Letters to the Editor
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Is myocardial contrast echocardiography ready to assume ‘gold standard’ status for quantification of collateral flow in humans?

Quantification of collateral flow in humans is most important and we recognize the valuable contribution by Vogel et al. towards this aim. However, some methodological issues related to the promising ultrasound-based method described should be resolved before it is pronounced the gold standard.

A fundamental source of error is the assumption that blood vessels are rigid tubes and that relative blood volume (rBV) is constant during a coronary occlusion despite a substantial drop in perfusion pressure. Experimental findings demonstrated that blood volume dynamically varies with pressure. This is in line with earlier observations by this group showing a significant increase in rBV in healthy volunteers upon adenosine-induced vasodilatation, which raises pressure in the microcirculation downstream of the resistance vessels.

An erroneous assumption of constant myocardial blood volume during coronary occlusion critically affects calculated collateral flow. The relationship with the pressure-derived collateral flow index (CFlp) is a function of the filling volume during proximal occlusion (represented by myocardial plateau intensity A). If the filling volume used in the fitting procedure is too high, the exchange frequency β is more than proportionally too small and, consequently, collateral blood flow is underestimated. In contrast, a smaller filling volume would lead to further underestimation of the relative perfusion index, CPI, by CFlp. Information on the period between coronary occlusion and start of the perfusion-refill sequence or on changes in filling volume of the collateral-dependent region with declining perfusion pressure is therefore essential to ascertain steady state after onset of the acute occlusion.

In our opinion, this fundamental issue at present precludes reliable application of this method to quantify collateral flow in humans or to validate pressure-derived CFI.

Additionally, heart contraction has a strong effect on coronary and collateral pressure-flow relations, especially on subendocardial perfusion. It would be a valuable contribution of myocardial contrast echocardiography if a distinction could be made between subendocardial and subepicardial perfusion, especially when investigating collateral flow. Although collateral flow may be measurable to a certain region, it may not help the subendocardium where it is needed most.

References


Jos Spaan
AMC
The Netherlands
E-mail address: j.a.spaan@amc.uva.nl

Maria Siebes
AMC
The Netherlands
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Is myocardial contrast echocardiography ready to assume ‘gold standard’ status for quantification of collateral flow in humans?: reply

We agree with the comment of Spaan and Siebes that blood vessels are not rigid and thus allow blood volumes to vary dynamically with perfusion pressure. Constant resistances in the coronary circulation are the core assumption of the theory describing the pressure-derived collateral flow index (CFlp). In contrast to that, the collateral perfusion index (CPI), reflecting collateral relative to normal myocardial blood flow (MBF), does not rely on assumptions regarding myocardial resistances or blood volumes.

The constituents of MBF (mL/min/g) as determined by myocardial contrast echocardiography (MCE), i.e. the relative blood volume (rBV, mL/mL) and its exchange frequency (β, 1/min), were assessed each during angioplasty and after successful revascularization. Therefore, the CPI accounts for dynamic changes of blood volumes, provided that they reach steady state prior to their measurement. Although steady-state conditions after revascularization can be guaranteed, the time to stable myocardial blood volumes after onset of coronary occlusion is not known in humans.

In our study, coronary arteries were occluded during 60 s. The acquisition of perfusion sequences took 15 s: the first two to three heart cycles were used to measure the plateau signal intensity A and rBV, respectively, followed by the contrast destruction during one to two heart cycles and the contrast refill during the remaining acquisition time. Perfusion sequences were acquired towards the end of the 1-min occlusion, thus allowing blood volumes to stabilize during 45 s prior to the measurement. From an ex vivo, non-contracting canine model, Spaan et al. suggested a time constant of ‘several seconds’ for intramural blood volumes. This value most likely represents an upper limit, as myocardial blood volumes were measured by an indirect technique that added further dynamics to the entire system. The period between the onset of the coronary occlusion and the start of perfusion sequence is sufficiently long to guarantee steady blood volumes, i.e. more than five time constants, provided that mechanical properties of the contracting human myocardium and the aforementioned model are similar.

We are aware that animal data may have limited significance for humans. However, these are the best data available, and in our opinion, they emphasize the gold standard status of MCE in conjunction with our protocol to assess collateral flow of the beating human heart.

References

1. Spaan J, Siebes M. Is myocardial contrast echocardiography ready to assume ‘gold standard’