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

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Objective: Despite profound differences in the neurohumoral milieu in patients undergoing on-pump and off-pump coronary artery bypass grafting, it is uncertain how this affects graft blood flow.

Methods: We prospectively recorded intraoperative transit-time flow measurements (MediStim BF 2004; MediStim AS, Oslo, Norway) in all internal thoracic artery, radial artery, and long saphenous vein conduits in patients undergoing off-pump and on-pump bypass grafting by a single surgeon. We calculated a flow/pressure ratio as a ratio of mean graft flow to mean arterial pressure for all the conduits just before chest closure.

Results: Transit-time flow measurements were recorded in 266 grafts (203 off-pump; 63 on-pump) in 100 patients (80 off-pump; 20 on-pump). Overall, mean graft flow (milliliters per minute) was higher for all grafts in the on-pump group despite a significantly lower mean arterial pressure compared with the off-pump group ($P < .05$). Consequently the flow/pressure ratio was greater for all grafts in the on-pump group (internal thoracic artery 0.55 vs 0.35, radial artery 0.61 vs 0.36, long saphenous vein 0.77 vs 0.55). Overall mean graft flow was significantly greater in the long saphenous vein than in the internal thoracic artery ($P < .001$) and radial artery ($P = .001$), but there was no significant difference in mean graft flow in internal thoracic artery or radial artery grafts within each group.

Conclusions: In comparison with the off-pump group, the overall mean graft flow and flow/pressure ratio were significantly higher and mean arterial pressure significantly lower for all grafts in the on-pump group. These findings are probably a result of vasodilatation resulting from cardiopulmonary bypass and reactive hyperemia resulting from a period of ischemia. There was no difference in the mean graft flow and flow/pressure ratio of arterial grafts, which were significantly less than for long saphenous vein grafts. In patients with unstable angina and/or hemodynamic instability, in whom rapid and maximum restoration of myocardial perfusion is a priority, potentially lower graft flow in arterial grafts and off-pump surgery should be considered.

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The need to assess intraoperative graft flow to detect and correct graft failure is supported by several studies.¹⁻⁵ In a recent prospective study, we⁶ reported that routine intraoperative assessment of graft patency identified a low but well-defined incidence of graft failure. There are concerns that graft failure rate may be even higher with the use of arterial conduits^{7,8} and off-pump coronary artery bypass grafting (OPCABG).⁹

Several studies have addressed the differing effects of on-pump CABG (ON-CABG) and OPCABG on intraoperative⁶ and postoperative¹⁰⁻¹⁶ graft patency rates (Table 1), with conflicting results, but few have specifically addressed the effects of these alternative surgical approaches on intraoperative graft flow rates.

Transit-time flowmetry (TTFM) is the most commonly used intraoperative technique for assessing graft patency.¹ TTFM measures mean graft flow (MGF) in

Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
FPR	= flow/pressure ratio
ITA	= internal thoracic artery
LSV	= long saphenous vein
MAP	= mean arterial pressure
MGF	= mean graft flow
ONCABG	= on-pump coronary artery bypass grafting
OPCABG	= off-pump coronary artery bypass grafting
RA	= radial artery
TTFM	= transit-time flowmetry

addition to providing a flow waveform and derived values such as a pulsatility index. Although TTFM has been used to assess intraoperative graft flow, there are conflicting reports in the literature regarding MGF in OPCABG and ONCABG.¹⁷⁻¹⁹ Crucially, these data do not take into account the key issue of the effects of mean arterial pressure (MAP) when measuring MGF. Consequently, we prospectively measured TTFM-defined graft flow in a consecutive series of 100 CABG patients undergoing both on-pump and off-pump surgery. Uniquely, to account for the effects of MAP on graft flow, we calculated a flow/pressure ratio (FPR) as a ratio of MGF to MAP for all conduits just before chest closure.

Patients and Methods**Study Approval**

This study was approved by the Oxfordshire research ethics committee (number CO2.233) and written informed consent was provided by all patients.

Patients

The patients in this study have previously been included in a prospective trial of TTFM and intraoperative fluorescence imaging for comparing graft patency,²⁰ but graft flows were not reported.

In brief, all patients undergoing CABG performed by a single surgeon (D.P.T.) between April 2003 and January 2004 were included in the study with the exception of a few cases in which the equipment was not available. The demographic data and the preoperative risk profile for both groups are detailed in Table 2. Off-pump total arterial grafting was performed whenever practical and feasible. In general, ONCABG was used in patients with poor left ventricular function (ejection fraction < 25%). Likewise, there was a higher use of vein grafts rather than radial artery (RA) grafts in patients with poor left ventricular function because of the higher likelihood of need for inotropic support.

Surgical Technique

All patients underwent CABG via a median sternotomy. Both internal thoracic arteries (ITAs) were harvested as skeletonized conduits. The skeletonized ITA was bathed in a swab containing topical papaverine. The RA was harvested and stored in heparinized blood containing phenoxybenzamine in the earlier patients²¹ and additional verapamil in the later patients before performing the anastomosis. The long saphenous vein (LSV) was harvested by a minimally invasive technique. Our principal surgical strategy for construction of the anastomosis and conduct of the procedure in both ONCABG and OPCABG techniques has been described previously.⁶ Some of the later patients in the ONCABG group with poor ventricular function were operated on with cardiopulmonary bypass but on a beating heart without the use of an aortic crossclamp to avoid any ischemic period.

Data Collection

The technique for use of TTFM has been described by D'Ancona and colleagues.¹ In brief, the TTFM Quickfit flow probes (MediStim AS, Oslo, Norway) were sterilized in Tristel sterilizing solution (The Tristel Company, Snailwell, United Kingdom) and prepared for intraoperative use. Patient data were entered into the MediStim BF 2004 flowmeter (MediStim AS), and real-time electrocardiographic and MAP data were directly displayed on the flowmeter. Ultrasound gel was applied to the flow probe lumen before positioning it on the graft such that the graft occupied at least 75% of the flow probe lumen. Simultaneous MGF, pulsatility index, and MAP data were collected before chest closure. To allow for the effect of dynamic

TABLE 1. Reports of postoperative angiographic graft patency in arterial and venous conduits in randomized controlled trials of OPCABG and ONCABG

Study and year	Overall patients enrolled (n)			Time to angiography (% undergoing angiography)	Graft patency (%)					
	Total	OPCABG	ONCABG		OPCABG			ONCABG		
					Overall	A	V	Overall	A	V
Nathoe 2003 ¹⁰	281	142	139	12 mo (64)	91	—	—	93	—	—
Widimsky 2004 ¹¹	400	208	192	12 mo (64)	70	91	49	74	91	59
Khan 2004 ¹²	103	54	49	3 mo (80)	91	92 (ITA) 76 (RA)	91	97	100 (ITA) 100 (RA)	95
Puskas 2004 ¹³	197	98	99	12 mo (78)	94	94	93	96	98	94
Kobayashi 2005 ¹⁴	167	81	86	3 wk (100)	93	93 (ITA) 95 (RA)	94	96	94 (ITA) 99 (RA)	100
Al-Ruzzeh 2006 ¹⁵	168	84	84	3 mo (90)	93	98 (ITA) 91 (RA)	82	94	97(ITA) 88 (RA)	88
Lingaas 2006 ¹⁶	120	60	60	12 mo (91)	85	94	80	90	96	87

OPCABG, Off-pump CABG; ONCABG, on-pump CABG; A, arterial; V, venous; ITA, internal thoracic artery; RA radial artery.

TABLE 2. Demographic data and preoperative risk profile for both groups

Variable	OPCABG	ONCABG	P value
Total	80	20	
Age (mean $\pm$ SD)	66 $\pm$ 9	68 $\pm$ 8	NS
Body mass index (mean $\pm$ SD)	28 $\pm$ 4	29 $\pm$ 4	NS
Smoker	45 (56%)	6 (30%)	<0.05
Diabetes mellitus	10 (13%)	2 (10%)	NS
Hypertension	45 (56%)	8 (40%)	NS
Hyperlipidemia	31 (39%)	8 (40%)	NS
Prior Q wave MI	15 (19%)	8 (40%)	0.04
EF < 50%	22 (28%)	17 (85%)	<0.01
Triple vessel disease	55 (69%)	14 (70%)	NS
NYHA class III/IV	27 (34%)	13 (65%)	0.01
CCS class III/IV	32 (40%)	11 (55%)	NS
Serum creatinine > 200 mmol/L	5 (6.3%)	2 (10%)	NS
CVA or TIA	9 (11%)	2 (10%)	NS
Peripheral vascular disease	7 (9%)	5 (25%)	0.05
Logistic EuroSCORE (mean $\pm$ SD)	3.2 $\pm$ 2.4	6.9 $\pm$ 3.6	<0.001

OPCABG, off-pump CABG; ONCABG, on-pump CABG; MI, myocardial infarction; EF, ejection fraction; NYHA, New York Heart Association; CCS, Canadian Cardiovascular Score; CVA, cerebrovascular accident; TIA, transient ischemic attack; NS, not significant.

variation in MAP on MGF, we devised the FPR. The FPR was calculated as an average of the ratio of MGF to MAP for each of the ITA, RA, and LSV conduit groups.

Statistical Analysis

Results for categorical variables are expressed as number (percent of total). Continuous variables are presented as mean $\pm$ standard deviation. The χ^2 test was used for comparison of categorical variables. The continuous variables were compared by the Student *t* test. Bonferroni correction was used for multiple comparisons. Nonparametric data were compared with the Mann–Whitney *U* test.

Results

Patient Groups

Of 100 CABG patients receiving 266 grafts, there were 80 OPCABG patients (receiving 203 grafts) and 20 ONCABG patients (receiving 63 grafts). The ONCABG group included 3 patients with simultaneous aortic valve replacement.

Distal Anastomoses

The mean number of distal anastomoses was 2.7 per patient, being 3.4 per patient for the ONCABG group and 2.5 per patient for the OPCABG group. The OPCABG group, however, had a higher proportion of patients with single or double vessel disease, and in patients with triple vessel disease the mean number of grafts for OPCABG and ONCABG groups was similar (OPCABG 3.2 $\pm$ 0.4 and ONCABG 3.4 $\pm$ 0.6).

Configuration of Conduits (Figure 1)

Of the 203 grafts in the 80 OPCABG patients, there were 126 ITA (62%), 44 RA (22%), and 33 LSV (16%). Of these 80 OPCABG patients, 55 (69%) had total arterial grafting, 46 had use of bilateral ITAs (58%), and 31 (39%) had composite arterial grafting. Of the 63 grafts in the 20 ONCABG patients, there were 22 ITAs (35%), 4 RAs (5%) and 37 LSVs (59%). Of these 20 ONCABG patients, 2 (10%) had total arterial grafting, 3 (15%) had use of bilateral ITAs, and none had composite arterial grafting. Although all patients in the study received at least 1 ITA graft, there were significantly more LSV grafts and significantly fewer RA grafts in the ONCABG group. The use of arterial grafts was significantly less in the ONCABG group, as a result of a majority of patients in this group having poor ventricular function and an increased likelihood of requiring inotropic support.

Overall Graft Flows (Table 3)

In comparison with the OPCABG group, the absolute MGF was approximately 30% higher for the ITA, RA, and LSV in the ONCABG group despite a lower MAP ($P < .05$). Consequently, when considering the MGF relative to MAP, the FPR was greater in the ONCABG group for all conduits, being 57% for the ITA ($P = .001$), 69% for the RA ($P = .13$

Figure 1. The flow diagram shows the configuration of conduits used in both on-pump (ONCABG) and off-pump coronary artery bypass grafting (OPCABG) groups. ITA, Internal thoracic artery group; RA, radial artery group; LSV, long saphenous vein group.

TABLE 3. Mean graft flow, mean arterial pressure, and flow/pressure ratios for all conduits in OPCABG and ONCABG groups

	ITA	RA	LSV	<i>P</i> value, ITA vs LSV	<i>P</i> value, RA vs LSV
Total					
No. of grafts	148	48	70		
Mean (SD) graft flow	29 (21)	31 (21)	47 (31)	<.001*	.001*
Mean (SD) arterial pressure	78 (14)	79 (15)	72 (12)	.001*	<.005*
Flow/pressure ratio	0.37	0.39	0.65	<.001*	<.001*
OPCABG					
No. of grafts	126	44	33		
Mean (SD) graft flow	28 (19)	31 (22)	41 (30)	.007*	.08
Mean (SD) arterial pressure	79 (14)	80 (15)	76 (14)	.25	.17
Flow/pressure ratio	0.35	0.36	0.55	<.01*	.04*
ONCABG					
No. of grafts	22	4	37		
Mean (SD) graft flow	37 (29)	40 (21)	52 (32)	.06	.5
Mean (SD) arterial pressure	70 (12)	64 (10)	69 (10)	.5	.5
Flow/pressure ratio	0.55	0.61	0.77	<.01*	.36
<i>P</i> value OPCABG vs ONCABG					
Mean graft flow	.2	.4	.04		
Mean arterial pressure	.01*	.08	.02*		
Flow/pressure ratio	.001*	.13	.03*		

OPCABG, Off-pump CABG; ONCABG, on-pump CABG; flow/pressure ratio, average of ratio obtained by dividing mean graft flow and mean arterial pressure for each of the conduits; ITA, internal thoracic artery; RA, radial artery; LSV, long saphenous vein. *Statistically significant.

because of small numbers), and 40% for the LSV ($P < .05$). Flows in the proximal limbs of composite grafts were analyzed separately.

ITA, RA, and LSV Graft Flows (Table 3)

Overall flow was similar for both the ITA and RA within each group despite being placed to different territories (ITA predominantly to left anterior descending and RA predominantly to posterior descending artery). In contrast, graft flow in the LSV conduits was around 30% higher than in ITA or RA conduits in both the ONCABG and OPCABG groups, despite similar MAPs for the various conduits within each group.

Composite Graft Flows (Table 4)

Overall, 148 ITA conduits (98 LITA and 50 RITA) were used to construct distal anastomoses in 100 patients. Using 98 LITA conduits, 77 simple grafts and 21 composite grafts were performed in 98 patients. A total of 50 RITA conduits were used to construct grafts to the left anterior descending artery in 41 patients and composite grafts in 9 patients. Collectively, when comparing flow in simple ITA grafts and the proximal limb of composite ITA grafts, the absolute MGF was around one third greater in the latter ($P = .07$). Consequently, because the MAP was very similar for the simple and composite groups, the FPR was also around one third greater in the composite group ($P = .03$).

Distribution and Graft Flows in RA and LSV (Tables 5 and 6)

The distribution of coronary grafts performed with LSV and RA conduits is detailed in Table 5. When comparing graft flow in LSV and RA conduits performed exclusively to the obtuse marginal and posterior descending artery branches, we observed that the FPR was higher in LSV conduits to both coronary arteries (LSV to obtuse marginal $P < .05$) (Table 6). However the MGF, MAP, and FPR for RA grafts placed to the obtuse marginal or posterior descending arteries

TABLE 4. Mean graft flow, mean arterial pressure, and flow/pressure ratios for internal thoracic artery conduits in all patients

Configuration of ITA graft	No. of grafts	MGF (mL/min), mean (SD)		MAP (mm Hg), mean (SD)		FPR	
Simple							
LITA-LAD	36	30 (21)	28 (14)	77 (12)	76 (11)	0.37	0.35
LITA-OM	41		24 (18)		77 (14)		0.32
RITA-LAD	41		35 (27)		78 (12)		0.42
Composite							
Proximal limb LITA Y-graft	21	39 (20)	34 (19)	79 (14)	77 (14)	0.48	0.43
Proximal limb RITA Y-graft	9		48 (21)		82 (14)		0.59
<i>P</i> value, simple vs composite		.07		.6		.03*	
<i>p</i> value, LITA-LAD vs RITA-LAD			.4		.3		.4

RITA, Right internal thoracic artery; LITA, left internal thoracic artery; MGF, mean graft flow; MAP, mean arterial pressure; FPR, flow/pressure ratio (average of ratio obtained by dividing mean graft flow and mean arterial pressure for each of the conduits). *Statistically significant.

TABLE 5. Distribution of coronary arteries grafted using long saphenous vein and radial artery conduits

Conduits (No.)	PDA	OM	RCA	DA	IM	LAD	LVBR
LSV (70)	24	21	11	7	1	4	2
RA (48)	20	7	3	10	6	2	—

LSV, Long saphenous vein; RA, radial artery; PDA, posterior descending artery; OM, obtuse marginal branch of circumflex artery; RCA, right coronary artery; DA, diagonal artery; IM, intermediate artery; LAD, left anterior descending artery; LVBR, left ventricular branch of right coronary artery.

were very similar as most were done as OPCABG. In contrast, MGF in LSVs placed to the obtuse marginal branch was around 16% higher than when placed to the posterior descending artery despite similar MAPs (as expected because most were ONCABG cases).

Discussion

This prospective study using TTFM provides detailed intraoperative information with simultaneous recording of MGF and MAP for all arterial and venous conduits in patients undergoing ONCABG and OPCABG. To date, three studies have reported TTFM flow values in OPCABG and ONCABG as summarized in Table 7. Schmitz and colleagues¹⁷ reported significantly lower graft flow values in the OPCABG group whereas Kjaergard and colleagues¹⁸

TABLE 6. Mean graft flow, mean arterial pressure, and flow/pressure ratios for long saphenous vein and radial artery conduits anastomosed to obtuse marginal and posterior descending arteries in both groups

Conduits (No)	Obtuse marginal artery (OM)	Posterior descending artery (PDA)	P value, OM vs PDA FPR
Radial artery (RA) (27)	n = 7 MGF = 34 (17) MAP = 81 (13) FPR = 0.43	n = 20 MGF = 36 (24) MAP = 80 (15) FPR = 0.44	.86
Long saphenous vein (LSV) (45)	n = 21 MGF = 59 (41) MAP = 72 (12) FPR = 0.83	n = 24 MGF = 51 (33) MAP = 73 (11) FPR = 0.70	.27
P value, RA vs LSV (FPR)	.04*	.1	
P value, RA vs LSV (MGF)	.1	.2	
P value, RA vs LSV (MAP)	.07	.1	

MGF, Mean graft flow; MAP, mean arterial pressure; FPR, flow/pressure ratio (average of ratio obtained by dividing mean graft flow and mean arterial pressure for each of the conduits).

reported no significant difference in graft flow between ONCABG and OPCABG groups but consistently lower MGF in women. Hassanein and colleagues¹⁹ reported lower OPCABG graft flow rates with the exception of the left anterior descending territory, which had flows similar to the ONCABG group. They concluded that this may be the result of technical reasons related to accessibility of target vessels in the lateral and posterior territories.

Although these recent studies compared conduit flow in both groups, they did not incorporate the effect of MAP on MGF. Except at extremes of systemic arterial pressures (which are uncommonly seen in clinical situations), MGF is directly proportional to MAP when coronary vascular resistance is unaltered. To understand graft flow in ONCABG and OPCABG, we devised the FPR to reflect the association between MGF and MAP.

Our study demonstrates that MGF and FPR were higher for all conduits in the ONCABG group despite a significantly lower MAP. In addition, the MGF and FPR were higher in LSV conduits when compared with ITA and RA conduits in both OPCABG and ONCABG groups, even for the same MAP, whereas the MGF for ITA and RA was similar within each group for the same MAP (Table 3).

There are two possible explanations for a higher MGF in the ONCABG group despite a lower MAP.

1. Systemic vasodilatation owing to a more pronounced systemic inflammatory response syndrome, from the increased release of immune mediators such as C3a and C5a, granulocyte elastase, and interleukins 1 and 6^{22,23} when compared with OPCABG.
2. The phenomenon of increased coronary blood flow associated with a fall in coronary vascular resistance may be attributed to reactive hyperemia in the microvascular bed after release of the aortic crossclamp. This may be similar to increased coronary flow velocity measured after discontinuing cardiopulmonary bypass in patients undergoing aortic valve replacement.²⁴

When ITA graft flow was analyzed, higher MGF and FPR were seen in the proximal limb of composite ITA grafts compared with simple ITA grafts. This possibly reflects the adaptive response of ITA grafts to increase their flow in response to myocardial demand when supplying a larger vascular bed. Likewise, marginally higher MGF and FPR were observed in the ITA to the left anterior descending compared with ITA to the obtuse marginal branch of the circumflex artery. This may be similarly attributed to an increased flow into a larger myocardial territory supplied by the left anterior descending artery (Table 4).

The FPRs for LSV grafts to the posterior descending and obtuse marginal coronary arteries were higher compared with those of RA grafts to the same territories (Table 6). Assuming the same myocardial territory being supplied by the arterial or LSV conduits, higher MGF and FPR in the LSV group may

TABLE 7. Review of studies comparing TTFM flow values in OPCABG and ONCABG groups

Article	Study type	No. of patients			MAP	MGF	MGF for composite arterial grafting	Flow rates in OPCABG and ONCABG
		Total	OPCABG	ONCABG				
Schmitz 2003 ¹⁷	Retrospective	896	201	695	—	Yes	No	Lower flows in OPCABG
Kjaergard 2004 ¹⁸	Retrospective	217	97	120	—	Yes	No	Similar flows in both groups
Hassanein 2005 ¹⁹	Retrospective	890	445	445 (case-matched)	—	Yes	No	Lower flows in OPCABG except in the LAD territory

MGF, Mean graft flow; MAP, mean arterial pressure; TTFM, transit-time flowmetry; OPCABG, off-pump coronary artery bypass grafting; ONCABG, on-pump coronary artery bypass grafting.

be simply explained by its larger diameter. The potential of venous grafts to increase the quantity of blood flow in response to myocardial oxygen demand may be of value in the perioperative period, especially in the presence of a pre-existing ischemic substrate. This observation corroborates the need to be aware of the possibility of lower graft flows in patients undergoing OPCABG with arterial grafts and especially in the situation of emergency revascularization, when rapid restoration of maximum myocardial blood supply is a priority.

Interestingly, revascularization with arterial grafts (particularly ITA to left anterior descending), although providing reduced immediate blood flow when compared with LSV grafts, does not appear to adversely affect long-term graft patency.²⁵ Similarly, when compared with ONCABG, even though OPCABG has reduced immediate graft flow, it has comparable postoperative angiographic patency¹⁴⁻¹⁶ and midterm to long-term survival.²⁶ These observations demonstrate that lower graft flow measured intraoperatively does not necessarily reflect reduced long-term graft patency, whereas, as discussed earlier, a higher immediate graft flow may be of significant value when revascularizing patients with unstable angina.

Limitations

This is an observational study comprising a low number of patients in the ONCABG group, with a consequent reduction in the number of RA conduits used in this group. Inasmuch as the two groups are unequal and not randomized, there may have been a selection bias that could influence the study outcome. This study only describes graft flows in the operating room; hence the results obtained may not necessarily reflect the long-term flow rates in either group.

Conclusions

In comparison with the OPCABG group, the overall MGFs and FPRs were significantly higher and MAPs significantly lower for all grafts in the ONCABG group. These findings are probably a result of vasodilatation owing to cardiopulmo-

nary bypass and reactive hyperemia owing to a period of ischemia. There was no difference in the MGF and FPR of arterial grafts, which were significantly less than for LSV grafts. In patients with unstable angina and/or hemodynamic instability, in whom rapid and maximum restoration of myocardial perfusion is a priority, *potentially* lower graft flow in arterial grafts and OPCABG surgery should be considered.

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