Coronary Physiologic Assessment and Imaging

Collateral Donor Artery Physiology and the Influence of a Chronic Total Occlusion on Fractional Flow Reserve

Andrew Ladwiniec, MA, MRCP; Michael S. Cunnington, BMedSci, MD, MRCP; Jennifer Rossington, BSc, MRCP; Adam N. Mather, BMedSci, MD, MRCP; Albert Alahmar, MRCP; Richard M. Oliver, DM, FRCP; Sukhjinder S. Nijjer, MRCP; Justin E. Davies, PhD, MRCP; Simon Thackray, MD, MRCP; Farquad Alamgir, MRCP; Angela Hoye, PhD, MRCP

Background—The presence of a concomitant chronic total coronary occlusion (CTO) and a large collateral contribution might alter the fractional flow reserve (FFR) of an interrogated vessel, rendering the FFR unreliable at predicting ischemia should the CTO vessel be revascularized and potentially affecting the decision on optimal revascularization strategy. We tested the hypothesis that donor vessel FFR would significantly change after percutaneous coronary intervention of a concomitant CTO.

Methods and Results—In consecutive patients undergoing percutaneous coronary intervention of a CTO, coronary pressure and flow velocity were measured at baseline and hyperemia in proximal and distal segments of both nontarget vessels, before and after percutaneous coronary intervention. Hemodynamics including FFR, absolute coronary flow, and the coronary flow velocity–pressure gradient relation were calculated. After successful percutaneous coronary intervention in 34 of 46 patients, FFR in the predominant donor vessel increased from 0.782 to 0.810 (difference, 0.028 [0.012 to 0.044]; P=0.001). Mean decrease in baseline donor vessel absolute flow adjusted for rate pressure product: 177.5 to 139.9 mL/min (difference −37.6 [−62.6 to −12.6]; P=0.005), mean decrease in hyperemic flow: 306.5 to 272.9 mL/min (difference, −33.5 [−58.7 to −8.3]; P=0.011). Change in predominant donor vessel FFR correlated with angiographic (%) diameter stenosis severity (r=0.44; P=0.009) and was strongly related to stenosis severity measured by the coronary flow velocity–pressure gradient relation (r=0.69; P<0.001).

Conclusions—Recanalization of a CTO results in a modest increase in the FFR of the predominant collateral donor vessel associated with a reduction in coronary flow. A larger increase in FFR is associated with greater coronary stenosis severity. (Circ Cardiovasc Interv. 2015;8:e002219. DOI: 10.1161/CIRCINTERVENTIONS.114.002219.)

Key Words: collateral circulation ■ coronary artery disease ■ physiology ■ pressure

The presence of a chronic total coronary occlusion (CTO) is a strong predictor of treatment strategy and is found in almost 1 in 5 patients with significant coronary artery disease on angiography. In the presence of a CTO, collateral blood supply originating from a major epicardial vessel other than the occluded vessel is usually present and is often sufficient to maintain resting perfusion and contractility in the collateral-dependent myocardium. In this setting, we would expect coronary flow to be increased relative to the same vessel in the absence of collateral donation. Restoration of antegrade flow by percutaneous coronary intervention (PCI) of a CTO has been shown to be associated with a rapid reduction in received collateral supply in the treated vessel and is likely to be coupled with an associated rapid reduction in flow in the collateral donor vessel amounting to the flow donated to the collateral-dependent myocardium before PCI.

In the setting of both single- and multivessel coronary disease, randomized trials support the use of fractional flow reserve (FFR) to guide PCI with an established treatment threshold of ≤0.8. Revascularization strategy based on angiographic assessment is frequently altered by FFR assessment. Although FFR is reported to be independent of changing hemodynamics, it is intimately related to total coronary flow through a stenosis, which in turn is related to perfused myocardial mass. In keeping with this, there have been several reports of large increases in collateral donor vessel FFR associated with PCI of a concomitant CTO and, therefore, reduction in perfused myocardium. However, there is inherent variability to FFR measurement and therefore selective reporting and publication bias might have exaggerated the magnitude (or even presence) of this phenomenon in the reported cases.
The purpose of this study is to serially investigate the changes in collateral donor vessel physiology, before and after successful PCI of a CTO and to test the hypothesis that there will be an associated significant change in collateral donor vessel FFR.

Methods

Study Patients

Forty-seven patients scheduled for PCI to a CTO for symptoms of angina (Canadian Cardiovascular Society class 1–3) were recruited and agreed by consensus. The nontarget vessel donating angiography by 2 independent observers blinded to hemodynamic measurements. The wire was normalized to aortic pressure at the tip of the catheter, advanced to the distal segment of each nontarget vessel, and manipulated to obtain a good Doppler trace. After administration of 100-μg intracoronary glyceryl trinitrate, once the hemodynamic response had settled, continuous recordings from the ComboMap were taken. Hyperemia was achieved by central venous administration of adenosine at 140 μg/kg per minute. Once steady state hyperemia had been reached and a continuous recording of ≥20 beats taken, adenosine infusion was ceased. The Combowire was withdrawn into the segment of the vessel proximal to any major side-branches and measurements repeated as described. Samples were recorded at 200 Hz and stored on disk for offline analysis.

After initial hemodynamic recordings, PCI of the CTO was undertaken at the discretion of the treating interventional cardiologist using an antegrade or retrograde approach. Once access to the vessel lumen distal to the point of occlusion was achieved, before restoration of antegrade flow, a microcatheter was placed into the distal vessel to facilitate delivery of the Combowire. The Combowire was positioned in a vessel segment angiographically free of a significant stenosis, then baseline and hyperemic measurements taken as described. PCI success was defined as stenting of the target vessel with <30% residual stenosis and thrombolysis in myocardial infarction grade III flow. If PCI was successful, nontarget vessel hemodynamic measurements were repeated as described preprocedure, including repeated central venous pressure measurement.

Recorded data were analyzed using dedicated custom software (Study Manager; Academic Medical Center, University of Amsterdam, The Netherlands and a Matlab [Mathworks Inc, Natick, MA] environment for wave intensity analysis; Imperial College London, London, United Kingdom).

Angiographic Assessment

Maximal nontarget vessel diameter stenosis (%) and proximal nontarget vessel diameters (at the point of proximal hemodynamic measurement) measured in 2 orthogonal views were calculated by 2 independent observers using quantitative coronary angiography (GE Centricity CA1000; GE Healthcare) using the guiding catheter luminal diameter as reference. Mean values from both observers were used for analysis. The nontarget vessel making the largest collateral contribution (the predominant collateral donor vessel), vessel collateral connection grade,19 and modified Rentrop score20 were assessed by 2 independent observers blinded to hemodynamic measurements and agreed by consensus. The nontarget vessel donating angiographically least/no collaterals to the occluded segment was considered the minor collateral donor vessel.

Data Analysis

FFR was calculated as (Pd-central venous pressure)/Pa-central venous pressure), using mean pressures taken over 5 cardiac cycles at stable hyperemia.24 An FFR of ≤0.80 was considered hemodynamically significant. Flow velocity was measured in cm/s, mean values are expressed as average peak velocity (APV), and instantaneous values as instantaneous peak velocity. Hyperemic microvascular resistance (HMR) was calculated as Pa/APV and hyperemic stenosis resistance as (Pa–Pd)/APV, both measured over 5 beats at stable hyperemia. Absolute coronary flow was estimated as ((proximal vessel radius)²×(proximal vessel APV/2))2.23 As resting absolute myocardial blood flow is closely related to rate pressure product, values for resting absolute coronary flow were divided by the respective rate pressure product/10,000.2 Coronary flow reserve (CFR) was calculated as APV at steady state hyperemia divided by APV at baseline, measured over 5 cardiac cycles.

Fractional collateral flow reserve was calculated as for FFR, with Pd measured in the occluded segment of the artery, before restoration of antegrade flow. Collateral flow velocity reserve was calculated as for CFR with flow velocities in the occluded segment measured at rest and steady state hyperemia.

The diastolic flow–velocity pressure gradient relation (DFV–PGR) describes the relationship between pressure and flow for a given stenosis or vessel segment.22,26 It was calculated using continuous
recordings of 30 cardiac cycles measured in the distal vessel from baseline to maximal hyperemia. Instantaneous pressures and flow velocities were extracted from the Study Manager program and Pa timings corrected to adjust for any time delay with respect to Pd. Instantaneous flow velocities from mid-diastole (after the diastolic upstroke in coronary flow velocity) to atrial activation (identified by the beginning of the p wave on ECG) were plotted against instantaneous pressure gradient (Pa-Pd). DFV–PGR was then calculated using Stata version 12 (StataCorp, College Station, TX), fitting the quadratic linear regression equation: $\Delta P = (F \times \text{instantaneous peak velocity}) + (S \times \text{instantaneous peak velocity}^2)$, where $\Delta P$ is the pressure gradient in mm Hg, $F$ is the coefficient of pressure loss because of viscous friction, and $S$ is the coefficient of pressure loss because of flow separation or localized turbulence downstream from the stenosis. Cumulative wave energy was calculated from simultaneous baseline pressure and flow measurements for the predominant and minor donor vessels. Pre- and postprocedural hemodynamic measurements for the predominant and minor donor vessels are detailed in Table 2.

Preprocedural predominant donor vessel FFR measured 0.782±0.117, which increased to 0.810±0.095 after CTO PCI (difference, 0.028; 95% confidence interval [CI], 0.012–0.044; $P=0.001$). We found no significant difference in the minor donor vessel. Individual FFR measurements are detailed in Figure 1. The treatment threshold for the predominant donor vessel was crossed from ≤0.8 to >0.8 in 4 patients (11.8%); however, 4 patients also crossed in the opposite direction from an FFR of >0.8 to ≤0.8.

### Hemodynamic Indices

Mean time in minutes from restoration of antegrade flow in the CTO vessel to post-PCI FFR measurement was 70.1±23.1 for the predominant donor vessel and 71.5±25.3 for the minor donor vessel. Pre- and postprocedural hemodynamic measurements for the predominant and minor donor vessels are detailed in Table 2.

Preprocedural predominant donor vessel FFR measured 0.782±0.117, which increased to 0.810±0.095 after CTO PCI (difference, 0.028; 95% confidence interval [CI], 0.012–0.044; $P=0.001$). We found no significant difference in the minor donor vessel. Individual FFR measurements are detailed in Figure 1. The treatment threshold for the predominant donor vessel was crossed from ≤0.8 to >0.8 in 4 patients (11.8%); however, 4 patients also crossed in the opposite direction from an FFR of >0.8 to ≤0.8.

### Coronal Flow

Satisfactory flow measurements were obtained in 32 of 34 subjects completing the study protocol. Changes in baseline and hyperemic absolute coronary flow are depicted in Figure 2. Predominant donor vessel absolute coronary flow under baseline conditions, adjusted for rate pressure product and expressed as mean ± standard deviation, was 49.7±25.4 cm3/minute. The treatment threshold of baseline-to-maximal hyperemia was crossed in 29 patients (85.3%). Of these, 25 patients (79.4%) crossed from ≤0.8 to >0.8, and 4 patients (11.8%) crossed from >0.8 to ≤0.8. Of these, 2 patients (5.9%) crossed from ≤0.8 to >0.8, and 2 patients (5.9%) crossed from >0.8 to ≤0.8.

### Statistical Analysis

Stata version 12 (StataCorp) was used for statistical analysis. Continuous values are expressed as mean±SD or median (25th percentile–75th percentile) as appropriate. Assuming a SD of the difference of 0.04 and success rate of CTO PCI of 70%; for the study to have 80% power to detect a 2-tailed change in FFR of 0.02, we estimated that 48 participants were required with procedural success in 33. Continuous variables were compared using a paired t test or Wilcoxon signed-rank test. Correlations were quantified using Pearson correlation coefficient. Probability values were 2 sided, and values of $P<0.05$ considered significant.

### Results

Of 47 patients recruited, 34 underwent successful CTO angioplasty, completed the study protocol, and were included in analysis. One was excluded because of significant left main stem disease found at the time of PCI not apparent on initial angiography. The presence of viable myocardium in the CTO territory was confirmed in all patients by myocardial perfusion scintigraphy (n=26; 76.5%), dobutamine stress echocardiography (n=1; 2.9%), or by the absence of a wall motion abnormality by echocardiography or left ventricular angiography without additional confirmation (n=7; 20.6%). Drug-eluting stents were used for all procedures. Demographics, angiographic, and procedural details are shown in Table 1.
Effect of a CTO on Collateral Donor FFR

Table 2. Hemodynamic Assessment Pre and Post Chronic Total Coronary Occlusion Percutaneous Coronary Intervention

<table>
<thead>
<tr>
<th></th>
<th>Preprocedure</th>
<th>Postprocedure</th>
<th>Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVP, mm Hg</td>
<td>5.6±2.9</td>
<td>6.1±3.1</td>
<td>0.5 (−1.7 to 0.7)</td>
<td>0.39</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>121.7±18.8</td>
<td>124.2±19.7</td>
<td>−2.5 (−9.9 to 4.9)</td>
<td>0.50</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>69.7±12.4</td>
<td>70.4±11.2</td>
<td>−0.6 (−3.5 to 2.3)</td>
<td>0.67</td>
</tr>
<tr>
<td>Predominant donor vessel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFR</td>
<td>0.78±0.117</td>
<td>0.810±0.095</td>
<td>0.028 (0.012 to 0.044)</td>
<td>0.001</td>
</tr>
<tr>
<td>Baseline flow, mL/min*</td>
<td>177.5±87.2</td>
<td>139.9±68.2</td>
<td>−37.6 (−62.6 to −12.6)</td>
<td>0.005</td>
</tr>
<tr>
<td>Hyperemic flow, mL/min†</td>
<td>306.5±149.0</td>
<td>272.9±151.1</td>
<td>−33.5 (−58.7 to −8.3)</td>
<td>0.011</td>
</tr>
<tr>
<td>CFR†</td>
<td>2.24±0.93</td>
<td>2.33±0.78</td>
<td>0.10 (−0.24 to 0.44)</td>
<td>0.57</td>
</tr>
<tr>
<td>HMR, mm Hg/cm²·s⁻¹†</td>
<td>1.92±0.71</td>
<td>2.47±1.35</td>
<td>0.55 (0.12 to 0.99)</td>
<td>0.014</td>
</tr>
<tr>
<td>HSR, mm Hg/cm²·s⁻¹†</td>
<td>0.50±0.37</td>
<td>0.50±0.30</td>
<td>−0.002 (−0.09 to 0.09)</td>
<td>0.95</td>
</tr>
<tr>
<td>Minor donor vessel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFR</td>
<td>0.808±0.104</td>
<td>0.813±0.110</td>
<td>0.005 (−0.015 to 0.023)</td>
<td>0.63</td>
</tr>
<tr>
<td>Baseline absolute flow,</td>
<td>157.6±80.3</td>
<td>141.4±98.1</td>
<td>−16.2 (−43.3 to 11.0)</td>
<td>0.23</td>
</tr>
<tr>
<td>mL/min†</td>
<td>274.4±147.7</td>
<td>270.6±185.3</td>
<td>−3.7 (−29.9 to 22.4)</td>
<td>0.77</td>
</tr>
<tr>
<td>CFR†</td>
<td>2.25±0.67</td>
<td>2.24±0.72</td>
<td>−0.01 (−0.24 to 0.27)</td>
<td>0.91</td>
</tr>
<tr>
<td>HMR, mm Hg/cm²·s⁻¹†</td>
<td>2.28±0.95</td>
<td>2.47±1.32</td>
<td>0.19 (−0.11 to 0.49)</td>
<td>0.20</td>
</tr>
<tr>
<td>HSR, mm Hg/cm²·s⁻¹†</td>
<td>0.48±0.28</td>
<td>0.54±0.43</td>
<td>0.06 (−0.03 to 0.15)</td>
<td>0.20</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; CFR, coronary flow reserve; CVP, central venous pressure; FFR, fractional flow reserve; HMR, hyperemic microvascular resistance; HSR, hyperemic stenosis resistance; and SBP, systolic blood pressure.

*Adjusted for rate pressure product.
†Satisfactory flow measurements were obtained in 32 patients.

Discussion

Our findings support the hypothesis that in a patient with a CTO, measurement of the FFR in an artery providing collateral supply to the myocardium beyond the occlusion is significantly lower than it would otherwise be in the absence of the CTO. Our estimate of the size of the effect in a group of unselected patients is smaller than suggested by case reports of the phenomenon.12–16 Several of our findings are suggestive of a possible physiological mechanism and reasons for variation in size of change; they are as follows: (1) there is an associated reduction in absolute coronary flow and increase in HMR; (2) the reduction in coronary flow is −29.6 to 37.7 mL/min; P=0.60). There was also no statistically significant change in mean CFR or hyperemic stenosis resistance in either the predominant donor vessel or the minor donor vessel.

HMR did increase after CTO PCI in the predominant donor vessel; preprocedure: 1.92±0.71 mm Hg·cm⁻²·s⁻¹; postprocedure: 2.47±1.35 mm Hg·cm⁻²·s⁻¹ (difference, 0.55 mm Hg·cm⁻²·s⁻¹; 95% CI, 0.12–0.99; P=0.014); there was no statistically significant change in the minor donor vessel.

It was possible to measure coronary flow velocity distal to the point of occlusion in 30 patients, 4 of which through a retrograde approach. Mean collateral flow velocity reserve measured 1.09±0.25 (excluding retrograde measurements, 1.08±0.26). We found no correlation between change in predominant donor vessel FFR and invasive measures of collateral perfusion measured distal to the occlusion; fractional collateral flow reserve: r=−0.08, P=0.66; collateral flow reserve: r=−0.10, P=0.62; or change in coronary flow velocity at the point of FFR measurement: r=0.11, P=0.55. In the predominant donor vessel, there was a trend to a smaller reduction in flow in more severe stenoses measured by DFV–PGR (r=0.33; P=0.068). We did find a relationship between maximal angiographic stenosis severity in the predominant donor vessel and change in FFR in the predominant donor vessel: r=0.44, P=0.009 (Figure 3).

Figure 4 shows an example of measurement and calculation of the DFV–PGR. There was a strong correlation between peak DFV–PGR slope in the predominant donor vessel and change in predominant donor vessel FFR; r=0.69, P<0.001 (Figure 5).

Wave Intensity Analysis

Wave intensity analysis was performed in 32 of 34 patients using measurements taken from the proximal nontarget vessels before any major branch; Figure 6 shows typical examples. In the predominant donor vessel, mean cumulative wave energy of the BEW decreased from 79.7±43.6×10⁵ J·m⁻²·s⁻² before PCI to 65.3±43.6×10⁵ J·m⁻²·s⁻² after PCI (difference, −14.3×10⁵ J·m⁻²·s⁻²; 95% CI, −25.9×10⁵ to −2.9×10⁵; P=0.016). We found no statistically significant difference in the minor donor vessel; Pre-PCI: 71.9±39.9×10⁵ J·m⁻²·s⁻², post-PCI: 67.1±42.3×10⁵ J·m⁻²·s⁻² (difference, −4.8×10⁵ J·m⁻²·s⁻²; 95% CI, −18.5×10⁵ to 9.0×10⁵; P=0.49). Change in cumulative wave energy correlated with change in resting coronary flow, unadjusted for rate pressure product: r=0.43, P=0.014.
associated with a reduction in size of the BEW; (3) the magnitude of reduction in flow is similar at baseline and hyperemia; (4) change in FFR is strongly related to donor vessel coronary stenosis severity; and (5) there is no demonstrable association between invasive indices of collateral function and change in FFR.

**Effect Size**

The increase in predominant donor vessel FFR associated with CTO PCI of \( \approx 0.03 \) is consistent with a smaller study examining the same phenomenon\(^3\); however, case reports suggest that the expected increase should be closer to 0.10.\(^1\)–\(^5\) This may be because measurement and remeasurement of an index such as the FFR is vulnerable to confounding by regression to the mean. If measurements are considered as a whole and not selected based on their values, regression to the mean will not influence overall effect size. However, individual measurement changes are much more likely to involve a contribution by regression to the mean.\(^3\) It can be estimated that the SD of the difference of repeated FFR measurements is 0.032 and coefficient of repeatability 0.063; this measurement variability is sufficient for regression to the mean to explain the disparity if the case reports are subject to selective reporting or publication bias. In addition, there seems to be a greater change in FFR in more severely diseased vessels. Including angiographically unobstructed vessels is likely to have reduced our effect size. However, it has been suggested that the phenomenon exists in unobstructed vessels\(^4\) and the mean pre-PCI FFR in the predominant donor vessel was 0.78, close to the widely practiced treatment threshold of 0.80 at which the phenomenon is most relevant.

**Reduction in Donor Vessel Flow**

A likely explanation for the change in predominant donor vessel FFR is the associated reduction in absolute coronary flow.
flow (Figure 2) and increase in HMR. Previous studies have shown a rapid reduction in recruitable collateral flow distal to the point of occlusion after CTO PCI,\(^4,5\) we have shown a reduction in coronary donor vessel flow at a similar interval. The absence of this finding in the vessel donating no/fewer collaterals suggests that the change is related to reduced collateral donation. A generalized effect of PCI on microvascular function seems less likely, whether mediated through an adrenergic effect\(^35\) or through myocardial stunning and an elevation in left ventricular end-diastolic pressure.\(^36,37\) An alternative mechanism that may work in synergy with the reduction in flow is that collateral contribution to distal pressure in the donor vessel might increase once the CTO is recanalized in the reverse direction to collateral flow before PCI.

**Mechanism of a Reduction in Donor Vessel Flow**

In support of the hypothesis that the observed reduction in donor vessel coronary flow is related to a reduction in collateral donation and perfused myocardial mass, we demonstrate a reduction in the size of the BEW in the predominant collateral donor vessel associated with CTO PCI. Moreover, the size of that reduction is related to the size of reduction in flow. A predominant pattern of 6 coronary waves measured by wave intensity analysis has been described. The BEW, caused by the relief of myocardial microcirculatory compression in early diastole, is responsible for the large increase seen in coronary flow in early diastole\(^30\) (Figure 6). Increased left ventricular contractility is associated with an increase in the size of the early backward compression wave.\(^38\) The size of the BEW, being driven by the reverse of the mechanism of the early backward compression wave, is likely to be related to the mass of myocardium relaxing in early diastole. A reduction in its size associated with a change in flow supports the hypothesis that a change in donor vessel antegrade flow is related to reduced collateral donation, rather than an increase in received collateral supply.

We describe a similar fall in predominant donor vessel absolute flow after CTO PCI at baseline and hyperemia. This is consistent with the fall in coronary flow being the component of pre-PCI flow donated to the collateral-dependent myocardium. Flow in well-collateralized occluded vessel segments responds to an arteriolar vasodilatory stimulus in a similar fashion to flow beyond a severe stenosis.\(^39\) The microcirculation beyond a severe stenosis is already maximally vasodilated, so a further vasodilatory stimulus is unlikely to increase flow.\(^39\) Coronary flow distal to a CTO can actually diminish with adenosine infusion (a CFR of <1), a phenomenon known as coronary steal.\(^34,41\) The mean collateral flow velocity reserve measured in the occluded segment in this study was 1.09, with coronary steal evident in 9 patients (26%). The small relative proportion of donor vessel absolute flow attributable to the collateral circulation at hyperemia may explain the relatively small increase in FFR.
Change in FFR Is Related to Stenosis Severity

We report an association between predominant donor coronary stenosis severity and change in FFR in the predominant donor vessel associated with CTO PCI, assessed both angiographically and hemodynamically (Figures 3 and 5). Although functional stenosis severity assessment by angiography is limited, it is independent of individual variation in measurement of FFR and, therefore, the relationship with pre/post measurement should not be confounded by regression to the mean.33

The DFV–PGR describes the pressure gradient as a result of overall lesion severity, encompassing lesion length, diameter stenosis, and induced turbulence as coronary flow velocity changes (Figure 4). The slope of the curve is independent of the absolute difference in Pd and Pa and so in addition to describing the effect of a change in flow on pressure-based physiological lesion indices, it should also be less susceptible to confounding by regression to the mean compared with indices dependent on absolute values of Pa and Pd. The observed strong association between a steeper predominant donor peak DFV–PGR slope and a greater change in predominant donor FFR (Figure 5) is supportive of the hypothesis that any change in pressure gradient (and therefore FFR) is related to reduced flow.

Relationship of Change in FFR and Indices of Collateral Function in the Occluded Segment

The absence of a relationship between the change in predominant donor flow and measured indices of collateral function is surprising. It may be that overall collateral-dependent myocardial mass is more important than the measurement of collateral function for a given myocardial mass. This could be evaluated by comparing left anterior descending artery with non–left anterior descending artery CTOs, but would require a study population larger than reported here. The absence of a correlation between change in predominant donor vessel flow and change in predominant donor FFR may reflect an interaction between the effect of donor vessel stenosis severity on collateral flow and the effect of the change of flow. Coronary steal, and therefore reduced collateral flow at hyperemia, is more prevalent if a collateral donor vessel has a lower FFR.34 We report a trend toward a smaller change in hyperemic flow associated with CTO PCI in predominant donor vessels with more severe stenoses. A smaller change in flow may, therefore, be associated with a steeper DFV–PGR slope, masking any relationship.

Clinical Implications

This study confirms that the presence of a CTO is associated with a lower FFR in the predominant collateral donor vessel than if the CTO were absent. The change is smaller than might be expected and is closely related to lesion severity such that greater changes are largely confined to stenoses of severities that remain below the treatment threshold of ≤0.8 in spite of a large increase in FFR. The number of patients in the study population that cross the treatment threshold is small. A small number have also crossed the FFR treatment threshold in the opposite direction to that expected, most likely because of measurement variation and possibly short-term PCI-related effects on the microvasculature. When planning multivessel revascularization in the presence of a concomitant CTO, physiological lesion assessment by FFR is reliable. If measurements are close to the current established treatment threshold of ≤0.80, a probable small increase in FFR should be considered when deciding on treatment strategy.

Limitations

This is a single-center study, and the number of patients with a significant lesion in the predominant donor vessel was small. The study population had a preponderance of right
coronary CTOs, with fewer left anterior descending artery CTOs. This is a reflection of practice and is in keeping with other publications in the field but may have reduced the size of the observed effect.

Measurements were repeated early after PCI; therefore, transient procedural-related changes such as microvascular dysfunction because of distal embolization, catecholamine release, left ventricular stunning, or a hyperemic stimulus related to side-branch occlusion may have influenced donor vessel physiology. However, if the observed effect was because of transient global effects of PCI, we would expect a similar effect on the vessel donating no/less collaterals angiographically. In addition, other than the hyperemic effect of side-branch occlusion, these mechanisms would result in a larger reduction in donor vessel flow and larger increase in FFR. Given the smaller than expected change we observed, it seems unlikely that these additional mechanisms are contributing greatly to the overall change; however, they may have contributed to individual variation.

Conclusions
Recanalization of a CTO results in a modest increase in the FFR of the collateral donor vessel associated with a reduction in coronary flow. The magnitude of the change is closely related to lesion severity such that the largest changes are observed across stenoses, which remain hemodynamically significant in spite of a large increase in FFR. In vessels with less severe stenoses, the effect is likely to be so small that it is masked by variations in physiology both related and unrelated to PCI, as well as measurement variation.

Sources of Funding
This study was funded by a grant provided by The Hull & East Yorkshire Cardiac Trust Fund.

Figure 6. Wave intensity analysis, ensemble averaged coronary pressure (solid line) and flow velocity (dashed line) measured in the proximal predominant donor vessel pre (left) and post (right) percutaneous coronary intervention of a chronic total coronary occlusion. Top row, Proximal right coronary artery (RCA) donating collaterals to a chronically occluded left anterior descending artery (LAD). Bottom row, Proximal LAD donating collaterals to a chronically occluded RCA. *Backward expansion wave.
Disclosures

None.

References


Collateral Donor Artery Physiology and the Influence of a Chronic Total Occlusion on Fractional Flow Reserve

Andrew Ladwiniec, Michael S. Cunnington, Jennifer Rossington, Adam N. Mather, Albert Alahmar, Richard M. Oliver, Sukhjinder S. Nijjer, Justin E. Davies, Simon Thackray, Farquad Alamgir and Angela Hoye

Circ Cardiovasc Interv. 2015;8:
doi: 10.1161/CIRCINTERVENTIONS.114.002219

Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7640. Online ISSN: 1941-7632

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circinterventions.ahajournals.org/content/8/4/e002219

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Interventions can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Interventions is online at:
http://circinterventions.ahajournals.org//subscriptions/