Coronary collaterals provide a constant scaffold effect on the left ventricle and limit ischemic left ventricular dysfunction in humans

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Hoole SP, White PA, Read PA, Heck PM, West NE, O’Sullivan M, Dutka DP. Coronary collaterals provide a constant scaffold effect on the left ventricle and limit ischemic left ventricular dysfunction in humans. J Appl Physiol 112: 1403–1409, 2012. First published February 9, 2012; doi:10.1152/japplphysiol.01304.2011.—Coronary collaterals preserve left ventricular (LV) function during coronary occlusion by reducing myocardial ischemia and may directly influence LV compliance. We aimed to re-evaluate the relationship between coronary collaterals, measured quantitatively with a pressure wire, and simultaneously recorded LV contractility from conductance catheter data during percutaneous coronary intervention (PCI) in humans. Twenty-five patients with normal LV function awaiting PCI were recruited. Pressure-derived collateral flow index (CFI): CFI0 = (Pv − Pa)/Pv was calculated from pressure distal to coronary balloon occlusion (Pv), central venous pressure (Pa), and aortic pressure (Pv). CFI0 was compared with the changes in simultaneously recorded LV end-diastolic pressure (∆LVEDP), end-diastolic volume, maximum rate of rise in pressure (∆LVEDP/dtmax; systolic function), and time constant of isovolumic relaxation (ΔLV τ; diastolic function), measured by a LV cavity conductance catheter. Measurements were recorded at baseline and following a 1-min coronary occlusion and were duplicated after a 30-min recovery period. There was significant LV diastolic dysfunction following coronary occlusion (∆LVEDP: +24.5%, P < 0.0001; and ∆LV τ: +20.0%, P < 0.0001), which inversely correlated with CFI0 (∆LVEDP vs. CFI0: r = −0.54, P < 0.0001; ∆LV τ vs. CFI0: r = −0.46, P = 0.0009). Subjects with fewer collaterals had lower LVEDP at baseline (r = 0.33, P = 0.02). CFI0 was inversely related to the coronary stenosis pressure gradient at rest (r = −0.31, P = 0.03). Collaterals exert a direct hemodynamic effect on the ventricle and attenuate ischemic LV diastolic dysfunction during coronary occlusion. Vessels with lesions of greater hemodynamic significance have better collateral supply.

low-flow ischemia; LV contractility; diastolic dysfunction

MYOCARDIAL ISCHEMIA CAUSES left ventricular (LV) diastolic dysfunction, resulting in a reduction in LV wall compliance and raised LV end-diastolic pressure (LVEDP) (4, 14, 17, 30). Coronary collaterals reduce myocardial ischemia during coronary occlusion. They are associated with less angina, ST-segment deviation on ECG, and LV systolic dysfunction during percutaneous coronary intervention (PCI) (25, 29) and by reducing ischemia, may blunt rises in LVEDP. They improve long-term prognosis in patients with stable coronary disease (23, 24). Coronary collateral blood flow can be objectively quantified by intracoronary distal pressure, when antegrade flow is prevented by coronary balloon occlusion (21, 22, 28, 34).

There is hemodynamic “cross talk” between the epicardial vasculature and the LV cavity (32), and it has been hypothesized that collateral channels exert a direct hemodynamic effect on the LV. Good collateral flow may increase rather than decrease LVEDP (8, 26) by increasing epicardial vascular turgor and reducing LV compliance, acting like an external scaffold, similar to the observed difference in LVEDP between low-flow and normal-flow ischemia (7). Collaterals may also preserve systolic function by reducing ischemia or through the Gregg effect, where myofibril stretch, from preserved microvascular volume provided by good collaterals, maintains membrane calcium influx into the cardiac myocyte and contractile force (12). This is also termed the “garden-hose” effect. In addition, LV hemodynamic changes (ΔLV) may be transmitted to the myocardial interstitium, compressing collaterals and affecting flow, as described by the Waterfall effect (9). Coronary collaterals demonstrate the vascular Waterfall effect and collapse at a threshold of ~25 mmHg–30 mmHg (6, 11). This can occur at higher backpressures when the LVEDP is elevated.

We aimed to re-evaluate the relationship between quantitatively derived coronary collateral flow and LV hemodynamics, measured simultaneously during PCI. We hypothesized that the coronary collaterals would influence indices of diastolic and systolic function during coronary occlusion, predominantly by reducing ischemic LV dysfunction.

METHODS

Study Population

Twenty-five consenting patients awaiting elective PCI to a proximal American College of Cardiology/American Heart Association type-A stenosis and with normal LV function (ejection fraction (EF) > 55%) were recruited. Patients were excluded if they were having an emergency procedure, if they had suffered a myocardial infarction in the preceding 3-mo period, if they had significant valvular heart disease or peripheral vascular disease, or if they had a permanent pacemaker. The Local Research Ethics Committee approved the study protocol (09/H0311/17). The study conformed to the principles outlined in the Declaration of Helsinki.

Preprocedural Protocol

Variables that could alter coronary physiology were minimized. Patients were asked to abstain from caffeine, alcohol, nicotine, and oral/sublingual nitrate and nicorandil use for a 24-h period prior to
their procedure. All subjects fasted for 6 h and received aspirin 300 mg, clopidogrel 300 mg, and diazepam 5 mg at least 6 h prior to PCI. The catheter laboratory was maintained at a constant ambient temperature (21°C ± 0.5°C), and noise was kept to a minimum.

**Procedural Protocol**

**Cardiac catheterization.** Bilateral femoral arterial (6F and 7F) and venous (5F) sheaths were inserted. A catheter was placed into the right atrium to record central venous pressure (Pc). PCI was performed using 6F guiding catheters. All patients were anticoagulated with a heparin bolus (70–100 U/kg) after arterial sheath insertion to achieve an activated clotting time >250 s. No hemodynamic altering medication was administered during the procedure.

After the research measurements, all patients underwent PCI with angiographic success, defined as a residual stenosis of <15% and thrombolysis in myocardial infarction complete perfusion (TIMI 3 flow) in the target vessel. Angiographic stenosis severity, before and after stenting, was assessed by quantitative coronary angiography (QCA; Cardiac Viewer CV 1000, Version 2.1.0; InfiMed, Liverpool, NY).

**LV hemodynamic calibration.** The conductance catheter technique has been described previously in detail by Baan et al. (3) to determine LV pressure-volume relations. Briefly, a 7F, eight-electrode conductance catheter with an integrated micromanometer tip (Millar Instruments, Houston, TX) was advanced via a femoral sheath into the LV apex (Fig. 1A). It was placed along the longitudinal axis of the ventricle to minimize motion during the cardiac cycle.

The catheter was connected to a signal conditioning and processing unit (CD Leycom, Zoetermeer, The Netherlands), and signals were acquired using custom software at 250 Hz. A 20-kHz, 30-pA current was applied to the distal and proximal electrodes, and the remaining six electrodes were used to measure a time-varying ventricular conductance [G(t)] as the sum of the intervening five segments. The relationship between the time-varying volume [V(t)] and the G(t) is given by the formula V(t) = 1/α·L2·r[G(t) - G(p)], where α is the ratio of the conductance-derived volume to true ventricular volume, L is the interelectrode distance, r is the resistivity of blood in Ω/cm, and G(p) is the parallel conductance due to the conductance of structures outside the ventricular blood pool. Volume correction (Vc) for G(p) was calculated from the formula Vc = 1/α·L2·r[G(p)], estimated by the hypertonic saline injection technique described by Baan et al. (3).

Three rapid injections of 5 to 10 ml, 8.4% saline into the main pulmonary artery during held-expiration were performed, increasing LV conductivity alone, without a changing volume. Regression analysis of LV end-diastolic volumes (LVEDVs) vs. LV end-systolic volumes (LVESVs) from these beats during transient-increased conductivity yields a linear relationship. Extrapolation of this linear relation to the point of zero blood conductivity [LVEDV = LVESV, with no apparent stroke volume (SV)] gave an estimate of the volume signal outside of the ventricular blood pool (Vc). The slope coefficient (α), calculated to correct for inhomogeneity of the electric field, was determined by an average Fick cardiac output, measured three times.

**LV hemodynamic measurements.** Conductance catheter data were analyzed offline using PVAN software (Millar Instruments). Five cardiac cycles, at baseline and after 1-min balloon occlusion (just before balloon deflation), were recorded (Fig. 1B). Mean index of diastolic function [time constant of LV isovolumic relaxation (LV τ)], systolic function [maximum rate of pressure generation (LV dP/dtmax)], LVEDP and LVEDV, SV, and EF was calculated for comparison with the coronary data. Conductance catheter-derived P0—measured from the time of peak rate of pressure decline (dP/dtmax) to 5 mmHg above end-diastolic pressure—was used to calculate LV τ, derived from the monoexponential decay of the pressure wave form:

\[ P_0 = Ke^{-\beta t}. \]

LV τ is the slope of the log P0 vs. t relation (τ = −1/slope, assuming P0 = 0). A simplified equation and first derivative are sometimes used as P0 ≠ 0 in normal physiology:

\[ P = (P_0 - P_0e^{-\beta t}) + P_0' + \frac{dP}{dt} = (-1/\tau)P - P_0/\tau. \]

Linear regression of dp/dt vs. P yields τ = −1/slope.

**Coronary hemodynamic calibration.** A 0.014-in. pressure wire (Volcano Therapeutics, Rancho Cordova, CA) was used, enabling

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Fig. 1. A: a right anterior oblique fluoroscopic image of a conductance catheter in the left ventricular (LV) cavity and pressure wire in the mid left anterior-descending artery during proximal balloon occlusion; B: LV pressure-volume loops at baseline (red) and during 1-min coronary occlusion (blue); C: a circuit diagram of the coronary measurements during occlusion [central venous pressure (Pc)]: an example of simultaneously recorded aortic pressure (P0; red) and wedge pressure (Pw; yellow) during balloon occlusion; and deflection are shown.
intracoronary pressure measurements during PCI. The measurements were recorded digitally at each PCI stage onto a ComboMap (Volcano Therapeutics) console for offline analysis.

The wire was calibrated to atmospheric pressure outside of the patient, prior to insertion, and then advanced via the guiding catheter to the ostium of the left main stem, where aortic and wire-tip pressures were equalized. The tip of the wire was then positioned 3–5 cm beyond the stenosis.

**Coronary hemodynamic measurements.** The mean pressure distal to the stenosis (Pd) was recorded from an average of five beats and compared with the mean aortic pressure (Pao), simultaneously measured at the guiding catheter to derive the coronary stenosis pressure gradient (Pd/Pao). Distal coronary and aortic pressures were then acquired during a low-pressure balloon occlusion at less than four atmospheres for 1 min. Coronary occlusion was confirmed by contrast injection during balloon inflation. An average of five beats was used to calculate mean coronary wedge pressure distal to the balloon occlusion (Pw) and Pao just prior to balloon deflation. After 30 min recovery, baseline and balloon occluded coronary measurements were repeated. The pressure-derived collateral flow index (CFIw) was calculated (Fig. 1C) as: CFIw = (Pw − Pd)/(Pd − Pao).

**Statistical Analysis**

Data are expressed as a mean ± SD. LV hemodynamic data after balloon occlusion were converted to a percentage change from baseline values to facilitate data comparison. Correlations between LV and coronary collateral data were analyzed using Pearson’s coefficient. Comparisons between data were made using the paired Student’s t-test. A probability level of P < 0.05 was considered significant. All calculations were done with SPSS for Windows, v 14 (SPSS, Chicago, IL).

**RESULTS**

**Patient Demographics**

Patient demographic data are summarized in Table 1. Collateral and LV data were acquired in all but one patient, providing 48 paired datasets for analysis. All of the patients were treated successfully by PCI. There was no significant difference in mean CFIw between nitrate and non-nitrate users (CFIw: 0.192 vs. 0.136; P = 0.24).

**Coronary and LV Hemodynamic Data**

**Coronary data.** The serial low-pressure balloon inflations did not alter the coronary stenosis severity measured by QCA (P = 0.62) or Pd/Pao: 0.76 (0.20) vs. 0.78 (0.20); P = 0.26. Serial measurements of CFIw were highly reproducible (r = 0.97, P < 0.0001). Repeated, 1-min coronary occlusion did not recruit collaterals acutely (CFIw: 0.150 vs. 0.146; P = 0.49). CFIw and Pw strongly correlated with each other (r = 0.89, P < 0.0001). CFIw and Pao had a modest inverse correlation to the Pd/Pao at rest (r = −0.31, P = 0.03; r = −0.30, P = 0.04, respectively; Fig. 2).

**LV hemodynamic data.** There were substantial ∆LV hemodynamic measurements after a 1-min balloon occlusion (Table 2): mean ∆LVEDP: +24.5%, P < 0.0001; mean ∆LVSV: −12.4%, P = 0.003, but there was no significant change in mean ∆LVEDV: −2.0%, P = 0.29. As a result, LVEF fell: −11.3%, P = 0.001. LV systolic function was significantly impaired after balloon occlusion (∆LV dP/dtmax: −10.7%, P < 0.0001), as was LV diastolic function compared with baseline (∆LV τ: +20.0%, P < 0.0001).

**Coronary collaterals and LV hemodynamic data.** Changes in LVEDP after 1-min coronary balloon occlusion were inversely correlated with CFIw (r = −0.54, P < 0.0001; Fig. 3A). This was largely driven by differences in Pw, which also inversely correlated with ∆LVEDP (r = −0.55, P < 0.0001; Fig. 3B), whereas Pao remained constant (Table 2). Patients with lower Pw values had a lower baseline LVEDP (r = 0.33, P = 0.02; Fig. 3C), as did those with lower CFIw (r = 0.29, P < 0.05). LVEDP, during coronary occlusion, was not related to Pao (r = 0.06, P = 0.68; Fig. 3D).

Diastolic dysfunction during coronary balloon occlusion in subjects with poorer collaterals was confirmed by an inverse correlation between ∆LV τ and the degree of collaterals (CFIw: r = −0.46, P = 0.0009; Pw: r = −0.45, P = 0.0012; Fig. 4, A and B). This was driven by LV τ during coronary occlusion, inversely correlating with Pw (r = −0.47, P = 0.0008; Fig. 4C). Systolic dysfunction measured by ∆LV dP/dtmax did not correlate with CFIw (r = 0.07, P = 0.62) nor did ∆LVSV (r = 0.14, P = 0.35). There was also no correlation between CFIw and ∆LVEF (r = 0.10, P = 0.67), and ∆LVEDV was too small to reliably establish a correlation with the degree of coronary collaterals.

**DISCUSSION**

This is the first study to simultaneously assess coronary collateral and LV hemodynamics during coronary balloon occlusion in humans. Coronary balloon occlusion caused diastolic and systolic LV dysfunction. The development of diastolic LV dysfunction during coronary balloon occlusion was attenuated in subjects with good collaterals to the occluded

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**Table 1. Patient demographic data**

<table>
<thead>
<tr>
<th>Age, years</th>
<th>60.6 (10.3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>24 males, 1 female</td>
</tr>
<tr>
<td>Risk factors</td>
<td>30.7 (3.9)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>10 (40%)</td>
</tr>
<tr>
<td>LDLc, mmol/l</td>
<td>1.9 (0.6)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Random blood glucose, mmol/l</td>
<td>5.4 (1.0)</td>
</tr>
<tr>
<td>Previous myocardial infarct</td>
<td>9 (36%)</td>
</tr>
<tr>
<td>Canadian Cardiac Society Angina Class</td>
<td>21 (18)</td>
</tr>
<tr>
<td>Medication</td>
<td>21 (18)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>25 (100%)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>25 (100%)</td>
</tr>
<tr>
<td>Statin</td>
<td>23 (92%)</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>22 (88%)</td>
</tr>
<tr>
<td>ACE inhibitor or ARB</td>
<td>16 (64%)</td>
</tr>
<tr>
<td>Nitrates</td>
<td>11 (44%)</td>
</tr>
<tr>
<td>Hemodynamics</td>
<td>66 (11)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>68 (10)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>82.1 (11.3)</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>58 (10)</td>
</tr>
<tr>
<td>Stenosis</td>
<td>82.1 (11.3)</td>
</tr>
<tr>
<td>Location: LAD/LCx/RCA, n</td>
<td>21, 2, 2</td>
</tr>
<tr>
<td>Severity: QCA DS, %</td>
<td>82.1 (11.3)</td>
</tr>
</tbody>
</table>

Categorical data are expressed as frequency (%) and continuous data as mean (SD). LDLc, LDL concentration; ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; bpm, beats/min; LAD, left anterior descending; LCx, left circumflex; RCA, right coronary artery; QCA DS, quantitative coronary angiography diameter stenosis.
vessel. The baseline LVEDP was elevated in patients with evidence of good collaterals. Vessels with lesions of greater hemodynamic significance had better collateral supply. Our observations suggest that collaterals can have a direct effect on the LV in diastole as well as attenuating ischemic LV diastolic dysfunction during coronary occlusion.

**Coronary-LV Cross Talk**

**Coronary collateral effect on LV.** An improvement in coronary perfusion pressure and microvascular flow has been shown to increase contractile function due to increased calcium influx secondary to myofibril stretch. This is known as the Gregg or garden-hose effect and helps match supply and demand (2, 12, 18). Coronary perfusion pressure may also reduce LV diastolic compliance—a phenomenon known as the Salisbury effect (27). LV hemodynamic changes are different if induced by coronary balloon occlusion (low-flow ischemia) compared with pacing-induced ischemia or hypoxemia (normal-flow ischemia) (5, 7). Normal-flow ischemia reduced LV end-diastolic compliance to a greater extent than low-flow ischemia, resulting in a higher LVEDP. The authors proposed that their observations could be explained by an increase in vascular turgor during normal-flow ischemia, resulting in a scaffold effect. Similarly, the Salisbury effect from collateral turgor has been reported to explain the reduction in LV diastolic compliance and subsequent increase in LVEDP in patients with good collaterals (8, 26).

Our observations that Pw correlated with baseline LVEDP supports a significant scaffold effect from collaterals to the LV cavity in humans. It also implies that collateral channels are “open” and exerting a hemodynamic effect at baseline, even when the recipient artery is not occluded. During ischemia, those with poor collaterals (lower CFIp) have an increase in ΔLVEDP due to ischemia, whereas in those with adequate collaterals the LVEDP remains constant. Similar observations occurred when comparing collateral flow with LV τ. Previous work has shown a positive correlation between coronary collateral filling and the preservation of LV wall motion in the area supplied during ischemia (13, 15, 29). Our data concur; ischemic LV diastolic dysfunction inversely correlated with CFIp. Perhaps surprisingly, we did not observe a similar maintenance of systolic function in patients with better collateral flow. This may be explained by the ischemic cascade, where diastolic ischemic dysfunction precedes systolic ischemic dysfunction. We speculate that a more prolonged coronary occlusion time may be required to cause greater systolic dysfunction, which may have made a relationship between collaterals and systolic function apparent. An alternative explanation is that collateral flow, as with coronary flow, occurs predominantly in diastole rather than systole and as a result, may exert less of a hemodynamic effect on systolic indices of contractility.

**LV effect on coronary collaterals.** The effect of cardiac muscle on the coronary vasculature is based on the Waterfall model: flow within a coronary vessel becomes backpressure (Pp) independent, due to external compression, which will eventually lead to vessel collapse (9). This explains why ischemia is mostly subendocardial at the site of greatest wall stress. Coronary collaterals have been reported to demonstrate the vascular Waterfall effect and collapse at a threshold of ~25 mmHg–30 mmHg (6, 11). Overestimation of collaterals by CFIp has been attributed to the outward transmission LV cavity pressure to the distal coronary (8).

We have demonstrated no correlation between LVEDP during coronary occlusion and Pw, and the observation that increasing LVEDP is associated with lower rather than higher Pw values refutes a significant transmission of LV preload affect-

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**Table 2. Comparison of hemodynamic variables at baseline and during coronary balloon occlusion**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Balloon occlusion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm</td>
<td>57.8 (9.5)</td>
<td>61.8 (12.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>LVEDP, mmHg</td>
<td>14.7 (4.2)</td>
<td>18.3 (5.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVEDV, ml</td>
<td>145.6 (42.1)</td>
<td>142.7 (35.8)</td>
<td>0.29</td>
</tr>
<tr>
<td>LVESV, ml</td>
<td>62.9 (25.1)</td>
<td>70.2 (28.7)</td>
<td>0.01</td>
</tr>
<tr>
<td>LVSV, ml</td>
<td>82.7 (24.7)</td>
<td>72.5 (29.0)</td>
<td>0.0005</td>
</tr>
<tr>
<td>CO, l/min</td>
<td>4.6 (1.5)</td>
<td>4.3 (1.9)</td>
<td>0.10</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>55.8 (12.4)</td>
<td>49.5 (15.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>LV dP/dtmax, mmHg/s</td>
<td>1407 (331)</td>
<td>1256 (315)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV τ, ms</td>
<td>519 (8.7)</td>
<td>62.3 (11.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pw, mmHg</td>
<td>95.5 (23.7)</td>
<td>93.4 (19.8)</td>
<td>0.14</td>
</tr>
<tr>
<td>Pd, mmHg</td>
<td>719 (22.6)</td>
<td>98.9 (11.0)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Mean (SD). LVEDP, left ventricular (LV) end-diastolic pressure; LVEDV, LV end-diastolic volume; LVESV, LV end-systolic volume; SV, stroke volume; CO, cardiac output; EF, ejection fraction; LV dP/dtmax, LV maximum rate of pressure generation; LV τ, LV time constant of isovolumic relaxation; Pw, aortic pressure; Pd, distal coronary pressure.
The Waterfall model is an oversimplification to explain LV–coronary interaction, as it ignores vascular emptying, alterations in myocardial elastance, and the deformation of vessels by the myocardium affecting perfusion, independent of cavity pressure (16, 33). Coronary resistance is mainly determined by thick-walled coronary arterioles, which may be less susceptible to compression, and venules may off-load blood volume from the interstitium, acting as a sump to dissipate interstitial pressure. Nevertheless, extrapolation of our data shows that LVEDP is stable when Pw is in excess of 30 mmHg, which approximates to the reported collapsible threshold of collaterals (6, 11). Our data confirm that a Pw > 30 mmHg provides sufficient myocardial perfusion pressure via collaterals to maintain LV function during coronary occlusion at rest.

**Stenosis hemodynamic significance and collaterals.** Mamas and colleagues (19) have demonstrated a linear correlation between resting Pd/Pa and fractional flow reserve (FFR) post-pharmacological hyperemia (r = 0.74, P < 0.0001). We have demonstrated that higher resting Pd/Pa gradients have fewer collaterals as quantified by CFIp and Pw. Ischemia stimulates compensatory collateral development via VEGF and nitric oxide-dependent processes (20). Hence, patients with less-
significant lesions will have fewer collaterals and subsequently more ischemic diastolic LV dysfunction during coronary occlusion.

Limitations

This is a small study compared with previous studies, which used angiographic assessment of coronary collaterals (8). However, the size of our study is compensated by the use of a quantitative and accurate assessment of collaterals during simultaneous LV hemodynamic data acquisition. Angiographic collateral assessment is a semiquantitative technique, sensitive to the variability of manual contrast injection, and this is reflected in a poor correlation of invasive and angiographic assessment of collateral function (31). We repeated the simultaneous measurement of collateral function and LV hemodynamics to increase the power of the study. As we and others (1, 10) have shown, a 60-s balloon occlusion does not alter coronary collaterals. P, has also previously been shown to remain constant (8) and therefore, was not measured repeatedly. As with all previous studies, measurement of collaterals suffers from a “Heisenberg-like” effect—the act of measuring the collateral prevents their quantification at baseline (without occlusion).

We did not measure coronary sinus lactate to confirm ischemia as a cause for the observed LV dysfunction during coronary occlusion. This would have been desirable but was not feasible within the protocol design. It was also not ethically justified to elicit greater systolic dysfunction with more prolonged coronary occlusion. The demonstrated, modest inverse correlation between lesion hemodynamic significance and CFIp at rest requires confirmation with the more robust assessment of lesion significance measured during hyperemia by FFR.

Conclusion

This study demonstrates that well-developed coronary collaterals minimize ischemic diastolic dysfunction during coronary occlusion. Baseline LVEDP at rest may be high in patients with good collaterals, due to a direct scaffold effect of collateral channels on the LV cavity. Vessels with lesions of greater hemodynamic significance have better collateral supply.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: S.P.H. and D.P.D. conception and design of research; S.P.H., P.A.W., P.M.H., N.E.W., and M.O. performed experiments; S.P.H., P.A.W., and P.A.R. analyzed data; S.P.H. and P.A.W. interpreted results of experiments; S.P.H. and P.A.W. prepared figures; S.P.H. drafted manuscript; S.P.H., M.O., and D.P.D. edited and revised manuscript; S.P.H., N.E.W., M.O., and D.P.D. approved final version of manuscript.

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