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An Arteriovenous Fistula Model of Intimal Hyperplasia for Evaluation of a Nitinol U-Clip Anastomosis

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ABSTRACT

Objectives: The aim of this study was to create an ovine arteriovenous fistula (AVF) model which would closely replicate a human forearm fistula and use this to quantify the degree of intimal hyperplasia in those created with the U-Clip compared to a conventional sutured anastomosis.
Materials and methods: Twenty AVFs were created in 10 Border Leicester–Merino sheep between the superficial femoral artery and vein of each hind limb. On one side the U-Clip and on the other a continuous polypropylene suture was used to perform the anastomosis. The animals were sacrificed at 2 ($n = 3$), 4 ($n = 4$), 6 ($n = 3$) weeks and histological slices were taken of each AVF in cross section to determine the intimal media area per unit length (IMA/L).
Results: Intimal hyperplasia (IH) was observed at all time points with one AVF found occluded with thrombus at the time of harvest. The IMA/L was significantly lower in the U-Clip groups by 24% at 2 weeks, 32% at 4 weeks and 23% at 6 weeks (Two-way ANOVA, $p = 0.019$, observed power = 0.825, time or side $p \geq 0.766$, type $p = 0.001$; Paired *t*-test, $p < 0.001$ between matched anastomotic types). Time taken to perform the anastomosis was similar between the two anastomotic techniques (Polypropylene 14(8–18) vs. U-Clip 15.3(11–23) min; $p = 0.47$).
Conclusion: This ovine AVF model results in IH similar to that seen in a human AVF. The IH that occurs with the U-Clip is less than that of continuous polypropylene suture.

Introduction

Intimal hyperplasia (IH) is ubiquitous after the vascular injury that occurs during surgery. It affects all types of vascular anastomosis but is most pronounced in the arteriovenous fistula (AVF) created for hemodialysis access. This IH results in restenosis, which threatens AVF patency and causes significant morbidity. The failure or dysfunction of arteriovenous fistulae has an annual cost of more than $1 billion dollars in the United States[1–3] where there were almost 328,000 patients receiving hemodialysis therapy at the end of 2006.[4]

The primary patency of an AVF is less than 50% after 3 years and may be as low as 20% in patients who are elderly, diabetic or female.[5,6] Despite such poor durability alternatives to AVF such as cuffed central venous catheters and synthetic arteriovenous grafts suffer higher rates of infectious complications, central venous stenoses and even lower patency rates.[6,7] The AVF remains therefore the best option for patients with end stage renal disease who require hemodialysis.

The nitinol U-Clip device (Medtronic, Minneapolis, MN, USA) is designed to reduce the use of sutures thus eliminating knot tying whilst facilitating the creation of a circumferentially interrupted vascular anastomosis[8] (Fig. 1). In support of this device's efficacy a single prospective human study has shown superior patency and maturation rates of forearm AVFs created with U-Clips when compared to continuous polypropylene suture.[9] The aim of our study was to create an AVF model with vessel size, handling properties, configuration and hemodynamic stresses akin to human forearm AVFs to quantify the degree of intimal hyperplasia and make comparison between continuous polypropylene suture and the Nitinol U-Clip anastomosis.

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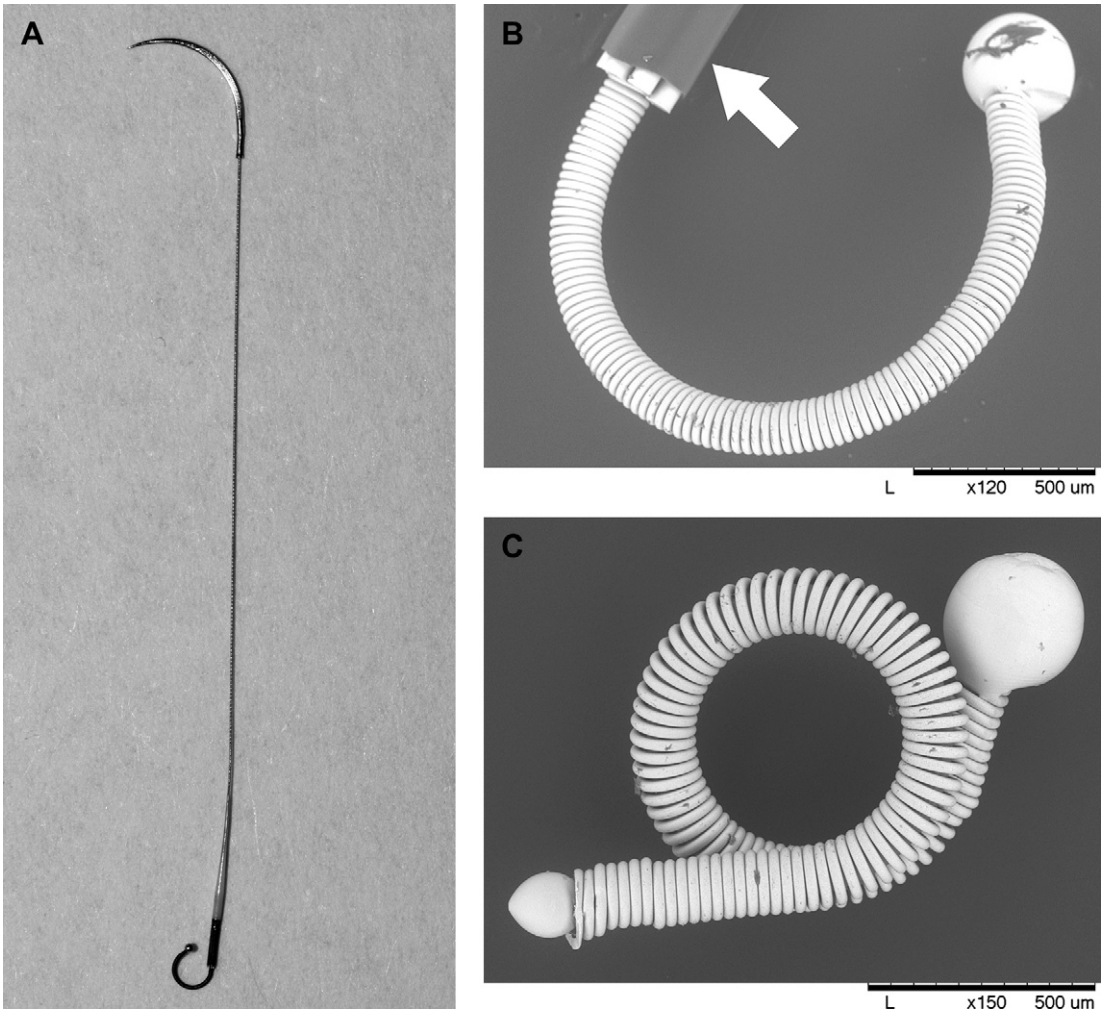

Figure 1. The nitinol U-Clip with its delivery apparatus intact (A), demonstrating the release trigger point (B, Arrow) and resuming its circular shape (C). (B and C Images taken with environmental scanning electron microscopy (TM-1000, Hitachi, Japan)).

Materials and Methods

Animals

Ten 2-year old crossbred Border Leicester–Merino wethers were used with the approval of our local Animal Care and Ethics Committee (ACEC 08/113A). They were kept in the research facility at the St. George Hospital Campus, University of New South Wales in accordance with the research guidelines of the National Health and Medical Research Council of Australia.

Surgery

Sheep were first sedated with Intramuscular Zolazopam (8–12 mg/kg), analgesed with subcutaneous Carprofen (2–4 mg/kg) and intramuscular Burprenorphine (0.005 mg/kg) then administered inhaled Isofluorane (2–3%) and 100% oxygen (3 L/min) throughout the surgery. Laryngoscopy was performed and an endotracheal tube placed above the carina for ventilation. Antibiotics (Intravenous Cephalothin 0.016–0.024 mg/kg; Benacillin 0.079–0.122 ml/kg IM) were administered and crystalloid fluids (Hartmann's solution) were given intravenously at 4–10 ml/kg/h prior to and during the surgery.

Both hind limb groin creases were cleaned with povidone-iodine and draped in accordance with conventional surgical practice. Skin crease incisions were made just below the inguinal ligament and the incision deepened to expose both the superficial femoral artery and vein. 5000 IU of Sodium Heparin was administered intravenously and the vessels were double slung both proximally and distally to achieve hemostasis for AVF creation. A 2 cm length longitudinal arteriotomy and corresponding venotomy was performed in the superficial femoral vessels. This length was standardized for all anastomoses and all animals. A conventional Brescia-Cimino side-to-side anastomosis was created using continuous 6–0 polypropylene (Prolene, Ethicon, Johnson & Johnson, Warren, NJ, USA) in one hind limb and interrupted U-Clips in the contralateral one[10] (Fig. 2). In each anastomosis care was taken to evert the vessel edges and avoid adventitia within the suture line. Flushing with heparinised saline and hemostasis were given careful attention at the time of sling release. A marking suture was placed at the cephalad and caudad ends of the anastomosis to aid and orient the cadaveric dissection. Patency of fistula was confirmed with pulse and thrill at the end of the anastomosis. Layered closure of fascia and skin with 3–0 polypropylene suture (Prolene, Ethicon, Johnson & Johnson, Warren, NJ, USA) was performed. The side of hind limb chosen for suture/U-Clip was alternated in consecutive animals.

The nitinol U-Clip is applied with a standard needle and suturing action. It is connected to the surgical needle by a fine wire and released by grasping a trigger point with the teeth of the needle holder, at which point it resumes its circular shape holding the blood vessel walls in apposition (Fig. 1A,B). The retention knob at