Transit-Time Flow Measurement and Outcomes in Coronary Artery Bypass Graft Patients

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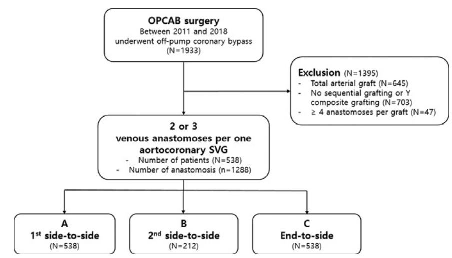
Transit-time flowmetry (TTFM) is commonly used during coronary artery bypass grafting for intraoperative graft assessment. This study aimed to investigate whether TTFM values were predictive of graft failure and major adverse cardiac and cerebrovascular events (MACCEs). Between 2011 and 2018, 1933 patients with 3-vessel coronary artery disease who underwent off-pump coronary artery bypass were retrospectively analyzed. Among them, 1288 sequential venous grafts in 538 consecutive patients were measured using TTFM's 2 parameters, pulsatility index (PI) and flow (mL/min). The anastomoses were divided in the 3 groups depending on the anastomotic site: group A, first side-to-side anastomoses (n = 538), group B; second side-to-side (n = 212), group C; end-to-side (n = 538). MACCEs were related to TTFM. The mean clinical follow-up time was 64.8 ± 21.2 months. Postoperative graft patency was confirmed with multi-slice computed tomography or coronary angiography (follow-up interval: 64.8 ± 50.4 and 27.8 ± 20.5 months based on the date of examination). The 5-year survival rate was 93.7%. The mean graft flow was 59.1 ± 31.3, 41.0 ± 25.2, and 38.9 ± 22.8 mL/minute, and the PI was 2.2 ± 1.3, 2.5 ± 3.4, and 2.4 ± 2.5, in groups A, B, and C, respectively. Graft failure occurred in 23/1055 (2.2%) anastomoses. The 5-year MACCE rate was 6.9% (37/538 patients). Kaplan-Meier analysis revealed that graft patency was significantly lower in low MGF (p = 0.044) and high PI (p < 0.001). Multivariable logistic analysis showed that high PI (>5; HR 2.276; 95%CI 2.188-2.406, p < 0.001) was an independent risk factor for MACCEs. The cutoff values for PI of sequential grafts were 3.65, 3.55, and 3.17 in groups A, B, and C, respectively for the prediction of MACCE. A high PI predicts



Summary flow diagram of the study population. Anastomoses were divided to serial site.

Central Message

The pulsatility index may be more suitable for predicting clinical outcomes than the mean graft flow for sequential venous grafting

Perspective Statement

A high pulsatility index in transit time flow measurements predicts graft failure and poor clinical outcomes for sequential venous grafts after surgery. Different pulsatility index cutoff values should be applied according to the anastomotic location. These findings may improve understanding of the effects of the sequential grafting technique and provide guidance to assist the surgeon's decision-making

Abbreviations: CAG, coronary artery angiography; CABG, coronary artery bypass grafting; CAOD, coronary artery obstructive disease; CKD, chronic kidney disease; CTO, Chronic total occlusion; ICU, intensive care unit; IMA, internal mammary artery; LAD, left anterior descending artery; LCX, left circumflex artery; LIMA, left internal mammary artery; MACCE, major adverse cardiac and cerebrovascular event; MDCT, multi-slice computed tomographic angiography; MGF, mean graft flow volume; MI, myocardial infarction; OPCAB, off-pump coronary artery bypass; PCI, percutaneous coronary intervention; PI, pulsatility index; RCA, right coronary artery; RIMA, right internal mammary artery; ROC, receiver operating characteristic; SVG, saphenous vein graft; TTFM, transit time flow measurements

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more predictive poor outcomes of sequential venous grafts after surgery than the low mean graft blood flow.

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INTRODUCTION

Early graft failure may occur after coronary artery bypass grafting (CABG). Studies using intraoperative and early postoperative coronary angiography to assess graft patency have demonstrated significant variations in patency, and an early graft failure incidence of approximately 5% for internal mammary artery (IMA) grafts, and 11% for vein grafts.[1-5] These findings strongly suggest the need for intraoperative assessment of bypass grafts, which allows early detection and correction of technical problems.

Although postoperative angiography remains the gold standard for anastomotic evaluation, transit-time flow measurement (TTFM) is a suitable method for a quick and reproducible intraoperative assessment of graft function.[6-8] TTFM is a reliable method to assess graft function before completion of the operation, and may improve outcomes. Although many studies have validated the usefulness of TTFM, definite guidelines for TTFM cutoff values are not well established.

Furthermore, increasing numbers of patients with multiple coronary diseases are being referred for surgical revascularization, and sequential grafting is also increasing.[9,10] There is no predictive value of TTFM for sequential grafting. Therefore, we evaluated TTFM findings in 585 consecutive patients to assess whether this method could predict postoperative graft patency and major adverse cardiac and cerebrovascular events (MACCE).

METHODS

Ethics Statements

This study was approved by the Ethics Committee/Review Board of the Severance Hospital, Republic of Korea [IRB number: 4-2019-0216 (2019.04.25)]; the committee waived the requirement for informed consent from the individual patients owing to the retrospective nature of the study. The authors received no funding for this study.

Patient Selection

This single-center, retrospective study included 1933 consecutive patients who underwent off-pump coronary artery bypass graft surgery (OPCAB) between January 2011 and December 2018. We excluded patients with total arterial grafting, no sequential grafting, or more than 4 anastomoses per saphenous vein graft (SVG). Finally, 538 patients with 2-or 3-vessel coronary artery obstructive disease (CAOD) and who underwent 2 or 3 sequential anastomoses using an SVG were included in the study. Three vessel disease was defined as one or more lesion in each of the 3 major coronary arteries.

Definition Of the Groups

Total anastomoses were divided into 3 groups depending on the anastomotic site: first side-to-side anastomosis (Group A, n = 538), second side-to-side anastomosis (Group B, n = 212), or end-to-side anastomosis (Group C, n = 538). The surgeons determined their surgical strategies according to each patient's conditions.[11] The patient flowchart is shown in Figure 1.

Operative Techniques

Surgical Technique

OPCAB was performed as previously described.[12] Preoperative clinical evaluations of SVG quality and size was performed using intraoperative ultrasonography in all cases. SVGs were harvested using an atraumatic open no-touch technique and avoiding excessive handling, including distension, to prevent injury to the endothelium.

All operations were performed through as median sternotomy. After full median sternotomy, heparin (0.7−1.0 mg/kg) was administered to achieve the target activated clotting time (ACT; >300 sec). A SVG as anastomosed to the aorta using the Heartstring III device (MAQUET Holding B.V. & Co. KG, Rastatt, Germany) and polypropylene 6−0 sutures. The lateral and inferior walls were exposed by means of a combination of a deep pericardial stay suture, Trendelenburg and right decubitus position. Regional myocardial immobilization was achieved with a tissue-stabilizer (Octopus Evaluation AS, Maquet-Acrobat-i. OM-10000) under 200 mm-Hg negative-pressure. The target coronary vessels were snared proximally with silastic slings. An intracoronary shunt (Synovis Flo-Thru intraluminal shunt, Baxter) was used during small vessel or expected good native flow. Side-to-side anastomoses were performed with a diamond configuration for the middle anastomoses in the sequential grafts. The side-to-side anastomosis was completed using polypropylene 7−0 suture. In the cases that target vessels have thin wall, 8−0 suture was used. The end-to-side anastomoses of the SVG to target vessels were performed in the following steps. The arteriotomy, made at an axial plane to the course of the target artery, was constructed in a parachute manner after 6 throws. A surgical CO_2 blower/mister device was

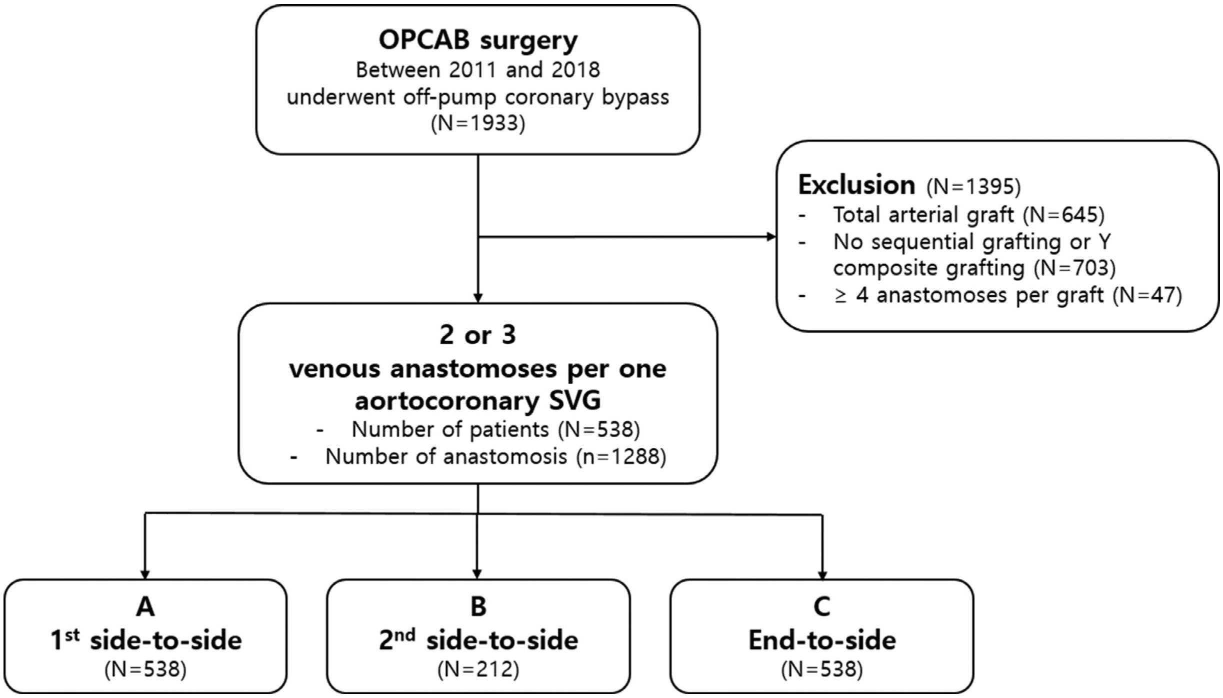

Figure 1. Summary flow diagram of the study population. OPCAB, off-pump coronary artery bypass; SVG, saphenous vein graft; N; number of patients; n; number of anastomoses.

used to enhance visualization (Beijing Medos AT biotechnology Co., China).

Flow Measurement

The TTFM values of all grafts were recorded intraoperatively in a standardized fashion when the hemodynamic condition was assessed as stable (systolic blood pressure between 100 and 120 mm-Hg, diastolic blood pressure above 60 mm-Hg) to exclude the effects on flow of excessively low or high blood pressure. The flow measurement values were obtained using the VeriQ system TTFM device (MediStim Inc., Oslo, Norway, Video 1). To achieve the best possible ultrasonic coupling, skeletonization of a small segment of the pedicled LIMA/SVG graft is generally necessary.[13] The following variables were recorded and evaluated: (1) mean graft flow volume (mL/min), and (2) pulsatility index (PI): [(maximum flow volume−minimum flow volume)/mean flow volume]. PI values were measured one by one during sequential grafting. The PI of first side-to-side was examined and collected just after anastomosis before proceeding second anastomosis. For flow measurement, the flow was measured and calculated from the distal anastomosis zone to proximal portion.

Endpoints

The primary endpoint was graft patency rate and MACCE, defined as the composite of all-cause death, cerebral events (stroke or transient ischemic attack), myocardial infarction (MI), or repeat revascularization.

Follow-Up

To assess graft patency, patients underwent multi-slice computed tomographic angiography (MDCT) 7 days, 1 year, and 5 years after OPCAB. Transthoracic echocardiography was performed on days 3 and 7 after surgery, then annually. Coronary angiography (CAG) follow-up was performed only in symptomatic patients, those with newly developed wall motion abnormality, or those with a positive exercise stress test. We started this study on January 2020 and finished the analysis on July 2020.

The graft patency status was classified into 1 of 3 descriptive MDCT imaging categories: patent (<50% luminal stenosis), faint (visualization but >50% stenosis or diffuse spasm), or non-visualization (occlusion). For CAG, graft patency was defined according to the FitzGibbon classification (grade A, graft with unimpaired run-off; grade B, reduced graft caliber >50%; and grade O, occlusion).[14] In this study, graft occlusion was defined as faint or non-visualization on MDCT or as grade B or O on CAG. Furthermore, sequential bypass grafts that were not visualized from the inflow site to the side-to-side anastomosis while showing patency beyond the side-to-side anastomosis were assessed as an occluded proximal portion and a patent distal portion.[15] The clinical follow-up rate was 98.7%. The mean period of MDCT follow-up was 64.8 ± 50.4 months (IQR, 36.1−97.4) and angiographic follow-up was 27.8 ± 20.5 months (IQR, 12.3−40.2).

Statistical Analysis

Categorical variables were summarized using frequencies and percentages, and were compared using a Pearson's chisquare test. Continuous variables were analyzed using the mean standard deviation with median and interquartile range and were compared using an independent t-test or ANOVA test.

The Kaplan-Meier method was used to generate survival curves and freedom from MACCEs. The Cox proportional hazards model for the overall population was used to estimate the independent effect of graft patency or MACCE of the TTFM measurements, adjusting for multiple baseline covariates. Receiver operating characteristic (ROC) curves were used to assess particular cutoff values for the MGF or PI with regard to graft patency or MACCE. Spearman's rank correlation test was used, and the appropriate correlation coefficient was calculated to describe the correlation between the measured MGF and PI. Differences were considered statistically significant at $p < 0.05$, and all tests were 2-sided. IBM SPSS Statistics package (version 23.0, IBM SPSS Inc., Armonk, NY) was used for all statistical analyses.

RESULTS

Clinical Characteristics

The baseline demographic, clinical, and echocardiographic parameters are shown in Table 1. The mean age at the time of surgery was 67.0 ± 8.1 years, and patients were predominately male (73.0%). A history of previous MI was recorded in 4.1% of the patients (22/538), and 15.8% of patients (85/538) had a recent MI. Three-vessel disease was present in 494 patients (91.8%). A total of 51 patients (9.5%) with EF ≤35% and 115 patients (21.4%) had left main involvement.

Table 1. Baseline Characteristics in All Patients

Variable	Entire Cohort (n = 538)
Age, years	67.0 ± 8.1
Male, n (%)	393 (73.0)
BMI, kg/m^2	23.1 ± 3.5
Hypertension, n (%)	302 (56.1)
Diabetes mellitus, n (%)	233 (43.3)
CKD (Grade III-V), n (%)	65 (12.1)
COPD, n (%)	12 (2.2)
CVA history, n (%)	53 (9.9)
Smoking history, n (%)	145 (27.0)
Dyslipidemia, n (%)	69 (12.8)
Previous PCI history, n (%)	38 (7.0)
Old MI	22 (4.1)
STEMI	19 (3.5)
NSTEMI	66 (12.3)
CAOD 3vd	494 (91.8)
Left main disease	115 (21.4)
LVEF, %	52.3 ± 15.5
LVEF <35%, n (%)	51 (9.5)
NYHA class III-IV	204 (37.9)

BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; PCI, percutaneous coronary intervention; MI, myocardial infarction; STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; CAOD, coronary artery occlusive disease; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Operative Data

The patients received 3.4 ± 0.5 anastomoses using the LIMA (n = 518), right internal mammary artery (RIMA, n = 19), SVG (n = 538), and radial artery (n = 28) (Table 2). The average size of vein grafts was 3.32 ± 1.60 mm and the distribution was in Supplementary Figure 1, and 'quantile- quantile' plot showed normal distribution of diameter. Vascular condition of the SVG was good/satisfactory (96.1%) when checked with ultrasound sonography and visually. We used poor qualified vein graft to avoid radial harvesting in the patients with CKD stage IV or V (n = 16/21). Moreover, massive forearm hematoma after transradial coronary angiography (n = 4/21) and short length of forearm were also a reason for avoiding radial harvesting (n = 1/21).

In all 538 patients included in this study we used the aorta as a proximal inflow to sequential SVG grafting. Of these, 326 (60.6%) underwent OPCAB with 2 venous anastomoses per aortocoronary SVG, and the remaining 212 patients (39.4%) received 3 venous anastomoses. LCX (50.5%) was the most common target territory for sequential SVG grafting, followed by RCA (38.4%) and diagonal (11.1%).

At the individual anastomotic site, the range of target vessel diameter was in 0.8−3.0mm (median value was 1.5mm, Supplementary Figure 2). We adapted the anatomical classification and defined complete revascularization as performing at least 1 bypass for each diseased main vessel. Complete revascularization containing a culprit lesion was performed in 96.3% (518/538) patients (Table 2).

TTFM Measurements

Supplementary Table 1 shows the TTFM data of 538 consecutive grafts that were recorded and analyzed at 1,228 anastomotic sites. The total for each site decreased as the MGF moved distally (p = 0.020, 0.001, 0.003). There was a significant difference in PI at the LCX territory depending on the order of anastomosis (p = 0.030).

The distribution of PI values for each suture site was in Supplementary Figure 3. In first side-to-side anastomosis, a PI value of 6 or higher was observed in 1.3% (n = 7), 2.8% (n = 6) in second side-to-side and 2.4 % (n = 13) in end-to-side. In 5 patients the side-to-side anastomoses and 11 patients the distal end anastomoses were revised using re-opening and re-anastomosis technique had shown unfavorable graft flow (mean graft flow volume <20ml/min). After reconstruction in the 14 patients, there was the significant improvement of graft flow. However, 2 patients with small vessel (≤0.8mm) had no improvement of flow after anastomotic revision.

Early And Late Clinical Outcomes

Supplementary Table 2 shows the early and late clinical outcomes. Overall mortality was observed in 23 and cardiac death in 3 patients. The overall MACCE rate was 6.9% (37/538

Table 2. Intraoperative Variables in All Patients

Variable		Entire Cohort (n = 538)	
Operative time, min		219.4 ± 57.4	
Number of conduits per patient		2.0 ± 0.2	
LIMA		518 (96.3)	
RIMA		19 (3.5)	
Radial artery		28 (5.2)	
Number of total distal anastomoses, *n* (%)		3.4 ± 0.5	
Complete revascularization, *n* (%)		518 (96.3)	
Aortocoronary proximal anastomosis of SVG		538 (100)	
Anastomoses per SVG			
2		326 (60.6)	
3		212 (39.4)	
SVG target territory	Patients		Anastomosis
LAD (diagonal)	59 (11.0)		143 (11.1)
LCX	229 (42.5)		651 (50.5)
RCA	250 (46.5)		494 (38.4)
Target vessel stenosis	Stenosis degree		Critical stenosis (>90%)
LAD (diagonal)	81.3 ± 14.6		23/ 59 (39.0%)
LCX	80.0 ± 18.8		122/ 229 (53.3%)
RCA	83.2 ± 20.8		131/ 250 (52.4%)
First side-to-side		79.8 ± 14.2	
second side-to-side		81.2 ± 17.7	
End-to-side		86.7 ± 14.5	
Overall		83.4 ± 16.3	
SVG vessel quality			
Good/ Satisfactory		517 (96.1)	
Poor		21 (3.9)	
Clockwise anastomosis of SVG		512 (95.2)	

LIMA, left internal mammary artery; RIMA, right internal mammary artery; SVG, saphenous vein graft; LAD, left anterior descending; LCX, left circumflex artery; RCA, right coronary artery.

patients). During the follow-up period, nonfatal MI occurred in 6 patients. Two patients underwent repeat revascularization with percutaneous coronary intervention (PCI), and one patient underwent CABG. Revascularization was performed according to the judgement of experts, and a multidisciplinary approach was made for this. The overall 5-year graft patency was 92.1% (Fig. 2). Graft patency was not associated with the anastomosis method (side-to-side vs end-to-side, p = 0.396, Fig. 3A), nor did it correlate with target vessel territories (LAD, LCX, or RCA, p = 0.074) (Fig. 3B).

The Relationship Between TTFM And Graft Patency Or MACCE

The rate of angiographic follow-up (MDCT or CAG) was 90.5% (487/538 patients), covering 1055 of 1228 anastomoses (81.9%). In the conduits with complete angiographic follow-up, the rate of graft failure was 2.2% (23 of 1055 anastomoses) (Supplementary Table 2). Kaplan-Meier analysis revealed that graft patency was significantly different between high and low MGF (p = 0.044, Fig. 3C). Patients with high PI parameters experienced a significantly higher incidence of graft failure events than those with low PI (p < 0.001, Fig. 3D).

To assess graft patency according to TTFM measurements, 1055 anastomoses of 487 grafts were visualized. Of these, 1032 anastomoses were patent (97.8%), and 23 (2.2%) were occluded. A total of 356 patients had an MGF <20 ml/min, whereas 699 had an MGF >20 ml/min. Among the anastomoses with low flow, 4.2% (15/356) were occluded, which was significantly higher than those with high flow anastomosis (1.1%, 8/699, p = 0.037). The patency rate was significantly different between the anastomoses with high compared with low PI (44.2% vs 0.4%, p = 0.024) (Supplementary Table 3, left panel).

The 5-year freedom from MACCE rate was 85.6% (Fig. 4A). No relationship was observed between the number of anastomoses per graft (85.4% vs 85.6%, p = 0.290, Fig. 4B) and MACCE. The MGF in TTFM measurements was also not associated with postoperative MACCE (p = 0.286, Fig. 4C). A high PI (>5) tended to increase the risk of MACCE (p = 0.084, Fig. 4D).

An MGF >20 did not affect the results (3.9% vs 4.1%, p =0.819). The overall MACCE was significantly higher among patients with grafts with a high PI (8.3%) compared with those with low PI (6.8%, p = 0.045) (Supplementary Table 3, right panel).

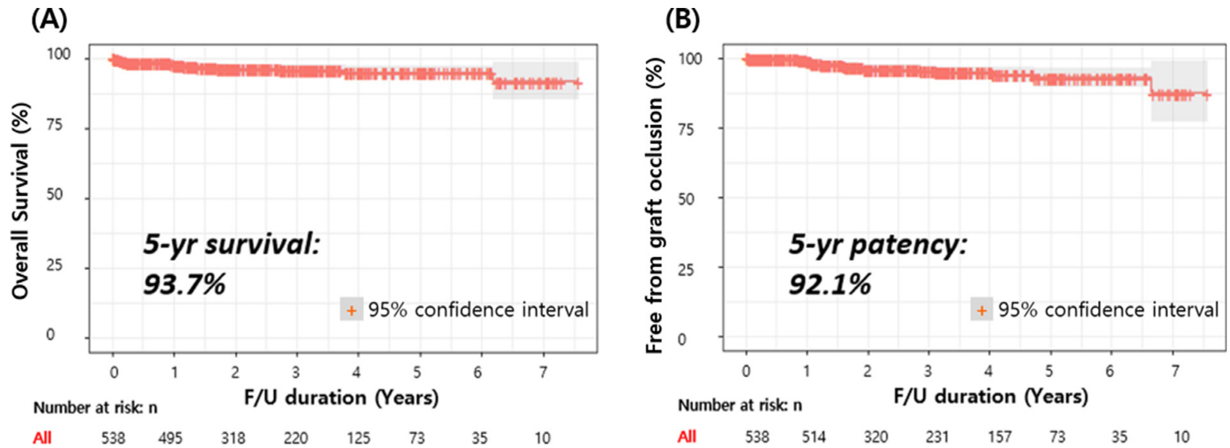

Figure 2. Kaplan-Meier plots of (A) overall survival, (B) freedom from graft occlusion, F/U, Follow-up. 95% CI, 95% confidence interval (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)

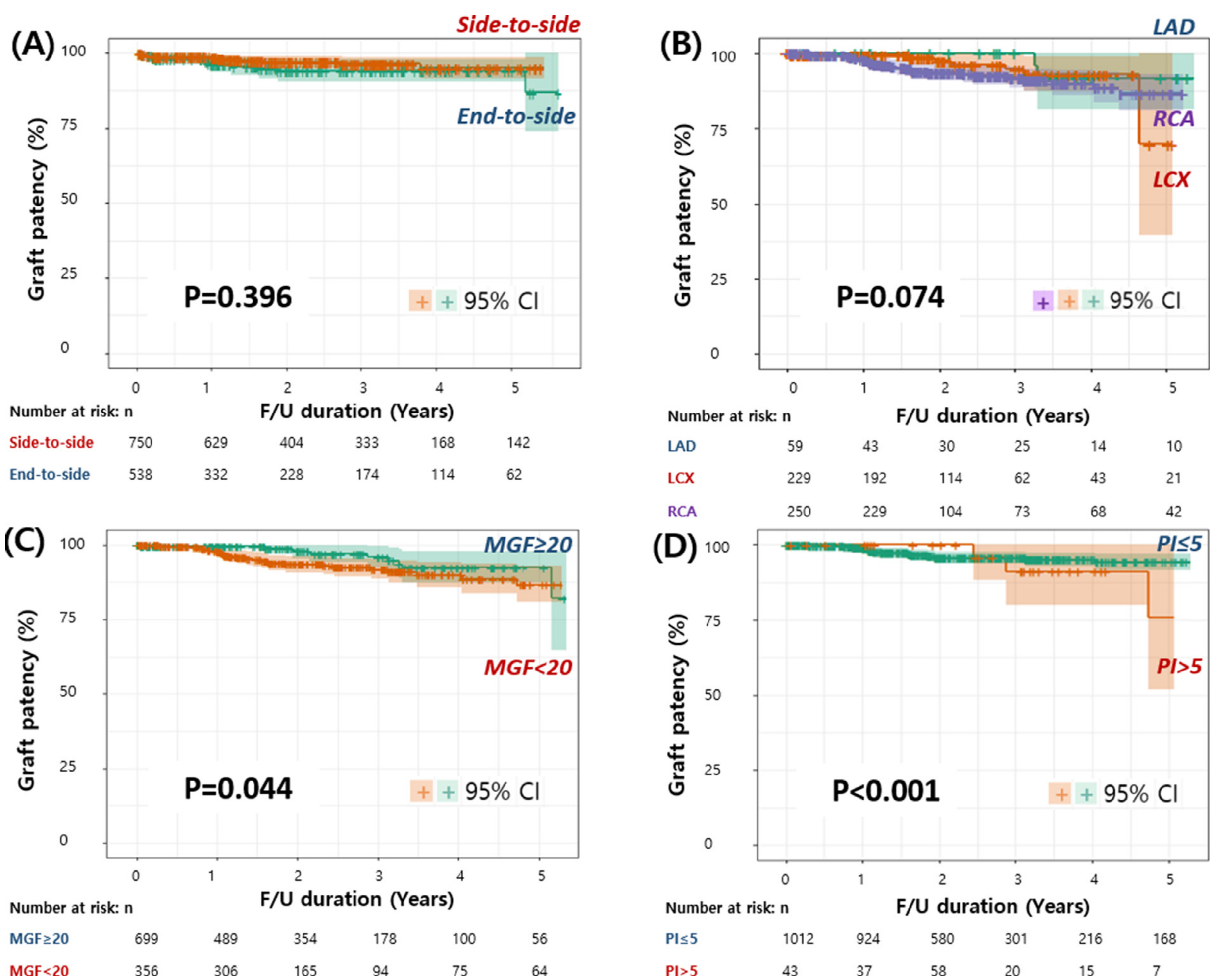

Figure 3. Kaplan-Meier plots of (A) graft patency according to side-to side versus end-to-side anastomosis method ($p = 0.396$), (B) graft patency depending on target vessel territories ($p = 0.074$). (C) graft patency between high and low MGF ($p = 0.044$), and (D) graft patency between high and low PI ($p < 0.001$). LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery, MGF, mean graft flow volume; PI, pulsatility index, F/U, Follow-up. 95% CI, 95% confidence interval (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)

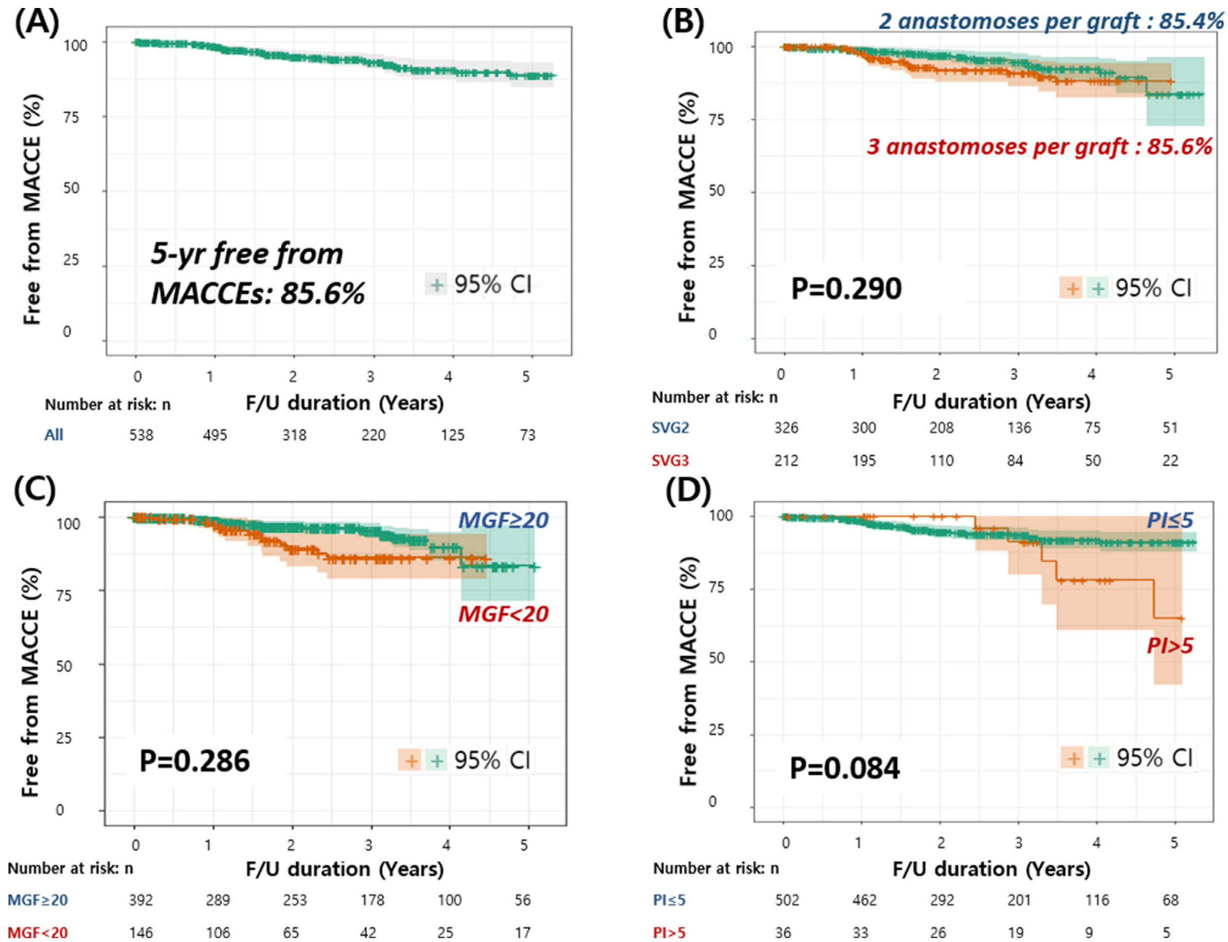

Figure 4. Kaplan-Meier plots of (A) overall MACCE (5-year free from MACCE rate: 85.6%), and freedom from MACCE, according to (B) the number of sequential anastomoses (p = 0.290), (C) MGF (p = 0.286), and (D) PI (p = 0.084). MACCE; major adverse cardiac and cerebrovascular events, MGF, mean graft flow volume; PI, pulsatility index, F/U, Follow-up. 95% CI, 95% confidence interval (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)

Predictability Of TTFM For Graft Patency Or MACCE

Cox regression multivariate analysis showed that CKD and high PI (>5) were independent risk factors of graft failure (Table 3) (HR 1.169, 95% CI, 1.008−1.693, p = 0.034; HR 1.362, 95% CI 1.311−1.955, p = 0.015, respectively). The independent risk factor for MACCE was high PI (>5, HR 2.276, 95% CI 2.188−2.406, p < 0.001). Interestingly, low MGF (<20 ml/min) did not affect graft failure or MACCE. Target vessel size and stenosis degree were also not significant relation with graft failure or MACCE. Furthermore, SVG quality was also not a predictor of risk of poor graft patency or worse MACCE.

In univariate analysis, we found that the MACCE rate was significantly different between chronic total occlusion (CTO) legions and non-CTO legions (p = 0.061). However, in multivariate analysis, there was no significantly different in the 2 groups (HR 1.611, 95% CI 1.346−1.816, p = 0.129). This was maybe the effect of the effort to complete revascularization including the CTO legion (Table 3).

Cutoff Value of TTFM For MACCE

The cutoff values for MACCE of PI were 3.65 in the first side-to-side (sensitivity: 89.5%, specificity: 60.5%), 3.55 in the second side-to-side (sensitivity: 88.6%, specificity: 67.7%), and 3.17 in the end-to-side (sensitivity: 89.5%, specificity: 62.3%), respectively (Fig. 5). The PI and MGF values correlated negatively and significantly with each other (p < 0.001) (Supplementary Figure 4). Supplementary Figure 5 shows the ROC analysis for the MACCE of the MGF parameters; there was no diagnostic correlation.

As we mentioned that in Supplementary Table 2, there was postoperative cardiac ischemic events [perioperative MI (n = 20, 3.7%), low cardiac output syndrome (n = 4, 0.7%) and newly onset atrial fibrillation (n = 68, 12.6%)]. To analysis their correlation with high PI values, these events were designated as composite clinical outcomes. In this correlation analysis, the high PI values and perioperative MI showed a significant correlation (Supplementary Table 4).

Table 3. Cox Regression Analysis on Graft Failure and Major Adverse Cardiac and Cerebrovascular Events

Variables	Graft Failure				MACCE			
	Uni-	Multivariate			Uni-	Multivariate		
	p Value	HR	95% CI	*p* value	*p* Value	HR	95% CI	*p* value
Age >70years	0.856	-	-	-	0.788	-	-	-
Male gender	0.979	-	-	-	0.184	-	-	-
DM	0.012	1.192	0.728–1.884	0.114	0.170	-	-	-
CKD (G III-V)	0.004	1.169	1.008–1.693	0.034	0.783	-	-	-
Low EF (<35%)	0.414	-	-	-	0.932	-	-	-
LM disease	0.795	-	-	-	0.078	0.595	0.331–1.069	0.083
Previous PCI	0.198	-	-	-	0.096	1.590	0.552–4.580	0.390
Recent MI	0.175	-	-	-	0.036	1.209	0.619–2.361	0.057
Poor SVG quality	0.242	-	-	-	0.379	-	-	-
Target vessel size	0.320				0.384			
Target vessel stenosis degree	0.140				0.277			
CTO lesion	0.195				0.061	1.611	0.837–1.816	0.129
MGF <20ml/min	0.082	1.331	0.877–3.485	0.190	0.054	1.240	0.781–1.968	0.363
PI>5	0.028	1.362	1.311–1.955	0.015	0.007	2.276	2.188–2.406	<0.001

MACCE, major adverse cardiac and cerebrovascular events; DM, diabetes mellitus; CKD, chronic kidney disease; EF, ejection fraction; LM, left main; PCI, percutaneous coronary intervention; MI, myocardial infarction; SVG, saphenous vein graft; CTO, chronic total occlusion; MGF, mean graft flow volume; PI, pulsatility index

DISCUSSION

In this study, we demonstrated that intraoperative TTFM could assess graft function and predict early graft function, thus allowing the prediction of long-term outcomes regarding graft patency and MACCE. Further, ROC analysis, conducted to identify the TTFM cutoff value parameters at individual sequential sites, revealed that high PI values could predict a high incidence of graft failures and MACCE.

Benefits of Sequential Grafting In CABG

The advantages of sequential saphenous grafting include: fewer proximal anastomoses, less aortic damage, shorter operation duration, and better long-term outcomes.[16,17] Nordgaard et al. and Kim et al. have used intraoperative TTFM to compare the hemodynamic characteristics of blood flow to find that the total blood flow in sequential venous grafts was significantly higher than that in a single vein graft.[18,19] We found that the sequential grafting technique was reliable and safe based on low overall graft failure and MACCE values.

Cutoff Value for MGF In Sequential Venous Grafts

The European Association for Cardio-Thoracic Surgery and the European Society of Cardiology guidelines recommend an MGF of ≥20 ml/min and a PI of ≤5 as acceptable perioperative results for TTFM.[20-23] A study has found a direct correlation between outcome and initial MGF, with consecutively proposed cutoff values for acceptable MGF flow rates of ≥20 ml/min for LIMA grafts and ≥40 ml/min for SVGs.[24] Our study showed that sequential graft failure could be predicted when the same criteria with ESC/EACTS guideline were applied.[25] The anastomosis with low flow below 20 ml/min or high PI (above 5) was revised using re-opening and re-anastomosis technique. Because poor TTFM maybe induce low shear stress, known to predispose grafts to develop intimal hyperplasia, which results in graft failure.

Statistically significant correlations have been found between flow and graft patency at midterm[26] and long-term follow-up.[27] Our study showed that graft patency was significantly lower in low MGF (p = 0.044). Furthermore, we showed that correlation between graft flow and patency based on univariate analysis (p = 0.082). However, our study found no correlation between graft flow and patency based on multivariate analyses (p = 0.190). This could be attributed to small sample sizes or because MGF depends on several variables including hemodynamics. Determining a clear cutoff value for the MGF remains difficult.

Cutoff Value for PI In Sequential Venous Graft

Although a statistically significant correlation between TTFM and flow at follow-up remains controversial, most studies agree that PI is directly and independently related to an increased risk of graft failure or adverse cardiac events.[13,26-28] Low PI values indicate adequate bypass, and a high PI indicates technical failure and flow competition with the bypass graft. Kieser and colleagues found that a PI > 5 was significantly associated with occurrence of MACE (17% vs 5%, p = 0.005) and mortality (32% vs 12%, p = 0.011) in the patients undergoing arterial revascularization.[29] We also showed that a high PI was a predictor of sequential graft patency and clinical outcomes after CABG. We suggest definite pathological PI values depending on the anastomotic site for a subgroup analysis of occluded grafts at follow-up. These findings may improve the

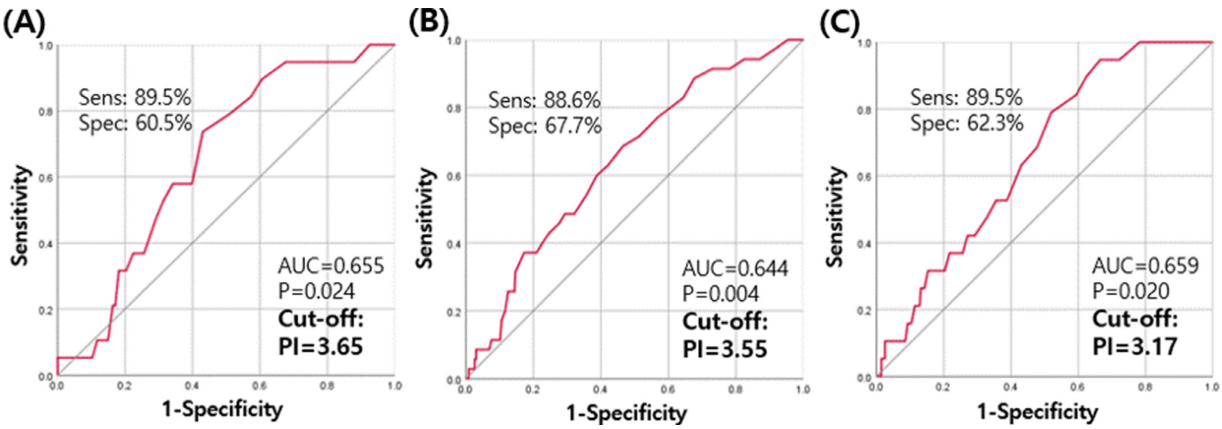

Figure 5. Receiver operating characteristic curves to determine cutoff values of the pulsatility index depending on the anastomotic site for major adverse cardiac and cerebrovascular events (A) first side-to-side, (B) second side-to-side, (C) end-to-side. Sens, sensitivity; Spec, specificity. AUC, area under the curve; PI, pulsatility index (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)

understanding of the effects of the sequential grafting technique and provide guidance to inform the surgeon's decision-making.

Other Mechanisms That Can Affect Sequential Venous Grafts

Multiple factors influence long-term SVG patency, including the quality of the target vessel and the anastomosis, bypass run-off, postoperative medical therapy, progression of coronary artery disease, and the quality of the SVG itself, which strongly depends on harvesting and handling as well as intraoperative storage and preservation.[30-34] Several modifications to CABG surgery have been proposed to improve graft patency, including the choice of conduit, distal target selection, and a sequential anastomotic technique. In this study, the rate of severe target stenosis (>70%) of sequential grafts was 78.7% in the diagonal, 94.8% in the LCX, and 96.4% in the RCA territory. We did not perform a subgroup analysis on target stenosis. Further studies are needed to determine the influence of these parameters on sequential venous grafting.

Study Limitations

The limitations of this study include its retrospective nature and the small data set from a single center. The analysis did not include factors associated with hemodynamic changes that may affect the differences in myocardial resistance between the left and right ventricles. A limitation of TTFM measurement was the lack of standard curves and flow values for different types of grafts and revascularized vessels. Standardization of TTFM findings was difficult because of the large biologic variability among different patients, and within the same patient. Temporary occlusion was not used in this study, so there is a limitation in that there may be measurement errors. Furthermore, the high PI value may mean a small vessel, severely calcified target, poor run-off or potential graft-target mismatch. We did not include all of these factors in our analysis.

Interpretation of flow curves and TTFM findings was largely dependent on the surgeon's personal experience. Each group was performed heterogeneously by each surgeon. However, in our institution 2 special coronary vascular surgeons have more than 10 years of experience as independent operators performing more than 200 cases per year; thus their surgical results including OPCAB did not vary widely, which rules out bias from different surgeons. We did not include all of these factors in our analysis.

We could not analyze to angiographic outcomes in all patients, because of renal function, rejection or local reasons. This could be a factor as bias. Lastly, we did not routinely examine CAG; instead, MDCT was used to evaluate anastomotic quality and graft patency. We could not analyze to angiographic outcomes in all patients. In Korea Health Insurance, although bypass surgery was performed, only when angina pectoris or myocardial infarction occurred, angiography is covered with. Additionally, according to our experience, Korean patients prefer follow-up with a less invasive method, such as CT, after CABG surgery.

CONCLUSIONS

We found that TTFM provides real-time information about the intraoperative hemodynamic characteristics of the graft, and affects long-term outcomes. The PI of TTFM measurements was highly predictive of long-term outcomes after CABG using a sequential venous graft. Our findings suggest that different individual cutoff values could be applied according to the anastomotic site in sequential venous grafting (Fig. 6).

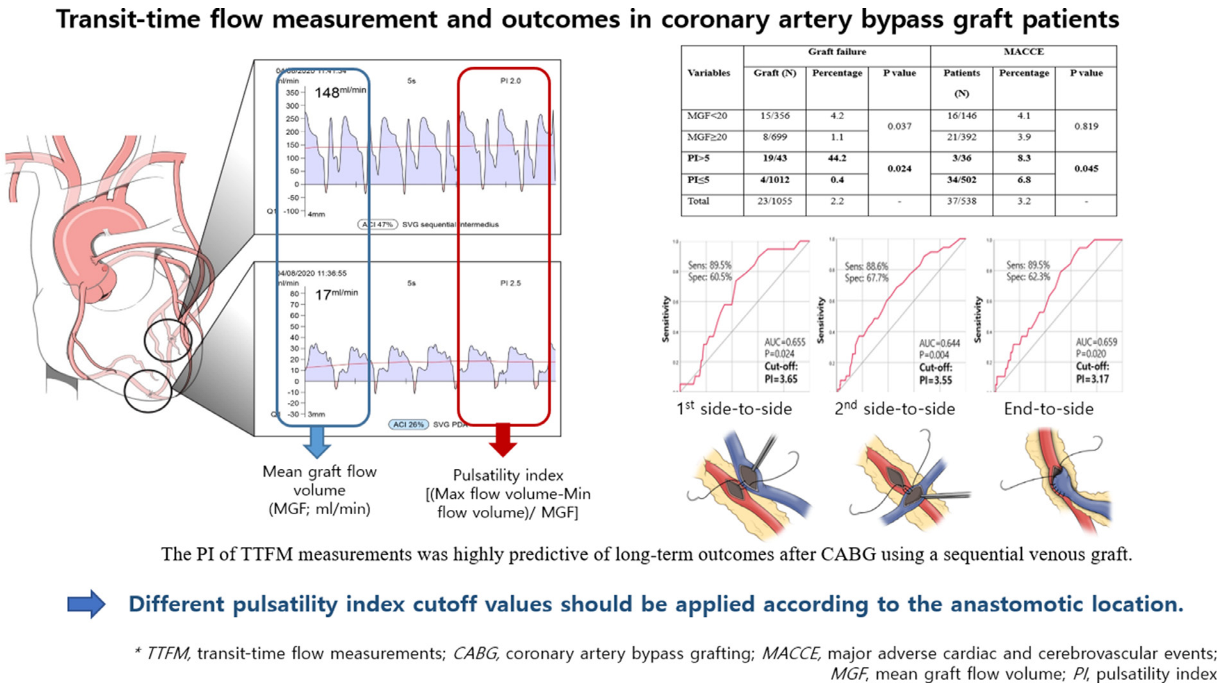

Figure 6. Graphical Abstract. This study found that Transit-time flow measurements (TTFM) provides real-time information about the intraoperative hemodynamic characteristics of the graft, and affects long-term outcomes. The PI of TTFM measurements was highly predictive of long-term outcomes after CABG using a sequential venous graft. TTFM, transit time flow measurements; CABG, coronary artery bypass grafting, PI, pulsatility index, MGF, mean graft flow volume (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)

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SUPPLEMENTARY MATERIAL

Scanning this QR code will take you to the article title page to access supplementary material.

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