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# Off-pump or On-pump? Single-vessel Coronary Artery Bypass Grafting Surgery

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#### **Abstract**

**Objectives:** Off-pump coronary artery bypass grafting (OPCAB) was introduced to avoid the adverse effects of cardiopulmonary bypass used in on-pump coronary artery bypass grafting (ONCAB). While OPCAB is performed on a beating heart, often in a more challenging surgical field, ONCAB provides a stable, bloodless environment with the heart arrested. Despite extensive research comparing the two techniques, consensus on the optimal approach, particularly for single-vessel disease, remains unclear. Single-vessel disease accounts for approximately 3% of coronary bypass cases, with surgical intervention often preferred for proximal left anterior descending artery (LAD) lesions.

**Methods:** A total of 336 patients aged 20–80 who underwent elective or emergency LAD bypass between 2015 and 2021 were included in the study. Patients were divided into OPCAB (n=125) and ONCAB (n=211) groups. Exclusion criteria included concomitant surgeries, prior cardiac surgery, endarterectomy, non-LAD single-vessel bypass, redo surgeries, hemodynamic instability, and severe arrhythmias. Pre-operative (age, gender, ejection fraction [EF], diabetes, chronic kidney disease), intraoperative (use of left internal mammary artery), and post-operative outcomes (drainage, transfusions, complications, intensive care unit (ICU)/hospital stay, 30-day mortality) were analyzed. Emergency cases included unstable angina or myocardial infarction, while elective cases involved stable coronary disease.

**Results:** Results indicated that the OPCAB group had older patients with lower EFs. There were no significant differences in post-operative complications or mortality rates between the two groups, although OPCAB patients experienced shorter ICU and hospital stays. Importantly, OPCAB demonstrated comparable effectiveness to ONCAB, particularly in older patients and those with lower EFs. Factors influencing mortality included new-onset cerebrovascular accidents and acute renal failure.

**Conclusion:** This study contributes to the limited literature on single-vessel disease and suggests that OPCAB should be considered the first choice in suitable patients due to its reliability and potential benefits. Further research is encouraged to explore these findings in a broader context.

**Keywords:** Coronary artery bypass grafting; left anterior descending artery; off-pump coronary artery bypass; on-pump coronary artery bypass; single-vessel coronary artery disease.

# Off-pump mı Yoksa On-pump mı? Tek Damar Koroner Arter Baypas Greftleme Cerrahisi

#### Özet

Amaç: Bu çalışmanın amacı, izole tek damar hastalığında, özellikle sol ön inen arterin (LAD) revaskülarizasyonunda, off-pump (OPCAB) ve on-pump (ONCAB) koroner arter bypass greftleme tekniklerinin sonuçlarını karşılaştırmaktır.

Gereç ve Yöntem: 2015–2021 yılları arasında izole LAD bypassı uygulanan, yaşları 20–80 arasında değişen toplam 336 hasta retrospektif olarak analiz edildi. Hastalar OPCAB (n=125) ve ONCAB (n=211) olmak üzere iki gruba ayrıldı. Preoperatif (yaş, cinsiyet, ejeksiyon fraksiyonu, komorbiditeler), intraoperatif (LIMA kullanımı) ve postoperatif (drenaj, kan transfüzyonu, komplikasyonlar, yoğun bakım/servis kalış süresi, 30 günlük mortalite) veriler karşılaştırıldı.

This study was accepted as an oral presentation and presented at the 72<sup>nd</sup> European Society of Cardiovascular and Endovascular Surgery (ESCVS) Congress held in Istanbul in 2024.

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**Bulgular:** OPCAB grubundaki hastalar daha ileri yaşta ve daha düşük ejeksiyon fraksiyonuna sahipti. Postoperatif komplikasyonlar ve mortalite oranları açısından gruplar arasında anlamlı fark yoktu. Ancak yoğun bakım ve hastanede kalış süresi OPCAB grubunda anlamlı derecede daha kısaydı. Yeni gelişen serebrovasküler olay (SVO), akut böbrek yetmezliği (ABY) ve ejeksiyon fraksiyonu mortaliteyi etkileyen bağımsız değişkenler olarak saptandı. **Sonuç:** OPCAB, özellikle yaşlı ve düşük ejeksiyon fraksiyonuna sahip hastalarda, LAD'ye yönelik tek damar cerrahisinde ONCAB'a güvenli ve etkili bir alternatiftir. Daha kısa yoğun bakım ve hastane kalış süresi ile benzer komplikasyon oranları göz önünde bulundurulduğunda, uygun hastalarda ilk tercih olarak değerlendirilebilir. Uzun dönem sonuçların değerlendirilmesi için ileriye dönük çalışmalara ihtiyaç vardır.

**Anahtar sözcükler:** Koroner baypas cerrahisi; sol ön inen arter; off-pump koroner baypas; on-pump koroner baypas; tek damar koroner arter hastalığı.

#### Introduction

Off-pump coronary artery bypass grafting (OPCAB) was introduced to avoid the adverse effects of cardiopulmonary bypass (CPB) used in on-pump coronary artery surgery (ONCAB). It has been actively practiced in cardiac and vascular surgery for approximately 30 years. Despite numerous studies in the literature comparing OPCAB and ONCAB techniques, consensus on which technique is optimal has not yet been reached. [2,3]

In OPCAB, anastomoses are performed under beating heart conditions without using CPB, often in a relatively more bloody surgical field. In the ONCAB technique, anastomoses are performed under a more stable condition with the heart arrested, typically in a less bloody surgical field. While OPCAB avoids the need for a stable anastomosis field, working in areas such as the right coronary artery and circumflex artery can be challenging and may create an environment prone to hemodynamic instability. ONCAB, on the other hand, accepts the recognized adverse effects of CPB and invasive aortic interventions.

A review of the literature indicates that patients undergoing coronary artery bypass surgery with single-vessel disease constitute approximately 3% of the cases.<sup>[4,5]</sup> Surgical intervention is particularly favored for lesions in the proximal left anterior descending artery (LAD). Studies comparing OP-CAB and ONCAB techniques have predominantly focused on multi-vessel disease, with limited attention given to single-vessel disease. Performing a bypass to the LAD using the OPCAB technique is generally easier compared to the same technique applied to the right coronary and circumflex coronary artery regions. The LAD can be exposed without excessive traction on the heart, and hemodynamic problems are typically absent during the anastomosis. Many surgeons can comfortably perform this procedure without requiring advanced expertise. One of the primary considerations for patients with single-vessel disease scheduled for surgery is whether to use the OPCAB or ONCAB technique. It is our observation that surgeons generally perceive the OPCAB technique as more acceptable and feasible for single-vessel disease.

In this study, we will discuss the surgical strategy that should be selected for patients requiring single-vessel coronary bypass. This study was accepted as an oral presentation and presented at the 72nd European Society of Cardiovascular and Endovascular Surgery Congress held in Istanbul in 2024.

#### **Materials and Methods**

## **Ethics Approval and Consent to Participate**

This study was approved by the hospital's ethics committee (Protocol No: 569, Date: February 8, 2022) in full compliance with the principles of the Helsinki Declaration and applicable local regulations. The Ethics Committee determined that the publication of this research was appropriate.

#### **Patient Selection**

A total of 336 patients, aged between 20 and 80, who underwent elective or emergency isolated LAD coronary artery bypass grafting between January 1, 2015, and December 31, 2021, were included in our study. The cases were evaluated in two groups: OPCAB (n=125) and ONCAB (n=211). Exclusion criteria for the study included patients with other concomitant surgeries, a history of any previous cardiac surgery, those who underwent coronary endarterectomy, carotid endarterectomy, and single-vessel bypass surgery other than the LAD, and redo surgeries. In addition, hemodynamically unstable patients and those with severe ventricular arrhythmias were not included in the study.

The pre-operative, intraoperative, and post-operative processes of the patients were examined. In the pre-operative period, factors such as age, gender, ejection fraction (EF), elective or emergency status, diabetes mellitus (DM), and chronic kidney disease (CKD) were investigated. During the intraoperative period, the focus was on whether the left internal mammary artery (LIMA) was used. In the post-operative period, we analyzed the drainage amounts on the first post-operative day, bleeding and tamponade revisions, usage amounts of erythrocyte suspension (ES), fresh frozen plasma (FFP), platelet suspension (PLT), whole blood (WB), prolonged mechanical ventilation (PMV), the necessity of extracorporeal membrane oxygenation (ECMO), acute kidney failure (AKF), new cerebrovascular events (CVA), intensive care unit (ICU) length of stay, hospital length of stay, and 30-day mortality.

When categorizing patients as emergency or elective, those in the emergency group were selected based on the presence of unstable angina, non-ST elevation myocardial infarction, or ST-elevation myocardial infarction. Patients in cardiogenic shock were excluded from the study. The elective patient group consisted of those with stable coronary artery disease.

In the pre-operative period, diabetes was defined as a fasting blood glucose level of 126 mg/dL or higher. CKD was defined

as a creatinine level of 1.4 mg/dL or higher in men, and 1.2 mg/dL or higher in women. In the post-operative period, PMV was defined as patients remaining intubated for more than 2 days. Post-operative AKF was defined as newly developed kidney failure requiring dialysis. In our study, CVA encompassed conditions ranging from transient ischemic attacks to overt neurodeficits occurring in the post-operative period. The primary endpoint of the study was 30-day mortality. In addition, factors influencing mortality were also examined.

Blood products were administered to patients in cases of ongoing bleeding and when hematocrit levels dropped to 24% or below.

The surgical decision for patients with single-vessel disease was made in accordance with the 2021 American Heart Association/American College of Cardiology guidelines. Surgery was particularly performed on patients with complex lesions based on the SYNTAX score.

### Surgical Method

All cases were performed using median sternotomy. The LIMA was preferred as the graft. In cases where LIMA was not used, the vena saphena magna (VSM) was utilized.

In the OPCAB group, following median sternotomy, LIMA was harvested. The pericardium was opened, heparinization was performed, and an activated clotting time (ACT) of 250-300 s was maintained. With the aid of gauze placed posteriorly to the heart, the area of the LAD was visualized. Subsequently, the LAD was encircled with rubber slings at the proximal and distal anastomosis sites. Surgical field stabilization was achieved using an Octopus stabilizer. The slings were tensioned to perform an arteriotomy. Coronary shunts were used only in cases of hemodynamic instability, ST-segment changes, or limited visibility. The LIMA-LAD continuous end-to-side anastomosis was then performed using 7-0 prolene sutures. In cases where LIMA was not used, VSM was anastomosed to the ascending aorta at the proximal anastomosis using a side-biting clamp technique. Heparin was not antagonized with protamine. Mediastinal and thoracic drains were placed, and the sternum was closed with wires. The skin and subcutaneous tissue were closed in a standard manner. Subsequently, the patient was transferred to the ICU.

Following median sternotomy in the ONCAB group, the LIMA was harvested, and then the pericardium was opened and appropriately suspended. Heparinization was performed, maintaining an ACT of over 480 s. Arterial cannulation was performed through the aorta, and a two-stage venous cannulation was performed through the right atrium. After cross-clamping, the heart was arrested using antegrade cardioplegia, administered intermittently every 20 minutes as needed. Isothermic potassium-enriched blood cardioplegia was used. Moderate hypothermia (34°C) was maintained throughout the procedure. Subsequently, with the heart arrested, the LIMA-LAD continuous end-to-side anastomosis was performed using 7–0 prolene sutures. In cases where VSM was used, the proximal anastomosis was performed under cross-clamp. The cross-clamp was

then released, and the patient was gradually weaned off CPB. Protamine was administered for heparin reversal. After ensuring hemostasis, mediastinal and thoracic drains were placed, and the sternum was closed with wires. The skin and subcutaneous tissues were closed in a standard manner, and the patient was transferred to the ICU.

### **Statistical Design**

In the study, IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The normality of parameters was assessed using the Kolmogorov–Smirnov test. Descriptive statistical methods (minimum, maximum, mean, standard deviation, median, frequency) were used to evaluate study data. For quantitative data comparisons between two groups, Student's t-test was used for parameters showing normal distribution, and Mann–Whitney U test was used for parameters not showing normal distribution. For comparisons of qualitative data, the Chi-square test, Fisher's Exact Chi-square test, and Continuity (Yates) Correction were used as appropriate. A significance level of p<0.05 was considered statistically significant.

#### Results

In Table I the study, a total of 336 cases were included, with ages ranging from 20 to 85 years. Of these, 256 (76.2%) were male and 80 (23.8%) were female. The mean age was  $59.54\pm10.35$  years. The cases were divided into two groups: OPCAB (n=125) and ONCAB (n=211).

OPCAB group had a statistically significantly higher mean age compared to the ONCAB group (p=0.020; p<0.05). The mean EF in the OPCAB group was statistically significantly lower than that in the ONCAB group (p=0.001; p<0.05). The proportion of male cases in the OPCAB group (82.4%) was statistically significantly higher than in the ONCAB group (72.5%) (p=0.040; p<0.05).

There was no statistically significant difference between the groups in terms of emergency/elective status, rates of DM, and CKD (p>0.05).

Table I. Evaluation of groups' pre-operative data

		pump 125)	On- (n=	р	
	n	%	n	%	
Age, mean±SD	61.25	±10.48	58.54	10.020*	
EF, mean±SD	53.34	±13.04	57.84	10.001*	
Gender					
Male	103	82.4	153	72.5	<sup>2</sup> 0.040*
Female	22	17.6	58	27.5	
Elective/emergent					
Elective	114	91.2	176	83.4	30.065
Emergent	11	8.8	35	16.6	
DM>126	49	39.2	84	39.8	20.912
CKD>1.2	15	12.0	25	11.8	31.000

<sup>1:</sup> Student t test; 2: Chi-Square test; 3: Continuity (yates) Correction; \*: p<0.05. EF: Ejection fraction; DM: Diabetes mellitus; CKD: Chronic kidney disease.

Table 2. Evaluation of groups' intraoperative and post-operative data

		oump 125)	On-p (n=	р	
	n	%	n	%	
Post-operative 0-day drainage, mean±SD (median)	712±387.06 (650)		650.38±40	10.082	
LIMA	111	88.8	198	93.8	<sup>2</sup> 0.151
Revision	9	7.2	6	2.8	<sup>2</sup> 0.111
ES	29	23.2	71	33.6	30.043*
ES usage, mean±SD (median)	512.41±364.64 (270)		489.44±438.52 (270)		10.590
FFP	57	45.6	122	57.8	<sup>3</sup> 0.030*
FFP usage, mean±SD (median)	506.84±222.82 (540)		524.67±28	10.940	
PLT	5	4	15	7.1	<sup>2</sup> 0.355
PLT usage, mean±SD (median)	326±13.42 (320)		410±257	<sup>1</sup> 0.744	
WB	12	9.6	29	13.7	<sup>2</sup> 0.342
Whole blood usage, mean±SD (median)	491.67±129.39 (450)		543.79±17	10.192	
PMV>3 day	2	1.6	5	2.4	41.000
ECMO	1	0.8	2	0.9	⁴I.000
ARF	2	1.6	4	1.9	41.000
CVA	3	2.4	4	1.9	40.714
ICU stay (day), mean±SD (median)	2.11±2.07 (1)		2.58±2	10.004*	
Hospital stay (day), mean±SD (median)	7.82±6.47 (6)		8.83±7	10.001*	
Mortality	3	2.4	8	3.9	40.546

<sup>1:</sup> Mann Whitney U Test; 2: Continuity (yates) Correction; 3: Chi-square test; 4: Fisher's Exact test; \*: p<0.05. SD: Standard deviation; LIMA: Left internal mammary artery, ES: Erythrocyte suspension; FFP: Fresh frozen plasma; WB: Whole blood; PMV: Prolonged mechanical ventilation; ECMO: Extracorporeal membrane oxygenation; ARF: Acute renal failure; CVA: Cerebrovascular events; ICU: İntensive care unit.

Table 3. The independent predictive factors affecting mortality

Univariant logistic regression							Multivariant logistic regression						
	В	Wald	Sig.	OR	95% CI for EXP(B)			В	Wald	Sig.	OR	95% CI for EXP(B)	
					Lower	Upper						Lower	Upper
Electivity (1)	2.549	15.39	0.000	12.78	3.580	45.685	Electivity (1)	1.523	2.708	0.100	4.58	0.74	28.127
CVA(I)	3.692	17.15	0.000	40.12	6.991	230.28	CVA(I)	4.12	6.3	0.012	61.7	2.47	1543.42
PMV (I)	2.652	8.635	0.003	14.17	2.418	83.118	PMV (I)	0.17	0.01	0.90	1.19	0.05	23.966
LIMA (I)	2.012	9.207	0.002	7.478	2.039	27.429	LIMA (I)	0.847	0.6	0.420	2.33	0.29	18.267
EF	-0.07	10.55	0.001	0.928	0.887	0.971	EF	-0.07	5.2	0.022	0.92	0.87	0.989
ARF(I)	4.522	22.81	0.000	92.00	14.39	588.15	ARF(I)	3.39	4.7	0.030	29.7	1.39	634.252

CVA: Cerebrovascular events; PMV: Prolonged mechanical ventilation; LIMA: Left internal mammary artery; EF: Ejection fraction; ARF: Acute renal failure; OR: Odds ratio; CI: Confidence interval.

In table 2 there was no statistically significant difference between the groups in terms of post-operative day 0 drainage amounts, LIMA usage, revision rates, and per-patient usage of ES, FFP, PLT, WB, and mortality (p>0.05). The rate of ES and FFP usage was statistically significantly lower in the OPCAB group compared to the ONCAB group (p<0.05). There was no significant difference between the groups in terms of PMV, ECMO application, incidence of acute renal failure (ARF), or CVA development (p>0.05). The mean duration of ICU stay and hospital stay was statistically significantly shorter in the OP-CAB group compared to the ONCAB group (p=0.004; p<0.05). In Table 3, independent predictive factors influencing mortality were examined. According to the multivariate logistic regression analysis, new-onset CVA (p=0.012), EF (p=0.022), and ARF (p=0.03) were identified as independent predictive factors affecting mortality.

#### **Discussion**

In the literature, there are numerous studies comparing off-pump and on-pump techniques.<sup>[6-9]</sup> However, there is a scarcity of studies specifically comparing these techniques in single-vessel disease. Our study addresses this gap by focusing on a limited surgical approach involving LIMA-LAD anastomosis, which eliminates the confounding factor of multi-vessel disease and partially mitigates the surgeon's experience requirement.

Our study aims to shed light on the preference between these surgical techniques in single-vessel disease, which sets it apart from other studies in the field.

In the current study, we observe that preoperatively, patients undergoing OPCAB have lower EF values and consist of older individuals. In contrast, the ONCAB group includes a higher proportion of female patients. Apart from these factors,

there were no differences between the two groups in terms of pre-operative and intraoperative risk factors. From this, it can be concluded that the OPCAB technique is preferred more in older patients with lower EF values. The similarity in mortality rates and post-operative complication rates suggests that OPCAB yields successful outcomes in high-risk groups. Indeed, this observation has been noted in the literature. [1.6.10.11]

Furthermore, the similarity in rates of ECMO requirement, ARF, and CVA across patient groups indicates that OPCAB maintains physiological conditions and effectively preserves tissues with pulsatile flow. We believe that OPCAB, performed in single-vessel disease, maintains hemodynamic stability effectively. Demonstrating a successful track record in high-risk profiles characterized by age and low EF, OPCAB raises the question of why it should not be considered for use in lower-risk patient groups.

When examining bleeding rates in the literature, the Best Bypass Surgery Trial<sup>[6]</sup> reported that the revision rate for bleeding in the OPCAB group was found to be twice as high as in the ONCAB group, attributed to the absence of heparin antagonization. Similarly, in the DOORS study,<sup>[10]</sup> despite heparin antagonization, bleeding rates were higher in the OPCAB group. Conversely, the JOCRI study<sup>[12]</sup> found no difference in bleeding between the groups. In addition, there are studies indicating that OPCAB reduces revision for bleeding.<sup>[1,13,14]</sup>

In our study, despite not antagonizing heparin in the OPCAB group, the rates of ES and FFP usage were lower than those in the ONCAB group. We attribute this to hemodilution due to pump use. Most patients in the studies mentioned above have multi-vessel coronary artery disease. We believe that the anastomoses performed in the right and circumflex coronary artery regions play a role in bleeding in multi-vessel disease.

Patients who underwent OPCAB surgery had shorter stays in the ICU and hospital. As noted in the literature, shorter hospital stays contribute to reduced exposure to hospital-acquired infections. [15] In addition, it helps lower hospital costs, thereby contributing to the national economy. [16] Moreover, rapid discharge of patients allows quicker access to treatment for other surgical patients awaiting procedures.

Our study specifically aims to clarify the treatment approach for patients with single-vessel coronary artery disease. Despite similarities, patients treated with the OPCAB technique, whether they have single-, double-, or triple-vessel disease, represent distinct patient groups. Anastomosis difficulty is notably higher in the circumflex and right coronary artery territories compared to the LAD territory. Indeed, studies have highlighted lower revascularization and patency rates in patients with multi-vessel disease, ultimately leading to increased repeat revascularization rates. [3,6,17]

In single-vessel disease patients, there is no likelihood of low revascularization probability. After all, in a patient selected for surgery for single-vessel disease, skipping this anastomosis is not an option. At worst, an ONCAB conversion may be performed. We believe that accessibility to the anastomosis site and ease of anastomosis in this area will increase patency rates in the long term. A study examining LIMA patency rates

found similar LIMA patency rates between OPCAB and ONCAB groups, which supports our hypothesis.<sup>[18]</sup>

In contemporary practice, single-vessel and two-vessel OPCAB surgeries are increasingly performed. <sup>[19]</sup> In a study involving 5203 patients, no OPCAB subgroup other than those undergoing single-vessel OPCAB showed mortality as low as ONCAB. <sup>[4]</sup> Similarly, studies comparing outcomes of OPCAB and ONCAB at I month, I year, and 5 years with 4752 patients consistently show the superiority of OPCAB in single-vessel disease. <sup>[7,8,20]</sup>

Although no significant difference in stroke incidence was observed between groups, we believe that OPCAB may offer advantages in terms of CVA as patient numbers increase. This is because, in cases using LIMA, even a side-biting clamp is not utilized. In cases using VSM, minimal intervention to the aorta is done with a single side-biting clamp. Unlike in ONCAB, invasive procedures are not applied to the aorta. High-volume studies have emphasized that the OPCAB technique reduces the incidence of stroke. [17,21]

In light of these findings, our study has segmented OPCAB into segments focusing specifically on single-vessel coronary artery disease. Literature on this topic is sparse. Today, the OPCAB technique is increasingly applied to single-vessel patients, with its benefits particularly evident in elderly and low EF patients. However, we believe that OPCAB for single-vessel disease is not limited to elderly and low EF patients but is also a suitable treatment option for all patients who are hemodynamically stable, without significant arrhythmias or severe coronary atherosclerosis.

Over the past 30 years, delving deeper into the debate between OPCAB and ONCAB, we consider that our study provides at least some answers to the question of which technique should be used for single-vessel disease. Alternatively, we believe that our study could provide insights into the literature and pioneer future studies in this direction.

Since our study is a retrospective observational study, there may be a selection bias in the choice between OPCAB and ONCAB. It is noteworthy that no conversions from OPCAB to ONCAB were encountered in our study, which may be associated with underreporting. During surgical evaluation before anastomosis, patients with severely calcified vessel structures might have been preferentially selected for ONCAB, potentially biasing outcomes against the ONCAB group.

It is important to acknowledge that our study lacks long-term follow-up of patients.

#### Conclusion

This study contributes to the limited body of evidence comparing off-pump (OPCAB) and on-pump (ONCAB) techniques in single-vessel coronary artery bypass grafting (CABG), specifically focusing on LAD revascularization. Our results demonstrate that OPCAB is a safe and effective alternative to ONCAB, with comparable post-operative complication and mortality rates, despite being preferentially utilized in older patients and those with lower EFs. Notably, OPCAB was associated with shorter ICU and hospital stays, suggesting potential benefits in resource utilization and patient recovery.

The absence of significant differences in major adverse events (e.g., stroke, ARF, or mortality) reinforces the reliability of OPCAB in selected patients, particularly for single-vessel disease, where technical challenges are minimized. However, the choice between techniques should be individualized, considering patient-specific factors such as hemodynamic stability and anatomical complexity.

While our findings align with prior studies favoring OPCAB in high-risk subgroups, the retrospective nature of this analysis and the lack of long-term follow-up remain limitations. Future prospective studies with larger cohorts and extended follow-up are warranted to validate these results and assess long-term graft patency and survival.

In summary, for isolated LAD disease, OPCAB should be considered a viable first-line surgical strategy, offering comparable outcomes to ONCAB while potentially reducing hospital resource burden.

#### **Disclosures**

**Ethics Committee Approval:** The study was approved by the Kartal Koşuyolu Ethics Committee (no: 569, date: 08/02/2022).

**Informed Consent:** Informed consent was obtained from all participants.

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