A novel transit-time flow metric, diastolic resistance index, detects subcritical anastomotic stenosis in coronary artery bypass grafting

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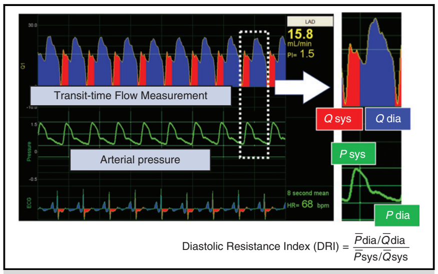
ABSTRACT

Objective: Transit time flow measurement (TTFM) can detect critical anastomotic stenosis during coronary artery bypass grafting. However, the identification of subcritical stenosis remains challenging. We hypothesized that diastolic resistance index (DRI), a novel TTFM metric, is more effective in evaluating subcritical stenosis than the currently available TTFM metrics. DRI is used to measure changes in the diastolic versus systolic resistance of distal anastomosis.

Methods: A total of 123 coronary bypass anastomoses in 35 patients were prospectively analyzed. During coronary artery bypass grafting, the mean graft flow (Q_{mean}), pulsatility index, and diastolic filling were obtained. DRI was calculated using the intraoperative recordings of TTFM and arterial pressure. Postoperatively, stenosis of anastomoses was categorized into successful (<50%), subcritical (50%-74%), and critical (≥75%) via multidetector computed tomography scan.

Results: In total, 93 (76%), 13 (10%), and 17 (14%) anastomoses were graded as successful, subcritical, and critical, respectively. DRI and diastolic filling could distinguish subcritical from successful anastomoses ($P < .01$ and $< .01$, respectively), whereas Q_{mean} and pulsatility index could not ($P = .12$ and .39, respectively). The receiver operating characteristic curves were established to evaluate the diagnostic ability for detecting ≥50% stenosis. In left anterior descending artery grafting ($n = 55$), DRI had the highest area under the curve (0.91), followed by diastolic filling (0.87), Q_{mean} (0.74), and pulsatility index (0.65).

Conclusions: DRI and diastolic filling had a reliable diagnostic ability for detecting ≥50% stenosis during coronary artery bypass grafting. In left anterior descending artery grafting, DRI had a more satisfactory detection capability than other TTFM metrics. (JTCVS Techniques 2023;17:94-103)



DRI is calculated using the simultaneous recordings of graft flow and arterial pressure.

CENTRAL MESSAGE

DRI, a novel TTFM metric, evaluates changes in diastolic/systolic resistance of coronary anastomosis and has a high diagnostic value for detecting critical (≥75%) and subcritical (50%-74%) stenoses.

PERSPECTIVE

TTFM has been used in confirming critical anastomotic stenosis (≥75%). However, subcritical stenosis (50%-74%) is challenging to detect using TTFM. DRI is a novel metric derived via diastolic/systolic resistance analysis. This study showed that DRI is a viable parameter for detecting ≥50% stenosis at a sensitivity higher than that of other currently available TTFM metrics.

Blood flow in the graft is critical for determining the clinical outcomes of coronary artery bypass grafting (CABG). Graft failure is a major cause of cardiac adverse events that occur in up to 11% of bypass grafts, affecting approximately 10% of all patients after CABG.[1,2] The cause of graft failure is, in part, believed to be correlated with technical errors that could be corrected at the time of operation.[3] The risk of graft occlusion owing to imperfect anastomosis is amplified in technically demanding off-pump CABG.[4]

Transit time flow measurement (TTFM) is a less invasive and the most frequently used technique for intraoperative graft assessment during CABG surgery and has been able to detect 2% to 4% of grafts that require revision.[5,6] Although TTFM could identify highly stenotic anastomoses,[7] it may not be reliable in detecting subcritical stenosis

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Abbreviations and Acronyms

AUC = area under the curve
CABG = coronary artery bypass grafting
CCT = coronary computed tomography
DF = diastolic filling
DRI = diastolic resistance index
FFR = fractional flow reserve
ITA = internal thoracic artery
LAD = left anterior descending artery
LCx = left circumflex artery
PBS = posterior balanced sensitivity
PI = pulsatility index
Q_{mean} = mean graft flow
RCA = right coronary artery
ROC = receiver operator characteristic
SVG = saphenous vein graft
TTFM = transit-time flow measurement

with consideration of few modifications in the hemodynamic performances of grafts at this level based on previous clinical studies.[1,8] In an earlier TTFM study, Morota and colleagues[9] identified diastolic flow fraction, also known as diastolic filling (DF), as the most reliable TTFM indicator for detecting graft stenosis in a swine model with an intentionally constricted internal thoracic artery (ITA) graft to the left anterior descending artery (LAD). The most striking result of the aforementioned study is the progressive shift in flow rate distribution from diastole to systole with increasing graft occlusion. Considering that vessel flow resistance is strongly dependent on its cross-sectional diameter, stenotic anastomosis becomes the primary factor for insufficient diastolic flow and systolic-dominant waveform. Thus, DF is a possible independent predictor of failed anastomosis despite being rarely reported as a predictive marker in clinical settings[10] perhaps due to the influence of other patient-specific flow dynamics, including intraoperative circulatory status and competitive coronary flow, on DF.

Herein, we introduce the clinical use of diastolic resistance index (DRI), a novel TTFM metric with a more conceptually tangible link to anastomotic quality. DRI is basically an extension of DF. Further, DF can identify changes in the diastolic-delivered blood volume versus the total-delivered blood volume, whereas DRI can detect changes in the diastolic versus systolic resistance of the distal anastomosis plus its connected coronary network. Similar to DF, DRI quantifies the gradual shift from diastolic to systolic dominance with increasing occlusion observed in the CABG flow rate waveform. Further conception and physiological background of DRI were reported in the TTFM theoretical article by Drost and colleagues.[11] We hypothesized that DRI can be a true metric of anastomosis resistance and can detect $\geq$50% stenosis at a higher sensitivity than other currently available TTFM metrics.

METHODS

Study Cohort

Between September 2019 and October 2020, 35 patients who underwent CABG were prospectively enrolled. A total of 123 anastomoses involving 55 (45%) anastomoses for LAD or diagonal branches, 39 (32%) anastomoses for left circumflex arteries (LCx), and 29 (23%) anastomoses for right coronary arteries (RCA), were analyzed. Postoperatively, percent stenosis of the coronary anastomoses was confirmed using coronary computed tomography (CCT) scan. Patients with renal dysfunction or known contraindications to contrast media were excluded. This prospective observational study was approved by the review board of Nippon Medical School Institutional (No. 30-11-1029) on May 15, 2019. All patients provided a written informed consent for the publication of study data.

Surgical Strategy

The study cohort underwent isolated off-pump CABG or concomitant on-pump CABG with other procedures. For LAD grafting, an in situ ITA was used if available. For diagonal branch, an in situ ITA or a saphenous vein graft (SVG) was utilized as an individual or sequential bypass graft. For LCx, an in situ ITA or an SVG was used in the same manner as diagonal branch grafting. In some cases, the in situ ITA was extended with radial artery or right gastroepiploic artery for sequential bypass grafting. For RCA, an in situ right gastroepiploic artery or an SVG was used. A Y composite graft was not used in this study.

Intraoperative TTFM Acquisition

During off-pump CABG, the flow profile with TTFM was obtained just after each bypass conduit was created. During on-pump CABG with a concomitant procedure, the flow profile was obtained after weaning from cardiopulmonary bypass. First, standard graft patency assessment was performed using the VeriQ flowmeter (Medistim) for each anastomosis. Once the graft flow was accepted, additional data acquisition was performed on the same graft using the AureFlo flowmeter (Transonic Systems Inc). The AureFlo could be connected to the vital sign monitor to record real-time arterial pressure measured via an arterial line placed in the radial or femoral artery (Figure 1). The following parameters were measured and recorded: mean graft flow (Q_{mean}) measured in milliliters per minute, pulsatility index (PI) measured as (maximal flow − minimal flow)/mean flow, and % DF measured as diastolic-delivered volume/systolic + diastolic delivered volume. To assess the effect of competitive flow on all TTFM parameters, these flow profiles were measured with and without the proximal coronary snare applied for each anastomosis (Figure E1). The measurement results were stored in the AureFlo for later retrieval by Transonic System Inc, blind to any clinical outcome data.

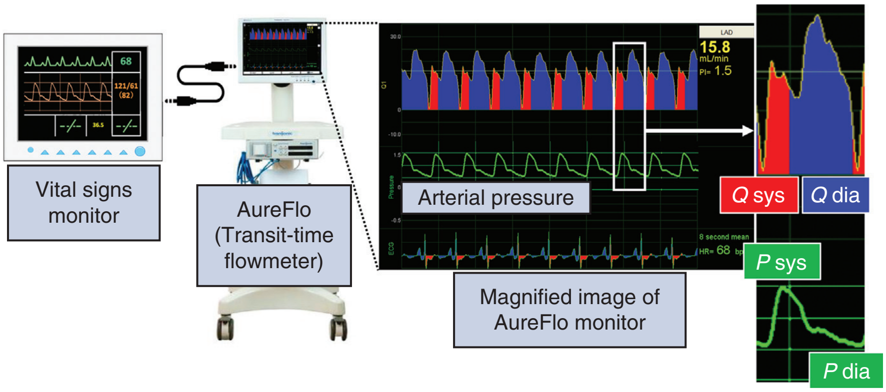
Postoperative DRI Computation

This study was conducted in cooperation with Transonic Systems Inc, a consultant responsible for DRI data processing and technical support. Postoperatively, the TTFM dataset was sent to Transonic System Inc, which then calculated DRI using the simultaneous recordings of graft flow rate and arterial blood pressure with the following equation:

$$\mathrm{DRI}=\frac{\bar{P}\mathrm{dia}/\bar{Q}\mathrm{dia}}{\bar{P}\mathrm{sys}/\bar{Q}\mathrm{sys}}$$

The association between DRI and DF can be expressed as follows:

$$\mathrm{DRI}=\frac{\bar{P}\mathrm{dia}}{\bar{P}\mathrm{sys}}\,\frac{T\mathrm{dia}}{T\mathrm{sys}}\,\frac{100-\mathrm{DF}}{\mathrm{DF}}$$



$$\text{Diastolic Resistance Index (DRI)} = \frac{\bar{P}\text{dia}/\bar{Q}\text{dia}}{\bar{P}\text{sys}/\bar{Q}\text{sys}}$$

FIGURE 1. The process of calculating the diastolic resistance index (DRI). AureFlo (Transonic Systems Inc), which could be connected to the vital sign monitor to record the patient's real-time arterial pressure measured via the arterial line placed in the radial artery or in the femoral artery. The DRI was calculated using the simultaneous recordings of the graft flow rate and arterial blood pressure using the abovementioned equation. *Q* is the time-varying rate of volume flow, and *P* is the arterial blood pressure. *sys*, Systole; *dia*, diastole.

Q is the time-varying rate of volume flow, P is the arterial blood pressure, and T is the period over which averaging is performed (ie, systole and diastole). The dia and sys indicate diastole and systole, respectively. Transonic Systems reported flow parameters, including DRI back to Nippon Medical School for outcome comparison and study conclusions.

Postoperative CCT Evaluation

CCT examination, the accepted noninvasive approach for assessing percent stenosis between newly created grafts and native coronaries,[12,13] was performed postoperatively. Images were evaluated using axial slices, thin-slab maximum intensity projections, and 3-dimensional rendering images on a postprocessing workstation. Each consecutive anastomosis in case of sequential graft was counted as separate graft segments. Independent radiologists blinded to TTFM data reviewed the CCT images and calculated percent stenosis as the ratio of luminal diameters between the anastomosis site and the native coronary artery. Then, the radiologists categorized each anastomosis into the following 3 patency classes: successful (no or <50%), subcritical (50%-74%), and critical (≥75%). Figure 2 shows the representative 3-dimensional rendering images exhibiting each patency class. CCT examination was generally performed after discharge in this study.

Statistical Analysis

All continuous variables were presented as median (interquartile range [IQR]), considering skewness and kurtosis due to the small cohort size. For group comparisons, the nonparametric tests of hypothesis testing were performed using the Kruskal-Wallis test, followed by the pairwise Dunn tests with Holm-Sidak correction. To explore the correlation between each TTFM metric and patency grades of anastomoses assessed via CCT, the Spearman (r_S) correlation coefficient was calculated as appropriate (Figure 3). To evaluate the diagnostic ability of a TTFM metric for detecting ≥50% stenosis, the receiver operating characteristic (ROC) curves and area under the curve (AUC) were constructed with 95% CI. To calculate ROC curves (Figure 4) and corresponding AUC values, the subcritical and critical groups were combined. Hence, the 2 classes remained: successful (<50%) and subcritical + critical (≥50%). Alternatively, all 3 classes can be retained, and the performance can be evaluated using the 3-class Bayesian statistical framework. In this setting, classwise posterior sensitivities and the overall, posterior balanced sensitivity (PBS) were evaluated, with a significance level of 5%.[14,15] The patency class predicted based on the value of a metric was compared with the true patency class based on CCT, thereby storing the results in a confusion matrix. Based on the number of true and false negatives for each class, the beta distributions representing the classwise posterior sensitivity were derived. The probability distribution of the overall PBS was obtained by convolution of the classwise probability distributions (ie, probabilistic equivalent of averaging). Further explanation about Bayesian multiclass statistics is described in the DRI theoretical article by Drost and colleagues.[11] All statistical analyses were performed using R (R Foundation for Statistical Computing).

RESULTS

Characteristics of the Participants

Table 1 shows the characteristics of the patients. In total, 26 (74%) were men, and the patients' median age was 67 years (IQR, 60-72 years; range, 48-85 years). Off-pump CABG was performed on 32 (91%) patients and an on-pump CABG with a concomitant procedure on 3 (9%). For LAD and diagonal branch grafting (n = 55), an in situ ITA was used in 47 (85%) anastomoses and an SVG in 8 (15%). For LCx grafting (n = 39), an in situ ITA was used in 16 (41%) anastomoses and an SVG in 23 (59%). For RCA grafting (n = 29), an in situ gastroepiploic artery was used in 8 (28%) anastomoses and an SVG in 21 (72%).

Evaluation of CCT Patency Grade

A total of 123 anastomoses were successfully evaluated via CCT examination. Accordingly, 93 (76%), 13 (10%), and 17 (14%) anastomoses were graded as successful (no or <50%), subcritical (50%-74%), and critical (≥75%), respectively. Graft occlusion or string sign was observed in 2 (2%) anastomoses, and the primary patency rate was 98% (121 out of 123). In grafting for LAD or diagonal

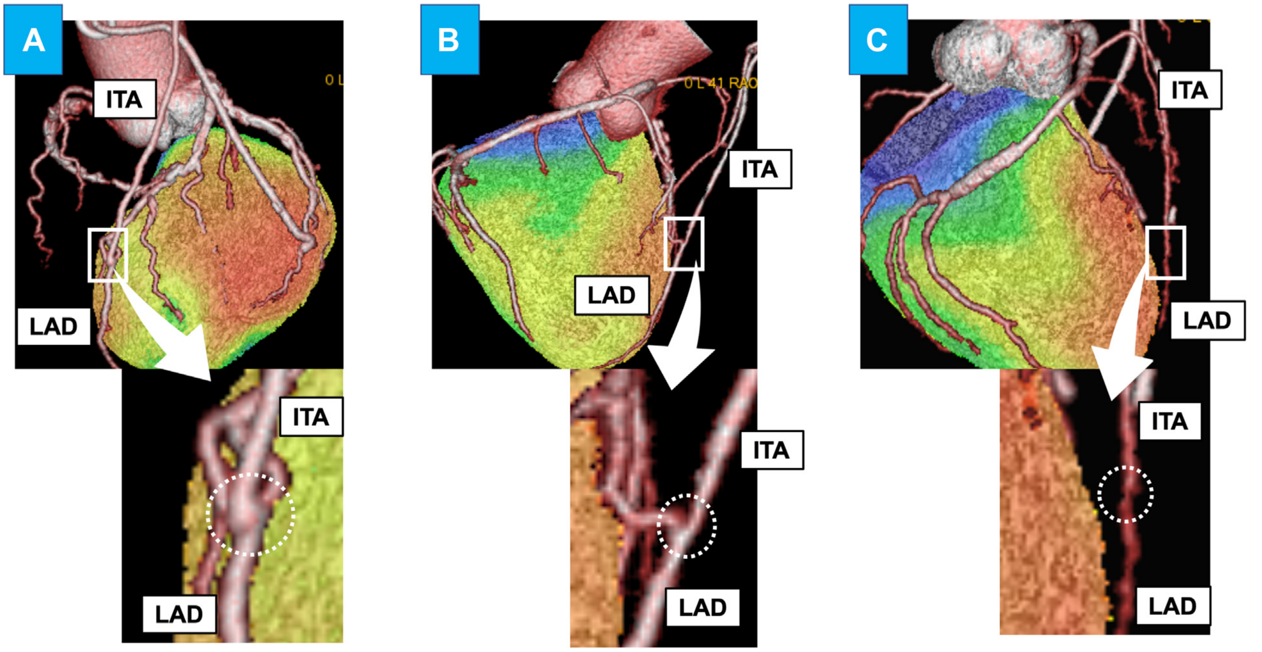


FIGURE 2. Representative 3-dimensional rendering images of coronary computed tomography scan assessing percent stenosis of coronary arterial anastomosis. Independent radiologists blinded to transit-time flow measurement data reviewed the images and categorized each anastomosis into three patency grades. A, Successful (no or <50% stenosis), anastomosis of the left internal thoracic artery (*ITA*) to the left anterior descending artery (*LAD*) showing an ideal external shape with adequate bulge. B, Subcritical (50%-74% stenosis), anastomosis of ITA to the LAD showing mild stenosis just proximal to the anastomosis site. C, Critical (≥75% stenosis), anastomosis of ITA to the LAD showing highly stenosed anastomosis with low contrast enhancement of the LAD.

branch (n = 55), 42 (76%), 8 (15%), and 5 (9%) anastomoses were graded as successful, subcritical, and critical, respectively. Among them, graft occlusion or string sign was observed in 1 (2%) anastomosis, which was an SVG sequenced to the diagonal branch. The median time interval from CABG surgery to CCT examination was 33 days (IQR, 19-89 days; range, 6-160 days).

TTFM Predictive Value of Anastomotic Stenosis

Table 2 depicts the TTFM data. The first 3 columns show basic quantitative TTFM metrics within each patency class. The intergroup *P* values in the final 3 columns expressed the significance of differences between these TTFM metrics. Q_{mean} and PI could distinguish between successful and critical classes, but could not distinguish between successful and subcritical classes. Meanwhile, DF and DRI had *P* values indicating significance in distinguishing between successful and subcritical classes and between successful and critical classes. Table E1 presents the thresholds of each TTFM metric to define subcritical and critical anastomoses.

Figure 3 shows the box plots of TTFM values according to each patency class. The patency class showed the strongest and significant correlation with DF ($r_S = -0.51$; $P < .01$) and DRI ($r_S = 0.51$; $P < .01$) in the analysis of all anastomoses involving the LAD, LCx, and RCA. Based on the evaluation of LAD and diagonal branch grafting (n = 55), DRI had the strongest correlation with patency class ($r_S = 0.62$; $P < .01$), followed by DF ($r_S = -0.57$; $P < .01$), Q_{mean} ($r_S = -0.37$; $P < .01$), and PI ($r_S = -0.22$; $P = .1$).

Figure 4 shows the ROC curves of each TTFM metric for detecting ≥50% stenosis. In the analysis of all anastomoses, DRI had the highest AUC value (0.85; 95% CI, 0.77-0.92), followed by DF (0.84; 95% CI, 0.78-0.89), Q_{mean} (0.75; 95% CI, 0.67-0.83), and PI (0.66 95% CI, 0.56-0.77). DRI had a higher AUC than PI ($P = .03$ [significant]), Q_{mean} ($P = .15$ [not significant]), and DF ($P = .85$ [not significant]). In the analysis of LAD and diagonal branch grafting (n = 55), DRI had the highest AUC value (0.91; 95% CI, 0.83-0.99), followed by DF (0.87; 95% CI, 0.78-0.95), Q_{mean} (0.74; 95% CI, 0.61-0.87), and PI (0.65; 95% CI, 0.48-0.81).

Table 3 shows the Bayesian 3-class analysis results. The performance of DRI was significantly better than that of PI ($P < .01$) and DF ($P = .03$). However, it was not significantly better than that of Q_{mean} ($P = .17$). Q_{mean} had the best sensitivity for the critical class. Meanwhile, DRI had the best sensitivity for the successful class; the strengths of these metrics can be combined, thereby resulting in a PBS of 67%.

DISCUSSION

The current study aimed to validate the ability of TTFM metrics for detecting the subcritical stenosis of CABG

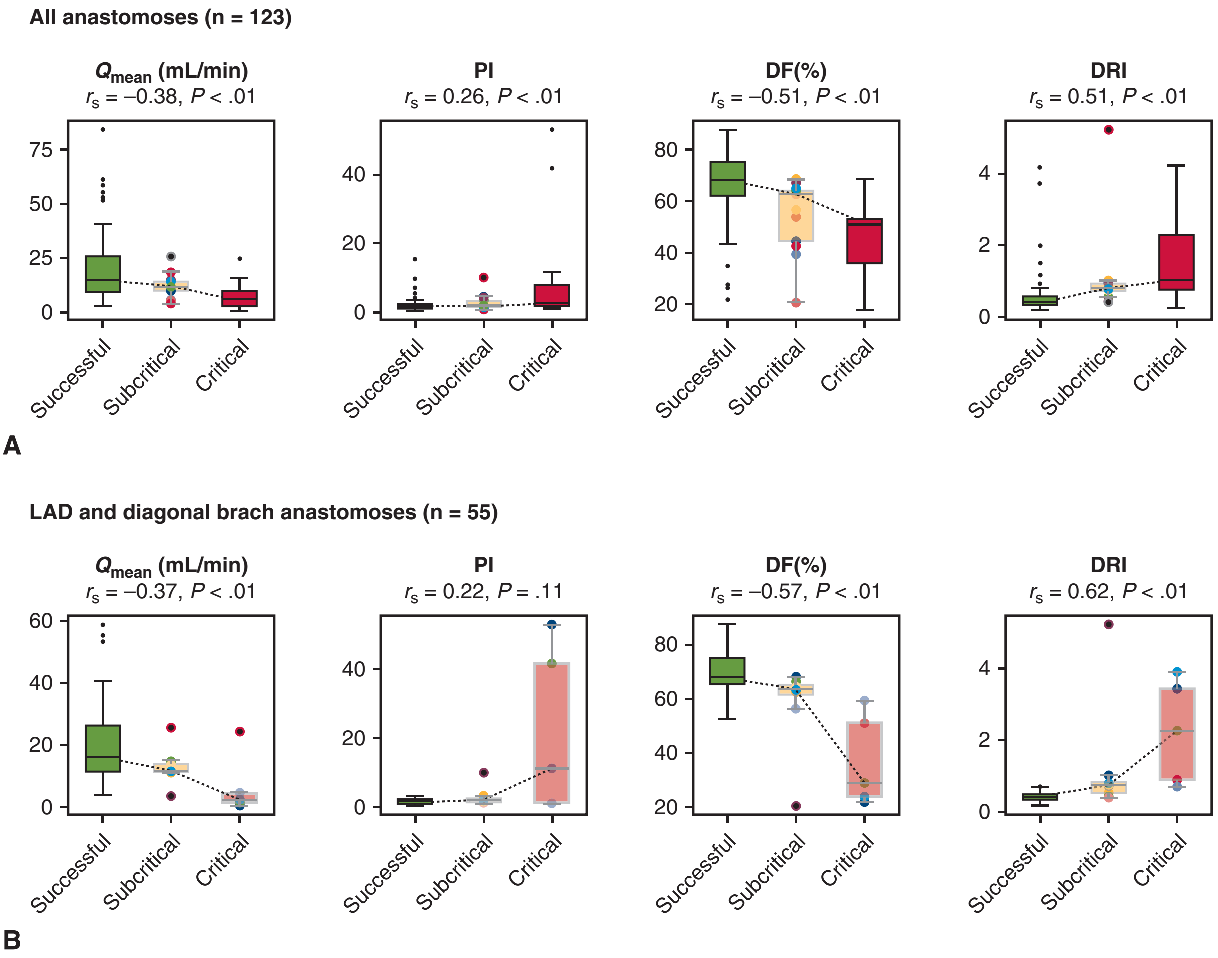


FIGURE 3. A, Box plots of each transit-time flow measurement parameters according to the 3 anastomotic patency grades for all anastomoses (n = 123) involving the left anterior descending arteries (*LAD*), diagonal branch, left circumflex arteries, and right coronary arteries. B, Box plots for LAD and diagonal branch grafting (n = 55). The middle horizontal line represents the median value (50th percentile), whereas the box contains the 25th to 75th percentiles of dataset. The lower and upper whiskers represent the minimum and maximum values of nonoutliers. Extra dots represent outliers. If the number of subjects or measurements is 14 or fewer, each value is plotted as different-colored dots. Q_{mean}, Mean graft flow; *PI*, pulsatility index; *DF*, diastolic filling; *DRI*, diastolic resistance index; r_s, Spearman correlation coefficient.

anastomosis. The 3 main findings were as follows. First, DF and DRI could distinguish subcritical (50%-74%) grafts from successful (no or <50%) grafts with statistical significance, whereas Q_{mean} and PI could not. Second, DRI had the highest AUC for detecting ≥50% stenosis in LAD and diagonal branch grafting. Third, combined Q_{mean} and DRI could provide improved patency class discrimination.

A previous study has reported the intraoperative utility of TTFM in confirming or excluding a technical graft failure and in reducing the rate of postoperative adverse events.[16] The definition of graft failure was not uniform in the previous literature, whereas graft occlusions and string signs were common parameters and applied by most authors.[10] In this study, 10% (13 out of 123) and 14% (17 out of 123) of grafts were categorized as subcritical and critical stenosis, respectively. This categorization is unique to this study and even critical stenosis included milder stenosis than conventional definition of graft failure such as occlusions or string signs. Thus, the ratio of stenotic grafts of the current study may be relatively higher than that of previous studies. In addition, the current study aimed to detect subcritical stenosis intraoperatively. Meanwhile, this degree of stenosis, as shown in Figure 2, *B*, might have been considered as successful in previous studies, and have been allowed to be left unattended. However, even subcritical anastomotic stenosis may cause altered wall shear stress and abnormal flow pattern, thereby leading to intimal hyperplasia and possible short-term graft failure.[17,18] Hence, more sensitive TTFM metrics and algorithms are urgently needed for more accurate intraoperative assessment of anastomotic quality.

The results of this study added new knowledge about intraoperative TTFM analysis to previous studies. DF and

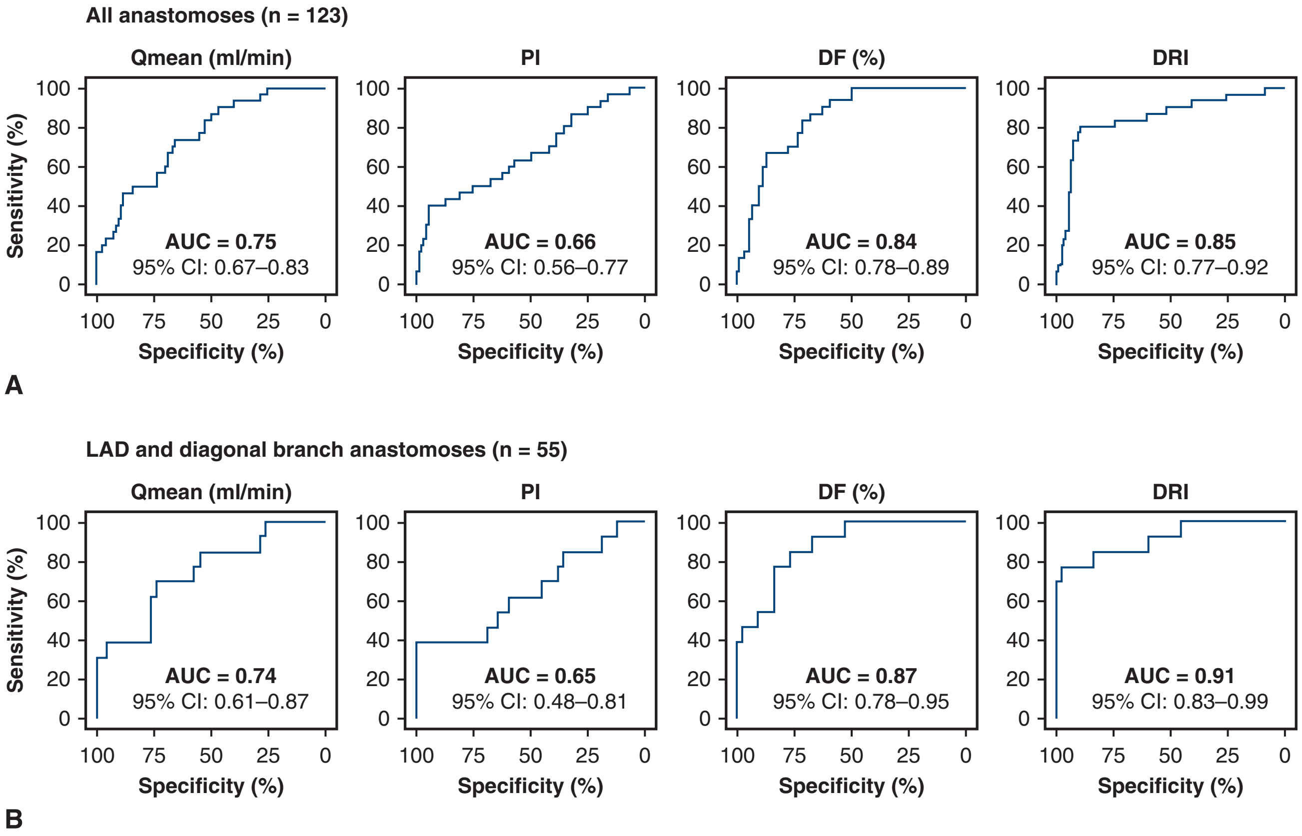


FIGURE 4. A, Receiver-operating characteristic (ROC) curves of transit-time flow measurement parameters for detecting ≥50% stenosis of coronary anastomosis for all anastomoses (n = 123) involving the left anterior descending arteries (*LAD*), diagonal branch, left circumflex arteries, and right coronary arteries. B, Receiver operator characteristic (ROC) curves for LAD and diagonal branch grafting (n = 55). Q_{mean}, Mean graft flow; *PI,* pulsatility index; *DF*, diastolic filling; *DRI*, diastolic resistance index; *AUC*, area under the curve.

DRI could be significantly effective in distinguishing subcritical anastomotic stenosis from successful grafts, whereas Q_{mean} and PI could not. Considering that a good graft to the left heart is diastolic-dominant, diastolic/systolic waveform analysis can provide an additional value for detecting stenotic anastomosis by quantifying the diastolic-dominant characteristic of the coronary flow waveform and the shift toward systolic dominance with increasing occlusion. DRI is a completely new metric of anastomotic resistance derived from fluid dynamics considerations and observations in an earlier animal model study.[9] The results of the binary ROC-curve analysis (Figure 4) and Bayesian three-class analysis (Table 3) are similar in that DRI and PI had the best and worst overall performances, respectively. The most striking difference of the abovementioned 2 analyses was that Q_{mean} had better performance than DF in the 3-class analysis, whereas its AUC was lower (0.75 vs 0.84) in the binary ROC-curve analysis. The most likely reason for this can be observed in the box plots in Figure 3. The DF IQRs are relatively wide, particularly for the subcritical and critical classes, thereby resulting in a high number of incorrect classifications and low posterior sensitivity for the subcritical class.

Notably, a disadvantage of the diastolic/systolic waveform analysis is that the systolic-dominant characteristic may not only indicate stenotic grafting but also low volume delivery during the diastole. This phenomenon may occur particularly in patients with competitive coronary arterial flow.[5,10,19] Competitive flow influences the systolic waveform more than the diastolic waveform, thereby creating negative-going excursions in systolic flow[20] and reducing the DRI. Thus, if the presence of competitive coronary arterial flow is apparent (low Q_{mean} and a sharp negative flow spike at the start of systole) and is a part of troubleshooting a questionable anastomosis, the surgeon may measure the same parameters with the coronary proximal snare applied. Vascular stiffness is another possible source of variance for the diastolic/systolic waveform analysis. Vascular stiffness, particularly in the myocardial wall, influences how resistance varies with transmural pressure. In a normal vessel, a decrease in transmural pressure leads to a smaller diameter, which, in turn, results in an increase in resistance. If the vessel is stiffer, this effect becomes smaller. Thus, even with a fully patent graft, resistance can be higher than normal, and the contrast between systolic and diastolic flow can be smaller than normal, thereby leading to lower

TABLE 1. Clinical and operative characteristics (N = 35)

Variable	Result
Age (y)	67 (60-72)
Male sex	26 (74)
Diabetes mellitus	17 (49)
Nonelective surgery	7 (20)
Isolated CABG	32 (91)
Off-pump CABG	32 (91)
On-pump CABG	0 (0)
Concomitant CABG	3 (9)
On-pump CABG + aortic valve replacement	2 (6)
On-pump CABG + surgical ventricular restoration	1 (3)
Intra-aortic balloon pump support during surgery	4 (11)
No. of anastomoses	4 (3-4.5)
No. of grafts	3 (2-3)
Use of arterial graft for LAD	34 (97)
Use of arterial graft for diagonal branch	14 (70)
Use of arterial graft for LCx	16 (41)
Use of arterial graft for RCA	8 (28)
Time interval from CABG to CCT (d)	33 (19-89)

Values are presented as median (interquartile range) or n (%). *CABG*, Coronary artery bypass grafting; *LAD*, left anterior descending artery; *LCx*, left circumflex artery; *RCA*, right coronary artery; *CCT*, coronary computed tomography.

DF. For DRI, things are more complicated because of its dependence on aortic blood pressure, which is often elevated in patients with high vascular stiffness. However, the weaker pressure-resistance relation can influence DRI in a similar way as DF.

The current study showed that the diagnostic ability of DRI is more accurate in the analysis of LAD and diagonal branch grafting than that in the analysis of LCx or RCA grafting. In RCA grafting, diastolic/systolic waveform evaluation does not always reflect the anastomotic quality because the endocardial muscle contraction is milder in the right heart, and its coronary flow profile is systolic–diastolic balanced rather than diastolic-dominant.[1] Therefore, any shift in the CABG flow toward a systolic-dominant flow profile created by anastomotic technical error will be milder. In addition, the intraoperative TTFM data of LCx and RCA grafting were obtained by lifting the apex using a heart positioner, which may cause deviation in TTFM values. However, based on our opinion, this finding does not impair the utility of TTFM-based diastolic/systolic waveform evaluation because the patency of LAD grafting is among the most significant determinants of long-term survival after CABG.[16]

Regarding the clinical implications of currently available TTFM metrics, this study recommends that any TTFM protocol should use combined Q_{mean} and DF for intraoperative patency evaluation in the current clinical setting. If Q_{mean} is sufficiently high, this can ensure high anastomosis quality. In case of an intermediate Q_{mean}, the value of DF should be considered, with high and low values of DF indicating success and failure, respectively. If DRI is a more sensitive metric than DF, it should be used by treatment protocols. In the current study, PI was an inadequate parameter for assessing the technical failure of a graft. Similar to Q_{mean} along, a PI >5 identified only severely constricted vessels with extremely small Q_{mean} or with competitive flow.

The use of coronary angiography versus CCT for the postoperative evaluation of anastomosis stenosis remains controversial. This study used CCT because the evaluation of asymptomatic patients with coronary angiography should be prevented with consideration of adverse events. Although CCT might have overestimated or underestimated anastomotic percentstenosis compared with coronary angiography, recent multislice CCT exhibits satisfactory sensitivity and specificity for detecting stenotic anastomosis.[21] In addition, the time of CCT evaluation from the original operation varies, with a median duration of 33 days (IQR, 19-89 days). Previous research revealed that the time from graft implantation does not affect the sensitivity and specificity of CCT detection of significant CABG stenosis.[21] Because there is concern about renal damage when using a contrast agent in the early postoperative period, CCT examination was basically performed after discharge in this

TABLE 2. Summary of transit-time flow measurement (TTFM) data according to patency class

	Category*			*P* value		
Variable	Successful (n = 93)	Subcritical (n = 13)	Critical (n = 17)	Successful vs subcritical	Successful vs critical	Subcritical vs critical
Q_{mean} (mL/s)	15.8 (9.66-26.8)	11.8 (9.88-14.1)	5.92 (2.79-9.93)	.12	<.01	.12
PI	2.02 (1.58-2.62)	2.17 (1.77-3.74)	2.98 (2.02-8.17)	.39	<.01	.25
DF (%)	68.3 (62.1-75.2)	62.8 (44.5-63.9)	51.0 (36.0-53.1)	<.01	<.01	.28
DRI	0.42 (0.35-0.57)	0.81 (0.73-0.92)	1.03 (0.76-2.27)	<.01	<.01	.73

Values are presented as median (interquartile range). For group comparisons, the nonparametric tests of hypothesis testing were performed using the Kruskal-Wallis test, followed by the pairwise Dunn tests with Holm-Sidak correction. Q_{mean}, Mean graft flow; *PI*, pulsatility index; *DF*, diastolic filling; *DRI*, diastolic resistance index. *Stenosis categories: successful (<50%), subcritical (50%-74%), and critical (≥75%).

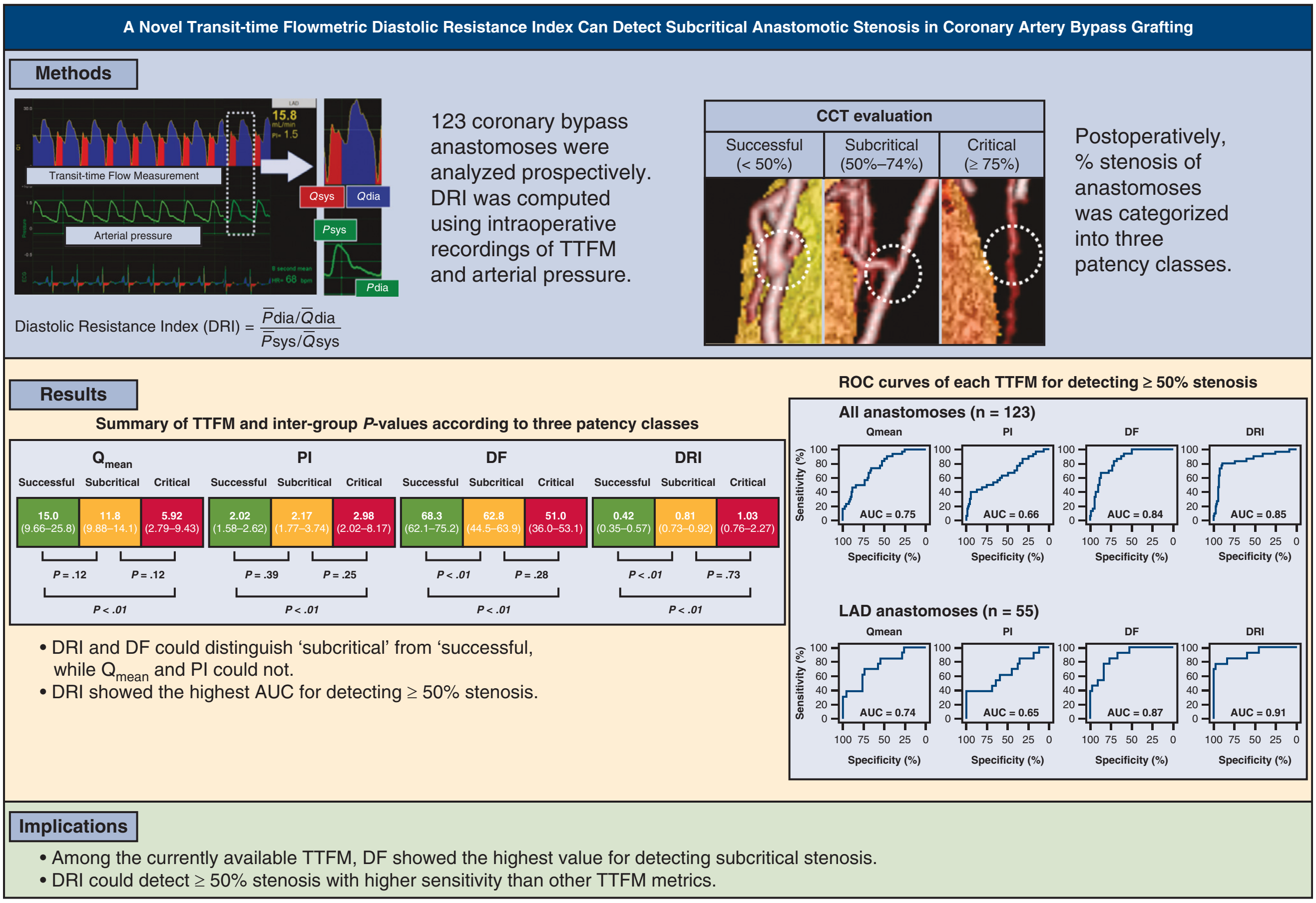
TABLE 3. Bayesian 3-class analysis for the performance comparison of each transit-time flow measurement (TTFM) metric

		Classwise posterior sensitivity		
Metric	PBS	Successful (n = 93)	Subcritical (n = 13)	Critical (n = 17)
Q_{mean}	60 (50-68)	50 (41-58)	62 (39-79)	71 (50-84)
PI	41 (35-50)	76 (68-83)	7.7 (2.6-30)	35 (20-55)
DF	47 (39-56)	75 (67-82)	15 (6.1-38)	47 (29-66)
DRI	64 (55-73)	90 (84-94)	62 (39-79)	41 (24-61)
Q_{mean} + DRI	67 (57-76)	88 (81-92)	62 (39-79)	53 (34-71)

Values are presented as % (95% CI). *PBS*, Posterior balanced sensitivity; Q_{mean}, mean graft flow; *PI*, pulsatility index; *DF*, diastolic filling; *DRI*, diastolic resistance index.

study. Recently, the importance of functional flow reserve (FFR) has been recognized in coronary angiography and even in CCT to assess physiologically significant lesions. However, this study did not include FFR because CCT-derived FFR computation requires the use of offsite supercomputers or computational fluid dynamics algorithm, which can be time-consuming and cost-intensive, limiting its widespread clinical utility.[22]

This study had some limitations. First, its sample size was relatively small. This clinical pilot study first validated the TTFM value (including DRI) for detecting ≥50% anastomotic stenosis. Hence, a sample size of 120 to 150 grafts can initially expect to demonstrate at least a medium effect (Cohen's $d \geq 0.5$), with a statistical power of 95%. Second, the current analysis did not include long-term follow-up data to determine the late prognostic significance of TTFM. Accordingly, whether TTFM-detected subcritical anastomosis should be revised or not intraoperatively to improve subsequent clinical outcomes remains a major question. Further follow-up evaluation should be performed



A Novel Transit-time Flowmetric Diastolic Resistance Index Can Detect Subcritical Anastomotic Stenosis in Coronary Artery Bypass Grafting

Methods

Diastolic Resistance Index (DRI) = $\frac{\overline{P}\text{dia}/\overline{Q}\text{dia}}{\overline{P}\text{sys}/\overline{Q}\text{sys}}$

123 coronary bypass anastomoses were analyzed prospectively. DRI was computed using intraoperative recordings of TTFM and arterial pressure.

CCT evaluation

Successful (< 50%)	Subcritical (50%–74%)	Critical (≥ 75%)

Postoperatively, % stenosis of anastomoses was categorized into three patency classes.

Results

Summary of TTFM and inter-group *P*-values according to three patency classes

	Successful	Subcritical	Critical	P (Successful vs Subcritical)	P (Subcritical vs Critical)	P (Successful vs Critical)
Q_{mean}	15.0 (9.66–25.8)	11.8 (9.88–14.1)	5.92 (2.79–9.43)	*P* = .12	*P* = .12	*P* < .01
PI	2.02 (1.58–2.62)	2.17 (1.77–3.74)	2.98 (2.02–8.17)	*P* = .39	*P* = .25	*P* < .01
DF	68.3 (62.1–75.2)	62.8 (44.5–63.9)	51.0 (36.0–53.1)	*P* < .01	*P* = .28	*P* < .01
DRI	0.42 (0.35–0.57)	0.81 (0.73–0.92)	1.03 (0.76–2.27)	*P* < .01	*P* = .73	*P* < .01

- DRI and DF could distinguish 'subcritical' from 'successful, while Q_{mean} and PI could not.
- DRI showed the highest AUC for detecting ≥ 50% stenosis.

ROC curves of each TTFM for detecting ≥ 50% stenosis

All anastomoses (n = 123)

LAD anastomoses (n = 55)

Implications

- Among the currently available TTFM, DF showed the highest value for detecting subcritical stenosis.
- DRI could detect ≥ 50% stenosis with higher sensitivity than other TTFM metrics.

FIGURE 5. Graphical summary of the study showing that the new transit-time flow metric (*TTFM*) parameter diastolic resistance index (DRI) shows high diagnostic ability for detecting subcritical anastomotic stenosis in coronary artery bypass grafting. *CCT*, Coronary computed tomography; *sys*, systole; *dia*, diastole; *ROC*, receiver-operating characteristic; Q_{mean}, mean graft flow; *PI*, pulsatility index; *DF*, diastolic filling; *AUC*, area under the curve; *LAD*, left anterior descending artery.

to explore the prognostic value of these TTFMs for predicting long-term patency and clinical outcomes.

CONCLUSIONS

Among the currently available TTFM metrics for evaluating anastomotic quality during CABG, DF had the highest diagnostic value for detecting $\geq$50% stenosis. In addition, DRI had a more satisfactory detection capability for $\geq$50% stenosis in LAD and diagonal branch grafting than the currently available TTFM. Hence, the novel TTFM metric DRI had a more tangible link to anastomotic quality, and it facilitates the detection of subcritical anastomotic stenosis with a higher sensitivity than other currently available TTFM metrics (Figure 5).

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: coronary artery bypass grafting, transit-time flow measurement, intraoperative graft evaluation, anastomotic stenosis

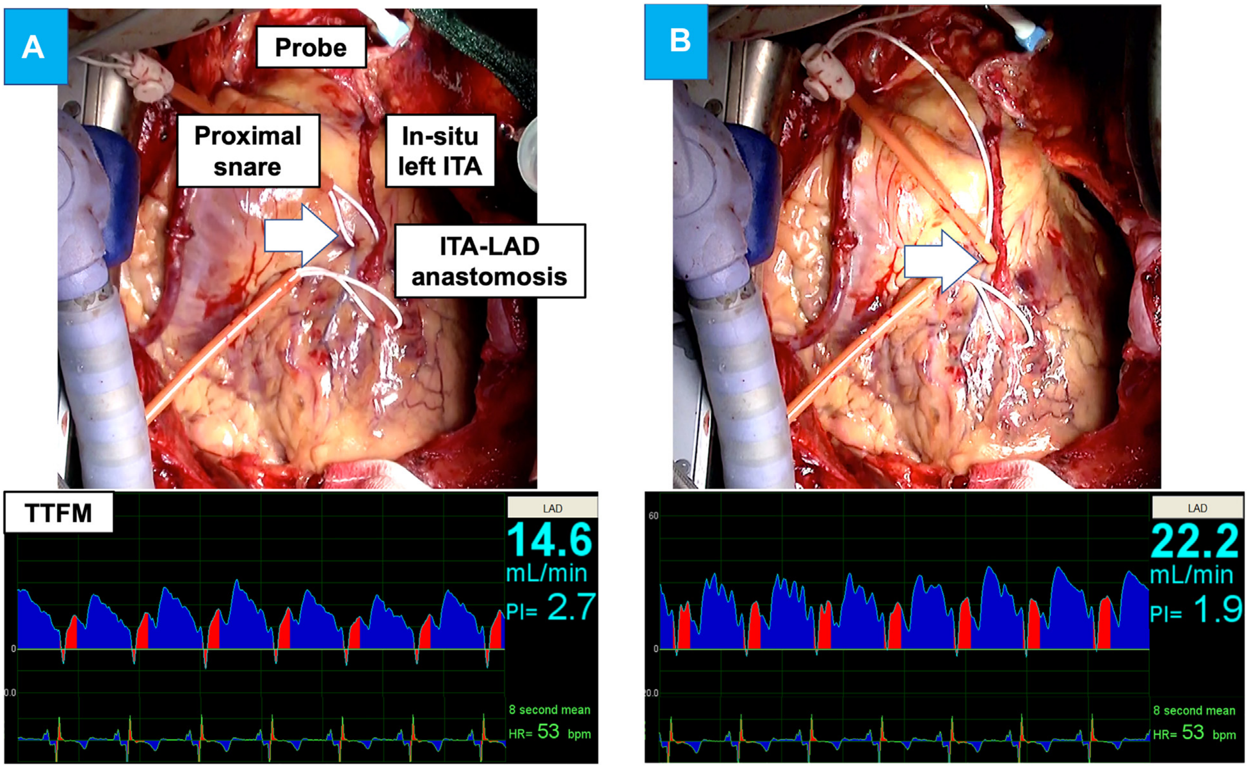

FIGURE E1. Transit-time flow measurement (*TTFM*) was obtained with and without the application of a coronary proximal snare. This TTFM collecting protocol was performed for each anastomosis to prevent misleading values due to proximal coronary competitive flow. A, The TTFM profile of the in situ left internal thoracic artery (*ITA*) was measured with the proximal left anterior descending artery (*LAD*) opened (*arrow*). Intermediate values of the mean graft flow indicated the presence of competitive coronary flow. B, The TTFM profile of the left ITA with the proximal LAD closed (*arrow*) showed sufficient mean graft flow and pulsatility index values.

TABLE E1. Thresholds of each transit-time flow measurement (TTFM) metric to define subcritical and critical anastomoses

Metric	Subcritical	Critical
Q_{mean} (mL/min)	<15.2	<9.53
PI	>2.68	>4.54
DF (%)	<61.7	<50.1
DRI	>0.73	>1.30

Q_{mean}, Mean graft flow; *PI*, pulsatility index; *DF*, diastolic filling; *DRI*, diastolic resistance index.