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Changes in the Arterial Graft Flow Pattern after Intermittent Occlusion of the Anterior Descending Coronary Artery during Off-Pump Coronary Surgery in the Porcine Model

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Abstract

Background: During off-pump coronary surgery, temporary occlusion of the left anterior descending coronary artery (LAD) is often necessary as a preconditioning method or during the performance of the anastomosis. Our aim is to describe the effect of prolonged and intermittent occlusion of the LAD on the measurement of mean graft flow (MGF) and arterial graft pulsatility index (PI). **Methods:** Off-pump coronary surgery (internal mammary artery in situ to LAD) was performed on 8 pigs of the Landrace genotype. Tourniquets were placed proximal and distal to the site of the anastomosis. Intraoperative flow measurements were performed by the transit time method in the following phases: the baseline, during distal snaring of LAD, proximal snaring, and distal and proximal snaring at the same time; subsequently on up to 5 occasions, we repeated this proximal/distal occlusion for 5 minutes and measured the graft flow after its proximal and distal release. **Results:** During distal occlusion and simultaneously proximal and distal occlusion, the MGF decreased, and the PI increased ($P < 0.05$). After intermittent proximal/distal occlusion of the LAD and its subsequent release, the MGF progressively decreased, and the PI increased to become significant from the 3rd release ($P < 0.05$) compared with the baseline measurement. Within 10 minutes of the fifth release, the flow pattern normalised. **Conclusion:** Intermittent and/or prolonged proximal/distal occlusion of LAD may temporarily alter the flow pattern of the graft (decreased MGF and increased PI) once released. Temporary arterial vasospasm in coronary arteries with little atherosclerosis may be the explanatory cause of this phenomenon.

Subject Areas

Cardiology

Keywords

Coronary Surgery, Porcine Model, Vasospasm

1. Introduction

The leading cause of death in developed countries remains ischaemic heart disease. Percutaneous coronary intervention (PCI) or surgical coronary artery bypass graft intervention (CABG) saves thousands of lives worldwide every year. CABG still remains the best strategy for treating multivessel coronary disease in stable ischaemic heart disease, because of its better results in terms of survival and freedom for reoperation [1].

CABG can be done using cardiopulmonary bypass or off-pump CABG (OPCAB). The choice of one or another technique depends on the surgeon's preferences and the patient's characteristics. OPCAB may reduce post-surgical morbidity and may be appropriate in high-risk patients, while comparing the two techniques in terms of very long-term survival outcomes still remain controversial [2] [3].

The most commonly used graft to revascularize the left anterior descending coronary artery (LAD) is the left internal mammary artery (LIMA), as it has long demonstrated greater long-term patency and survival than the saphenous vein graft [4].

Multiple methods have been proposed to control the quality of grafts during CABG surgery, such as electromagnetic flowmetry, flow rate measurement by pulsed Doppler, transepicardic echocardiography, transit-time flow (TTF) measurement and fluorescent angiography with Indocyanine green. Intraoperative graft evaluation with TTF for CABG surgery is recommended (class IIa recommendation, level of evidence B) in the last Guidelines for Myocardial Revascularisation of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC) [5]. A mean graft flow (MGF) of ≥20 ml/min and a pulsatility index (PI) of ≤5 are considered an acceptable outcome [6], but reaching a consensus to establish a threshold is difficult because of the great heterogeneity in the published data due to the great variability of the parameters involved, such as the different haemodynamic data during the flow assessment, the location of the TTF probe (e.g. proximal or distal on the graft), different types of grafts or different degrees of coronary stenosis [7]. TTF measurement is the most frequently used technique for graft assessment and has been able to detect that 4.3% of grafts require revision [5] [7], but its measurement can sometimes fail to detect distal stenosis or technical failures during the procedure [6] [7].

Various systems have been developed (such as direct clamping, intracoronary shunting, gas jet insufflation, and snaring sutures) to obtain a bloodless field at the coronary anastomotic site [2] [3]. The temporary occlusion of the artery to perform the anastomosis comfortably is usually not for long, but sometimes, due to technical difficulties, it is necessary to keep it closed for a long time or even occlude it intermittently several times. To the best of our knowledge there are no studies that measure the impact of these coronary occlusions on the flow pattern in TTF measurements.

The aim of this study is to determine in a porcine model how these intermittent proximal/distal anterior descending coronary occlusions affect the flow pattern of arterial grafts by means of TTF measurement.

2. Methods

2.1. Premedication and Anaesthesia

Eight Landrace pigs weighing a mean of 45 kg underwent OPCAB with LIMA-to-LAD anastomosis. All animals were treated by the same anaesthesiologist and surgical team.

All the pigs received intramuscular premedication administered at neck level (at the level of the trapezius and cleido-occipital muscles), using a 20 G needle and a 10 ml adapted syringe with a 120 cm extension tube, the latter so as not to restrict the animal's movement and thus not cause it any stress. Ketamine 15 mg/kg, Midazolam 0.4 mg/kg and Medetomidine 4 mg/kg were administered and used as sedation and immobilisation to cannulate the marginal vein of the ear (abbocath 20 G) and transfer to the operating theatre.

Propofol 1.66 mg/kg and rocuronium 0.6 mg/kg were used intravenously as a hypnotic in the induction of the anaesthetic plane. To maintain the anaesthetic, individualised doses of propofol were used in continuous perfusion, starting at 4 mg/kg/h. In addition, continuous perfusion of rocuronium was used at 0.3 mg/kg/h, which was started 30 minutes after the initial bolus. To maintain the intravenous line, physiological saline solution was administered and 200 cc boluses were administered in case of hypotension. Remifentanil at 0.15 microgr/Kg/min was used as the intraoperative analgesia

The pigs were intubated with a tracheal tube (7.0 mm; Unomedical, Lejre, Denmark) using a laryngoscope with a 30-cm Miller blade (Welch Allen, Skaneateles Falls, NY, USA). The pigs were then connected to a mechanical ventilator, the ventilation volume used (in litres), was the body weight divided by 10 and the ventilation frequency was 16/min.

Once the animals became unconscious, an intravenous catheter was placed in a peripheral line (outer ear, marginal vein of the ear) to provide a route for the administration of drugs and the volume thereof. The femoral artery was then cannulated for blood pressure monitoring, the cannulation being done by an ultrasound guided technique. Also, electrocardiograms and pulse oximetry were monitored for saturation. Blood pressure was continuously monitored. In case of hypotension during the intervention, 1 mg/mL of adrenaline (Amgros, Copenhagen, Denmark) was administered by continuous infusion. Amiodarone 150 mg and hexamethonium chloride 20 mg/kg were given to avoid arrhythmias. 300 IU/kg of Heparin were administered to maintain an activated coagulation time of more than 200 seconds.

This study complied with Spanish animal experiment regulations and the European convention on animal care and was approved by the National Animal Experiments Board.

After finishing the experiment, the animal was euthanised on the operating table itself by means of an IV anaesthetic overdose with Thiopental, a muscle relaxant overdose with Atracurium (2.5 mgr/Kg), and finally, for the cessation of cardiac function, 20 mEq of potassium chloride was administered intravenously.

2.2. Surgical Procedure

A midline sternal incision was made from the suprasternal gap to the xiphoid process. The median sternotomy was performed with an oscillating saw, starting from the xiphoid process in a proximal direction. To avoid damaging the heart and large vessels during this manoeuvre, the sternum was raised by means of 2 Langenbeck retractors.

The left internal mammary artery (LIMA) was located and dissected from the internal thoracic wall in a skeletonised fashion. The pericardiotomy was performed by exposing the heart using traction sutures with 3-0 polyglactin sutures.

The place where we will perform the anastomosis was located in the medial LAD, in all cases, always distal to the first diagonal branch. Two 4-0 Prolene sutures were placed widely around the proximal and distal to the anastomosis for transient occlusion at a site between <1 cm from the anastomosis (**Figure 1**). The middle portion of the LAD was immobilised with the OCTUPUS stabiliser (Medtronic, Minneapolis, MN). We first tightened only the proximal snare, with the anastomosis being created in the usual fashion as with conventional CABG. The LIMA was grafted to the LAD with an 8-0 polypropylene suture (Prolene; Ethicon). The field is kept free of blood with a humidified CO2 blower (DLPp; Medtronic, Inc, Minneapolis, MN).

The intraoperative flow measurement of the graft was performed by TTF method using a 2 or 3 mm flow probe in the following phases (**Figure 2**): the baseline (after grafting the LIMA to the LAD without occlusion of either the proximal or distal LAD), after tightening the distal snare, after proximal snaring (to simulate 100% stenosis of the LAD) and after proximal/distal snaring with 2 minutes of reperfusion in between. Subsequently, we proceeded to the proximal/distal occlusion of the LAD for 5 minutes, the proximal/distal snare was then loosened for 2 minutes, and the same measurements were made again intermittently up to 5 times. The last flow measurement on the LIMA was made after 10 minutes from the last release after local application of hot water.

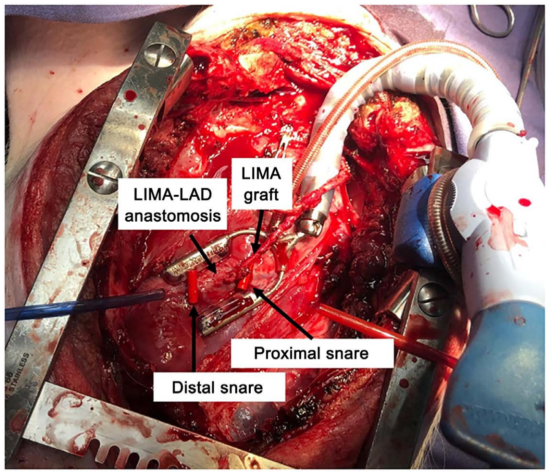

Figure 1. Coronary artery bypass graft model of the left internal mammary artery (LIMA) grafted to the left anterior descending artery (LAD) showing the proximal and distal snaring sites.

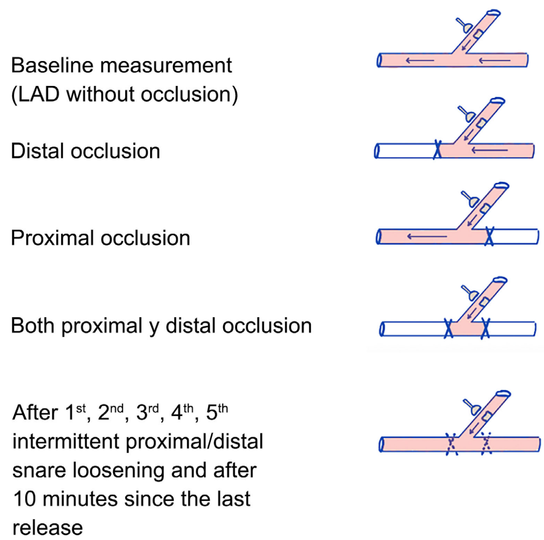

Figure 2. Layout of the intraoperative flow measurement of the graft performed by transit time method (TTF) in the different phases. LAD, left anterior descending artery.

2.3. Measurements

TTF measurements

At each time point, we measured the TTF and the PI on the LIMA with a 2 or 3 mm pericoronary QuickFit probe (Medistim, Oslo, Norway) connected to a VeriQ system (Medistim, Oslo, Norway).

Mean graft flow. MGF is expressed in mL/minute and is useful for indicating how a bypass is flowing. But it is a poor indicator of the quality of the anastomosis because the flow can be altered by many variables such as systolic blood pressure, coronary vascular resistance, the size and quality of the graft or the quality of the anastomosis performed. In general ≥20 ml/min values are considered an acceptable result, flows below this will make us look more carefully at other parameters and a <3 ml/m flow should always alert us that there may be a technical problem [6] [8] [9].

Pulsatility index. The PI is expressed as an absolute value and is considered to be a good indicator of the anastomotic flow pattern, and consequently, of anastomotic quality. The PI can be used as an estimator of vascular resistance and it is obtained by dividing the numeric difference between the maximum flow and the minimum flow by the mean flow. An index between 1 - 5 is considered normal [6].

Diastolic filling (DF). DF indicates the proportion of diastolic graft flow during the entire graft flow. DF in a proper graft should range from 45% to 80%. DF of <25% is considered to mean an inadequate graft [8].

Systolic reverse flow (SRF). Reverse, or backward, flow during the systolic phase indicates flow competition between the bypass graft and the native coronary artery. It is measured as the percentage of the area below the zero line, compared with the total flow area. An SRF value of >3 can be considered a cut-off value that predicts early graft failure [9].

Ultrasound measurements.

In each of the phases, a flow measurement was made in the distal anterior descending coronary artery to the distal snaring site.

All measurements were made 5 times on each occasion in the most stable haemodynamic situation possible. The flow values were stored in a database and the flow curves were analysed off-line using the Medi-Stim 2.0 VeriQ software. Blood pressure, heart rate and O_2 saturation were also monitored and recorded throughout the study.

2.4. 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 <0.05. 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.

3. Results

TTF Measurements

The results of the TTF measurements can be seen in **Table 1**. The flow patterns of the mammary artery are shown in **Figure 3**, respectively. After distal tourniquet occlusion, and after proximal/distal occlusion, the mean TTF dropped and the PI increased significantly compared with the baseline. When the mean flow was <10 ml/m and/or the PI >10, neither the data nor the reverse systolic flow and DF were recorded as this did not provide any additional information.

In the measurements made during release after 5-minute intermittent proximal/distal occlusions, a progressive decrease in flow and an increase in PI are observed, with these values being significant from the third release onwards. Thus, during the third, fourth and fifth occlusion release, the mean flow of the arterial graft decreased significantly, and its mean PI increased significantly with respect to the mean baseline flow. In the measurement made after 10 minutes since the last release and application of hot water, the flow and PI were normalised to baseline values (no significant differences).

Ultrasound measurements.

Table 1 shows the flow measurement in the distal LAD at each stage, with lack of flow during the distal and proximal/distal snaring, and progressive decrease of flow in the measurements made during release after intermittent proximal/distal occlusions. These results are consistent with the findings found in TTF measurements of LIMA.

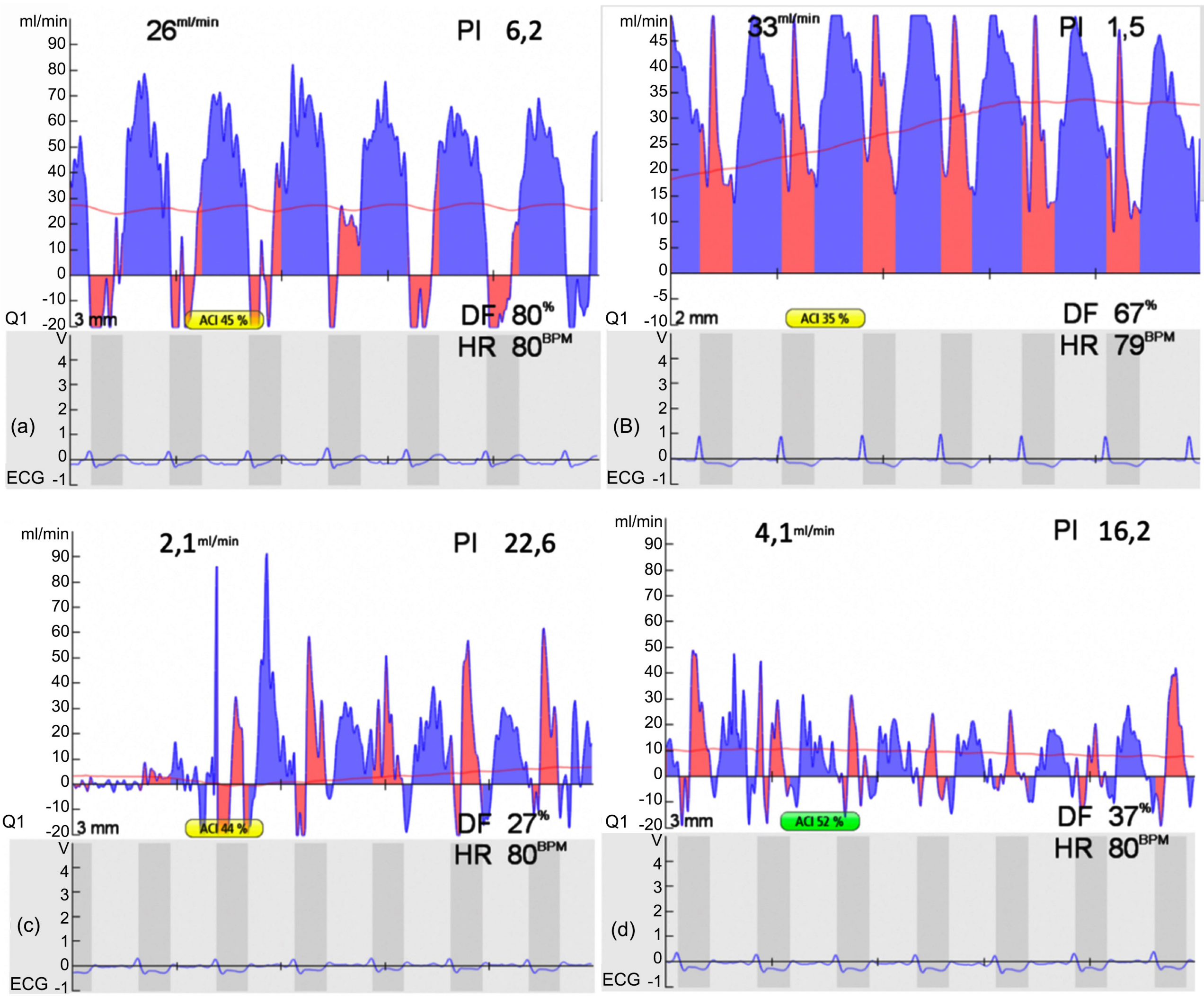

Figure 3. Transit time flow measurement on the left internal mammary artery. (a) Baseline flow with full competitive flow with no snaring of the proximal LAD. (b) Proximal snaring of the LAD. (c) Proximal and distal snaring of the LAD. (d) After the 5th intermittent proximal/distal snare loosening. LAD, left anterior descending artery; PI, pulsatile index; ACI, acoustical coupling indicator; DF diastolic filling; HR, heart rate.

Table 1. Transit time flow and ultrasound measurements.

	TTF (LIMA)						Ultrasound (Distal LAD)	
	Flow, mL/min	P	PI	P	DF (%)	P	Flow, mL/min	P
Baseline	22.1 ± 11.4		6.1 ± 4.2		71		27.1 ± 13.1	
Distal snaring	7.4 ± 5.1	**0.037**	16.4 ± 5.8	**0.490**	--		0	**0.007**
Proximal snaring	28.6 ± 10.3	0.354	4.3 ± 3.5	0.365	75		30.3 ± 14.7	0.786
Proximal /distal snaring	2.8 ± 1.5	**0.028**	20.8 ± 12.5	**0.383**	--		0	**0.013**
First proximal /distal snare loosening	22.8 ± 9.2	0.437	5.9 ± 4.7	0.492	75		28.3 ± 15.2	0.781
Second proximal/distal snare loosening	18.4 ± 11.1	0.310	6.3 ± 4.8	0.394	60		20.8 ± 14.9	0.601
Third proximal/distal snare loosening	9.4 ± 4.7	**0.046**	14.6 ± 7.3	**0.583**	--		12.6 ± 7.1	**0.048**
Fourth proximal /distal snare loosening	5.3 ± 3.6	**0.032**	15.4 ± 5.9	**0.047**	--		8.8 ± 4.3	**0.043**
Firth proximal /distal snare loosening	4.5 ± 2.3	**0.030**	17.5 ± 7.3	**0.043**	--		7.1 ± 4.1	**0.041**
10 minutes after the last snare loosening	20.1 ± 12.4	0.328	6.3 ± 4.8	0.439	70		26.9 ± 12.8	0.693

Note: Data are presented as the mean ± SD. *P* values are calculated with the Wilcoxon test (Boldface text, $P < 0.05$). Abbreviations: LAD, left anterior descending coronary artery. DF, diastolic filling. LIMA, left internal mammary artery; PI, pulsatile index; TTF, transit time flow.

Haemodynamic Data

Throughout all the interventions, blood pressure, heart rate and oxygen saturation remained constant, with no significant changes observed (Table 2). The same happened after proximal/distal snare loosening, without observing significant changes from those made at the baseline (Table 2).

4. Discussion

This CABG porcine model, using LIMA grafted to LAD, demonstrates that the TTF flow pattern can be altered after intermittent and repetitive occlusion of the LAD at the level of proximal/distal to the anastomosis, with full recovery of the normal flow pattern within 10 minutes of release.

During CABG surgery the most widely used diagnostic technique for assessing the permeability of grafts is the TTF measurement [7]. This method allows the surgeon to get an idea of the quality of the flow of the graft used after the anastomosis is performed, in a quick, easy and non-invasive way. Even so, the interpretation of the measurements can sometimes be misleading resulting in serious clinical consequences. Coronary vasospasm is one of those variables that could alter the flow pattern of the graft, but little is known about this phenomenon and its impact on the measurement of the MGF of the graft due to the lack of studies in this field.

4.1. Baseline Measurement

The baseline measurement of the MGF of the graft (without AD occlusion) showed a >20 ml/min flow with a lower than recommended diastolic curve, but with an absolute value within the figures which was considered acceptable and a

Table 2. Hemodynamic and saturation Data.

	Arterial Pressure, mmHg		Pulse, beats/min		Saturation, %	
	Mean	P	Mean	P	Mean	P
Baseline	65.8 ± 7.1		107.1 ± 19.4		96.4 ± 1.9	
Distal snaring	62.7 ± 8.1	0.453	110.4 ± 18.3	0.638	95.9 ± 1.9	0.456
Proximal snaring	61.8 ± 7.9	0.476	114.4 ± 16.4	0.467	95.5 ± 1.8	0.437
Proximal/distal snaring	62.6 ± 9.3	0.519	113.7 ± 17.9	0.435	95.2 ± 1.5	0.376
First proximal /distal snare loosening	63.7 ± 5.0	0.345	109.4 ± 17.4	0.567	96.3 ± 1.9	0.786
Second proximal /distal snare loosening	64.3 ± 6,8	0.358	108.2 ± 19.3	0.476	96.5 ± 1.6	0.893
Third proximal/distal snare loosening	62.1 ± 7.3	0.254	111.3 ± 17.9	0.324	96.1 ± 1.7	0.739
Fourth proximal /distal snare loosening	61.3 ± 8,4	0.264	113.7 ± 18.4	0.234	95.8 ± 1.4	0.564
Firth proximal/distal snare loosening	59.4 ± 6.9	0.097	116.6 ± 15.8	0.238	95.3 ± 1.5	0.342
10 minutes after the last snare loosening	62.6 ± 7.6	0.398	110.3 ± 19.1	0.548	96.7 ± 1.6	0.964

Note: Data are presented as the mean ± SD. *P* values are calculated with the Wilcoxon test.

PI of 6, which is slightly above the recommended figures in a CABG surgery. These findings are consistent with those observed in the study of graft flow patterns in a porcine model by Nordgaard, H. *et al.* [10], where it was demonstrated that measuring flow from the LIMA to the LAD without occlusion produces a significant decrease in flow and a significant increase in PI, given that competitive flow from the LAD without proximal lesions is complete. In the CABG porcine model study with 5 pigs, when measuring flow from LIMA to LAD without occlusion, Torstensson, G.N. *et al.* [11] observed a non-significant trend of decreasing flow and increasing PI. In these two porcine model studies, the flow pattern and figures for MGF and PI were very similar to those in our study [10] [11]. This increase in PI above 5 in mammary artery graft measurement has already been described as a possible indicator of competitive flow by many authors [6]. On a practical level, in CABG surgery this high competitive flow is unlikely because the coronaries to be revascularised are vessels with luminal sis >50%, and therefore, the competitive flow from the LAD should never be complete. On the other hand, there are clinical studies that suggest the influence of competitive flow in arterial grafts such as LIMA is greater than in saphenous vein grafts. This might be related to the fact that saphenous vein grafts are not muscular, which means they cannot adjust their lumen in response to metabolic requirements unlike arterial grafts [12]. In any case, the effect of this competitive flow on the long-term permeability of the LIMA graft remains controversial [13].

4.2. Distal Occlusion of LAD

Our study demonstrated a decrease in MGF and an increase in PI in the LIMA graft when the LAD was occluded distally to the anastomosis. This scenario could simulate the clinical situation during coronary surgery where due to a technical error the anastomosis is occluded in the distal part of the LAD. This result is consistent with that obtained in the CABG porcine model study with 5 pigs by Torstensson, G.N. *et al.* [11]. The explanation for this phenomenon may be that the flow from the LAD competes with the flow from the LIMA, both without finding a distal outlet, as Nordgaard pointed out when studying the different flow patterns in the porcine model [10].

4.3. Proximal Occlusion of LAD

During this stage there were no significant differences in MGF or PI with respect to baseline values, but there was a trend towards higher flow and lower PI (<5), on there not being competitive flow through the LAD. This flow pattern was the same as that observed by Torstensson, G.N. *et al.* [11]. This flow pattern is what it is usually found in a conventional CABG surgery.

4.4. Both Proximal and Distal Snaring of LAD

Since there is no flow outlet to any branch and there is a high resistance, the MGF of the LIMA decreases and the PI increases very significantly. Torstensson, G.N. *et al.* [11] did not find this behaviour, they obtained a high flow and a low PI, similar to those found at the baseline level. These results are explained by the finding of abundant septal branches with a flow between the proximal and distal occluded portion of the LAD. However, in our study, this is unlikely to happen because, unlike Torstensson, G.N. *et al.*, the proximal and distal occlusion was made very close to the anastomosis (<1 cm) leaving no margin for septal branches between the proximal and distal occlusions. In this sense, no blood arising from septal branches was observed when the anastomosis was finished.

4.5. After the Release of Intermittent Proximal and Distal Occlusion of LAD

The results obtained in the measurements, showing a decrease in MGF and an increase in IP, significantly from the third release, suggest that the trauma of repetitive occlusion causes a vasospasm in the coronary artery at that level, simulating an occlusion. However, the measurement made after 10 minutes since the last release, with a normalisation of the flow pattern with respect to baseline values, suggests that this vasospasm is transitory and reversible.

There are authors who do not recommend the use of occluders during CABG because of the evidence found of coronary endotelial injury on electron microscopy after different occluding techniques in patients before removal of the recipient heart before transplantation [14]. However, a functional study in swine by Perrault and colleagues showed that snaring (with 4-0 Gore-Tex thread) to achieve haemostasis at the anastomotic site does not cause any endothelial dysfunction in healthy coronary arteries [15].

The mechanisms involved in coronary vasospasm and its different treatments have been widely studied and described [16] [17]. Coronary vasospasm related to CABG surgery is rare, but sometimes it has catastrophic clinical implications which are difficult to resolve, such as the intraluminal injection of vasodilators or emergency PCI [18] [19]. As far as we know, this is the first study in a porcine model showing the flow pattern of the mammary artery graft after induction of coronary vasospasm and its subsequent recovery.

4.6. Limitations

This is a study limited by the use of only 8 pigs presumably with normal coronary arteries and good run-off, so this animal model may not be directly comparable to that of human patients with advanced coronary disease. In addition, the values of the measured flows may be different in different species. The statistical limitations were the multiple comparisons and the use of a limited number of measurements. No further measurements could be made because of the increased risk of arrhythmias. All surgery and intraoperative measurements were carried out by the first 2 authors.

5. Conclusions

In this study our results showed that in a CABG porcine model intermittent and/or prolonged occlusion on LAD may temporarily alter the flow pattern of the arterial graft once released.

Taking these results to a practical level, this porcine model would simulate OPCAB with longer than usual proximal and distal occlusion or with technical problems that would force intermittent coronary occlusion to optimize distal anastomosis. In this context early TTF measurement of the MGF of the graft after completion of the anastomosis may be misleading showing a flow pattern that simulates a technical complication due to an error in the anastomosis suture. The complete recovery of the normal flow pattern after 10 minutes, just applying hot water, indicates that the vasospasm produced by the prolonged and intermittent trauma is reversible. These findings suggest that we should be patient when assessing the correct flow measurements of the grafts in this clinical context.

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Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] De Palo, M., Quagliara, T., Dachille, A., Carrozzo, A., Giardinelli, F., Mureddu, S., *et al.* (2019) Trials Comparing Percutaneous and Surgical Myocardial Revascularization: A Review. *Reviews on Recent Clinical Trials*, **14**, 95-105.

https://doi.org/10.2174/1574887114666190201102353

[2] Takagi, H., Ando, T. and Mitta, S. (2017) Meta-Analysis Comparing ≥ 10-Year Mortality of Off-Pump versus On-Pump Coronary Artery Bypass Grafting. *The American Journal of Cardiology*, **120**, 1933-1938. https://doi.org/10.1016/j.amjcard.2017.08.007

[3] Kawajiri, H., Yaku, H., Glineur, D. and Ruel, M. (2017) Clampless versus Clamped Coronary Bypass Grafting: Does It Make a Difference? *Current Opinion in Cardiology*, **32**, 737-743. https://doi.org/10.1097/HCO.0000000000000451

[4] Loop, F.D., Lytle, B.W., Cosgrove, D.M., Stewart, R.W., Goormastic, M., Williams, G.W., *et al.* (1986) Influence of the Internal-Mammary-Artery Graft on 10-Year Survival and Other Cardiac Events. *The New England Journal of Medicine*, **314**, 1-6. https://doi.org/10.1056/NEJM198601023140101

[5] Sousa-Uva, M., Neumann, F.J., Ahlsson, A., Alfonso, F., Banning, A.P., Benedetto, U., *et al.* (2019) 2018 ESC/EACTS Guidelines on Myocardial Revascularization. *European Journal of Cardio-Thoracic Surgery*, **55**, 4-90. https://doi.org/10.1093/ejcts/ezy289

[6] Niclauss, L. (2017) Techniques and Standards in Intraoperative Graft Verification by Transit Time Flow Measurement after Coronary Artery Bypass Graft Surgery: A Critical Review. *European Journal of Cardio-Thoracic Surgery*, **51**, 26-33. https://doi.org/10.1093/ejcts/ezw203

[7] Thuijs, D.J.F.M., Bekker, M.W.A., Taggart, D., Kappetein, A.P., Kieser, T.M., Wendt, D., *et al.* (2019) Improving Coronary Artery Bypass Grafting: A Systematic Review and Meta-Analysis on the Impact of Adopting Transit-Time Flow Measurement. *European Journal of Cardio-Thoracic Surgery*, **56**, 654-663. https://doi.org/10.1093/ejcts/ezz075

[8] Di Giammarco, G., Pano, M., Cirmeni, S., Pelini, P., Vitolla, G. and Di Mauro, M. (2006) Predictive Value of Intraoperative Transit-Time Flow Measurement for Short-Term Graft Patency in Coronary Surgery. *The Journal of Thoracic and Cardiovascular Surgery*, **132**, 468-474. https://doi.org/10.1016/j.jtcvs.2006.02.014

[9] Leong, D.K., Ashok, V., Nishkantha, A., Shan, Y.H. and Sim, E.K. (2005) Transit-Time Flow Measurement Is Essential in Coronary Artery Bypass Grafting. *The Annals of Thoracic Surgery*, **79**, 854-857. https://doi.org/10.1016/j.athoracsur.2004.06.010

[10] Nordgaard, H., Nordhaug, D., Kirkeby-Garstad, I., Løvstakken, L., Vitale, N. and Haaverstad, R. (2009) Different Graft Flow Patterns Due to Competitive Flow or Stenosis in the Coronary Anastomosis Assessed by Transit-Time Flowmetry in a Porcine Model. *European Journal of Cardio-Thoracic Surgery*, **36**, 137-142. https://doi.org/10.1016/j.ejcts.2009.02.036

[11] Torstensson, G.N., Torp, T.L., Rasuli-Oskuii, N. and Kjeldsen, B.J. (2013) Graft Flow Unaffected by Full Occlusion of Left Anterior Descending Artery during Coronary Artery Bypass Grafting in a Porcine Model. *The Heart Surgery Forum*, **16**, E107-E113. https://doi.org/10.1532/HSF98.20121112

[12] Sabik, J.F. and Blackstone, E.H. (2008) Coronary Artery Bypass Graft Patency and Competitive Flow. *JACC: Journal of the American College of Cardiology*, **51**, 126-128. https://doi.org/10.1016/j.jacc.2007.09.029

[13] Gaudino, M., Alessandrini, F., Nasso, G., Bruno, P., Manzoli, A. and Possati, G. (2002) Severity of Coronary Artery Stenosis at Preoperative Angiography and Midterm Mammary Graft Status. *The Annals of Thoracic Surgery*, **74**, 119-121. https://doi.org/10.1016/S0003-4975(02)03614-7

[14] Hangler, H.B., Pfaller, K., Antretter, H., Dapunt, O.E. and Bonatti, J.O. (2001) Coronary Endothelial Injury after Local Occlusion on the Human Beating Heart. *The Annals of Thoracic Surgery*, **71**, 122-127. https://doi.org/10.1016/S0003-4975(00)02181-0

[15] Perrault, L.P., Menasché, P., Bidouard, J.P., Jacquemin, C., Villeneuve, N., Vilaine, J.P., *et al.* (1997) Snaring of the Target Vessel in Less Invasive Bypass Operations Does Not Cause Endothelial Dysfunction. *The Annals of Thoracic Surgery*, **63**, 751-755. https://doi.org/10.1016/S0003-4975(96)01118-6

[16] Yasue, H., Mizuno, Y. and Harada, E. (2019) Coronary Artery Spasm—Clinical Features, Pathogenesis and Treatment. *Proceedings of the Japan Academy*, *Ser. B*, *Physical and Biological Sciences*, **95**, 53-66. https://doi.org/10.2183/pjab.95.005

[17] Mitchel, J.F., McKay, R.G., Azrin, M.A., Aretz, T., Waters, D.D. and Fram, D.B. (1997) Effect of Low Grade Radiofrequency Heating on Arterial Vasospasm in the Porcine Model. *Catheterization and Cardiovascular Diagnosis*, **42**, 348-355. https://doi.org/10.1002/(SICI)1097-0304(199711)42:3<348::AID-CCD28>3.0.CO;2-G

[18] Lorusso, R., Crudeli, E., Lucà, F., De Cicco, G., Vizzardi, E., D'Aloia, A., *et al.* (2012) Refractory Spasm of Coronary Arteries and Grafted Conduits after Isolated Coronary Artery Bypass Surgery. *The Annals of Thoracic Surgery*, **93**, 545-551. https://doi.org/10.1016/j.athoracsur.2011.09.078

[19] Kaku, B., Ikeda, M., Kato, H., Takabatake, S., Hayashi, T., Taguchi, T., *et al.* (2007) Coronary Artery Multistenting in the Treatment of Life-Threatening Refractory Coronary Spasm after Coronary Artery Bypass Grafting. *International Heart Journal*, **48**, 379-385. https://doi.org/10.1536/ihj.48.379

Abbreviations

CABG: Surgical coronary artery bypass graft intervention.
DF: Diastolic filling.
EACTS: European Association for Cardio-Thoracic Surgery.
ESC: European Society of Cardiology.
LAD: Anterior descending coronary artery.
LIMA: Left internal mammary artery.
MGF: Mean graft flow.
OPCAB: Off-pump CABG.
PI: Pulsatility index.
PCI: Percutaneous coronary intervention.
SRF: Systolic reverse flow.
TTF: Transit-time flow.