Injectable sclerosing agent: a new strategy to prevent endoleak after endovascular aneurysm repair

MC Bonneviot, G Soulez, J Raymond, S Lerouge.
CHUM research center, Department of Radiology, University of Montreal, Montreal, Quebec, Canada

Statement of Purpose: Endovascular Aneurysm Repair (EVAR) is a minimally invasive alternative to open surgery which prevents rupture of abdominal aortic aneurysms (AAA). It is however limited by frequent complications, including persistent blood flow within the aneurysmal sac after stent-graft (SG) deployment. This phenomenum, called endoleak, affects about 20% of patients (1). Understanding mechanisms leading to endoleaks and establishing strategies to prevent them are major interests at our lab. Bilateral canine models of aneurysms reproducing persistent type I and II endoleaks after EVAR have been created (2). In these models, leak areas were shown to be delimited by endothelial lining which prevents occlusion with time. The endothelial lining has been also already shown to be responsible for residual flow within the neck of incompletely treated intracerebral aneurysms (3). It is also known to be involved in recanalization following arterial occlusion. Endothelial denudation was shown to inhibit the recanalization process routinely found in canine arteries or in bifurcation aneurysms after coil embolization. Therefore, we hypothesized that endothelial denudation prior to SG implantation could prevent the formation of persistent leaks after EVAR. The aims of this study were, first, to confirm the potential of endothelial denudation to prevent leak formation and second, to prepare and test an injectable sclerosing gel able to achieve endothelial destruction in a minimally invasive way.

Methods: Bilateral models of aneurysms were surgically constructed on iliac arteries of 6 mongrel dogs using a jugular vein patch. In the left aneurysm, the luminal side of the venous patch was mechanically desendothelialized whereas in the right aneurysm, the patch was sutured with preservation of the endothelial lining. Ballon-expandable Jostent SG were implanted on both side under fluoroscopic guidance. Type I leaks was created by inducing SG deformation at proximal neck, according to our previous protocol (4). In 6 other dogs, the experimental model was modified to create a collateral flow by reimplanting a collateral vessel in the middle portion of both aneurysm. SG were then implanted to create a type I leak with collateral outflow. Presence of endoleak and aneurysm size was followed by angiography and ultrasonography until animal sacrifice and histology at three months. Since mechanical denudation is not suitable for clinically practice, an injectable sclerosing agent able to achieve endothelial denudation of the aneurysm during SG implantation was developed. A gel was created with ethanol, a well known sclerosing agent already used to treat varicose vein and other venous malformations. In order to increase its viscosity, ethyl cellulose (EtC, Sigma Aldrich, 70 000 g/mol), an ethanol soluble polysaccharide was added. Lipiodol™ (Guerbet) was chosen as contrast agent for gel traceability during injection. Good radioopacity is achieved with 20%Vol concentration of Lipiodol™. The optimal concentration of EtC was determined using viscosity measurements at room and body temperature, with or without Lipiodol™, using a Brookfield rheometer equipped with a temperature-regulated recipient. The injectability and sclerosing effect of the gel was demonstrated in vivo on renal arteries. Endothelial denudation was assessed by immunohistology with factor VIII staining. Gel efficiency to prevent endoleak is investigated in a bilateral model of aneurysm reproducing type I leak with collateral outflow.

Results/Discussion: In the group without collateral, moderate type I endoleaks were persistent in 6 of 6 aneurysms having an intact endothelial layer whereas no endoleak was observed in mechanically denuded aneurysms at 3 months ($p = 0.03$, Wilcoxon test) (see table). In the group with collateral, leaks on untreated aneurysms were larger than on treated aneurysms however endothelial denudation was not sufficient to prevent persistent leaks. This suggests that an effective injectable gel should not only be sclerosing but also temporarily block the endoleak. While addition of EtC in ethanol rapidly formed aggregates, addition of Lipiodol™ allowed to reach an homogeneous gel of much higher viscosity, up to 3000 cp at 37°C (Fig.1). Both techniques (mechanical or chemical denudation) led to the destruction of the endothelium, although some non-denudated areas remained visible. Gel injection effective-ly prevented primary leak formation in our canine model.

Number of leaks	Denudation	No denudation
Without collateral	0 / 6	6 / 6
With collateral	4 / 6	4 / 6

Table 1. Presence of leaks 3 months after EVAR in aneurysm with/without mechanical denudation

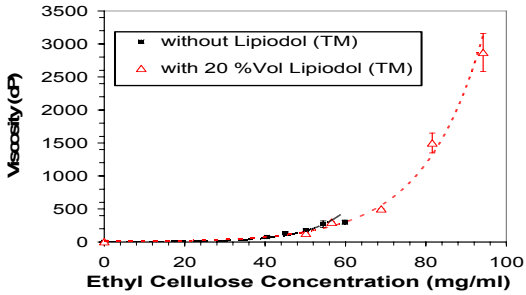

Figure 1. Gel viscosity against EtC concentration

Conclusions: The novel radioopaque sclerosing embolizing gel that we developed could help reducing risks of blood leakage after EVAR.

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References : (1) Buth J. J Vasc Surg 2000;31:134-146 **(2)** Lerouge S, JVIR 2004;15:971-979 **(3)** Raymond J. Stroke 2004;35:1471-1475 **(4)** Soulez G. JVIR (accepted).