

# Graft flow evaluation with intraoperative transit-time flow measurement in off-pump versus on-pump coronary artery bypass grafting



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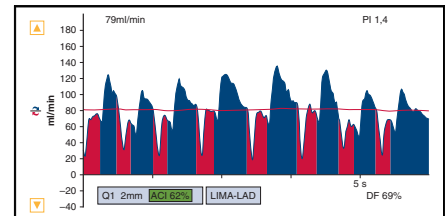
## ABSTRACT

**Objective:** We aimed to compare transit-time flow measurement (TTFM) parameters for on-pump (ONCAB) and off-pump (OPCAB) coronary artery bypass procedures.

**Methods:** The database of the Registry for Quality AssESmenT with Ultrasound Imaging and TTFM in Cardiac Bypass Surgery (REQUEST) study was retrospectively reviewed. Only single grafts were included (ie, no sequential or Y/T grafts). Primary end points were mean graft flow (MGF), pulsatility index (PI), diastolic fraction (DF), and backflow (BF). Unadjusted and propensity score-matching comparisons were performed.

**Results:** Of 1016 patients in the REQUEST registry, 846 had at least 1 graft for which TTFM was performed. Of these, 512 patients (60.6%) underwent ONCAB and 334 (39.4%) OPCAB procedures. Mean arterial pressure (MAP) during measurements was higher in the OPCAB group. After propensity score-matching, 312 well balanced pairs were left. In these matched patients, MGF was higher for the ONCAB versus the OPCAB group (32 vs 28 mL/min, respectively, for all grafts [ $P < .001$ ]; 30 vs 27 mL/min for arterial grafts [ $P = .002$ ]; and 35 vs 31 mL/min for venous grafts [ $P = .006$ ], respectively). PI was lower in the ONCAB group (2.1 vs 2.3, for all grafts;  $P < .001$ ). Diastolic fraction was slightly lower in the ONCAB group (65% vs 67.5%;  $P < .001$ ). The backflow was also lower in the ONCAB group (0.6 vs 1.3;  $P < .001$ ) with trends similar to MGF and PI for venous and arterial grafts. There were 21 (3.3%) revisions in the OPCAB group and 14 (2.1%) in the ONCAB group ( $P = .198$ ).

**Conclusions:** ONCAB surgery was associated with higher MGF and lower PI values, especially in venous grafts. Different TTFM cutoff values for ONCAB versus OPCAB surgery might be considered. (JTCVS Techniques 2022;15:95-106)



Typical result of a graft evaluation using TTFM.

## CENTRAL MESSAGE

On-pump bypass surgery was associated with higher flows and lower pulsatility indices than off-pump coronary bypass.

## PERSPECTIVE

We sought to investigate if there is a difference in TTFM parameters between on-pump and off-pump CABG. We found that on-pump surgery was associated with higher mean graft flows and lower pulsatility indices, especially in venous grafts. Different TTFM cutoff values for on-versus off-pump bypass surgery might be considered.

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**Abbreviations and Acronyms**

ACI	= acoustic coupling index
BF	= backflow
CABG	= coronary artery bypass grafting
DF	= diastolic fraction
LAD	= left anterior descending
LIMA	= left internal mammary artery
MAP	= mean arterial pressure
MGF	= mean graft flow
OM	= obtuse marginal
ONCAB	= on-pump coronary artery bypass
OPCAB	= off-pump coronary artery bypass
PI	= pulsatility index
PSM	= propensity score matching
RA	= radial artery
REQUEST	= Registry for Quality AssESsmenT with Ultrasound Imaging and TTFM in Cardiac Bypass Surgery
RIMA	= right internal mammary artery
SVG	= saphenous vein graft
TTFM	= transit-time flow measurement

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Technological advances paved the way for the development of devices that can be used to assess grafts for intraoperative failure. Graft patency can be measured in various ways, but the most widespread technique is transit-time flow measurement (TTFM) because of its ease of use.<sup>1</sup> A meta-analysis by Thuijs and colleagues<sup>1</sup> revealed a pooled rate of graft revisions of 4.3% per patient, and 2.0% per graft. In the grafts with an abnormal measurement, the pooled rate of graft revision was 25.1%. This frequency implies that there will be improvement in clinical outcomes with higher adoption rates and improved quality of intraoperative graft assessment,<sup>2</sup> as shown in the recent Registry for Quality AssESsmenT with Ultrasound Imaging and TTFM in Cardiac Bypass Surgery (REQUEST) trial.<sup>3</sup>

There is still debate regarding the possible advantages and disadvantages of on-pump (ONCAB) versus off-pump (OPCAB) coronary artery bypass graft procedures.<sup>4-6</sup> Regardless of these perceived advantages and disadvantages, few previous reports have compared the

flow rates in these 2 types of procedures, and conflicting results have been reported.<sup>7-11</sup> However, these studies were limited by being either single-center series, by a relatively small sample size, or by type of grafts used and the parameters measured. If differences in flow rates do indeed exist, this discrepancy might suggest that there should be different thresholds for the TTFM parameters when evaluating graft quality in ONCAB versus OPCAB.

In this study, we sought to quantify differences in TTFM parameters for ONCAB and OPCAB using a retrospective review of the REQUEST trial—a large, multicenter cohort. Any existing differences could be used to help correlate successful procedures with specific cutoff values for each type of procedure, and eventually improve the quality of intraoperative decision-making in coronary artery bypass grafting (CABG).

**METHODS****Study Design**

REQUEST is an international, multicenter, prospective registry that enrolled 1016 patients in 7 cardiac surgery centers (4 in Europe and 3 in North America) between April 2015 and December 2017. Patients underwent isolated CABG with intraoperative assessment of multiple surgical sites, such as the ascending aorta (for cannulation, crossclamping, and proximal anastomoses, if any), coronary targets, conduits, and finally proximal and distal anastomoses, using high-frequency ultrasound and graft assessment using transit time flowmetry (TTFM) with the MiraQ or VeriQ C devices (Medistim ASA).

The registry was designed to capture information on any changes in the proposed surgical procedure on the basis of high-frequency ultrasound and/or TTFM findings. The results, along with the study protocol, were reported in a previous publication.<sup>3</sup>

Institutional review board approval from each participating center was obtained before screening and enrollment. Informed consent was obtained from all enrolled patients (approval number for the various institutions: site 1: June 30, 2015 [15-63060-BO]; site 2: April 23, 2015 [REB15-0090]; site 3: August 6, 2015 [HS 053-15]; site 4: June 18, 2015; site 5: April 22, 2015 [15/SC/0194]; site 6: April 24, 2015 [01,731]; and site 7: July 20, 2015 [MEC-2015-448]).

The original REQUEST study<sup>3</sup> was funded by Medistim. The principal investigators and authors had complete scientific freedom. This subanalysis received no funding. The study is registered at [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02385344) (NCT02385344).

**Overall Patient Population**

Patients diagnosed with multivessel coronary artery disease and scheduled for isolated CABG were eligible to be included. Patients were excluded from enrollment if undergoing emergency surgery, when concomitant surgical procedures were planned (eg, valve repair or replacement, surgery for arrhythmias, etc), if the medical history included the presence of a muscle disorder (eg, myopathy, myalgia, myasthenia), or if the patient was known to be suffering from any psychological, developmental, or emotional disorder. The decision of performing the CABG operation with versus without the aid of cardiopulmonary bypass (ONCAB vs OPCAB) was left to the discretion of the operating surgeon.

It was highly recommended, but not mandatory, to assess each conduit used for CABG intraoperatively using TTFM. Only TTFM studies with an acoustic coupling index (ACI; as a correlate of the quality or reliability of the TTFM measurements) >30% were included in the analysis.

The following 4 TTFM parameters were defined as the primary outcome and were measured and recorded: mean graft flow (MGF; usually

represented in mL/min and coupled with electrocardiogram), pulsatility index (PI; this is an absolute number that provides information on resistance and flow patterns with lower values representing lower resistance), diastolic fraction (DF; this is the percent of diastolic flow in the graft. Ideally, this should be more than 50%) and backflow (BF; this represents the percent of backward flow over the anastomosis during 1 cardiac cycle). Such parameters were measured after protamine administration for heparin reversal. When a graft was revised, the measurements included in the analysis were those measured after graft revision.

### Inclusion and Exclusion Criteria

We considered only single grafts (ie, with only 1 distal anastomosis and no or 1 proximal anastomosis) with postprotamine TTFM performed with an ACI >30 (Figure 1). Sequential and Y/T grafts were therefore excluded from our analysis. We compared the median values of such parameters in ONCAB versus OPCAB procedures, considering all conduits (venous, arterial, and combined venous-arterial), completely arterial conduits, completely venous conduits, and specific conduit to target subsets: left internal mammary artery (LIMA) to left anterior descending (LAD), right internal mammary artery (RIMA) to LAD, RIMA to obtuse marginal (OM), radial artery (RA) to OM, RA to posterior descending artery, saphenous vein graft (SVG) to diagonal branch, SVG to OM, SVG to posterior descending artery, and SVG to right coronary artery.

### Statistical Analysis

Continuous data are reported as median (25th-75th percentile; ie, interquartile range), and categorical data as number (percentage). Comparisons were performed using the  $\chi^2$ , Fisher exact, and Wilcoxon rank sum tests as deemed appropriate (because normality was not established on the basis of Q-Q plots and the Shapiro-Wilk test), with the co-primary (ie, TTFM parameters) end points analyzed with  $P < .0125$ , taking into account multiple testing (Bonferroni correction). As a secondary analysis, propensity score matching (PSM; 1:1 ratio) was performed to balance the OPCAB and the ONCAB groups. The PSM was done using Greedy matching, and it was performed for all unbalanced variables (ie, age, body mass index, and New York Heart Association classification). The co-primary end points

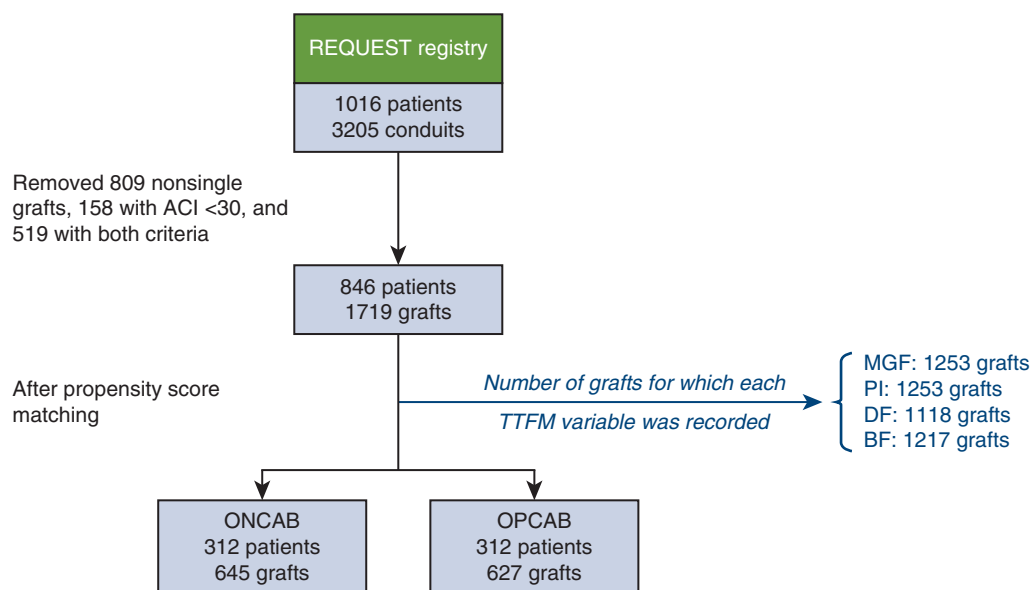
were analyzed with  $P < .0125$ , considering multiple testing (Bonferroni correction). We also analyzed the number of grafts not reaching specific parameter thresholds (MGF <20 mL/min, PI < 5, BF >3%, DF < 50%) and reviewed whether these grafts were revised. Analyses were performed using SAS 9.4 software (SAS Institute Inc).

## RESULTS

### Patient Groups

Of 1016 patients enrolled in the REQUEST registry, 846 had at least 1 single graft for which TTFM was performed (after protamine administration) with an ACI >30% and were included in our study (809 grafts were excluded for sequential grafting or Y/T grafting, 158 had an ACI <30%, and 519 grafts had both exclusion criteria). Of these, 512 patients (60.6%) underwent ONCAB and 334 (39.4%) OPCAB, corresponding to 1050 ONCAB grafts (61.1%) and 669 OPCAB grafts (38.9%).

Baseline characteristics and postoperative in-hospital outcomes are reported in Table 1. Before PSM, patients in the ONCAB group were slightly older compared with the OPCAB patients (68 years vs 66 years, respectively;  $P = .006$ ). Patients in the ONCAB group had a slightly lower rate of type 2 diabetes mellitus (28.3% vs 32.0%, respectively;  $P = .27$ ). Other than age, the only other difference between groups was the body mass index, which was slightly lower for the ONCAB group than the OPCAB group (27.6 vs 28.3;  $P = .03$ ). In-hospital morbidity and mortality rates were very low, with a numerically lower rate of stroke in the OPCAB group (1.8% for ONCAB vs 0.3% for OPCAB;  $P = .1$ ) Use of PSM resulted in 2 well balanced groups of 312 patients each (Table 2).



**FIGURE 1.** Inclusion and exclusion criteria. *REQUEST*, Registry for Quality Assessment with Ultrasound Imaging and TTFM in Cardiac Bypass Surgery; *ACI*, acoustic coupling index; *TTFM*, transit-time flow measurements; *MGF*, mean graft flow; *PI*, pulsatility index; *DF*, diastolic fraction; *BF*, backflow; *ONCAB*, on-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass.

**TABLE 1. Baseline characteristics and in-hospital outcomes of patient who underwent on- versus off-pump coronary artery bypass grafting**

	ONCAB (n = 512 patients)	OPCAB (n = 334 patients)	P value
Baseline characteristics			
Age, y	66.6 (9.9)	65.1 (8.7)	.024
Female sex	14.3 (73/512)	13.5 (45/334)	.75
Body mass index	28.4 (5.1)	29 (5.3)	.07
Diabetes mellitus	28.3 (145/512)	32.0 (107/334)	.25
History of stroke	5.7 (29/512)	6.3 (21/334)	.71
History of myocardial infarction	35.2 (180/512)	31.1 (104/334)	.23
History of revascularization			
CABG	0.4 (2/512)	0	.52
PCI	24.0 (123/512)	26.4 (88/334)	.45
NYHA classification			
I	42.4 (197/465)	31.1 (97/312)	.001
II	37.0 (172/465)	50.6 (158/312)	
III	16.8 (78/465)	15.7 (49/312)	
IV	3.9 (18/465)	2.6 (8/312)	
In-hospital postoperative MACCE			
Death	0.6 (3/512)	0.9 (3/334)	.69
Myocardial infarction	0.4 (2/512)	0	.52
Stroke	1.2 (6/512)	0.3 (1/334)	.25
Repeat revascularization	0	0	NA

Data are reported as mean (standard deviation) or % (n/N). ONCAB, On-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; NYHA, New York Heart Association; MACCE, major adverse cardiac and cerebrovascular events; NA, not applicable.

### Grafts

Results of the comparison of ONCAB and OPCAB grafts (per graft analysis after PSM) are reported in [Table 3](#) and [Figure 2](#). Of note, 64% of LAD grafts in the ONCAB group

were available for analysis and 75% of the LAD grafts were available in the OPCAB group. Most of the exclusions in this group of grafts were because of sequential grafting with a low ACI being the second most common reason

**TABLE 2. Baseline characteristics and in-hospital outcomes of patient who underwent on-versus off-pump coronary artery bypass grafting after propensity score matching**

	ONCAB (n = 312 patients)	OPCAB (n = 312 patients)	P Value
Baseline characteristics			
Age, y	65.3 (10.1)	65.2 (8.7)	.87
Female sex	12.5 (39/312)	13.5 (42/312)	.72
Body mass index	28.9 (4.9)	28.9 (5.2)	.81
Diabetes mellitus	30.5 (95/312)	32.7 (102/312)	.55
History of stroke	5.8 (18/312)	6.1 (19/312)	.87
History of myocardial infarction	32.1 (100/312)	31.4 (98/312)	.86
History of revascularization			
CABG	0.64 (2/312)	0	.50
PCI	26.9 (84/312)	25.3 (79/312)	.65
NYHA classification			
I	31.1 (97/312)	31.1 (97/312)	.88
II	49.4 (154/312)	50.6 (158/312)	
III	17.6 (55/312)	15.7 (49/312)	
IV	1.92 (6/312)	2.6 (8/312)	
In-hospital postoperative MACCE			
Death	0.64 (2/312)	0.96 (3/312)	>.99
Myocardial infarction	0.64 (2/312)	0	.50
Stroke	0.96 (3/312)	0.32 (1/312)	.62
Repeat revascularization	0	0	NA

Data are reported as mean (standard deviation) or % (n/N). ONCAB, On-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; NYHA, New York Heart Association; MACCE, major adverse cardiac and cerebrovascular events; NA, not applicable.

**TABLE 3. Comparison of transit time flowmetry parameters of on-versus off-pump coronary artery bypass procedures after propensity score matching**

	ONCAB		OPCAB		P value
	Grafts, n	Value	Grafts, n	Value	
All					
MGF	633	32 (20-54)	620	28 (18-40)	<.001
PI	633	2.1 (1.6-2.9)	620	2.3 (1.8-3.1)	<.001
DF	556	65 (57-72)	562	67.5 (59-75)	.0007
BF	621	0.6 (0-2.7)	596	1.3 (0.1-3.8)	<.001
Arterial					
MGF	307	30 (18-49)	359	27 (16-36)	.002
PI	307	2.2 (1.8-2.9)	359	2.3 (1.8-3)	.036
DF	279	70 (63-75)	326	71 (63-76)	.081
BF	301	1.3 (0.1-3.8)	345	1.6 (0.3-4.1)	.174
Venous					
MGF	326	35 (21-58)	261	31 (19-44)	.005
PI	326	1.9 (1.5-2.8)	261	2.4 (1.7-3.5)	<.001
DF	277	61 (54-67)	236	62 (54-69)	.055
BF	320	0.2 (0-1.9)	251	1 (0-3.7)	<.001
LIMA to LAD					
MGF	194	34 (18-54)	212	26 (17-36)	.002
PI	194	2.2 (1.8-2.9)	212	2.4 (2-3.1)	.006
DF	170	71 (66-76)	193	74 (69-78)	.015
BF	191	1.7 (0.2-4)	205	2.2 (0.5-5.1)	.062
RIMA to LAD					
MGF	5	31 (25-35)	21	31 (18-43)	.922
PI	5	2.1 (1.4-2.1)	21	2.1 (1.7-3)	.378
DF	5	72 (72-74)	21	73 (70-77)	.744
BF	5	1.3 (0-1.9)	20	1.6 (0.3-3.8)	.357
RIMA to OM					
MGF	29	25 (19-32)	7	18 (12-23)	.180
PI	29	2.2 (1.6-3.1)	7	2.1 (1.7-2.3)	.688
DF	27	69 (63-73)	6	68 (62-72)	.606
BF	29	0.5 (0-2.8)	7	0.1 (0-1.5)	.744
RA to OM					
MGF	19	36 (23-58)	33	26 (13-44)	.061
PI	19	1.9 (1.4-3)	33	2.3 (1.7-3.1)	.241
DF	18	66 (61-77)	27	63 (59-72)	.577
BF	18	0.2 (0-3)	29	1.2 (0.1-3.9)	.143
RA to PDA					
MGF	13	34 (30-53)	17	26 (22-32)	.065
PI	13	1.7 (1.2-2)	17	2 (1.7-2.7)	.160
DF	13	65 (55-70)	17	60 (51-66)	.208
BF	12	0.2 (0-2.5)	16	0.1 (0-1.2)	.902
SVG to Diag					
MGF	31	37 (25-45)	34	30.5 (20-39)	.226
PI	31	1.9 (1.5-2.6)	34	2 (1.8-2.4)	.406
DF	26	69 (63-76)	30	71.5 (67-75)	.542
BF	31	0.3 (0-1.6)	31	0.8 (0.1-2.6)	.121
SVG to OM					
MGF	104	36.5 (19.5-61)	76	30 (20-44.5)	.084
PI	104	1.8 (1.4-2.5)	76	2.3 (1.7-3.3)	.002
DF	86	63 (58-69)	71	64 (56-71)	.381
BF	102	0.1 (0-2.1)	74	1 (0-3.8)	.011

(Continued)

TABLE 3. Continued

	ONCAB		OPCAB		P value
	Grafts, n	Value	Grafts, n	Value	
SVG to PDA					
MGF	93	36 (20-52)	81	32 (19-48)	.344
PI	93	2.2 (1.6-3)	81	2.5 (1.7-3.9)	.095
DF	86	58.5 (52-63)	74	61 (54-66)	.305
BF	90	0.4 (0-2.1)	78	0.8 (0-3.1)	.196
SVG to RCA					
MGF	56	36 (24-75)	34	36.5 (25-49)	.303
PI	56	1.9 (1.3-2.9)	34	2.6 (1.7-3.3)	.038
DF	47	55 (47-61)	31	57 (48-62)	.339
BF	56	0.1 (0-1.1)	32	0.9 (0-2.8)	.074

Data are reported as median (interquartile range). Units: MGF, mL/min; DF, %; and BF, %. Postprotamine TTFM measurements. ONCAB, On-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass; MGF, mean graft flow; PI, pulsatility index; DF, diastolic fraction; BF, backflow; LIMA, left internal mammary artery; LAD, left anterior descending artery; RIMA, right internal mammary artery; OM, obtuse marginal; RA, radial artery; SVG, saphenous vein graft; Diag, diagonal; PDA, posterior descending artery; RCA, right coronary artery.

(no major between group differences). Of the 406 single LIMA grafts in this analysis, 4 (0.98%) were free grafts anastomosed to the aorta. Of the 62 single RIMA grafts available for analysis, 11 (17%) were free grafts. MAP during measurements was higher in the OPCAB group. MGF was higher for ONCAB versus OPCAB (32 mL/min vs 28 mL/min, respectively, for all grafts;  $P < .001$ ). This difference was more pronounced in venous than in arterial grafts (35 mL/min vs 31 mL/min [ $P = .005$ ] and 30 mL/min vs 27 mL/min [ $P = .002$ ], respectively). MGF was higher in ONCAB procedures for most conduit to target subsets taken together (apart from RIMA to LAD and SVG to RCA).

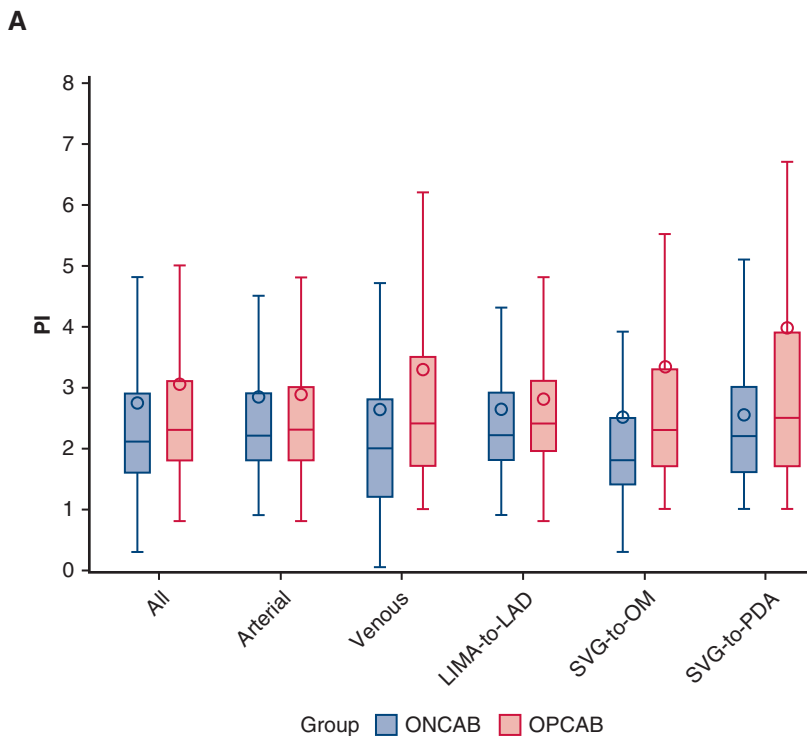
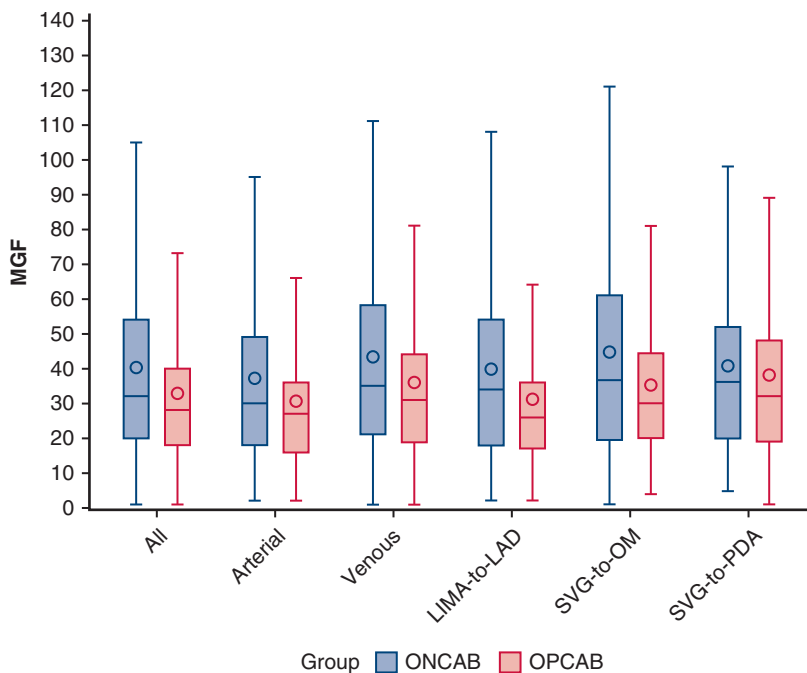
PI was lower in the ONCAB group (2.1 vs 2.3, for all grafts;  $P < .001$ ). This difference was more pronounced in venous grafts than in arterial grafts (1.9 vs 2.4 [ $P < .001$ ] and 2.2 vs 2.3 [ $P = .369$ ], respectively). DF was slightly lower in the ONCAB group than in the OPCAB group (65% vs 67.5%, respectively;  $P < .001$ ). The DF measured separately for venous and arterial grafts showed the same trend. The BF was also lower in ONCAB than in OPCAB (0.6 vs 1.3, respectively, for all grafts;  $P < .001$ ) with similar trends for venous and arterial grafts as MGF and PI (Figure 3). Regarding anastomotic revisions, there were 21 (3.3%) revisions in the OPCAB group and 14 (2.1%) in the ONCAB group ( $P = .198$ ; Table 4). In the OPCAB group, most of these revisions were for a LIMA to LAD and in the ONCAB there was a more equal distribution (Table 4). Between group comparisons of grafts that did not meet parameter thresholds showed that almost 50% of grafts had at least 1 parameter that did not reach the accepted parameter threshold (Table 5). The only parameter that was different between ONCAB and OPCAB was BF for which it was much more common for OPCAB patients to not reach the threshold (32.9% OPCAB vs 23.9% ONCAB;  $P = .006$ ). For the 2 most common threshold

parameters (ie, MGF and PI), we also checked whether grafts not reaching the thresholds were more likely to undergo revision and found no difference for the 2 groups (Table 5).

## DISCUSSION

In one of the largest multicenter cohorts existing thus far, ONCAB MGF was higher than OPCAB MGF and ONCAB PI was lower than OPCAB PI, despite consistently higher MAP values during measurement in the OPCAB patients. This finding was true for all grafts and for most coronary territories, but the difference was more pronounced in venous than in arterial grafts. The difference in MGF values ranged from no difference (RIMA to LAD and SVG to RCA) to 10 mL/min (RA to OM;  $P = .061$ ) whereas the difference in PI ranged from no difference (RIMA to OM and RIMA to LAD) to 0.5 (SVG to OM;  $P = .002$ ). These differences in MGF and PI for ONCAB and OPCAB could be an inherent characteristic of the procedures (ie, due to vasodilatation resulting from the use of cardiopulmonary bypass and the reactive hyperemia resulting from ischemic arrest) or a sign of the higher technical demands of OPCAB grafting. Regardless of the reason—this difference might have clinical implications, especially regarding MGF in venous grafts for which differences were substantial compared with the accepted cutoff value of 20 mL/min.

Previous reports have shown conflicting results regarding whether the differences in MGF and PI are inherent to the procedures themselves or a marker of the technical difficulty of OPCAB.<sup>7-11</sup> Schmitz and colleagues<sup>7</sup> reported significantly lower graft flow values in the OPCAB group but with less myocardial damage, as reflected by lower postoperative cardiac enzyme levels in the OPCAB group (896 patients, 695 ONCAB and 201 OPCAB), with a total of 2247 grafts (1952/295, respectively). They attributed the higher flow rates and the higher levels of cardiac enzymes

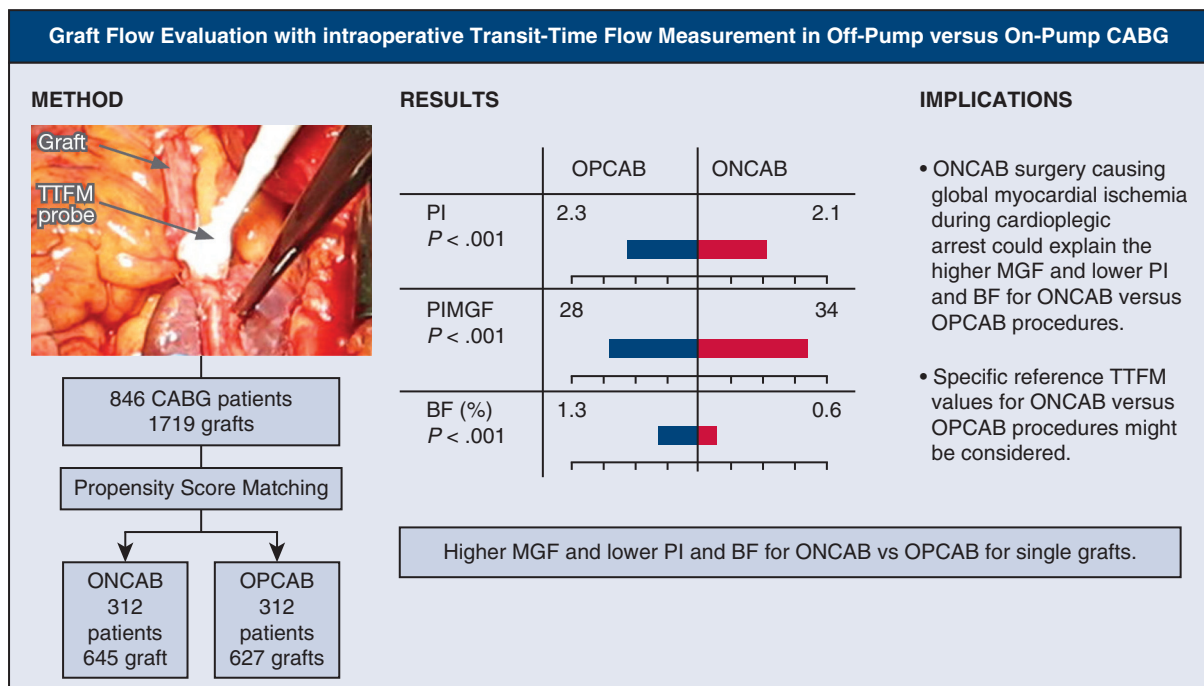


**B**

**FIGURE 2.** A, Mean graft flows and (B) pulsatility indices for on-pump coronary artery bypass (ONCAB) versus off-pump coronary artery bypass (OPCAB) in all grafts, arterial grafts, venous grafts, and according to territory: single grafts with ACI > 30. The box upper and lower limits represent the 75th and 25th quartiles, respectively. The lower and upper whiskers represent the minimum and maximum values of nonoutliers. The middle horizontal line represents the median and the circle represents the mean. Data are reported as medians. MGF, Mean graft flow; PI, pulsatility index; ACI, acoustic coupling index; LIMA, left internal mammary artery; LAD, left anterior descending; SVG, saphenous vein graft; OM, obtuse marginal; PDA, posterior descending artery.

in the ONCAB group to myocardial hyperemia in response to metabolic acidosis caused by myocardial ischemia during crossclamp application. In contrast, Kjaergard and

colleagues<sup>8</sup> reported no significant difference in graft flow values for the ONCAB and OPCAB groups after correction for flow per anastomosis; they attributed the lower total flow



**FIGURE 3.** Visual summary of main findings. CABG, Coronary artery bypass grafting; TTFM, transit-time flow measurement; OPCAB, off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; PI, pulsatility index; MGF, mean graft flow; BF, backflow.

rates in the OPCAB group to fewer total grafts (120 ONCAB, 97 OPCAB). Hassanein and colleagues<sup>9</sup> reported lower OPCAB graft flow rates and higher PI values in all myocardial territories except for the LAD territory, which had flow rates and PI values similar to the ONCAB group (445 OPCAB patients paired with 445 ONCAB with 845 bypasses in each group). They concluded that this discrepancy between the OPCAB flow rates and PI of the LAD territory and the other territories might be the result of technical reasons related to accessibility of target vessels in the lateral and posterior territories. Balacumaraswami and colleagues<sup>10</sup> reported higher MGF and a higher flow-to-pressure ratio (because MGF is dependent on MAP) for all conduits in the ONCAB group despite a significantly lower MAP (80 OPCAB patients and 20 ONCAB; 203/63 grafts, respectively). They offered 2 explanations for this finding—the aforementioned increase in coronary blood flow as a result of ischemia in ONCAB and systemic vasodilatation as a result of a more pronounced inflammatory response in the ONCAB. Last, in a more recent report, Amin and colleagues<sup>11</sup> focused on grafts to the left system, reported higher flows in arterial grafts in ONCAB versus OPCAB (with higher MGF rates measured in the arterial and the venous grafts compared with the REQUEST database). They reported no difference in PI for ONCAB and OPCAB, both in arterial and venous grafts.

In a recent meta-analysis of intraoperative graft flow profiles ONCAB versus OPCAB MGF was compared as a

secondary outcome.<sup>12</sup> The authors combined data from 8 studies with a total of 5041 grafts and reported MGF was higher in ONCAB versus OPCAB surgery with no difference in PI for the 2 procedures.

The original REQUEST study<sup>3</sup> was designed to prospectively evaluate the implementation of intraoperative graft quality assessment with TTFM and high-frequency ultrasound. It enrolled 1046 patients who underwent CABG, 30 of whom were excluded on the basis of predetermined criteria. Of the procedures, 39.6% (402/1016) were performed off-pump with a total of 1606 ONCAB grafts and 1069 OPCAB grafts. There was no difference in in-hospital mortality for the 2 groups. There was also no difference in in-hospital major cardiac and cerebrovascular events, strokes or transient ischemic attacks, myocardial infarctions, or repeat revascularizations. We retrospectively reviewed the REQUEST database to compare TTFM parameters for ONCAB versus OPCAB procedures. MGF was higher for ONCAB versus OPCAB (32 mL/min vs 28 mL/min, respectively, for all grafts; *P* < .001). This difference was more pronounced in venous than in arterial grafts (35 mL/min vs 31 mL/min [*P* = .005] and 30 mL/min vs 27 mL/min [*P* = .002], respectively). The PI was lower in the ONCAB versus the OPCAB group (2.1 vs 2.3, respectively; *P* < .001) with a more pronounced difference in the venous grafts.

Anastomotic revision rates were lower in this specific cohort (3.3% OPCAB, 2.1% ONCAB; Table 4) than in



**TABLE 4. Anastomotic revision rates and details according to group**

	OPCAB (n = 627)	ONCAB (n = 645)	P value
Revision rate	21 (3.3%)	14 (2.1%)	.20
Grafts			.29
LIMA	11	4	
RIMA	2	5	
RA	4	2	
SVG	4	3	
Target			.38
LAD	10	3	
Diagonal	N/A	1	
OM	4	5	
RCA	2	1	
PDA	5	4	
Change			.05
Distal	15	5	
Proximal	2	1	
Other	4	8	

OPCAB, Off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; LIMA, left internal mammary artery; RIMA, right internal mammary artery; RA, radial artery; SVG, saphenous vein graft; LAD, left anterior descending artery; OM, obtuse marginal; RCA, right coronary artery; PDA, posterior descending artery.

the REQUEST trial. This might stem from the fact that we used only single grafts in this analysis (in an attempt to reduce confounding) and thus less complex grafting required fewer revisions. There were more LIMA to LAD revisions in the OPCAB group, but the numbers were small, preventing comparison.

When interpreting TTFM values as threshold values (Table 5) we found that almost 50% of grafts had at least 1 parameter that did not meet parameter thresholds. Regarding revision rates for the most frequently used parameters (MGF and PI), we could not ascertain that surgeons have a different approach to cutoff values for OPCAB and ONCAB.

**CONCLUSIONS**

In our cohort, the increased MGF in ONCAB procedures did not correlate with better in-hospital clinical outcomes in the REQUEST trial. This finding is in accordance with previous studies that showed comparable postoperative angiographic patency for ONCAB and OPCAB, despite these reduced TTFM parameters.<sup>13,14</sup> It follows that the lower flow rates and higher PI values measured in OPCAB surgery could be intrinsic to the procedure. These differences probably result from the lack of ischemia (and subsequent hyperemia) in OPCAB.<sup>15</sup> If this hypothesis is true, then we must examine the clinical implications that these data might have. We need to consider for example, the higher immediate graft flow in ONCAB (especially when using venous grafts) when choosing the most appropriate surgical revascularization technique in an urgent scenario (ie, a patient in an acute myocardial infarction or in cardiogenic shock)

**TABLE 5. Grafts not reaching threshold parameters and revision rates**

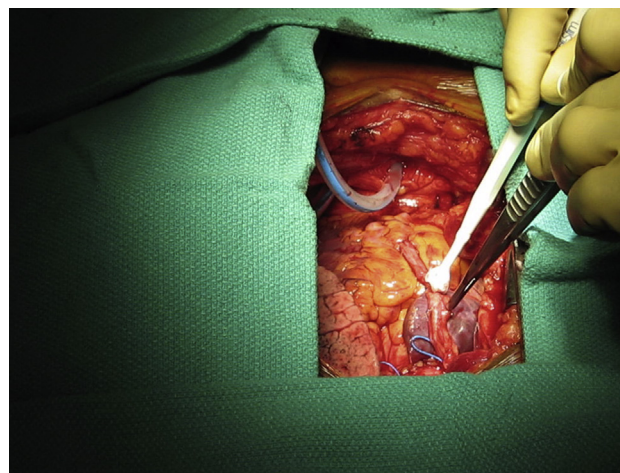
Parameter (threshold)	OPCAB, %	ONCAB, %	P value
Any abnormal parameter	298 (47.5%)	291 (45.1%)	.38
MGF (<20 mL/min)	206 (33.2%)	172 (27.1%)	.02
Revisions	11 (5.3%)	6 (3.5%)	.38
PI (>5)	41 (6.6%)	31 (4.9%)	.19
Revisions	7 (17%)	2 (6.45%)	.28
DF (<50%)	56 (9.96%)	75 (13.5%)	.06
BF (>3%)	196 (32.8%)	149 (23.9%)	.0006

OPCAB, Off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; MGF, mean graft flow; PI, pulsatility index; DF, diastolic fraction; BF, back-flow.

versus an elective CABG. Furthermore, investigation is needed to correlate off- and on-pump parameters with graft patency and determine specific, clinically significant cutoff values for each type of procedure because lower MGF might still be satisfactory in the OPCAB patient. This is especially relevant when considering that a cutoff value of MGF >20 mL/min is considered adequate and the difference in flow for OPCAB and ONCAB reached 10 mL/min in some of the grafts in our study. By tracking this change in flow for ONCAB versus OPCAB we hope to improve intraoperative decision-making in the evaluation of graft quality using TTFM (Video Abstract).

**Limitation**

The major limitation of this study stems from the lack of randomization of the patients in the REQUEST trial to ONCAB versus OPCAB. Furthermore, there was no equal distribution of OPCAB procedures performed in the various



**VIDEO 1.** Intraoperative image of a probe used to measure flow in a LIMA to LAD. Video available at: [https://www.jtcvs.org/article/S2666-2507\(22\)00274-7/fulltext](https://www.jtcvs.org/article/S2666-2507(22)00274-7/fulltext).

participating centers. As such, the differences in flow parameters in this study might have been the result of unidentified and unmeasured confounding variables for ONCAB and OPCAB patients not controlled for by PSM or the result of divergent surgical techniques of the different centers. Follow-up was limited to 30 days with no angiographic results, limiting our ability to draw clinical conclusions from our findings.

### Webcast

You can watch a Webcast of this AATS meeting presentation by going to: <https://www.aats.org/resources/1944>.

Graft Flow Evaluation with Intraoperative Transit-Time Flow Measurement in Off-Pump versus On-Pump coronary artery bypass grafting



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### Conflict of Interest Statement

D. J. Thuijs, G. Di Giammarco, D. Wendt, T. M. Kieser, A. P. Kappetein, S. J. Head, J. D. Puskas, and D. P. Taggart reported traveling support/speaking fees from Medistim. A. P. Kappetein and S. J. Head reported Medtronic employment. D. P. Taggart reported Medistim research funding, speaking, traveling honoraria, and consultant. All other authors reported no conflicts of interest.

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### References

1. Thuijs DJFM, Bekker MWA, Taggart DP, Kappetein AP, Kieser TM, Wendt D, et al. Improving coronary artery bypass grafting: a systematic review and meta-analysis on the impact of adopting transit-time flow measurement. *Eur J Cardiothorac Surg*. 2019;56:654-63.
2. Niclauss L. Techniques and standards in intraoperative graft verification by transit time flow measurement after coronary artery bypass graft surgery: a critical review. *Eur J Cardiothorac Surg*. 2017;51:26-33.
3. Taggart DP, Thuijs DJFM, Di Giammarco G, Puskas JD, Wendt D, Trachiotis GD, et al. Intraoperative transit-time flow measurement and high-frequency ultrasound assessment in coronary artery bypass grafting. *J Thorac Cardiovasc Surg*. 2020;159:1283-92.e2.
4. Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Straka Z, et al. Five-year outcomes after off-pump or on-pump coronary-artery bypass grafting. *N Engl J Med*. 2016;375:2359-68.
5. Shroyer AL, Hattler B, Wagner TH, Collins JF, Baltz JH, Quin JA, et al. Five-year outcomes after on-pump and off-pump coronary-artery bypass. *N Engl J Med*. 2017;377:623-32.
6. Chikwe J, Lee T, Itagaki S, Adams DH, Egorova NN. Long term outcomes after off-pump versus on-pump coronary artery bypass grafting by experienced surgeons. *J Am Coll Cardiol*. 2018;72:1478-86.
7. Schmitz C, Ashraf O, Schiller W, Preusse CJ, Esmailzadeh B, Likungu JA, et al. Transit time flow measurement in on-pump and off-pump coronary artery surgery. *J Thorac Cardiovasc Surg*. 2003;126:645-50.
8. Kjaergard HK, Irmukhamedov A, Christensen JB, Schmidt TA. Flow in coronary bypass conduits on-pump and off-pump. *Ann Thorac Surg*. 2004;78:2054-6.
9. Hassanein W, Albert AA, Arnrich B, Walter J, Ennker IC, Rosendahl U, et al. Intraoperative transit time flow measurement: off-pump versus on-pump coronary artery bypass. *Ann Thorac Surg*. 2005;80:2155-61.
10. Balacumaraswami L, Abu-Omar Y, Selvanayagam J, Pigott D, Taggart DP. The effects of on-pump and off-pump coronary artery bypass grafting on intraoperative graft flow in arterial and venous conduits defined by a flow/pressure ratio. *J Thorac Cardiovasc Surg*. 2008;135:533-9.
11. Amin S, Madsen PL, Werner RS, Krasopoulos G, Taggart DP. Intraoperative flow profiles of arterial and venous bypass grafts to the left coronary territory. *Eur J Cardiothorac Surg*. 2019;56:64-71.
12. Silva M, Rong LQ, Naik A, Rahouma M, Hameed I, Robinson B, et al. Intraoperative graft flow profiles in coronary artery bypass surgery: a meta-analysis. *J Card Surg*. 2020;35:279-85.
13. Puskas JD, Williams WH, Mahoney EM, Huber PR, Block PC, Duke PG, et al. Off-pump vs conventional coronary artery bypass grafting: early and 1-year graft patency, cost, and quality-of-life outcomes: a randomized trial. *JAMA*. 2004;291:1841-9.
14. Lingaas PS, Hol PK, Lundblad R, Rein KA, Mathisen L, Smith HJ, et al. Clinical and radiologic outcome of off-pump coronary surgery at 12 months follow-up: a prospective randomized trial. *Ann Thorac Surg*. 2006;81:2089-95.
15. Jin XY, Gibson DG, Pepper JR. The effects of cardioplegia on coronary pressure-flow velocity relationships during aortic valve replacement. *Eur J Cardiothorac Surg*. 1999;16:324-30.

**Key Words:** coronary artery bypass grafting, on-pump coronary artery bypass grafting, off-pump coronary artery bypass grafting, transit-time flow measurement, flow

### Discussion

#### Presenter: Dr Dror Ben Leviner



**Dr George Tolis** (*Boston, Mass*). Congratulations on your presentation, and thank you very much for making the paper available about 2 months ago so I had plenty of time to review it. I have a disclosure. I started doing off-pump in 2002, and I was doing about 95%, and now I do about 99% on-pump. So, that's my disclosure before I start your discussion. And the main reason I did that was basically 3 reasons. When I would see a LAD and I could see the apical LAD very well but the more proximal LAD was hidden under fat and so on and so forth, I just didn't want to deal with cutting the fat and digging inside the muscle, so I would put the tip of the LIMA to the apical LAD.

When someone had a very tight [inaudible], I would not want to isolate the RCA because that's when all the V-tach starts and you've got to start pacing, and then you chase the vessel down toward the cava, so I would just lift the apex and put the vessel on the PDA. And then when there was a nice juicy ramus right next to the left atrial appendage, it was really difficult to do that and push the appendage out of the way, so I would always graft the OM after 1 or 2 bifurcations closer to the apex.

The point I'm trying to make is that even if you're an excellent technical surgeon, on off-pump, you have to graft

further distally than you do when you do an operation on-pump. You can do a great job with a more distal vessel and the op note reads exactly the same, but I'm not sure the operation is exactly the same.

My question to you is—there's 2 questions that I have for you, and the first one is do you really think that what you've shown here with the statistics is that on-pump surgeons graft their vessels more proximally than off-pump surgeons? And two, in terms of the propensity analysis that you did, are you sure that you're comparing apples to apples? Because like you said, this is not a randomized sample, and I'm not sure that you can take into account patients that someone wanted to do an off-pump and when they saw that the vessels were smaller, they can't isolate them well, they didn't convert, but just decided to change their intent to treat into an on-pump because if that's the case, then that would tilt more toward the favor of off-pump because you're grafting smaller vessels by definition when you're doing on-pump. So, these are my 2 questions but again, congratulations on your talk.



**Dr Dror Ben Leviner** (*Haifa, Israel*).

Thank you, and thank you for the thoughtful questions. So, regarding your first question, I don't know. And as you said, the op notes and for this matter, the Excel tables with all the data don't say where the graft was done. So, distal—unless of course, we have data on grafts or to the RCA itself. I can't remember off the top of my head what the differences were for RCA on- and off-pump. But I can answer what I think the main question is, and there are people here who can answer that much better than I do, and this goes back to Dr Taggart's comment. Should we be grafting very distal or should we be grafting proximal even if the disease isn't proximal? I definitely don't know the answer and there's much smarter people than me in the room because what we say, CABG is better because we graft distal, and no matter how much progression of disease there is, we still get that disease. So, I don't know what the answer is to that.

**Dr David P. Taggart** (*Oxford, United Kingdom*). If I could just add before we move on to another question, so the specific question you asked regarding the difference in flows and on-pump and off-pump, at my practice, we rarely are in a situation where we're grafting very proximal. We graft in the same place whether it's on-pump or off-pump. We don't make a choice. But what we did show and publish in JTCVS—I think it was in 2005—we look at this very question, and we introduced what we called a flow pressure ratio. So, the most important determination of [inaudible] graft is watch your blood pressure, and what we showed was when a patient had been done on-pump, they came off bypass with a relatively lower blood pressure than the off-pump patients but with far higher flows in the arterial

and the venous grafts, and we believe this was an ischemia-reperfusion thing. By having made the territory ischemic, when you reperfused it, you got a higher natural flow. So, that is still my interpretation of what these data show.

**Dr Tolis**. The numbers are great for both. I mean, if I had these PIs finishing a case, it really wouldn't matter, so I'm not entirely sure I see the clinical significance of your findings.

**Dr Leviner**. So, just to answer your question regarding—so, I think if I remember correctly, this was done in 7 centers, and most centers were either heavily toward off-pump or heavily toward on-pump, either/or. There was not that much variation in between the centers themselves—in the centers themselves. I have to admit—this is a confession—I am not sure that propensity score matching this way is the correct way to correct for the differences, but reviewer 2 thought that we should do propensity score matching, so we went ahead and did propensity score matching.

Was there anything else? I missed something.

**Unidentified Speaker 2**. [inaudible] from Texas. I have a simple question. Did you see, regardless on-pump or off-pump, see on the degree of coronary stenosis? Because I think in the general practice, that this depends what you measure with the TTFM because if you have low degrees, especially in the left main stenosis, 50% to 60%, you have a very different measurement. Did you see on the degree of the stenosis? That's a very important thing.

**Dr Leviner**. I did not have those data. I'm not sure if the request registry had it?

**Dr Taggart**. We didn't, no.

**Dr Leviner**. We didn't. And just there was I think another comment—and this, again, came up in the reviews many times—what's the clinical significance? So, I think we have to think of this in the context of the other data. Some of our grafts, there was more than 10 mL/min. Not all of the grafts, not on average, but there was more than 10 mL/min difference. Some other studies like the one I showed from JTCVS, there was, for some grafts, almost 20 mL/min difference. And when the cutoff value is set to 15 or 20 and there's a 10 mL difference on average, you have to think if this is relevant. I know you can, this is just statistics, but I think it has some relevance.

**Unidentified Speaker 2**. Thank you.

**Unidentified Speaker 3**. This is [inaudible] from Tokyo. In Japan, we perform average percent of the [inaudible] is nearly 60% and the [inaudible] from measurement is routine procedure in Japan because the government insurance, complete reimbursement for the [inaudible] measurement, and so we have lots of experience of [inaudible] measurement, especially in [inaudible] cases. And my question is, the flow after [inaudible] procedure, it changes

because right after the anastomosis, I always observe a better flow in case of the [inaudible] because [inaudible], as Dr [inaudible] said, hyperemia eruption. But so, I measure 3 times during the operation, immediately after the anastomosis, and then finally, before I close the chest, then the flow always decreases. So, I think that this kind of a study, the important point is what time, in which occasion you measure the [inaudible] flow for the patient? So, the timing is a very important factor to compare the flow in this kind of study, so that's my question.

**Dr Leviner.** I agree. For this study, we used only post-protamine measurements. I'm not sure. We didn't have in the database exactly when during the procedure this was done, but assuming postprotamine when you're very close to closing the chest. And by the way, we had another publication, another subanalysis from the REQUEST trial that

looked at that question; is there a difference between pre- and postprotamine measurements, and we found no such difference. But I agree, and blood pressure variations affect this hugely, so it really does matter when you measure.

**Dr Taggart.** Final comment. Thank you. I don't think these flows are relevant between on-pump and off-pump because they're so variable. If you've got a flow of 0, you've got a problem whether you are on-pump or off-pump, but the amount of difference flow can make by just changing the blood pressure by 20 mm Hg, you can double the phonograph. So, if you take in all of these variables—I mean, the importance of this technique is really making sure you don't have a graft with no flow or variable flow because then, you have a problem. So, on that point, thank you. We're now going to go on.