Temporary internal thoracic artery occlusion during off-pump coronary artery bypass grafting with the new poloxamer P407 does not cause endothelial dysfunction

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The positive effects of coronary revascularization are now well established. However, the application of vascular clamps to achieve a bloodless field during the anastomosis might alter the integrity of the internal thoracic artery.1 The reverse thermosensitive formulation of the poloxamer 407 (P407) makes it attractive for temporary vascular occlusion because it only solidifies when in contact with body temperature.2 Therefore, the purpose of this study was to assess the effect of occlusion with P407 on internal thoracic artery endothelium function.

Methods

Surgical procedure. The chests of 9 Landrace swine of either sex (25 ± 4 kg) were entered through a median sternotomy.3 The left internal thoracic artery was harvested as a pedicle from the subclavian artery. After distal section, the blood flow was controlled by means of proximal finger compression. P407 (20%, 200 mL) was injected with a Cardiac Control Syringe (Plumomed Inc, Woburn, Mass) into the arteries. The distal part of the catheter (made of polypropylene and styrene butadiene rubber) is smooth, with an olivary body extremity to render it atraumatic for the endothelium. After introduction of the catheter 15 mm into the thoracic arteries, the gel was rapidly injected with a progressive retracted movement to avoid uneven coating of the gel, which can compromise the efficacy of the occlusion. After a 15-minute period of occlusion, the thoracic artery was harvested and separated in 2 sections: P407 (vessel in contact with the gel) and control (no gel).

Vascular reactivity studies. Vascular reactivity was studied in organ chamber experiments, as previously described.3 The maximal contraction was determined with 100 mmol/L KCl, and all studies were performed in the presence of indomethacin (10^{-7} mol/L) and propranolol (10^{-7} mol/L). The nitric oxide–mediated relaxation pathway was studied by constructing concentration-response curves to acetylcholine and bradykinin. Endothelium-independent relaxations were studied in the presence of the nitric oxide donor sodium nitroprusside.

Endothelial coverage. The endothelial cell coverage was evaluated with silver nitrate staining, as previously described.3

Figure 1. Concentration-response curves to acetylcholine (ACh; A) and bradykinin (BK; B) in rings of thoracic arteries occluded with P407 (squares) and control rings (diamonds). Responses are expressed as the percentage of relaxation to the contraction induced by prostaglandin F2α. Results are presented as the mean ± standard error of the mean.
Results
The 15-minute period of occlusion was successful in all cases, with the necessity of a second injection only once. The mean quantity of the gel was 0.22 ± 0.02 mL, and the use of ice for the dissolution of the gel was needed in 8 of 9 cases.

Vascular reactivity studies. Concentration-response curves to acetylcholine and bradykinin of thoracic arteries occluded with P407 showed no significant difference compared with that seen in control rings (Figures 1 and 2). Moreover, relaxation reached 100% after the bolus of sodium nitroprusside in both groups (data not shown).

Endothelial coverage. Preservation of the endothelial layer was demonstrated in P407 rings, with no significant difference compared with that seen in control rings (Figure 2).

Discussion
The major findings of the present study are that injection of P407 (1) creates a successful occlusion of the thoracic arteries; (2) causes no significant decrease in endothelium-dependent relaxations mediated by the Gi and Gq protein pathways, as demonstrated by concentration-response curves to acetylcholine and bradykinin, respectively; and (3) does not alter the endothelial coverage.

The necessity of a bloodless field to obtain optimal visibility during performance of the anastomosis is an issue of concern in coronary artery bypass. The most widely used technique to occlude thoracic arteries in coronary reconstruction is fibrous jaw clamping. However, examination with scanning electron microscopy showed that jaw clamping causes focal endothelial denudation and atherosclerotic plaque rupture.1,4

Boodhwani and colleagues5 have demonstrated that temporary occlusion of the left anterior descending coronary artery with P407 does not cause abnormalities in coronary flow during the reperfusion, does not adversely affect regional myocardial function, and has no effect on endothelium-independent microvessel relaxation. Endothelium-dependent relaxation to adenosine diphosphate is preserved, whereas response to substance P is mildly impaired, perhaps because of a local effect of the gel.

In conclusion, the novel reversible thermosensitive gel P407 is safe and efficacious for temporary occlusion of the thoracic vessel.

References

Figure 2. Photomicrograph (original magnification 250×) of silver nitrate staining showing preservation of the endothelial layer of control strips (A) and strips occluded with P407 (100% of control values; B).