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Article

The Impact of Intraoperative Transit-Time Flow Measurement on Off-Pump and On-Pump Bypass Surgery Based on Three Months: A Propensity Score Matching Study

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Abstract

Background: The goal of this study was to investigate how transit-time flow measurement (TTFM) parameters influenced the success of coronary bypass surgeries using the on-pump coronary artery bypass (ONCAB) and off-pump coronary artery bypass (OPCAB) techniques and to compare the rates of early graft failure and major adverse cardiac and cerebrovascular events (MACCE). **Methods**: We retrospectively analyzed subjects who underwent coronary bypass surgery at our institution between 2017 and 2023 and compared the TTFM data of patients divided into two groups based on the surgical method: ONCAB and OPCAB. We compared the postoperative and first three months' MACCE data to assess the impact of TTFM on the two surgical methods. **Results**: Of the 2032 patients who underwent coronary bypass, we analyzed data from 1540 patients in the ONCAB group and 194 patients in the OPCAB group. After propensity score matching, the TTFM data of 192 patients in both groups were compared. In the ONCAB group, a mean of 3.28 ± 0.7 grafts per patient was used, while 2.22 ± 0.6 grafts were used in the OPCAB group ($p = 0.001$). TTFM identified problems with 19 (4.7%) grafts in the ONCAB group and 29 (8%) grafts in the OPCAB group, leading to their revision ($p = 0.001$). Overall, the pulsatile index (PI) values in the OPCAB group were significantly higher than in the ONCAB group. Hospital mortality was 3.1% in the ONCAB group and 2.6% in the OPCAB group ($p = 0.286$). MACCE and graft failure rates were similar in the first three months. **Conclusions**: Utilizing TTFM to assess graft quality during surgery enhances coronary bypass surgery in both ONCAB and OPCAB procedures. The enhanced results are particularly crucial for a process like OPCAB surgery, which necessitates the expertise and experience of a surgeon and is challenging to execute.

Keywords

transit-time flow measurement; coronary artery bypass graft surgery; on-pump; off-pump

Introduction

Establishing long-term graft patency and maintaining excellent clinical outcomes to improve quality of life remain the main goals of coronary artery bypass graft surgery (CABG) [1,2]. Satisfactory graft flow in patients who have undergone CABG is one of surgery's most important success indicators [3]. Insufficient flow in the graft after a recent anastomosis may cause new myocardial infarctions in the perioperative period, reducing the benefits of the surgery and leading to a significant increase in mortality [3]. In CABG surgery, many methods are available to assess graft flow and anastomosis quality. However, transit-time flow measurement (TTFM) is one of the most widely used measurement techniques and has been shown to be an easy-to-apply, effective, and safe method [4,5].

The effects of on-pump (ONCAB) and off-pump (OPCAB) coronary artery bypass graft procedures on graft patency and the clinical outcomes of these surgical techniques remain controversial issues in CABG surgery [5–8]. One study demonstrated similar clinical outcomes for both surgical procedures in the short and medium terms and at five years [6]. Another study found that off-pump CABG was associated with higher mortality, a higher incomplete revascularization rate, and a higher recurrent revascularization rate than on-pump CABG, with a mean follow-up of 6.8 years [7]. A meta-analysis and meta-regression demonstrated that off-pump CABG, when performed by experienced surgeons, produces comparable results to ONCAB regarding revascularization quality and long-term survival in well-selected patients [8]. Reports comparing TTFM parameters in these two procedure types have also documented different results [2,5,9–13]. The varying results may be related to the measurement parameters, graft types, surgical techniques, small sample sizes, and non-randomized and single-center studies. In general, the primary disadvantages of OPCAB surgery have been incomplete revascularization and insufficient graft patency [13].

Research evaluating graft patency using intraoperative and early postoperative coronary angiography has shown considerable variations in patency, with an early graft failure incidence of about 5% for internal mammary artery

(IMA) grafts and 11% for vein grafts, affecting roughly 10% of all patients [13–15]. These results point to the necessity of intraoperative bypass graft assessment, which enables the early identification and resolution of technical issues. For a rapid and reliable intraoperative assessment of graft performance, TTFM is a favorable option, even though postoperative angiography is still the gold standard for anastomotic evaluation. When used to evaluate graft function before completing the surgery, TTFM is a dependable technique with the potential to enhance results [13–15].

This study aimed to investigate the effect of TTFM measurement parameters on the success of coronary bypass surgeries using the ONCAB and OPCAB techniques. The rates of early graft failure and major adverse cardiac and cerebrovascular events (MACCE) were compared based on the three-month results.

Materials and Methods

Patient Selection

This single-center, retrospective cross-sectional study included consecutive patients who had undergone isolated coronary artery bypass surgery at the Cardiovascular Surgery Department of Atatürk University Faculty of Medicine between January 2017 and December 2023. The patients' data were obtained from the hospital registry system. We divided the subjects into two groups based on whether they had undergone surgery using ONCAB or OPCAB techniques. The study excluded patients who underwent CABG without TTFM, CABG using the on-pump beating heart technique, and minimally invasive direct coronary bypass (MIDCAB) [3]. Patients' demographics, pre-, per-, postoperative, and first three-month follow-up data were collected, recorded, and compared. We used the logistic EuroSCORE II to check the patients' risk before surgery. The left internal mammary artery (LIMA), radial artery (RA), and great saphenous vein (VSM) were used as bypass graft conduits. At the end of the operations, we checked the grafts in all patients by measuring transit-time flow. Necessary graft revisions were performed for patients with flow problems. All interventions and measurements were recorded.

Study Objectives

The study's primary goal was to evaluate the effect of intraoperative TTFM on graft quality and surgical outcomes by comparing cases undergoing CABG with ONCAB and OPCAB techniques. The secondary objective was to compare CABG cases performed using ONCAB and OPCAB techniques in our institution. The tertiary objective was to determine the differences in the TTFM parameters between these two techniques.

Surgical Procedures

We used standard anesthetic protocols to prepare all patients in both groups for CABG. Each patient was administered anesthesia using a combination of inhalation and intravenous narcotic methods. Following a median sternotomy, the LIMA and additional grafts were prepared concurrently. A coronary bypass was performed on all patients in the ONCAB group using a standard cardiopulmonary bypass (CPB). We administered 3–5 mg/kg of heparin for heparinization based on the initial activated clotting time (ACT). An antegrade cardioplegia cannula was placed in the aortic root after aortic arterial and two-stage venous cannulation when the ACT value was between 400 and 650 seconds. After implementing cross-clamping (CC) for myocardial protection in CPB, we induced cardiac arrest with antegrade cardioplegia and performed distal anastomoses under CC.

Myocardial protection was achieved with repeated cardioplegia every 20 minutes until the anastomoses were completed. Systemic hypothermia was administered (30–34 °C) after aortic CC. Proximal anastomoses were conducted under a side clamp placed on the aorta by removing the CC after all distal anastomoses were complete. Once we achieved the appropriate temperature and hemodynamics, we executed decannulation by weaning the patient from the CPB. After bleeding controls were provided, all patients' surgical and anesthesia procedures were terminated by closing the sternum and skin incisions. Patients in the OPCAB group underwent CABG surgery on the beating heart without entering the pump.

Intraoperative Measurement Technique

TTFM is a highly efficient technique for assessing the patency of grafts during surgery. While there may be varying opinions on the sensitivity and specificity of TTFM [16,17], European myocardial revascularization guidelines strongly advocate its use in monitoring graft openings. This recommendation is classified as Class IIa, with a level of evidence of B [18].

The technique was designed to assess the quality of the graft and quantify blood flow through the graft using a specialized probe. The equipment utilized by our clinic was the MediStim VQ-1101 (MediStim ASA, Oslo, Norway). The measurements were taken once the anastomoses were finished for all grafts, and the patients attained cardiac hemodynamic stabilization. The device provides a graphical representation of the flow pattern and computes the mean flow rate (mL/min), the pulsatile index (PI), and the percentage of diastolic filling (DF). A DF less than 50%, a PI greater than 5, or both indicate inadequate flow. The mean flow is employed as a stand-alone signal of inadequate flow and is assessed in conjunction with the other two metrics. Analyzing the collected numbers allows the determination of the need to alter a graft.

The decision to implement additional interventions was based on the values obtained prior to protamine administration. We measured all grafts involving at least two segments and assessed them by calculating the average. We analyzed the flow throughout the entire sequential bypass, including both the proximal and distal segments of the graft. Measurements were conducted with and without proximal closure of the original coronary artery to identify any potential flaws, specifically at the toe of the anastomosis, and to eliminate any competition from the native vessel in case a significant amount of retrograde blood flow existed. If the TTFM findings were not satisfactory, we examined the length and characteristics of the graft. Mechanical factors, such as torsion, spasms, and air were primarily eliminated in the grafts to achieve low PI and acceptable DF.

We administered papaverine and nitroglycerin to prevent spasms, especially in arterial grafts. If no apparent etiology was identified, the graft was accessed by making a tiny surgical cut around 1 cm from the anastomosis. We assessed the patency of the anastomotic site and the distal coronary artery using a tiny coronary probe to ensure they were open and unobstructed. A fresh anastomosis was performed using another graft on individuals who had a second serious lesion in the distal coronary artery. We also assessed the LIMA's patency using a coronary probe to evaluate the forward flow for patients with LIMA-LAD grafts and received unsatisfactory TTFM results. If we identified severe stenosis in the first section of the LIMA, we transected it and then anastomosed it to the aorta. Although we obtained satisfactory TTFM findings in the last measurement, we repeated all measurements before the closure of the sternum to confirm graft patency and to detect any possible new graft kinking or compression.

Follow-up

Our institution routinely follows up with patients who underwent CABG in our outpatient clinic on the seventh day and the first and third months after discharge. Afterward, we recommend a follow-up every three months in our outpatient or cardiology outpatient clinic. We recorded and analyzed the first three-month follow-up data of the patients included in the study. The analysis included MACCE, the need for intra-aortic balloon pump (IABP) placement, cardiac enzyme elevation, early graft failure, additional interventions, and mortality data.

Statistical Analysis

The results are presented as mean and standard deviation, median and interquartile range (IQR), number, and percentage. The relationships between categorical variables were assessed using Fisher's exact test or Pearson's chi-squared test. Normal distribution was tested using the Kolmogorov–Smirnov test. Propensity score matching (PSM) was conducted to reduce potential bias in comparing ONCAB and OPCAB patients. In comparisons of the two independent groups, the independent samples t-test was used when the normal distribution condition was met, and the Mann–Whitney U test was used if it was not. When comparing the two dependent groups, a paired samples t-test was used when the normal distribution condition was met, and a Wilcoxon test was used if it was not. The multivariate analysis assessed estimated risk factors between groups using logistic regression analysis, employing the possible risk factors identified in previous analyses. The statistical significance level was determined to be $p < 0.05$. All analyses used the Statistical Program for the Social Sciences (SPSS) Statistics for Windows version 21.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 2032 patients underwent CABG, including 226 OPCAB, 1686 ONCAB, 42 on-pump beating hearts, and 78 MIDCAB. The study excluded 178 patients due to the absence of TTFM during surgery and included 194 patients in the OPCAB group and 1540 in the ONCAB group (Fig. 1). Six patients who started off-pump surgery and switched to on-pump surgery due to hemodynamic deterioration were included in the ONCAB group. The main demographic and clinical characteristics of the patients are summarized in Table 1. Patients in the OPCAB group were slightly older (61.28 ± 10.08 in ONCAB and 62.54 ± 9.8 in OPCAB, p = 0.876). They had a statistically higher incidence of stroke history, hypertension, chronic obstructive pulmonary disease (COPD), and peripheral arterial disease (PAD) than the ONCAB group. Patients in the OPCAB group also had a higher history of previous coronary revascularization (Table 1).

When the number of diseased vessels was compared, patients with left main coronary artery disease (LMCA) and triple vessel disease were statistically significantly higher in the ONCAB group, while those with single-vessel disease were in the OPCAB group. The proportions of patients with double vessel disease were statistically similar in both groups (Table 1). To make the demographic, clinical characteristics, and graft number of the patient groups statistically similar, PSM was performed, with 192 patients identified in both groups because of matching. The data are summarized in Table 2. The EuroSCORE II risk scores of both groups were statistically similar at baseline demographic assessment and post-PSM assessment (Tables 1,2). Six (0.4%) patients in the ONCAB group and one (0.5%) patient in the OPCAB group had incomplete revascularization; after PSM, all patients in both groups had complete revascularization.

After the demographic and clinical characteristics of the patients in the two groups were equalized after PSM, we

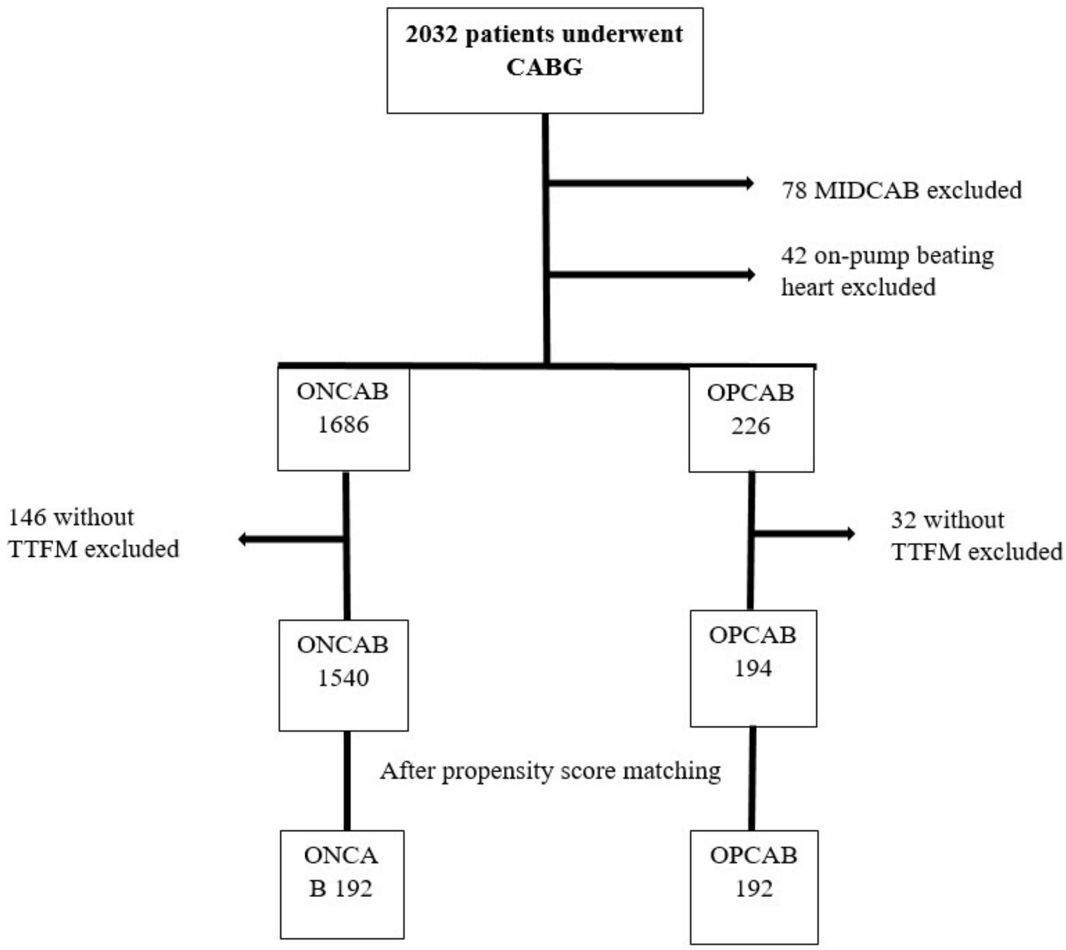

Fig. 1. The flow diagram for obtained patients each groups. CABG, coronary artery bypass grafting; ONCAB, on-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass; TTFM, transit-time flow measurement; MIDCAB, minimally invasive direct coronary bypass.

analyzed the graft characteristics (Table 3). A mean of 3.28 ± 0.7 grafts were used per patient in the ONCAB group, and 2.22 ± 0.6 grafts were used in the OPCAB group (p = 0.001). After the TTFM measurements, problems were detected in 19 (4.7%) grafts in the ONCAB group and 29 (8%) grafts in the OPCAB group and were revised (p = 0.001). The reasons for revising the grafts are shown in Table 3. Vasospasm was the most common problem in both groups and was statistically significantly more common in the OPCAB group [9 (2.2%) in ONCAB vs. 13 (3.6%) in OPCAB, p = 0.028]. Anastomotic problems were also statistically significant in the OPCAB group [2 (0.5%) in ONCAB vs. 8 (2.2%) in OPCAB, p = 0.001].

Other problems with revised grafts were graft curling and LIMA stenosis/dissection; the difference between the groups was not significant (Table 3). LIMA anastomosis to the LAD was planned for all patients in both groups. However, poor flow was detected in four patients in the ONCAB group and two in the OPCAB group due to severe stenosis or dissection in the LIMA graft; the RA was used instead (Table 3). The total number of distal anastomoses was 405 in the ONCAB group and 361 in the OPCAB group; the total number of grafts was 401 and 361, respectively (Table 3).

The mean operative times of patients in both groups were statistically similar, although slightly shorter in the OPCAB group (4.16 ± 0.6 h in ONCAB vs. 3.94 ± 0.6 h in OPCAP, p = 0.586). Reoperation for bleeding was significantly higher in the ONCAB group [7 (3.6%) vs. 3 (1.6%), p = 0.019]. IABP use, MACCE, additional intervention for early graft failure, and deep sternal infection were similar in both groups. Overall, postoperative morbidity rates were significantly higher in the ONCAB group (p = 0.038) (Table 4). The length of stay in the intensive care unit and hospitalization were similar in the groups. Hospital mortality was 3.1% in the ONCAB group and 2.6% in the OPCAB group (p = 0.286). All patients were followed up for the first three months. In the first three months of follow-up, there

Table 1. Baseline characteristics of on-pump versus off-pump coronary artery bypass garfting groups.

Characteristics	ONCAB (n = 1540)	OPCAB (n = 194)	*p*-value
Age (years) (mean ± SD)	61.28 ± 10.08	62.54 ± 9.8	0.876
Sex (female) (n, %)	436 (28.3)	52 (26.8)	0.589
BMI (kg/m^2) median (IQR)	28.74 (24.8, 31.2)	28.22 (24.7, 30.8)	0.568
Prior myocardial infarction (n, %)	564 (36.6)	69 (35.6)	0.622
Coronary revascularization history (n, %)	302 (19.6)	46 (23.7)	0.038
Prior CABG (n, %)	6 (0.4)	3 (1.5)	0.021
Prior PCI (n, %)	298 (19.4)	45 (23.2)	0.042
Stroke history (n, %)	74 (4.8)	17 (8.8)	0.028
Hypertension (n, %)	894 (58.1)	129 (66.5)	0.034
Hyperlipidaemia (n, %)	844 (54.8)	105 (54.1)	0.876
Diabetes mellitus (n, %)	622 (40.4)	81 (41.8)	0.587
COPD (n, %)	144 (9.4)	26 (13.4)	0.044
PAD (n, %)	82 (5.3)	22 (11.3)	0.023
CRF (n, %)	34 (2.2)	2 (1.0)	0.086
Smoking (n, %)	958 (62.2)	124 (63.9)	0.871
LVEF (%) (mean ± SD)	50.32 ± 8.3	48.74 ± 9.47	0.416
EuroSCORE II (mean ± SD)	1.84 ± 0.72	2.11 ± 1.04	0.578
Coronary lesions (n, %)			
LMCA	136 (8.8)	6 (3.1)	0.001
3 vessels disease	862 (56)	14 (7.2)	0.0001
2 vessels disease	429 (27.9)	59 (30.4)	0.824
1 vessel disease	113 (7.3)	115 (59.3)	0.0001

BMI, body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; IQR, interquartile range; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; SD, standard deviation; ONCAB, on-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass.

was no significant difference in either patient group regarding MACCE and additional intervention for graft failure.

Table 5 presents all flow measurements for both groups of patients. The mean values of all measurement parameters of the TTFM are given separately for all grafts. We first checked the grafts for torsion or kinking. Changes in the position of three saphenous vein grafts in the ONCAB group and five saphenous vein grafts in the OPCAB group resulted in significant improvements in PI and DF values; no additional intervention was required. In patients with PI values above five, vasospasm was detected in four radial arteries and 18 LIMA grafts. PI values were brought to acceptable limits with the topical application of papaverine and nitroglycerin. After LIMA-LAD anastomosis, proximal stenosis was detected in two grafts with inadequate flow measurements. The LIMA was transected proximally and anastomosed to the aorta as a free graft, thus obtaining acceptable TTFM values.

Anastomotic problems were detected in 10 patients, and satisfactory TTFM measurements were achieved after the necessary procedures were applied. Of these 10 patients, two were in the ONCAB group and eight were in the OPCAB group (Table 3). In the OPCAP group, two of these anastomotic problems were due to atherosclerotic plaque lifting at the LIMA-LAD anastomosis; the problem was solved by renewing the anastomosis more distally. One of the two anastomotic stenoses in the ONCAB group was at the saphenous graft to the right coronary artery (RCA) anastomosis, and the other was at the saphenous graft to the Cx. Of the remaining six anastomotic problems in the OPCAB group, two were in the Cx system with a saphenous vein graft, three were in the diagonal artery with one radial and two saphenous grafts, and one was in the RCA with a saphenous graft. Four of the anastomotic stenoses were due to technical defects, and the others were due to vessel structures and diameters. The anastomoses were renewed, and adequate TTFM values were obtained. Table 5 also shows that the overall PI values in the OPCAB group were significantly higher than in the ONCAB group.

Discussion

In this study, the investigators attempted to examine the efficacy of TTFMs in patients undergoing ONCAB and OPCAB and the differences in flow measurements between these surgical methods. Of the 2032 patients who underwent coronary bypass during the study period, 194 patients in the OPCAB group and 1540 in the ONCAB group were included. After analyzing all patients' basic clinical and

Table 2. Baseline characteristics of ONCAB and OPCAB groups after PSM.

Characteristics	ONCAB (n = 192)	OPCAB (n = 192)	*p*-value
Age (years) (mean ± SD)	62.08 ± 9.7	62.44 ± 10.01	0.626
Sex (female) (n, %)	50 (26)	51 (26.6)	0.896
BMI (kg/m^2) median (IQR)	28.84 (24.2, 30.8)	28.24 (24.4, 30.6)	0.875
Prior myocardial infarction (n, %)	67 (34.9)	69 (35.9)	0.796
Coronary revascularization history (n, %)	45 (23.4)	46 (24)	0.976
Prior CABG (n, %)	4 (2.1)	3 (1.6)	0.826
Prior PCI (n, %)	43 (22.4)	44 (22.9)	0.947
Stroke history (n, %)	19 (9.9)	17 (8.9)	0.608
Hypertension (n, %)	130 (67.7)	128 (66.7)	0.782
Hyperlipidaemia (n, %)	105 (54.7)	105 (54.7)	0.999
Diabetes mellitus (n, %)	82 (42.7)	80 (41.7)	0.628
COPD (n, %)	28 (14.6)	26 (13.5)	0.587
PAD (n, %)	20 (10.4)	21 (10.9)	0.872
CRF (n, %)	4 (2.1)	2 (1.0)	0.816
Smoking (n, %)	125 (65.1)	123 (64.1)	0.578
LVEF (%) (mean ± SD)	49.86 ± 9.84	49.04 ± 8.81	0.856
EuroSCORE II (mean ± SD)	1.96 ± 1.02	2.07 ± 1.42	0.738
Coronary lesions (n, %)			
LMCA	8 (4.2)	6 (3.1)	0.592
3 vessels disease	15 (7.8)	14 (7.3)	0.829
2 vessels disease	57 (29.7)	58 (30.2)	0.845
1 vessel disease	112 (58.3)	114 (59.4)	0.637

BMI, body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; IQR, interquartile range; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; PSM, propensity score matching; SD, standard deviation.

Table 3. Bypass graft numbers, locations and technical problems in groups (after PSM).

Variables	ONCAB (n = 192)	OPCAB (n = 192)	*p*-value
Total distal anastomosis	405	361	
*LAD anastomosis	198	192	
Cx system anastomosis	79	48	
RCA anastomosis	38	40	
DIA anastomosis	90	81	
Total number of grafts	401	361	
#LIMA	188	190	
Radial artery	74	58	
Saphenous vein graft	139	113	
Number of grafts per patient (mean ± SD)	3.28 ± 0.7	2.22 ± 0.6	0.001
Total number of revised grafts, n (%)	19 (4.7)	29 (8)	0.001
Curl in the grafts, n (%)	3 (0.8)	5 (1.4)	0.068
Vasospasm, n (%)	9 (2.2)	13 (3.6)	0.028
Stenosis/dissection in the LIMA, n (%)	5 (1.2)	3 (0.8)	0.689
Anastomosis problem, n (%)	2 (0.5)	8 (2.2)	0.001

LIMA, left internal mammary artery; LAD, left anterior descending artery; Ao, aorta; Cx, circumflex artery; RCA, right coronary artery; DIA, diagonal artery; PSM, propensity score matching; SD, standard deviation. *: In the ONCAB, the LAD underwent 188 LIMA-LAD bypasses, 4 of which were sequential, and four Ao-radial-LAD, and two additional Ao-saphenous-LAD bypasses. In the OPCAB, the LAD underwent 190 LIMA-LAD bypasses, and two Ao-radial-LAD bypasses. #: In total, LIMA could not be used in 6 patients due to poor flow and quality.

Table 4. Operative, postoperative and follow-up data of patients (after PSM).

Variables	ONCAB (n = 192)	OPCAB (n = 192)	*p*-value
Postoperative morbidities in total, n (%)	20 (10.4)	13 (6.8)	0.038
Intra-aortic balloon pump, n (%)	4 (2.1)	3 (1.6)	0.869
Re-exploration for bleeding, n (%)	7 (3.6)	3 (1.6)	0.019
MACCE, n (%)	7 (3.6)	6 (3.1)	0.689
Deep sternal infection, n (%)	2 (1)	1 (0.5)	0.826
Additional intervention for early graft failure, n (%)	2 (1)	2 (1)	0.999
Operation time (h) (mean ± SD)	4.16 ± 0.6	3.94 ± 0.6	0.586
Duration of intensive care unit (d), (mean ± SD)	2.4 ± 0.5	2.02 ± 0.5	0.853
Duration of hospital stay (d), (mean ± SD)	7.89 ± 2.9	6.92 ± 2.1	0.089
Total hospital mortality, n (%)	6 (3.1)	5 (2.6)	0.286
MACCE at follow-up, n (%)	3 (1.6)	4 (2.1)	0.886
Additional intervention at follow-up, n (%)	2 (1)	1 (0.5)	0.838

MACCE, major adverse cardiac and cerebrovascular events; PSM, propensity score matching; SD, standard deviation.

Table 5. Transit time flow measurement findings (after PSM).

Variables	PI		*p*-value	DF%		*p*-value	Mean Graft Flow (mL/min)		*p*-value
	ONCAB	OPCAB		ONCAB	OPCAB		ONCAB	OPCAB	
LIMA-LAD	2.5 ± 1.8	3.6 ± 0.9	0.001	73.2 ± 6.8	69.7 ± 9.7	0.096	42.1 ± 24.3	38.4 ± 22.8	0.068
Ao-Rd-LAD	2.6 ± 0.9	3.8 ± 0.7	0.001	64.8 ± 8.4	62.7 ± 9.2	0.385	58.1 ± 24.2	54.4 ± 28.5	0.086
Ao-Rd-OM	2.8 ± 1.2	3.3 ± 1.3	0.01	66.2 ± 9.4	64 ± 7.8	0.584	50.4 ± 14.3	51.3 ± 18.2	0.278
Ao-Rd-Cx	2.9 ± 1.4	3.2 ± 1.6	0.028	62.2 ± 6.9	65.1 ± 5.7	0.086	54.7 ± 22.8	52.4 ± 23.8	0.286
Ao-Rd-RCA	2.8 ± 1.3	3.0 ± 1.1	0.068	58.7 ± 5.4	56.8 ± 7.4	0.587	62.4 ± 28.6	59.2 ± 23.1	0.095
Ao-Sp-DIA	2.6 ± 0.9	3.7 ± 0.7	0.001	68.2 ± 9.8	66 ± 10.2	0.584	59.8 ± 15.4	56.7 ± 18.3	0.423
Ao-Sp-OM	2.9 ± 1.3	3.7 ± 0.8	0.001	64.2 ± 8.6	65.2 ± 8.3	0.727	62.3 ± 14.7	61.9 ± 15.2	0.384
Ao-Sp-Cx	3.1 ± 1.5	3.9 ± 0.9	0.01	62.8 ± 8.4	64 ± 9.1	0.826	60.3 ± 16.8	59.2 ± 17.4	0.522
Ao-Sp-RCA	3.2 ± 1.8	3.6 ± 0.9	0.428	63.6 ± 9.7	65.4 ± 8.9	0.632	64.3 ± 17.8	62.7 ± 16.4	0.527

PI, pulsatility index; DF, diastolic filling; LIMA, left internal mammary artery; LAD, left anterior descending artery; Ao, aorta; OM, obtuse marginal artery; Cx, circumflex artery; RCA, right coronary artery; DIA, diagonal artery; Rd, radial artery; Sp, saphenous vein graft; PSM, propensity score matching.

demographic data, PSM analysis was performed to eliminate bias and equalize the patients in both groups. After PSM, 192 patients obtained in both groups were compared regarding intraoperative TTFM parameters. In total, 405 distal anastomoses with 401 grafts were performed in the ONCAB group, and 361 distal anastomoses with 361 grafts were performed in the OPCAB group; their flowmeter records were retrieved. The number of grafts per patient was 3.28 ± 0.7 in the ONCAB group and 2.22 ± 0.6 in the OPCAB group (p = 0.001). The total number of revised grafts was 19 (4.7%) and 29 (8%), respectively (p = 0.001). Vasospasm and anastomosis problems as reasons for revision were significantly higher in the OPCAB group (p = 0.028 and p = 0.001, respectively). PI values in the OPCAB group anastomoses were generally higher than in the ONCAB group, whereas mean graft flow (MGF) and DF values were similar in both groups (Table 5).

The primary goal of any revascularization method, whether interventional or surgical, is to ensure adequate coronary flow. The aim is to preserve and maintain myocardial function by preventing ischemia or necrosis with increased coronary perfusion. Although intraoperative angiographic assessment of the quality of coronary/graft flow is the gold standard, it is not always useful in CABG operations [19,20]. Real-time measurements during the operation have generally been more useful. High-frequency epicardiac ultrasound (HF-ECUS), combined with TTFM and fluorescence coronary angiography using indocyanine green, is an intraoperative real-time imaging method [20–22]. The most widely accepted intraoperative graft quality assessment method is TTFM, but its utilization rate is around 30% worldwide [20,23].

In our clinic, we have been using the TTFM method to evaluate intraoperative graft quality since February 2006, and we have presented our experience in this regard in several studies [3,15,24]. Becit *et al.* [15] conducted an initial trial at our clinic, comparing two groups with and without TTFM. The study found that the TTFM group had lower rates of death, myocardial infarction during and after surgery, the need for more intervention, and the need for IABP support [15]. Kaya *et al.* [24] performed a retrospective analysis of the measurement data from 3596 grafts in

1240 patients who underwent ONCAB surgery at our clinic between 2007 and 2017. Their findings demonstrated that TTFM was a highly effective method for detecting graft failure during surgery and promptly addressing any issues [24]. Borulu *et al.* [3] conducted a recent study in our clinic. They compared the TTFM data of 110 patients who underwent CABG operations using three different methods: 48 ONCAB, 33 on-pump beating hearts, and 29 OPCAB. That study emphasized the importance of TTFM in solving technical problems related to grafts in CABG operations performed using three different methods [3].

Occlusion of 10–15% of saphenous vein grafts in the first month and subsequent re-occlusion of 5–10% within the first year are considered surgical technique failures. This is usually due to kinking or turning of the graft, stretching of the graft caused by inadequate graft length and technical defects in the anastomoses. Approximately half of venous grafts become occluded in a ten-year period [25,26]. The rapid assessment of graft patency and anastomotic quality during surgery and the identification and prompt resolution of problems are critical for successful surgical outcomes. In this study, we observed early graft failure before discharge in two patients in each group (1% for each group). In six saphenous vein grafts, all four patients showed occlusion. The index operation revised four of these grafts based on TTFM values, while the other two grafts with PI values above five did not undergo revision due to the thin and poor distal vascular bed.

During the three-month follow-up period, two patients in the ONCAB group and one in the OPCAB group had early graft failure requiring additional intervention. Three patients underwent angiographic intervention to treat the four saphenous vein graft occlusions. These four grafts' TTFM parameters were within acceptable limits. During the three months, the total early graft failure rate was 1.8%, with no difference between the two groups. These results were at reasonably acceptable levels according to the literature. We owe this success to the evaluation and revisions made during surgery. This study also found no significant difference between ONCAB and OPCAB regarding MACCE at three months.

TTFM provides data about the MGF, PI (shows resistance to flow), DF rate (indicating the dominant filling pattern in grafts), and backflow (BF) (reverse flow across the anastomosis, demonstrating flow competition between the graft and the native coronary artery). These measurement parameters alone cannot provide an adequate assessment to demonstrate graft and anastomotic quality. Using them together is important because many factors affect TTFM parameters, such as the size and quality of the conduit and the coronary target, the quality of the anastomosis, and the flow in the distal coronary vascular bed. Furthermore, when assessing graft function, we should also consider competitive flow and the hemodynamic conditions under which we make the measurements [3,15,20,24,27].

Using only the MGF value to assess graft and anastomotic quality may not be sufficient. A stenotic anastomosis can achieve high graft flow. Jaber *et al.* [28] found no significant decline in the average flow value when the anastomoses narrowed below 75%. Although TTFM parameters alone cannot adequately assess anastomotic quality, low MGF can be interpreted as a potential problem. This study obtained similar MGF values in patients from both operative technique groups after graft revisions (Table 5).

In determining anastomosis quality, PI is considered a crucial parameter [3,15,20,24,27]. In a study based on PI values and comparing on-pump surgery with off-pump surgery, the results were in favor of on-pump surgery [29]. Similarly, in our study, the ONCAB group had significantly lower PI values than the OPCAB group in the LIMA-LAD, Ao-Dia, and Ao-Cx system anastomoses for both arterial and venous grafts. However, the PI values of the Ao-RCA anastomoses were similar in both groups (Table 5). In parallel with these PI data, the number of revised grafts was significantly higher in the OPCAB group [29 (8%) vs. 19 (4.7%); p = 0.001] (Table 3). While vasospasm was the most common reason for revision, anastomotic problems were also significant, and both were significantly more common in the OPCAB group ([13 (3.6%) vs. 9 (2.2%); p = 0.028] and [8 (2.2%) vs. 2 (0.5%); p = 0.001], respectively) (Table 3). OPCAB surgery presents numerous challenges and necessitates a high level of surgical skill and experience. Anastomotic quality has been one of the major concerns associated with this procedure. We should emphasize the significance of instant TTFMs for this method. Although it is necessary to spend additional time, solving the anastomotic problem detected immediately before the end of the operation will prevent perioperative and early graft failure.

The DF represents the graft's diastolic flow ratio. The diastolic flow pattern in all grafts is more pronounced in the left coronary artery system than in the right coronary artery system. This is because the left coronary artery system has a higher transmyocardial pressure gradient [20]. DF differs depending on the location of the measurement site, with larger levels observed in the distal section of the graft [20]. The percentage of retrograde flow (%BF) indicates the amount of blood that reverses its direction and flows back into the graft through the anastomosis during a single cardiac cycle. Typically, it indicates that the graft and the native coronary artery compete for blood flow [20].

Repeated measurements at different time points during surgery can help with the early detection of graft failure [3,15,24,27]. In a sub-analysis of the Registry for Quality Assessment by Ultrasound Imaging and TTFM in Cardiac Bypass Surgery (REQUEST) data, Leviner *et al.* [30] found that after protamine was given, there was a statistically significant rise in mean flow and a significant fall in PI. However, they concluded that it was not clinically significant [30]. They also found that one measurement before or after the protamine infusion may be sufficient, and if needed, multiple measurements may be helpful [30]. The investigators in this study perform TTFM measurements before protamine to avoid the need for additional heparin if revision is required, and perform a final measurement before sternum closure because they believe that multiple measurements are more useful.

Flow parameters and their effects or predictive roles on graft patency and clinical outcomes in the early, mid, and long term have been the subject of recent studies on TTFM. These studies have reported varying results. A case-control study using data from the early-ended trial Graft Imaging to Improve Patency (GRIIP) reported that MGF was a significant indicator of early saphenous vein graft (SVG) failure, but not predictive of major adverse cardiac events (MACE) [31,32]. The study determined the cut-off value for MGF to be 31 mL/min [32]. A retrospective study by Di Giammarco *et al*. [16] found a correlation between the combination of MGF $\leq$15 mL/min, PI $\geq$3.0 and %BF $\geq$3% and graft failure at a mean follow-up of six months in both arterial grafts and SVGs. Similarly, Tokuda *et al*. [33] analyzed 261 grafts (169 arterial and 92 SVGs) and reported that MGF, PI, and %BF were associated with three-month graft failure. The authors also evaluated 104 grafts with follow-up angiography from one to four years and concluded that low MGF was an independent predictor of graft failure [17]. Kim *et al*. [34] evaluated 117 grafts of 58 patients who underwent total arterial off-pump CABG using coronary angiography on postoperative day one and correlated diastolic predominant flow pattern, MGF, PI, and %BF values with graft patency.

In a more recent study by Kim *et al*. [35], they analyzed the outcomes of 3,083 isolated CABG patients, 2919 (94.4%) of whom were off-pump. Over 20 years, TTFM guidance led to the revision of 109 (1.3%) out of 8585 distal anastomoses during surgery. Within seven days postoperatively, 2820 (96.6%) patients underwent early angiography. Angiographic patency rates were 99.0% (5484 out of 5540) for arterial conduits and 96.9% (3352 out of 3461) for venous conduits ($p < 0.001$). They found that after the introduction of TTFM, arterial conduit patency improved significantly (97.2% vs. 99.2%; $p = 0.038$), while free venous conduit patency did not improve significantly (86.0% vs. 91.4%; $p = 0.181$). Based on angiographic findings, they performed early reintervention in 76 (2.7%) patients [35].

In another prospective angiography-controlled study, Jokinen *et al*. [36] evaluated 75 elective CABG patients with 204 grafts by follow-up angiography approximately six months later. They reported that PI >3 was the best predictor of six-month graft failure, but TTFM values did not correlate with clinical outcomes (death, MI, stroke) [36]. Lehnert *et al*. [37] conducted a retrospective analysis of angiography data from 345 patients and 982 grafts at a one year follow-up. They stated that for every one mL/min increase in IMA MGF, there was a corresponding 4% reduction in graft failure [37]. Honda and colleagues found a relationship between TTFM parameters (MGF, PI, %BF) and the severity of stenosis in the native coronary artery. They highlighted the significance of competitive coronary flow in a retrospective analysis of 72 LIMA-LAD grafts [38].

In a study evaluating graft assessment by computed tomography angiography around postoperative day seven, Zientara *et al*. [39] examined 359 arterial grafts and 278 SVGs in patients undergoing off-pump CABG. They found that early silent graft failure occurred predominantly in SVGs with low MGF and high PI [39]. Quin *et al*. [2] used data from the randomized on-off bypass (ROOBY) trial to compare graft patency rates at one year and MACE at five years in patients who had and did not have TTFM measurements. In the TTFM group, 83% of grafts were patent compared to 78% in the non-TTFM group ($p < 0.01$), and TTFM patients were less likely to have at least one occluded graft (29% vs. 38%, $p = 0.01$). However, the groups had similar five-year MACE rates (death, MI, revascularization) [2,40].

In a study investigating whether TTFM values predict graft failure and MACCEs, Kim *et al*. [14] retrospectively analyzed 538 consecutive patients with 1288 sequential venous grafts out of 1933 patients undergoing off-pump CABG. They divided the patients into three groups according to sequential anastomoses and compared them based on flow and PI values. Multislice computed tomography or angiography confirmed graft patency. Graft failure occurred in 23/1055 (2.2%) anastomoses. Using Kaplan-Meier analysis, they found that graft patency was significantly lower at low MGF ($p = 0.044$) and high PI ($p < 0.001$). According to multivariate logistic analysis [14], they found that a high PI (>5; HR 2.276; 95% CI 2.188–2.406, $p < 0.001$) was an independent risk factor for MACCEs.

Taggart *et al*. [22] recently conducted a multicenter prospective large-scale trial, the REQUEST. A total of 1046 patients underwent graft assessment with TTFM or epicardial ultrasonography. Graft-related changes totaled 7.8%. Perioperative event rates for stroke, MI, and mortality were 1%, 0.3%, and 0.6%, respectively. The investigators noted that 25% of patients underwent surgical changes related to the aorta, conduits, coronary targets, and anastomosis, which were associated with low operative mortality and low major morbidity [22].

Rosenfeld *et al*. [41] examined three sub-analyses of the REQUEST study. They found that the OPCAB group had more changes to their strategy for the aorta (14.7% vs. 3.4%) and fewer changes for *in-situ* conduits (0.2% vs. 2.8%). There was no significant difference between the two groups regarding target vessels or graft revisions (4.1% vs. 3.5%) compared to the ONCAB patients. The study found that arterial grafts had a higher revision rate than venous grafts (4.7% vs. 2.4%). Additionally, inferior wall grafts had a higher rate of changes compared to anterior wall grafts (5.1% vs. 2.9%) and lateral wall grafts (5.1% vs. 2.8%) [41].

Finally, in a more recent study, Zeng *et al.* [42] conducted a five-year evaluation of 610 grafts from 202 off-pump CABG patients using TTFM measurement and angiographic control. The LIMA bypass graft had the best patency rate, single or sequential saphenous grafts had a similar patency rate, and MGF could better predict graft failure [42]. In this study, perioperative morbidity rates were higher in favor of ONCAB, which was due to postoperative revision surgery for bleeding in the ONCAB group. Both groups had similar intra-aortic balloon use, MACCE rates, deep sternal infection, and early graft failure rates. At the three-month follow-up, the MACCE and cardiac intervention rates due to graft failure were similar (Table 4). Our institution is conducting another study on the control and evaluation of grafts using operative TTFM data and mid- and long-term angiographic data; thus, we did not use more angiographic data in this study.

A systematic review and meta-analysis including 23 studies and 12,662 grafts reported that the pooled rate of graft revisions attributable to abnormal TTFM results was 2.0% [4]. Silva *et al.* [11] conducted another meta-analysis that included 25 studies and 4443 patients. They found that venous grafts had a higher MGF than arterial grafts (standardized mean difference between venous and arterial grafts, –0.28 [95% CI, –0.34 to –0.22]; $p < 0.001$) [11].

This study has several limitations. Data reliability was low and limited due to the retrospective observational design of the study. The surgical teams determined the surgical method to treat the patients based on their condition and their coronary lesions without applying randomization. In addition, the retrospective nature of the study precluded randomization. Although this was a single-center study, the overall sample size was strong. However, the proportion of OPCAB patients was low due to the surgeons' experience in this field and the general tendency to adopt the ONCAB technique. Another limitation of the study is that it relied on a three-month follow-up after surgery. Because our institution is in a rural region of the country, patients from other provinces, who make up almost half of the patient population, have a follow-up after three months in the provinces where they reside; this presents challenges in accessing the national database. The final limitation was demonstrating graft patency during the early postoperative period or mid- and long-term, a process best demonstrated angiographically through conventional or CT angiography. Performing an angiography on a patient without any ischemic complaints is not routinely feasible because of the ethical and cost implications as well as the potential for additional morbidities.

Conclusions

This study demonstrated that using TTFM to check the quality of the graft during surgery improved the outcomes of coronary bypass surgery in both ONCAB and OPCAB cases. These improved outcomes are especially important for a procedure such as OPCAB surgery, which requires surgeon skill and experience and is difficult to perform. The TTFM assessment resulted in more graft revisions in the OPCAB surgical procedure and higher PI values. Further prospective, randomized, large-scale, long-term studies can confirm the effects of TTFM parameters on bypass surgery outcomes.

Availability of Data and Materials

Datasets used and/or analyzed for this study are available from the corresponding author upon appropriate request.

Author Contributions

ESÇ and ÜA have individually contributed to this study. Both authors made significant contributions to the study's content/design or data collection. ESÇ contributed significantly to the analysis and interpretation. Both authors assume full responsibility for the study, drafted the manuscript, and critically reviewed important intellectual content. They have reviewed and approved the final version of the submitted manuscript. Both authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

The study was carried out according to the Declaration of Helsinki (as amended in 2013) and approved by the Ethics Committee of the Atatürk University Faculty of Medicine (B.30.2.ATA.0.01.00/714). For surgical procedures, patients' informed consend was acquired, however, since the study was retrospective and the data were anonymized, informed consent was waived.

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Conflict of Interest

The authors declare no conflict of interest.

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