SCIENTIFIC LETTER

Pharmacological vasodilatation in the assessment of pressure-derived collateral flow index

D Perera, S Patel, L Blows, E Tomsett, M Marber, S Redwood

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Assessment of the coronary collateral circulation by intracoronary pressure measurements was first described a decade ago and has rapidly become a clinically accepted standard for quantification of collateral flow. The pressure-derived collateral flow index (CFI) expresses collateral flow in relation to normal maximum myocardial perfusion and is calculated by simultaneous measurement of aortic (P_a), central venous (P_v) and coronary wedge (P_w) pressures, where $CFI = (P_w - P_v)/(P_a - P_v)$. In addition to these pressure gradients, collateral flow is determined by the resistances of collateral vessels and the myocardial microvasculature. Therefore, a flow index can only be derived from pressure measurements during conditions of maximum vasodilatation, when all resistances are minimised and held constant. Maximal and steady-state hyperaemia can be induced by administration of pharmacological agents such as adenosine or papaverine, which cause reproducible vasodilatation of resistance vessels.

CFI is assessed during transient coronary occlusion, which often induces myocardial ischaemia. The resulting hypoxia and accumulation of metabolites minimise microvascular resistance and therefore exogenous pharmacological vasodilators are often omitted during measurement of CFI. However, the depth of ischaemia and consequent effectiveness of the endogenous hyperaemic stimulus depend on a variety of anatomical, cellular and vascular factors, including collateral supply itself. Well-collateralised myocardium becomes less ischaemic¹ and this may attenuate the endogenous vasodilative stimulus during coronary occlusion. We hypothesised that failure to induce pharmacological steady-state hyperaemia would result in an artefactual CFI, particularly in patients with abundant collateral supply.

METHODS

Thirty three patients aged 61 (9) years (76% men) were studied during elective percutaneous coronary intervention. Patients with stable exertional angina and single-vessel coronary disease (55% left anterior descending, 24% right coronary and 21% circumflex artery lesions) were selected prospectively.

P_a was measured with a guide catheter and right atrial pressure with a multipurpose diagnostic catheter. A calibrated Pressurewire (Radi Medical Systems, Uppsala, Sweden) was advanced beyond the lesion to measure distal coronary pressure. P_w was measured after 90 s of balloon coronary occlusion and CFI was calculated as $(P_w - P_v)/(P_a - P_v)$. Pharmacological hyperaemia was then induced by a femoral venous infusion of adenosine at 140 $\mu\text{g/kg/min}$. CFI was reassessed when mean pressures reached a steady state. The study protocol was approved by the local research ethics committee and written informed consent was obtained from each patient at enrolment.

Patients were categorised into two groups: $CFI < 0.25$, poor collaterals; and $CFI \geq 0.25$, good collaterals. Continuous and categorical variables were compared by a Wilcoxon

signed rank test or Mann-Whitney U test and a Pearson χ^2 test, respectively, at a significance level of 5%. Data are expressed as mean (SD).

RESULTS

Eighteen patients had poor and 15 patients had good collateral supply. Those with well-developed collaterals had more severe coronary lesions (diameter stenosis 92 (12)% v 73 (16%), $p = 0.008$) but there were no other significant differences between groups.

In patients with poorly developed collaterals, CFI was 0.16 (0.07) with balloon occlusion alone and 0.16 (0.07) with additional pharmacological vasodilatation ($p = 0.41$). In the good collateral group, CFI with adenosine was significantly lower than with balloon occlusion alone (0.37 (0.07) v 0.33 (0.05), $p = 0.004$) (fig 1A). In the good collateral group, the drop in CFI was largely mediated by a decrease in P_w (from 38 (7) mm Hg to 34 (7) mm Hg, $p < 0.001$), whereas in the group with poor collaterals, P_w increased marginally with exogenous vasodilators (22 (6) mm Hg to 23 (6) mm Hg, $p = 0.03$). In the absence of adenosine, the error in CFI measurements was 11 (17)% (range -24% to 67%). There was a strong inverse correlation between baseline CFI and the change in CFI caused by pharmacological vasodilatation ($r = -0.63$, $p < 0.01$) (fig 1B).

DISCUSSION

It has been argued that balloon occlusion causes ischaemia, which in turn maximally dilates the distal vascular bed, such that an additional hyperaemic stimulus is not required during measurement of CFI. Several assumptions are inherent in this argument, which may not be valid in many cases. The first assumption is that transient balloon occlusion inevitably results in myocardial ischaemia. However, it has been shown that patients with a $CFI \geq 0.25$ may not experience ischaemia at rest, even when antegrade flow is abolished completely.¹ Given that CFI is proportional to the ratio of myocardial (R) and collateral (R_c) resistances (where $CFI = R/(R + R_c)$), the decrease in CFI with adenosine in the good collateral group suggests that myocardial vascular resistance was not minimised by balloon occlusion alone, due to amelioration of ischaemia by collaterals. Conversely, pharmacological vasodilatation had no impact on CFI measurements in patients with poor collaterals, which may reflect maximal microvascular vasodilatation after ischaemia. Inadequate perfusion of the distal myocardium may also have contributed to the decreased impact of adenosine in this group but, in practice, distal coronary perfusion can be optimised by administering vasodilators before balloon coronary occlusion.

The second assumption is that ischaemia, when it does occur, is sufficient to cause maximal vasodilatation of

Abbreviations: CFI, collateral flow index; P_a , aortic pressure; P_v , central venous pressure; P_w , coronary wedge pressure

Figure 1 (A) Collateral flow index (CFI) with and without adenosine (white and black bars, respectively). (B) Bland–Altman plot. The difference in CFI with adenosine is proportional to the degree of collateral supply.

coronary resistance vessels and overcome competing vasoconstrictor influences. However, several open-chest swine and dog experiments have shown that resistance vessels retain a degree of vasomotor tone, and therefore vasodilator reserve, even in low-flow ischaemic states.² Vasomotor tone in underperfused myocardium is thought to reside primarily in small calibre (< 100 µm) coronary arterioles, which are potentially vasodilated by adenosine.³

In conditions of submaximal hyperaemia, myocardial and collateral resistances remain labile, which in turn may lead to changes in P_w that are independent of distal coronary perfusion. In this context, the drop in P_w and CFI during hyperaemia in our study cannot necessarily be interpreted as evidence of coronary steal, as collateral flow per se may increase or decrease despite a drop in P_w .^{4–5} Given that only patients with single-vessel disease were included, coronary steal is unlikely to have occurred in this population, although this phenomenon can only be excluded by simultaneous measurement of collateral flow and coronary flow (velocity) reserve.

We conclude that failure to induce pharmacological hyperaemia results in artefactually high CFIs in patients with a well-developed collateral circulation. The absolute difference between hyperaemic and baseline CFI was small in the current study, but the errors introduced by this omission may limit the fidelity of CFI in clinical applications such as angiogenic drug trials, where subtle changes in collateral flow need to be detected.

Authors' affiliations

D Perera, S Patel, I Blows, E Tomsett, M Marber, S Redwood, Cardiovascular Division, The Rayne Institute, St Thomas' Hospital Campus, King's College London, London, UK

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Correspondence to: Dr Simon Redwood, Department of Cardiology, St Thomas' Hospital, London SE1 7EH, UK; Simon.Redwood@gstt.nhs.uk

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