Collateral blood flow between left coronary artery bypass grafts and chronically occluded right coronary circulation in patients with triple vessel disease. Observations during complete revascularisation of beating hearts

Jean-Philippe Verhoye, Issam Abouliatima, Agnes Drochon, Bertand de Latour, Christophe Leclercq, Alain Leguerrier, Hervé Corbineau

Department of Thoracic and Cardiovascular Surgery, University Hospital Centre, Rennes, France
School of Biotechnology, University of Compiegne, France
Department of Cardiology, University Hospital Centre, Rennes, France

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Abstract

Objective: Preoperative measurements of collateral blood flow in patients with triple vessel disease and chronic occlusions of the right coronary artery do not, currently, ascertain the need to revascularise an occluded right coronary artery. We performed direct measurements of flow across left coronary bypass grafts to determine their contributions to collateral blood flow.

Methods: Collateral blood flow was scored preoperatively according to Rentrop in 13 patients with triple vessel disease and chronic occlusions of the right coronary artery who underwent complete, off-pump, surgical revascularisation. The transit-time flow through the left coronary grafts was measured before and after unclamping of the right coronary artery bypass graft.

Results: Unclamping of the right coronary artery bypass graft was associated with a 5.9 ± 6.9 ml/min (mean ± SD) decrease in flow across the left circumflex territory (P = 0.009), which was proportional to the preoperative Rentrop score (P = 0.007). No significant change was observed in flow across the graft to the left anterior descending artery.

Conclusions: Grafts to the left circumflex system are the only grafts that supply a significant, albeit modest amount of collateral blood flow to chronically occluded right coronary artery. These observations confirm that (1) most collateral flow after revascularisation is supplied by the native network, and (2) revascularisation of an occluded right coronary artery is fully justified.

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Keywords: Collateral blood flow; Coronary artery bypass graft; Off-pump heart surgery; Coronary pathophysiology

1. Introduction

The coronary collateral circulation remains difficult to quantify, particularly in presence of chronic arterial occlusion. While the method developed by Pjils et al. [1] measures collateral blood flow (CBF) relative to maximum myocardial blood flow, it does not measure absolute CBF. Another method consists of measuring CBF during coronary catheterisation, derived from the diameter and blood flow rate in collateral vessels from the propagation rate of the contrast agent [2]. This method only approximates CBF, as it cannot be applied to small vessels, and the rate of contrast agent propagation is difficult to measure, since the residual pressure distal to the arterial occlusion is unknown.

This study describes a new method of measurement of CBF contributed by grafts to the left coronary arteries in patients with triple vessel disease and chronic occlusions of the right coronary artery (RCA), a pathophysiological setting where the collateral circulation to the occluded artery is difficult to ascertain. In a preliminary study performed during off-pump coronary revascularisation surgery, we measured the residual pressure distal to the occlusion, which allows the determination of pressure-derived collateral fractional flow reserve, a quantitative estimate of the CBF to an occluded artery relative to the maximum myocardial blood flow [3]. While we had observed that a high left ventricular ejection fraction (LVEF) predicted a high collateral fractional flow reserve, the latter has not been related with angiographic Rentrop score of collateral circulation [4]. Furthermore, the absence of change in this index after bypass surgery limited to the left...
coronary arteries suggested that these grafts did not provide enough CBF to (1) avoid revascularisation of an occluded RCA, or (2) allow the identification of the origin of its collateral blood supply.

The objective of this study, using the same clinical model of triple vessel coronary disease and chronic RCA occlusion, was to quantify the proportion and pinpoint the origin of CBF supplied by left-sided bypass grafts. The blood flow through left internal thoracic arteries (LITA) and right internal thoracic arteries (RITA) grafts measured directly by transit-time [5—8] before RCA revascularisation was examined as a function of Rentrop score, history of myocardial infarction, and LVEF. We specifically examined whether removing the clamp from the bypass graft implanted on the RCA significantly changed the blood flow in grafts implanted on the left coronary arteries.

2. Patient population and methods

This study was reviewed and approved by the Ethics Committee of our institution, and all patients granted their written informed consent to participate. The 14 patients included in this study presented with triple vessel coronary artery disease and chronic RCA occlusion, and needed revascularisation of all walls of the heart (Fig. 1). Patients whose RCA could not be revascularised, or with documentation of irreversible ischemia of the inferior wall by myocardial perfusion scintigraphy or dobutamine echocardiography, were excluded from the study. Patients with chronic occlusion of the left anterior descending (LAD), left circumflex (LCX) artery, or one of their branches were also excluded from the study. The collateral circulation to the RCA was scored by two independent observers according to the Rentrop classification. The right or left dominance and the presence of a stenosis on the LAD distal of the origin of the first septal branch were assessed in the same way. In case of discordant results, the coronary angiograms were reinterpreted by the same independent observers. Collateral filling of the RCA was scored as follows: 0 = no filling, 1 = filling of distal branches without visualisation of its epicardial segment, 2 = partial filling of the epicardial segment, and 3 = complete filling of the epicardial segment via collateral vessels [4].

2.1. Study protocol

2.1.1. Surgical techniques

Our surgical techniques have been reported previously [9]. In brief, a Swan—Ganz catheter was used to measure the right heart pressures and cardiac output, and the systemic blood pressure was continuously monitored by a radial artery catheter. Intraoperative anticoagulation was achieved with intravenous heparin, 200 units/kg, monitored to reach an activated partial thromboplastin time >300 s. Under normothermic conditions, a midline sternotomy was performed, the pericardium was opened, and the coronary vessels were inspected to confirm the revascularisation strategy. The various walls of the heart were exposed by pericardial traction sutures. LITA, RITA, and a long saphenous vein were harvested after identification of the target vessels. Particular attention was paid to the occluded...
distal RCA to confirm that it could be revascularised. The sites of anastomoses were immobilized by an Octopus® tissue stabilizer (Medtronic Inc., Minneapolis, MN). The usual sequence consisted of (1) anastomosis of a saphenous vein graft onto the distal RCA, or its branches, or both, then the proximal segment of the vein graft implanted on the RCA was anastomosed on the ascending aorta with lateral clamping, this graft remaining clamped, (2) revascularisation of the anterior wall by LITA implantation onto the LAD artery, and if necessary sequential anastomosis to a diagonal artery, and (3) implantation of a RITA, pedicled and tunnelled in the transverse sinus, onto the LCX or its main marginal branch, with or without sequential revascularisation. After the onset of perfusion of the grafts implanted onto the left coronary arteries, the heart was returned to its place. Complete revascularisation was performed in all patients with a mean of 3.14 ± 0.7 distal anastomoses per patient. The sequence of surgical and experimental interventions is summarised in Fig. 2.

2.2. Measurements of graft blood flow

Transit-time flow measurements across the internal thoracic arteries were made with a Butterfly Flowmeter 2001 (Medi-Stim, Oslo, Norway), with the heart left in its anatomical position, after haemodynamic stabilisation to a cardiac index > 2.0 l/min/m² and a systolic aortic pressure > 80 mmHg.

The thoracic grafts were skeletonized locally over 1.0 cm, at approximately 5.0 cm from their origin, to position transducers adapted to their diameter. Blood flow was measured simultaneously in LITA and RITA (LITA-PRE and RITA-PRE) during stable haemodynamics. The transducers were left in place, the RCA vein graft was unclamped and, after haemodynamic stabilisation, the simultaneous LITA and RITA blood flow measurements were repeated (LITA-POST and RITA-POST).

A single patient was excluded from the analysis because poor distal run-off observed intraoperatively precluded revascularisation of the LAD.

2.3. Statistical analysis

Values are expressed as means ± standard deviation (SD). The relationship between LITA-PRE and RITA-PRE and Rentrop score or history of inferior myocardial infarction was examined by Student’s t-test, and their relationship with LVEF was examined by linear regression. The differences between LITA-PRE and LITA-POST and between RITA-PRE and RITA-POST were examined by Student’s t-test for paired series, and Wilcoxon’s nonparametric test for paired series. A relationship between significant changes in blood flow, or Rentrop score, and a history of inferior myocardial infarction

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Sex/age (years)</th>
<th>History of IMI</th>
<th>Coronary artery stenoses (%)</th>
<th>LVEF (%)</th>
<th>Rentrop score</th>
<th>Right dominant system</th>
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IMI: inferior myocardial infarction; LM: left main; LAD: left anterior descending; LCX: left circumflex; LVEF: left ventricular ejection fraction; +: present; –: absent

* LAD stenosis distal of the first septal branch.
was examined by Student’s *t*-test, and a relationship with LVEF by linear regression. *P* values < 0.05 were considered statistically significant. Data were analysed with the SPSS 12.0 software (SPSS Inc., Chicago, IL).

### 3. Results

The individual preoperative characteristics of the 12 men and 1 woman included in this analysis are presented in Table 1. Their mean age was 62.5 ± 11.0 years, mean LVEF 57.0 ± 13.9%, and six patients had histories inferior myocardial infarction. The individual intraoperative measurements made in the 13 patients are presented in Table 2. The Rentrop score was 1 in one patient, 2 in five patients, and 3 in seven patients.

![Graph](image)

**Table 2**

<table>
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<tr>
<th>Pt.</th>
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<th>LITA(_{POST})</th>
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<th>RITA(_{PRE})</th>
<th>RITA(_{POST})</th>
<th>RITA(<em>{PRE})–RITA(</em>{POST})</th>
<th>RCA graft(^*)</th>
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<td>104</td>
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LITA: left internal thoracic artery (implanted in the left anterior descending artery); RITA: right internal thoracic artery (implanted in the left circumflex artery). LITA\(_{PRE}\) and LITA\(_{POST}\): flow across LITA before and after unclamping the saphenous graft on the right coronary artery, respectively; RITA\(_{PRE}\) and RITA\(_{POST}\): flow across RITA before and after unclamping the saphenous graft on the right coronary artery. RCA graft: flow across the saphenous graft on the right coronary artery.

\(^*\) Student's *t*-test for paired samples: *P* = 0.23; Wilcoxon's test for paired samples: *P* = 0.29.

\(^*\) Student's *t*-test for paired samples: *P* = 0.007; Wilcoxon's test for paired samples: *P* = 0.01.

\(^{**}\) Linear regression analysis between flow across the saphenous graft on the right coronary artery and variation of flow in RITA to the circumflex artery (RITA\(_{PRE}\)–RITA\(_{POST}\)): *P* = 0.146.

The mean LITA\(_{PRE}\) and RITA\(_{PRE}\) were 47.0 ± 35.4 (range: 11–115) and 43.2 ± 25.5 (range: 11–104) ml/min, respectively. Mean blood flow across LITA and RITA before unclamping of the saphenous vein graft was similar in patients with versus without histories of inferior myocardial infarction, and was unrelated to the Rentrop score. By linear regression analysis, a statistically significant correlation was observed between LVEF and LITA\(_{PRE}\) (**P** = 0.009), but not between LVEF and RITA\(_{PRE}\) (Fig. 3).

After unclamping the saphenous vein graft implanted on the occluded RCA delayed artery, a significant decrease in blood flow occurred across the RITA, corresponding to a mean 5.9 ± 6.9 ml/min difference between RITA\(_{PRE}\) and RITA\(_{POST}\) (*t*-test for paired samples: *P* = 0.009; Wilcoxon’s test for paired samples: *P* = 0.019). This significant difference was correlated neither with the presence versus absence of inferior myocardial infarction, nor with LVEF. However, the mean RITA\(_{PRE}\)–RITA\(_{POST}\) difference in seven patients with Rentrop score ≤2 was 1.33 ± 7.0 ml/min, versus 9.9 ± 3.8 ml/min in six patients with scores >2 (*t*-test: *P* = 0.018; nonparametric test: *P* = 0.045).

In contrast to the changes in blood flow measured across the RITA, no significant concomitant change in blood flow was observed across the LITA (LITA\(_{PRE}\)–LITA\(_{POST}\) = 1.8 ± 5.2 ml/min). This result is not modified when these variations are analysed according to the presence of a stenosis distally to the first septal branch (LITA\(_{PRE}\)–LITA\(_{POST}\) as a function of LAD stenosis: Student’s *t*-test: *P* = 0.115). No significant relationship was observed between the right dominance and the variation of flow observed in RITA; no significant relationship was observed between the blood flow in the unclamped RCA graft and the variation of flow observed in RITA (linear regression analysis, *P* = 0.146; Table 2).

### 4. Discussion

This study was the first to measure the proportion of CBF supplied to occluded RCA by grafts implanted onto the left...
coronary circulation. In this group of patients with chronic RCA occlusions, we observed (1) a significant decrease in blood flow across the RITA implanted onto the LCX after unclamping of the saphenous graft to the occluded RCA, and (2) a significant relationship between the difference in RITA flow before versus after unclamping and Rentrop score, suggesting that the CBF to the occluded RCA is, when effective, provided by the LCX artery. These observations are concordant with those of Pohl et al. [10] who reported a lower collateral flow index (CFI) in the LAD artery than in the LCX or RCA, in patients with coronary artery disease. This, however, was not confirmed by Wustman et al. [11] who observed no significant change in CFI during occlusion of angiographically normal coronary arteries. These combined observations are consistent with the two known main determinants of development of the collateral circulation, i.e., (1) the duration of coronary artery disease, and (2) the severity of stenosis of the artery involved [10,12,13]. Despite the availability of maximum CBF in case of chronic coronary artery occlusion, it might not be sufficient to systematically prevent the occurrence of a myocardial infarction in all patients. In this case, it has been shown that the collateral circulation develops between 1 and 4 weeks after the appearance of necrosis [14,15]. Therefore, the amount of collateral circulation that has developed months or years after myocardial infarction does not predict the likelihood of myocardial recovery after revascularisation of a chronically occluded artery [16], explaining, in our study, the absence of correlation between LVEF and difference in blood flow across the RITA, before and after unclamping of the RCA vein graft.

The collateral circulation of our patients, whose RCA was occluded for >4 weeks, was presumably well developed. However, the absolute blood flow provided by this collateral circulation, estimated from the changes in flow across the RITA and LITA, was evidently very low, and could not, in isolation, explain the absence of inferior myocardial infarction in seven of our patients [17,18]. This suggests that revascularisation of the RCA remains justified in these patients, since a sufficient CBF cannot be expected from left coronary artery revascularisation alone. Furthermore, this small amount of CBF supplied by left-sided bypass grafts, from the LCX artery in particular, implies that most of the left-to-right collateral circulation originates from vessels that are proximal to the left-sided coronary artery stenoses. We had already evoked this hypothesis after having observed the absence of changes in CFI after revascularisation of the left coronary arteries in patients with triple vessel disease and chronic RCA occlusions [3]. The absence of a significant increase in CBF after left-sided coronary revascularisation indicates that it is mostly contributed by other sources, proximal to the stenoses of the grafted vessels.

The calculation of CBF described by Rockstroh and Brown [2], based on the rate of propagation of contrast material and angiographic diameter of the dominant collateral, appears to be accurate, with an estimated flow capacity of 0.67—1.44 ml/min/mmHg. Assuming a mean pressure gradient of approximately 40 mmHg between the revascularised left arterial network and the occluded RCA [3], the CBF can be estimated to be between 26.8 and 57.6 ml/min. This latter value corresponds to the mean blood flow at rest in the RCA [17,18], explaining the myocardial protection conferred by the collateral circulation. We have also demonstrated a close correlation between CBF, estimated by the CFI, and LVEF [3]. This confirmation of the existence of a well-developed functional collateral circulation proximal to stenotic lesions via angiographically visible collateral connections highlights the value of Werner et al.’s [14] classification, validated in reference to haemodynamic parameters. These authors showed that a collateral vessel creating a continuous side branch-like connection, >0.4 mm in diameter, supplies sufficient collateral circulation to preserve the function of the left ventricle in the territory supplied by the artery.

4.1. Limitations of the study

The modest variations in blood flow that we detected must be interpreted in the light of the model that was chosen for this study. In a non-negligible proportion of patients with triple vessel disease, lesions along the left-sided coronary arteries are likely to be situated between the site of RITA implantation and the source of collateral circulation, predominantly ensured by type b collateral vessels (Fig. 1). Such distal stenoses evidently are in the way of a less effective collateral blood supply provided by left-sided bypass grafts. However, precise intraoperative measurements of blood flow in the native coronary network cannot be made with this technique in humans, for evident ethical as well as anatomical reasons.

Finally, while a sufficient collateral circulation can be confirmed preoperatively by measuring regional ventricular function at rest, and by visualising an abundant collateral supply in patients with occluded coronary arteries, it is currently not possible to determine its performance during effort. In this perspective, a measurement of absolute myocardial perfusion by contrast echocardiography would refine the indications for revascularisation of chronically occluded coronary arteries.

5. Conclusions

Measurements of changes in blood flow across grafts implanted onto left coronary arteries after unclamping saphenous RCA grafts showed that the LCX artery and its branches provided the only significant CBF toward chronically occluded RCA. However, the amount of collateral circulation supplied by this graft was modest, confirming that most CBF after revascularisation for triple vessel disease originates from the proximal, native collateral network. Therefore, revascularisation of an occluded RCA remains fully justified.

References


