

Graft Flow Unaffected by Full Occlusion of Left Anterior Descending Artery during Coronary Artery Bypass Grafting in a Porcine Model

Gustav Nils Johannes Torstensson, Thomas Lee Torp, Nader Rasuli-Oskuii, Bo Juel Kjeldsen

Department of Cardiothoracic Surgery, Odense University Hospital, Odense, Denmark

ABSTRACT

Background: We investigated in a porcine model whether measuring both the flow distal to an anastomosis and the graft transit time flow (TTF) gives a more accurate picture of the true blood flow in the left anterior descending artery (LAD) than graft TTF measurement alone.

Methods: We performed off-pump coronary artery bypass grafting (CABG)—left internal mammary artery (LIMA) to the LAD—on 5 Yorkshire-Landrace pigs. Snares were placed both proximal and distal to the anastomosis. Flow was measured with ultrasound and TTF. This was carried out on the LIMA and at 2 locations on the LAD. Measurements were performed at the following times: baseline, during proximal snaring, after proximal snare loosening, during distal snaring, after distal snare loosening, and during both proximal and distal snaring.

Results: During distal snaring, the TTF dropped ($P = .047$), and the pulsatile index (PI) increased ($P = .025$), while the ultrasound flow in the LAD dropped ($P = .002$). During proximal and distal snaring, the ultrasound flow dropped ($P = .005$), but the TTF value did not change significantly, compared with baseline.

Conclusion: A high flow and a low PI were seen in the graft, both proximal and distal to the anastomosis, despite a fully occluded LAD. This result suggests that graft TTF measurement alone is not sufficient when performing CABG, and measurement of flow distal to the anastomosis is also necessary to determine the true blood flow in the LAD.

INTRODUCTION

The choice between coronary artery bypass grafting (CABG) and percutaneous coronary intervention for treatment of ischemic heart disease is especially dependent on the severity and extent of disease [Serruys 2009; Cohen 2001].

During CABG, it is challenging to judge the quality of the graft flow and the newly established reperfusion of the affected myocardium. CABG can be performed with either the more common and well-validated conventional CABG involving the use of cardiopulmonary bypass, or by off-pump CABG (OPCAB), which may reduce postoperative morbidity by avoiding cardiopulmonary bypass. However, the DOORS study showed that OPCAB is equal to conventional CABG with respect to surgical safety for short to intermediate follow-up times [Houliind 2012].

Several methods, such as transit time flow (TTF) measurement, ultrasound, Doppler, and visible light spectroscopy, have been proposed for controlling the quality of grafts during CABG surgery [Ricci 1999; Budde 2006; D'Ancona 2008; Ho 2009; Tsirikos Karapanos 2011]. Arterial grafts, usually the internal mammary artery, have a longer durability than venous grafts (v. saphena magna) [Loop 1986; Sabik 2005; Walpoth 2008]. TTF measurement of the graft is widely used because of its simplicity and ease of use, but TTF measurement may fail to detect a distal stenosis and/or unintentional errors during surgery. Repeat CABG is necessary in 6% of all CABG cases, and 13% of patients who have undergone OPCAB have required reoperation [Petersen 2005]. Although these percentages are based on reoperation for all causes, the incidence of graft failure appears to be as high as 3% [Thielmann 2006; Laflamme 2012]. Consequently, an improved method for evaluating the graft may reduce the number of reoperations.

The aim of this study was to determine in a porcine model whether measuring both the flow distal to an anastomosis and the graft TTF gives a more accurate picture of the true blood flow in the left anterior descending coronary artery (LAD) than graft TTF measurement alone.

MATERIALS AND METHODS

Premedication and Anesthesia

Five Yorkshire-Landrace pigs weighing 65.4 to 73.7 kg were used. Premedication consisted of a solution containing 250 mg tiletamine and zolazepam (Zoletil 50, veterinary; Virbac Animal Health, Forth Worth, TX, USA), 6.25 mL xylazine (20 mg/mL Rompun, veterinary; Bayer Animal Health,

G. N. J. Torstensson and T. L. Torp contributed equally to this study.

Received October 3, 2012; accepted March 29, 2013.

Correspondence: Gustav Nils Johannes Torstensson, Skibbusvej 11, 5000 Odense, Denmark; 4528249907 or 46704050116 (e-mail: gustav@torstensson.net).

Leverkusen, Germany), 1.25 mL ketamine (100 mg/mL Ketaminol, veterinary; Intervet Schering-Plough Animal Health, Boxmeer, the Netherlands), and 2.5 mL butorphanol tartrate (10 mg/mL Torbugesic, veterinary; ScanVet Animal Health, Fredensborg, Denmark). The dose of the solution was 1 mL/10 kg. In our case, the pigs were given 6 to 7 mL, depending on the pig's specified weight on delivery. Administration was carried out in the pen with a 10-mL syringe, a 60-cm extension tube, and an 18-gauge needle. The premedication was given intramuscularly in the gluteus maximus muscle.

After approximately 20 minutes, we inserted 3 intravenous catheters into ear veins. Depending on the level of sedation, the pigs received a supplement of 1 to 12 mL of propofol (10 mg/mL Propofol B.Braun; B. Braun Melsungen, Melsungen, Germany) to allow intubation.

The pigs were intubated with a tracheal tube (7.0 mm; Unomedical, Lejre, Denmark). Because of the long pharynx in pigs, we used a laryngoscope with a 30-cm Miller blade (Welch Allen, Skaneateles Falls, NY, USA). If respiratory difficulties were seen after intubation, oxygen was given. The pigs were then connected to a mechanical ventilator, which ventilated with a combination of 50% oxygen and 50% atmospheric air. The ventilation volume used (in liters), was the body weight divided by 10. The ventilation frequency was 16/min, and 3.5% of the ventilation volume was 100% sevoflurane (Sevorane; Abbott Laboratories, Saint-Laurent, Québec, Canada) to maintain anesthesia.

A pulse oximeter was placed on 1 ear to monitor saturation, and a noninvasive 5-lead electrocardiogram device was used. A catheter (5F, 200 mm, Careflow; Becton Dickinson, Franklin Lakes, NJ, USA) was inserted into the femoral artery for invasive monitoring of blood pressure. We also inserted a urethral urinary Foley catheter (18F) into the bladder.

To avoid ventricular fibrillation, we administered a bolus consisting of 6 mL amiodarone (50 mg/mL Cordarone; Sanofi-Aventis, Paris, France) and 14 mL glucose (50 mg/mL) over 15 minutes after invasive blood pressure monitoring became available. Blood pressure was continuously monitored during the infusion, which was paused if the blood pressure fell too rapidly or below a systolic blood pressure of 70 mm Hg. The blood pressure usually normalized within minutes; however, if this was not the case, 1 mg/mL adrenaline (Amgros, Copenhagen, Denmark) was administered by infusion. To regulate blood pressure, we connected 3 infusions to the intravenous catheters. The first consisted of 1000 mL NaCl (9 mg/mL) administered continuously at a mean rate of 4 mL/min. The second infusion consisted of 6 mL amiodarone added to 500 mL glucose (50 mg/mL), which was administered continuously at a rate of 1 mL/min. The third infusion consisted of 2 mL adrenaline added to 500 mL NaCl solution, given at a rate of 1 mL/min. The amounts of amiodarone and adrenaline administered were the means given throughout the course of the surgery. At times it was necessary to regulate the volume of adrenaline and amiodarone given, depending on the blood pressure.

Heparinization was achieved with a bolus of 10,000 IU heparin (5000 IU/mL; Amgros). A 2500-IU supplement was given every 30 minutes, but to no more than 20,000 IU total.

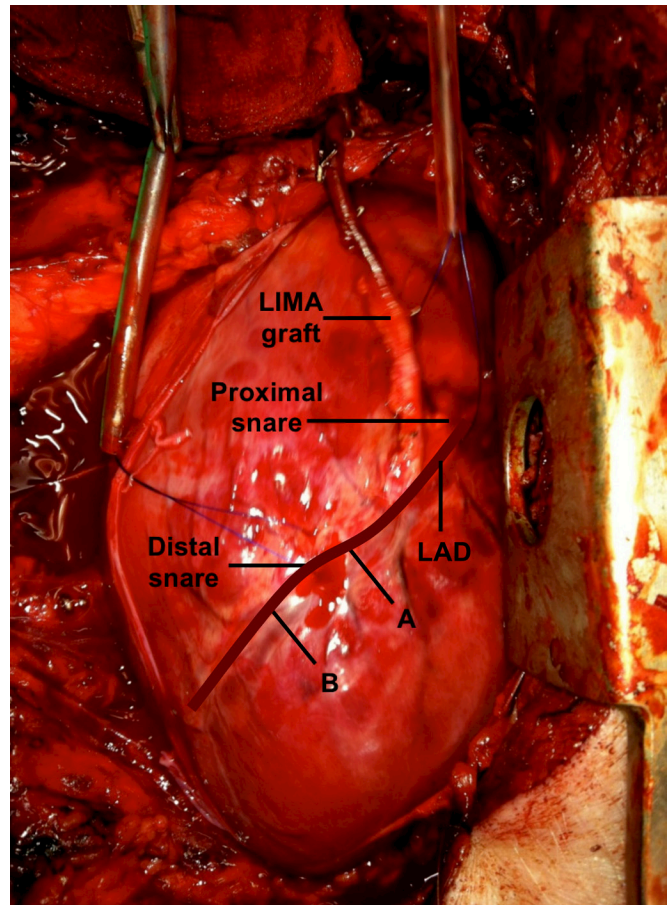


Figure 1. Coronary artery bypass graft model of the left internal mammary artery (LIMA) grafted to the left anterior descending artery (LAD) showing the proximal and distal snaring sites. Ultrasound measurements were made at locations A and B on the LAD.

Surgical Procedure

A midsagittal incision was made from the jugular notch to the xiphoid process. The sternum was freed from fat and connective tissue with a PSD-60 diathermy apparatus (Olympus Corporation, Tokyo, Japan). We used an oscillating saw to perform a median sternotomy, beginning with the xiphoid process and sawing proximally. The sternum was lifted with 2 Langenbeck retractors to avoid damaging the heart and major vessels.

We then located the left internal mammary artery (LIMA) and dissected it free of the internal thoracic wall. The LIMA diameter varied between 1.9 mm and 2.3 mm, and the diameter of the LAD varied between 2.1 mm and 2.5 mm. A pericardiotomy was carried out, and the pericardium was sutured to the skin with four 3-0 polyglactin 910 sutures (Vicryl, Ethicon, Somerville, NJ, USA). The shunt chosen depended on the size of the LAD (Clearview; Medtronic, Minneapolis, MN, USA). The LAD was stabilized with an Octopus Stabilizer (Medtronic); the LIMA was then grafted to the LAD with a 7-0 polypropylene suture (Prolene; Ethicon).

Table 1. Transit Time Flow (TTF) Measurements and Ultrasound Results*

	Ultrasound									
	TTF (LIMA)				LIMA (Graft)		Location A (LAD)		Location B (LAD)	
	Flow, mL/min	P	PI	P	Flow, mL/min	P	Flow, mL/min	P	Flow, mL/min	P
Baseline	21.7 ± 11.3		6.0 ± 2.8		26.8 ± 12.8		27.3 ± 10.6		27.4 ± 12.5	
Proximal snaring	24.6 ± 8.0	.346	5.0 ± 3.0	.309	31.4 ± 20.8	.675	27.5 ± 11.5	.917	30.4 ± 14.7	.773
Distal snaring	8.7 ± 4.6	.047	14.2 ± 6.8	.050	27.9 ± 14.0	.917	18.5 ± 13.0	.209	0	.007
Proximal and distal snaring	21.5 ± 23.1	.602	16.5 ± 19.0	.807	36.8 ± 14.9	.251	33.1 ± 8.9	.347	0	.014

*Data are presented as the mean ± SD. *P* values are calculated with the Wilcoxon test (Boldface text, *P* < .05). Location A is between the anastomosis and the distal snare on the left anterior descending coronary artery (LAD). Location B is distal to the distal snare on the LAD. LIMA indicates left internal mammary artery; PI, pulsatile index.

Table 2. Hemodynamic Data*

	Arterial Pressure, mm Hg		Pulse, beats/min		Extremity saturation, %	
	Mean	P	Mean	P	Mean	P
Baseline	62.4 ± 7.4		106.4 ± 18.4		96.6 ± 1.8	
Proximal snaring	60.6 ± 4.6	.753	107.4 ± 18.0	.600	95.8 ± 1.9	.448
Distal snaring	60.4 ± 6.8	.341	111.8 ± 16.5	.396	95.2 ± 1.1	.148
Proximal and distal snaring	55.2 ± 4.0	.059	113.5 ± 17.5	.463	96.6 ± 3.0	.916
ANOVA <i>P</i> value	.279		.845		.659	

*Data are presented as the mean ± SD. *P* values are calculated with the Wilcoxon test and analysis of variance (ANOVA).

Table 3. Baseline and Intermediary Measurements*

	TTF (LIMA)		Arterial Pressure, mm Hg	Pulse, beats/min	Extremity Saturation, %
	Flow, mL/min	PI			
Baseline	21.7 ± 11.3	6.0 ± 2.8	62.4 ± 7.4	106.4 ± 18.4	96.6 ± 1.8
Proximal snare loosening	14.2 ± 4.3	7.7 ± 2.0	59.6 ± 9.6	106.2 ± 14.0	96.8 ± 2.2
Distal snare loosening	22.8 ± 4.3	4.9 ± 2.2	57.6 ± 9.8	110.0 ± 16.7	97.7 ± 1.9
ANOVA <i>P</i> value	.0969	.194	.706	.869	.949

*Data are presented as the mean ± SD. *P* values are calculated with analysis of variance (ANOVA). TTF, transit time flow; LIMA, left internal mammary artery; PI, pulsatile index.

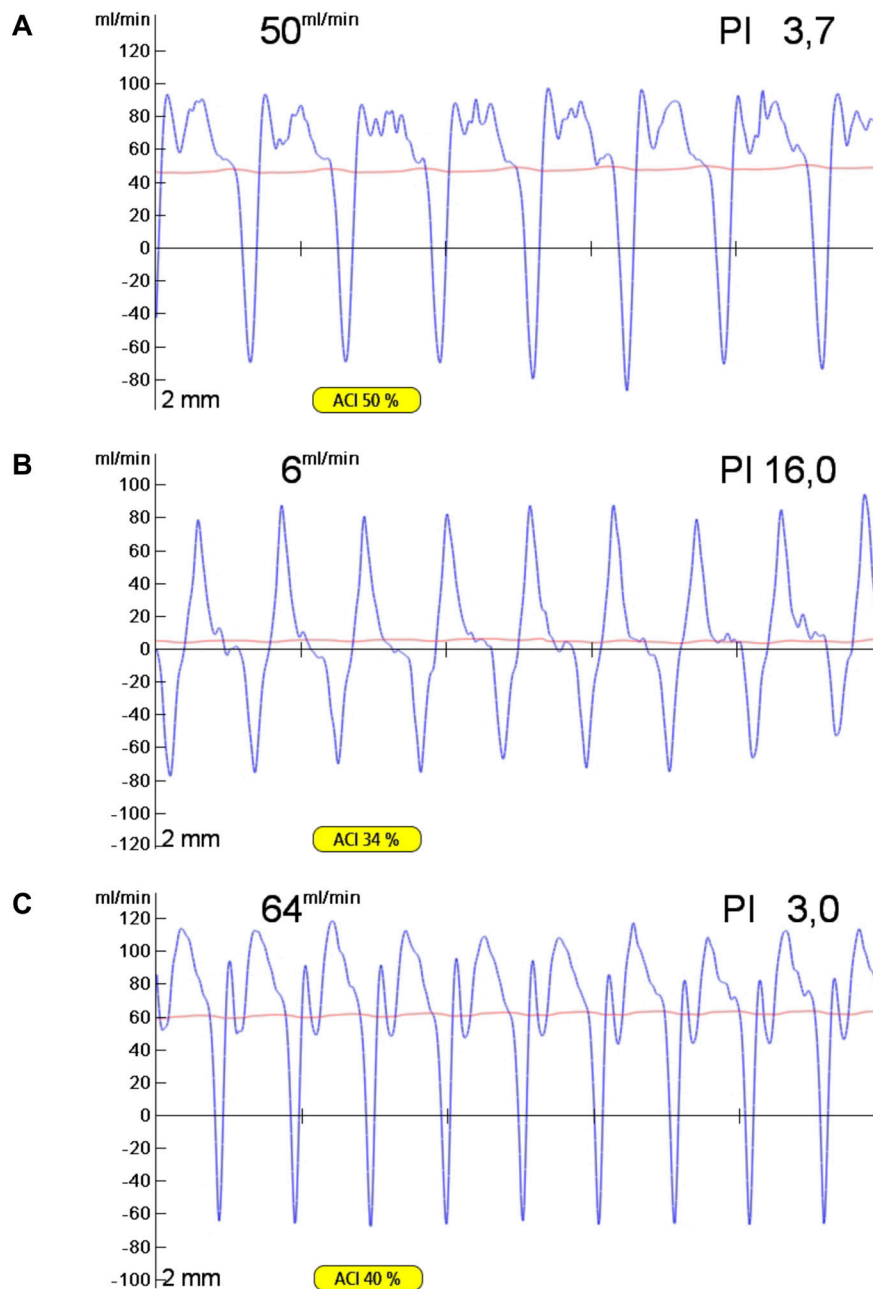


Figure 2. Fig 3. Transit time flow measurement on the left internal mammary artery during baseline (A), after distal snaring (B), and after both proximal and distal snaring (C). PI indicates pulsatile index; ACI, acoustical coupling indicator.

The main factor determining the location of the anastomosis was the ability to carry out measurements both proximal and distal to the anastomosis; however, the anastomosis was placed distal to the first diagonal branch in all 5 cases. The anastomosis site and the sites of the proximal and distal snares were marked with a surgical marker. After grafting the LIMA to the LAD, we removed the bulldog clamp. We defined this point as our baseline.

Using two 4-0 Prolene sutures, we snared the LAD proximal to the anastomosis at a site between 5 mm and 20 mm from the anastomosis. A second snare was placed between 15 mm and 35 mm distal to the anastomosis. We first tightened only the proximal snare to simulate 100% stenosis of the LAD (confirmed with ultrasound). Proximal snaring measurements were carried out. The proximal snare was then loosened, and the same measurements were made again. The

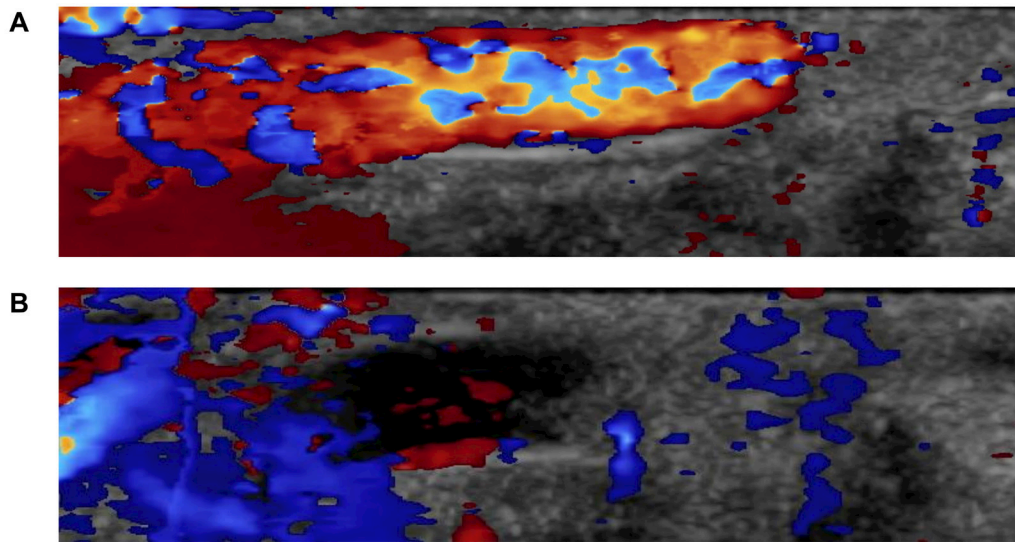


Figure 3. Pig 5. Ultrasound images showing the left anterior descending artery (LAD) distal to the distal snare during normal flow in the LAD (A) and during distal snaring of the LAD (B).

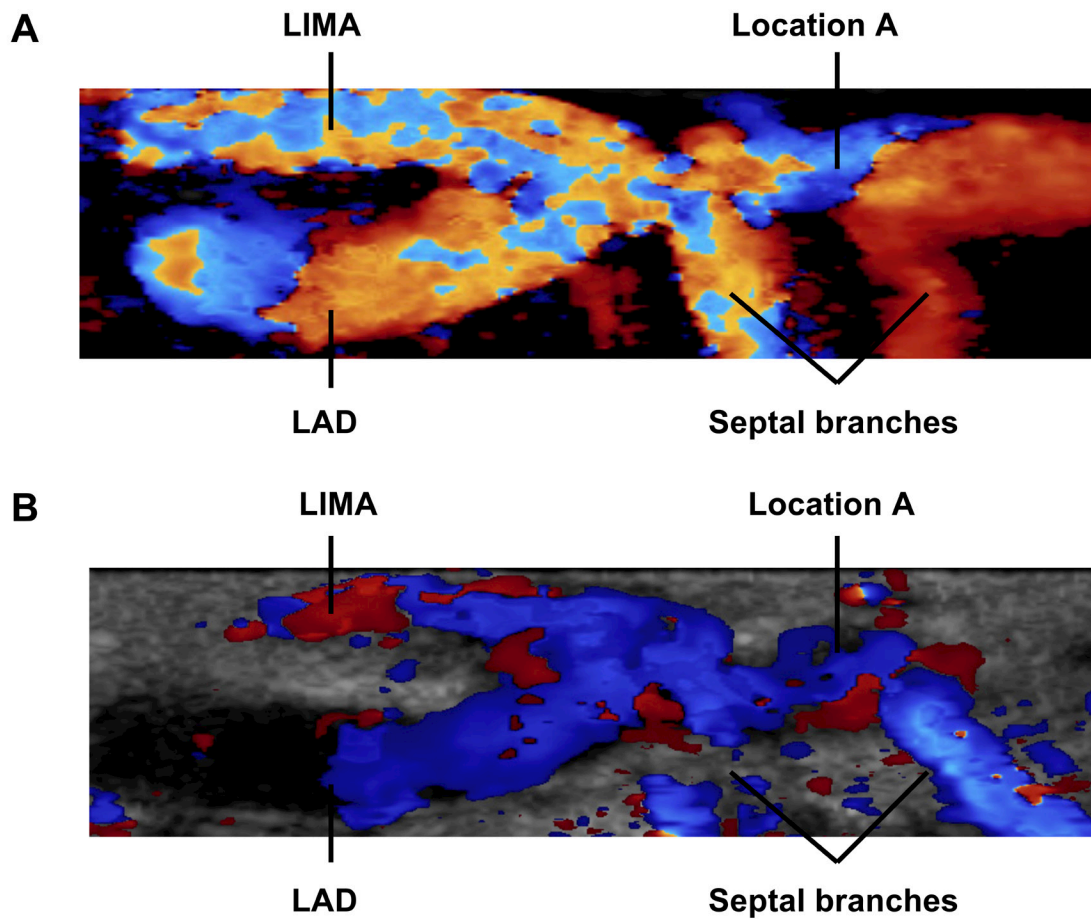


Figure 4. Pigs (A) 3 and 5 (B). Ultrasound images showing the left internal mammary artery (LIMA) grafted to the left anterior descending artery (LAD), with septal branches, after tightening of both the proximal and distal snare. Location A is situated between the anastomosis and the distal snare on the LAD.

distal snare was tightened, and distal snaring measurements were carried out. The distal snare was then loosened, and the same baseline measurements were made again. Finally, both the proximal and distal snares were tightened, and the same measurements were made again.

Measurements

At each time point, we measured the TTF and the pulsatile index (PI) on the LIMA with a 2-mm pericoronary QuickFit probe (Medistim, Oslo, Norway) connected to the VeriQ system (Medistim). An increase in the PI suggests increased vascular resistance, such as a stenosis. We measured the diameter of both the LIMA and the LAD by ultrasound with the L15-7io probe (Philips Healthcare, Andover, MA, USA) connected to the iE33 xMATRIX system (Philips Healthcare). Flow on the LIMA was measured by ultrasound between the anastomosis and the distal snare site (A in Figure 1), and distal to the distal snare site (B in Figure 1). All measurements were carried out 5 times each. Blood pressure (both systolic and diastolic), heart rate, and extremity saturation were monitored throughout the study.

This study complied with Danish animal experiment regulations and was approved by the National Animal Experiments Board. At the end of the experiment, we euthanized the pig humanely with 15 mL pentobarbital (200 mg/mL; Glostrup Apotek, Copenhagen, Denmark) while they were still under general anesthesia on the operating table.

Statistical Analysis

The Wilcoxon test was used to test for the statistical significance of differences between measurements. The level of statistical significance was set at a P level of $<.05$. We used analysis of variance to test for significant variation between >2 groups. We used STATA software (version 12.0; StataCorp, College Station, TX, USA) for statistical analyses.

RESULTS

TTF Measurements

When the distal snare was tightened, the mean TTF dropped significantly (8.7 ± 4.6 mL/min, $P = .047$). When both the proximal and distal snares were tightened, there was no significant difference in flow or PI compared with baseline (Table 1).

Ultrasound

During distal snaring, the flow measured at location B (Figure 1) was zero, hence a significant decrease ($P = .007$) compared with baseline measurements (27.4 ± 12.5 mL/min) (Table 1). During proximal and distal snaring, flow measured at location B decreased ($P = .014$), but flow in the LIMA did not change significantly.

Hemodynamic Data

Blood pressure, pulse, and extremity saturation remained constant throughout the course of each intervention, with no significant changes observed (Table 2).

The measurements taken after proximal snare loosening and after distal snare loosening were not significantly different

from those made at baseline (Table 3). Thus, we concluded that we returned to baseline conditions before each snaring intervention.

DISCUSSION

TTF measurement of the LIMA is of great benefit to patients undergoing CABG surgery; however, that does not completely eliminate the risk of overlooking suturing errors in the anastomosis. This porcine model of a coronary artery bypass with the LIMA showed that a high TTF can be measured in the graft, despite a fully occluded LAD both proximal and distal to the anastomosis.

TTF Measurements

Today, TTF measurement is widely used during cardiac bypass surgery as a tool for measuring graft flow [Kieser 2010]. This method is easy, quick, and gives the surgeon an idea of graft quality.

Our study showed a significantly lower flow and a higher PI in the LIMA graft when the distal snare was tightened and the proximal snare was open. Because the proximal snare was open in this scenario, it can be compared with the clinical situation in which the proximal stenosis is not complete and suturing errors in the anastomosis occlude the distal part of the LAD. Of note is that neither the flow nor the PI can stand alone when evaluating the quality of a graft [Kieser 2010]. As Figure 2B shows, the flow was 6 mL/min, a flow that may be acceptable in some cases; however, when seen together with a PI of 16.0, the surgeon should immediately become suspicious. Because competitive flow from the LAD reduces flow in the LIMA [Nordgaard 2009], the LIMA flow during distal snaring might have decreased in our study because of the flow from the LAD competing with the flow in the LIMA when it enters the septal branches. During both proximal and distal snaring, however, there was no competitive flow from the LAD; thus, a high flow in the LIMA was observed.

Figure 2C shows that a TTF measurement can show both a high flow and a low PI, similar to those at baseline (Figure 2A), even though the LAD is snared both proximally and distally. This finding shows that a distal flow measurement, such as ultrasound, is necessary to complement TTF measurement.

Ultrasound

The ultrasound apparatus allowed us to visualize the LIMA, the anastomosis, the LAD, septal branches, and the 2 snare sites. We were thus able to determine the quality of the anastomosis and the level of LAD occlusion during snaring and loosening, as well as determine the flow and diameter of the LAD and the LIMA.

None of the measurements were statistically significant compared with the baseline values, with the exceptions of the measurements made at location B during distal snaring and during distal and proximal snaring. These statistically significant results were not surprising, because we did expect blood flow at location B, owing to the 100% occlusion of the

LAD. During proximal snaring, we observed a trend toward an increased flow in the LIMA, which was also seen in a prior study [Tsirikos Karapanos 2011].

An unexpected finding was the lack of statistically significant differences between the distal and proximal snaring measurements and the baseline values. We had expected significant differences because of the full occlusion proximal and distal to the anastomosis. The abundant septal branches could explain the continuously high flow observed (Figure 4). Another possible factor may be the distance between the aortic root and the distal part of the LIMA. The higher peak flow in the LIMA than in the LAD is due to the delay in the systolic blood flow reaching the distal end of the LIMA when the heart is entering the diastolic phase. Hence, the flow in the LIMA is systolic and the flow in the LAD is diastolic, thus enabling the LIMA to increase the flow in the LAD.

In the clinical situation, this porcine model would simulate a patient having a complete proximal stenosis of the LAD that had become complicated with a suturing error, which would lead to full occlusion of the LAD distally. If the patient had abundant septal branches in the intermediate LAD, that could lead to falsely high TTF in the LIMA.

CONCLUSION

Our study has revealed that a high flow and a low PI can be seen in a porcine graft, despite a fully occluded LAD both proximal and distal to the anastomosis. Whether the same results can be seen in humans with coronary artery disease remains to be proved. Our results suggest that graft TTF measurement alone is not sufficient when performing CABG and that measuring the flow distal to the anastomosis is also necessary to determine the true blood flow in the LAD.

Limitations

This study was limited by our use of only 5 pigs, which were healthy young animals, presumably without cardiovascular disease. Few measurements were made during snaring of the LAD; however, spending more time on measurements was not possible because of the risk of arrhythmias. The results for all 5 pigs pointed in the same direction, showing that flow in the LIMA during snaring of the LAD was similar to the flow at baseline; however, further study is needed to determine whether similar results can be seen in humans.

All preanastomotic surgery and intraoperative measurements were carried out by the first 2 authors. The free dissection of the LIMA and grafting of the anastomoses were performed by an experienced senior surgeon from Odense University Hospital, Odense, Denmark.

ACKNOWLEDGMENTS

The authors thank Claire Gudex and the staff at the Laboratory of Biomedicine and the Department of Clinical Engineering, Region of Southern Denmark, Odense, Denmark. We also thank Medistim (Oslo, Norway) and ViCare Medical (Birkerød, Denmark) for lending us technical equipment.

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