et al. Off-pump techniques benefit men and women and narrow the disparity in mortality after coronary bypass grafting. *Ann Thorac Surg* 2007; 84: 1447–1454; discussion 1454–1446.
- 20 Fox K, Garcia MA, Ardissino D, et al. Guidelines on the management of stable angina pectoris: executive summary: The task force on the management of stable angina pectoris of the European Society of Cardiology. *Eur Heart J* 2006; 27: 1341–1381.
- 21 Task Force M, Montalescot G, Sechtem U, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* 2013; 34: 2949–3003.
- 22 Plomondon ME, Cleveland JC, Jr., Ludwig ST, et al. Off-pump coronary artery bypass is associated with improved risk-adjusted outcomes. *Ann Thorac Surg* 2001; 72: 114–119.
- 23 Oo AY, Grayson AD, Patel NC, et al. Is off-pump coronary surgery justified in EuroSCORE high-risk cases? A propensity score analysis. *Interact Cardiovasc Thorac Surg* 2003; 2: 660–664.
- 24 Al-Ruzzeh S, Ambler G, Asimakopoulos G, et al. Off-Pump Coronary Artery Bypass (OPCAB) surgery reduces risk-stratified morbidity and mortality: a United Kingdom multi-center comparative analysis of early clinical outcome. *Circulation* 2003; 108 Suppl 1: II1–II8.
- 25 Brignole M, Auricchio A, Baron-Esquivias G, et al. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). *Eur Heart J* 2013; 34: 2281–2329.
- 26 Lloyd-Jones DM, Wilson PW, Larson MG, et al. Framingham risk score and prediction of lifetime risk for coronary heart disease. *Am J Cardiol* 2004; 94: 20–24.