Editor’s Perspective

Coronary Venous Interventions
Failed Strategy or Inadequately Explored?

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Coronary revascularization can salvage ischemic myocardium, relieve symptoms, and prolong life in patients with high-risk acute coronary syndrome and in patients with severe coronary artery disease. It is no wonder that coronary artery bypass surgery and percutaneous coronary interventions (PCI) were performed on nearly 900,000 patients in the United States in 2010. Despite the advances with both revascularization techniques, there are many situations where improvement is still needed. For instance, myocardial salvage in ST-segment-elevation myocardial infarction with primary PCI averages only 40% to 50% of the area at risk despite timely reperfusion and many patients with multivessel disease continue to have severe angina and ischemia because of anatomy that is not amenable to revascularization. As many as 7% or 1.8 million individuals are estimated to be unrevascularizable and the treatment options for these patients are limited and often unsuccessful. Recently, several articles have been published suggesting that retrograde perfusion via the coronary sinus may have promise as a treatment option for these patients.

In a study by Verheye et al, 104 patients with severe angina who were not candidates for revascularization were randomized to partial coronary venous occlusion accomplished by placement of an hourglass stent in the coronary sinus or to a sham operation. The stent partially obstructs the coronary sinus leading to increased retrograde flow into the ischemic territory. At 6 months, angina and quality-of-life measures were significantly improved during exercise time and wall motion index during dobutamine stress imaging were not. The study demonstrated feasibility and safety accompanied by symptomatic improvement but it failed to show improvement on functional testing. Given the small size of the study, major adverse clinical outcomes were infrequent.

In a small pilot study, van de Hoef et al demonstrated that retrograde flow into the ventricles after ligation of the coronary sinus increased venous pressure to 50% to 70% of left ventricular systolic pressure but the diastolic pressure was identical to left ventricular diastolic pressure, presumably transmitted through Thebesian veins or from the myocardium or both.

Interventions through the coronary veins to treat coronary artery disease was first suggested by Pratt over 100 years ago but were not actively investigated until the 1937 when Gross et al demonstrated that retrograde flow into the ventricles after ligation of the coronary sinus in an experimental infarct model. The mortality in these experiments was high because of engorgement of the myocardium over time, so when Beck and Mako repeated these experiments in 1941 they used a partial occlusion rather than complete occlusion. This resulted in a significantly lower acute mortality in an infarct model. Subsequently, others demonstrated that combining a partial ligation of the coronary sinus with arterial cannulation further increased survival from arterial retroperfusion rather than venous. In experimental dog studies, Beck et al using newly developed vascular surgical techniques showed that arterial bypass with a free carotid artery conduit from the aorta to the partially occluded coronary sinus reduced mortality in an experimental animal study. He subsequently modified the technique for clinical use by using a brachial artery bypass from the aorta to the coronary sinus (the Beck II operation). In 1955, Beck reported his experience with 102 patients. He showed a reduction in angina or elimination of angina in 90% of patients with an operative mortality of 6.6%. It is important...
to remember that these studies were done before the introduction of cardiopulmonary bypass and before modern medical treatment of angina. The operation fell out of favor because of loss of effectiveness over time and the introduction of internal mammary implantation into the myocardium (Vineberg operation) in the 1940s and saphenous vein bypass surgery in the 1960s. Nevertheless, these pioneers demonstrate that coronary sinus occlusion and retroperfusion could reduce myocardial ischemia and could be done effectively in man.

A renewed interest in coronary sinus techniques occurred in the 1970s when Meerbaum et al.12 and Farcot et al.13 demonstrated that diastolic retroperfusion of arterial blood through a coronary sinus catheter reduced myocardial ischemia and associated wall motion abnormalities in experimental studies. The advantage of the technique was the retroperfusion only occurred during diastole, allowing for drainage of the venous system during systole.14 Subsequent studies have shown it to be effective for retrograde delivery of drugs and stem cells.15 Boekstegers et al.16 used a modified technique with selective suction and pressure regulated retroinfusion. In a study of 45 patients, retroperfusion reduced myocardial ischemia during PCI.

In 1984, Mohl.17 took another approach by intermittently occluding the coronary sinus. The occlusion was timed until the pressure reached a plateau usually over 3 to 4 cardiac cycle followed by deflation to allow venous drainage and washout.18 Experimental animal studies showed reduced ischemia in some studies but not all.19–21 Clinical trials of these techniques have been limited but positive results have been reported during cardiac surgery and in patients with acute coronary syndrome.22,23

Other novel ideas have been attempted in animal experiments that have included the creation of a shunt between the anterior vein and the LAD with a covered stent to provide retrograde venous flow distal to an occluded coronary artery. Another approach has been the creation of a shunt between an anterior coronary vein and left ventricle to allow for selective arterial retroperfusion from the left ventricle into the venous circulation serving an occluded LAD.24,25 No clinical experience has been reported for either technique.

Despite, 75 years of experimental studies of coronary venous interventions, only a few small clinical trials have been conducted following the work of Beck et al.26 Is it finally time to give up this approach since we have not been able to successfully develop a clinically useful technique by now? I would argue that we should not. Despite the long history of coronary sinus interventions, we still understand little about the hemodynamic and biological effects of these techniques. Emerging evidence suggests these techniques might provide additional benefit beyond retrograde perfusion and enhanced washout with restoration of vascular function and angiogenesis.18

The recent studies of 2 different coronary venous interventions are small and underpowered but they are provocative and should stimulate further study of coronary sinus interventions in the treatment of coronary artery disease. Exploration of other novel coronary venous techniques is also needed to exploit the potential that the coronary venous system has to offer. I would not rule out coronary sinus techniques as yet. Despite its history, we are still in the infancy of the technique.

Disclosures
None.

References


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