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The use of an absorbable collagen cover (NeuraWrap) improves patency of interpositional vein grafts

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Objectives: Autologous interpositional vein grafts are used in peripheral arterial bypass procedures. Sudden exposure of vein grafts to arterial blood pressure is associated with increased wall tension leading to overdistension of the graft and changes in flow patterns. Overdistension of vein grafts often results in anastomotic leaks, thrombosis, and loss of patency. This study was designed to evaluate the use of a biodegradable collagen cover as a means of preventing overdistension of venous bypass grafts in a rat model.

Methods: Twenty-two Sprague-Dawley female rats weighing 250-350 g were randomly assigned to two groups: study group (n= 15) and control group (n=7). In all the rats, a 10-mm segment of the left femoral vein was harvested and used as a graft in repair of a right femoral artery injury. Following this procedure, control rats remained untreated. After completion of the femoral artery repair in the study group, the graft was wrapped with a collagen cover of appropriate length (NeuraWrap Nerve Protector) and sutured to form a tube around the vein graft. At the end of the procedure, the intensity and duration of bleeding, and vessel patency were recorded and the proximal and distal arterial segments were examined by Doppler ultrasonography. All observations and measurements were repeated at 1 and 2 hours after surgery. After the second hour, all the rats were sacrificed and vein graft samples with the arterial portions were removed for histological study.

Results: After removal of the vascular clamps of the control group, a sudden distension was observed in all the vein grafts. In this group, bleeding at the anastomosis site lasted for 1 to 3 minutes and was followed by ballooning of the grafts. In the study group, however, none of the samples exhibited distension and ballooning. There was no bleeding in 11 samples at all, and bleeding time was less than one minute in the remaining four samples. In the control group, only one graft was patent at two hours, one of the grafts was occluded after only three minutes. In the study group, all the grafts were patent and no thrombosis was noted. The mean blood flow velocity of the control group measured at 0 hour by Doppler ultrasonography was 0.93±0.33 cm/sec in the proximal artery, and 0.73±0.44 cm/sec in the distal artery. The mean blood flow velocities in the proximal and distal arteries of the study group were as follows, respectively: at 0 hour: 0.45±0.27 and 0.46±0.22 cm/sec; at 1 hour: 0.40±0.22 and 0.62±0.40 cm/sec; and at 2 hours: 0.55±0.22 and 0.64±0.37 cm/sec.

Conclusion: Prevention of overdistension of vein grafts with the use of an external cover decreases anastomotic leaks, protects the intimal media, maintains blood flow, reduces the incidence of thrombosis, and thus provides a higher patency rate.

Key words: Anastomosis, surgical/methods; blood flow velocity; blood vessel prosthesis; rats; stress, mechanical; thrombosis; vascular patency; veins/transplantation.

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Autologous vein grafts are an ideal bypass conduit in peripheral arterial bypass procedures. The use of vein segments as a graft was first suggested by Alexis Carrel in 1910.[1] Kunlin was the first to use a saphenous vein graft for femoropopliteal bypass. Today, the use of autologous vein grafts has become a standard bypass procedure.[2,3]

Compared to less complex repair techniques, drawbacks of interposition vein grafts include a two-fold increase in the amount of microsurgical work than required for a simple anastomosis and increased risk for thrombosis. In addition, technical errors and increase in the number of sutures can reduce the likelihood of a successful anastomosis. The use of a vein graft requires distal and proximal anastomoses, doubling the surgical work and resulting in a two-fold increase in the complication rate.

Decreased flow or increased vascular resistance observed following flap surgery and revascularization surgery may often lead to graft thrombosis and failure.[4] Discrepant results have been reported in clinical studies suggesting a higher failure rate with vein grafts and animal studies showing no significant adverse effect of vein grafts.[5-7]

Surgical injury aggravated by compliance mismatch between the graft and artery has been suggested as an initiating factor for the development of wall thickening along the suture line. Studies of wall mechanics and fluid dynamics implicate the development of intimal hyperplasia as the initiator of ultimate graft failure.[8-10] Intimal hyperplasia, which is a form of physiological remodeling, is a consequence of abnormal conditions of blood flow and wall stress.[11] Disruption of venous graft endothelium and media by mechanical forces associated with pulsatile blood flow is likely to be the cause of such neointimal hyperplasia.[12] A vein graft subjected to a higher arterial pressure distends, undergoes elastic deformation, and becomes a rigid tube. Each additional strain on the distended vein graft by elastic deformation causes microtears on the vessel wall. Distension of the vein graft also impairs laminar blood flow.

Prevention of overdistension of venous bypass grafts by a nonrestrictive, microporous, elastic, and biodegradable extravascular support material may have a beneficial effect on graft wall adaptation to increased pressure and resultant stresses.[13,14]

Materials and methods

This experimental study was approved by the institutional ethics committee of Columbia University. Twenty-two Sprague-Dawley female rats weighing 250-350 g were randomly assigned to two groups: study group (n= 15) and control group (n=7). The rats were anesthetized with the use of intraperitoneal ketamine (70-80 mg/kg) and xylazine (5 mg/kg). The surgical area was shaved and cleansed with 70% ethanol. A standard anterior inguinal incision was used on both sides. Femoral arteries and veins were isolated in the right inguinal area under microscopic magnification. A 10-mm segment of the left femoral vein, just distal to the Murphy's branch, was harvested. Vein grafts were carefully prepared and placed in simple saline solution. Heparin was not used in order not no interfere with thrombus formation. Epigastric veins and arteries were ligated with 8/0 Ethilon sutures and cut for better visualization and better Doppler evaluation of the distal artery. After distal and proximal application of two single Acland clamps, the femoral artery was cut. Residual adventitia and blood were removed from the arterial ends. The femoral artery was repaired using a 10-mm vein graft. Microsurgical repairs were made with eight individual 10/0 Ethilon sutures.

After completion of vein graft repair in the study group, the graft was wrapped with a collagen cover of appropriate length (NeuraWrap Nerve Protector, Integra LifeSciences Corporation, NJ, USA). Care was taken for the correct length and width of wrapping and to keep the length of the cover as that of the graft so that the repair sites would not be obscured. The width of material was selected based on the precise radius of the graft. The wrap was loose enough to avoid strangulation and provided a buttressing effect. After placement of the cover around the graft with precise positioning, the two edges of the wrap were approximated and sutured to each other with 8/0 interrupted sutures to form a tube around the vein graft.

The distal clamp was removed first followed by the release of the proximal clamp. The intensity and duration of bleeding, and vessel patency were recorded. One milliliter of 1% lidocaine was used to prevent arterial spasm. The proximal and distal arterial segments were examined by Doppler ultrasonography (EME Companion Micro, Nicolet Vascular Inc., Madison, WI, USA). The surgical field was covered by an autolo-

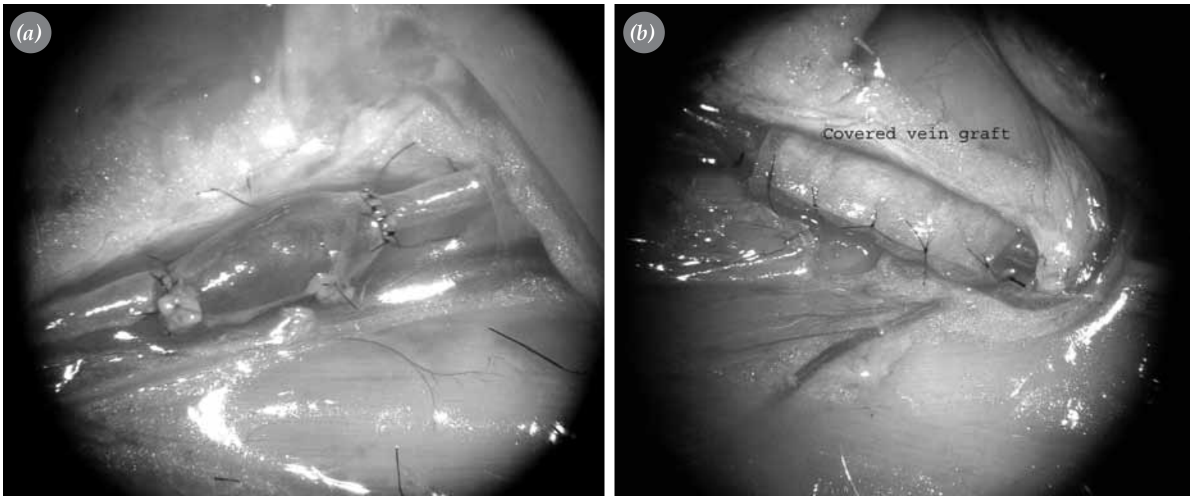

Fig. 1. **(a)** Distension of the vein graft exposed to arterial blood pressure (control group). **(b)** The appearance of a vein graft covered by NeuraWrap.

gous fat pad. All observations and measurements were repeated at 1 and 2 hours after surgery.

In the control group, all the procedures were the same with the exclusion of graft covering. After the second hour, all the rats were sacrificed and vein graft samples with the arterial portions were removed and preserved in 10% buffered formalin for histological study.

Results

After removal of the vascular clamps of the control group, a sudden distension of all uncovered vein grafts was observed (Fig. 1a). In all control animals, bleeding at the anastomosis site was followed by ballooning of the grafts, especially at the proximal repair site; this bleeding lasted for 1 to 3 minutes. In the study group, however, none of the samples exhibited distension and ballooning (Fig. 1b). Of these, there was no bleeding in 11 samples at all, and bleeding time was less than one minute in the remaining four samples.

In the control group, only one graft was patent at two hours, one of the grafts was occluded after only three minutes (Fig. 2a). In the study group, no thrombosis was noted (Fig. 2b).

The mean blood flow velocity of the control group measured at 0 hour by Doppler ultrasonography was 0.93±0.33 cm/sec in the proximal artery, and 0.73±0.44 cm/sec in the distal artery. The mean blood flow velocities in the proximal and distal arteries of the study group were as follows, respectively: at 0 hour: 0.45±0.27 and 0.46±0.22 cm/sec; at 1 hour: 0.40±0.22 and 0.62±0.40

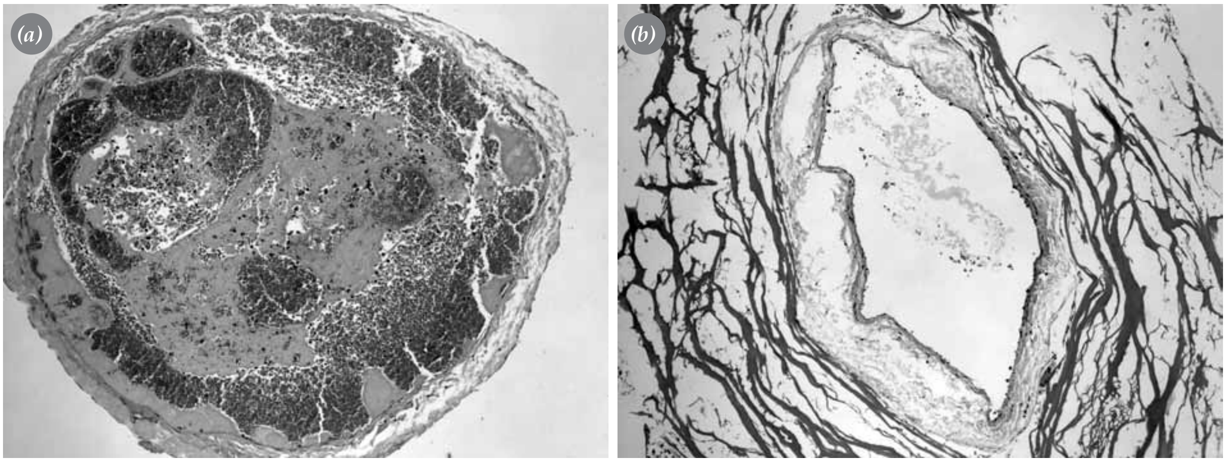

Fig. 2. **(a)** The appearance of thrombosis of the uncovered vein graft and thin media of the vessel wall (H-E x 10). **(b)** No thrombosis in the vein graft covered with NeuraWrap; the lumen of the vessel is patent (H-E x 10).

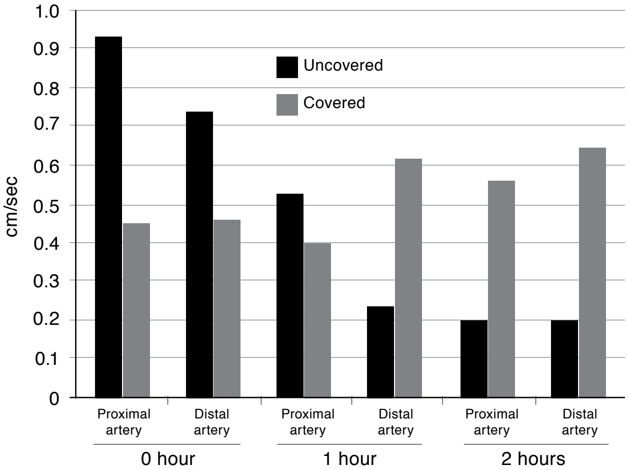

Fig. 3. Comparison of blood flow velocities in the control and study groups.

cm/sec; and at 2 hours: 0.55±0.22 and 0.64±0.37 cm/sec (Fig. 3). Doppler findings showed that blood flow velocities in the study group were more stable.

Discussion

Supporting a vein graft with a perivenous cover can prevent uncontrolled ballooning and distension by protecting the endothelium and media of the vein graft from mechanical destruction (Fig. 2b). To increase the risk for thrombus formation at the repair site, we did not use heparin and chose a vein graft having a larger diameter (contralateral femoral vein).

All the vein grafts covered by NeuraWrap were patent at 2 hours; none showed bleeding at the repair site or any sign of obstruction due to early thrombosis.

The use of a vein graft, with twice the number of anastomotic sites of a simpler repair, increases the risk for vessel thrombosis. In our control group, we observed a greater incidence of thrombosis.

When a vein graft is placed in the arterial circulation, the graft wall is subjected to two important mechanical factors: increased circumferential deformation and a significantly altered flow velocity. Both factors have serious effects on vein graft patency.[2,7]

After release of the vascular clamps in the control group, we observed a sudden distension of the vein graft (Fig. 1a). Distension was followed by bleeding at the anastomosis sites in all the uncovered grafts. In contrast, no ballooning and distension were observed in the covered grafts and there was minimal bleeding at the proximal repair site of only one graft.

The degree of vein graft distension is related to vein compliance. The ability of a blood vessel wall to expand and contract passively in response to changes in transmural pressure is an important function of large arteries and veins and is termed as vessel compliance (C), which is the ratio of the change in volume (ΔV) to the change in pressure (ΔP). According to Davies et al.,[15,16] the patency of a vessel graft is related to its compliance. Due to sudden increases in arterial blood pressure and consequent increases in wall tension, the vein graft becomes overdistended.[13,14,17] Overdistended vein grafts exposed to arterial pressure lose their compliance. It has been observed that de-endothelization and rupture of the media of vein segments occur within one hour of exposure to arterial pressure.[18] Structural insufficiency of the media of the vein wall accounts for these important changes. The comparatively thin media of vein walls cannot prevent ballooning of the vein graft upon exposure to the higher arterial pressure (Fig. 1a).

The most acute and well-known effects of this ballooning include stretching along the suture lines resulting in increased bleeding at repair sites, intimal rupture, and loss of laminar blood flow. Loss of laminar blood flow leads to turbulence that causes endothelial damage and subsequent thrombosis.

Bleeding, intimal rupture at the repair site, and turbulent blood flow constitute the main causes of early thrombosis and failure. De-endothelization of the vessel may increase the rate of thrombosis at the site of microvascular anastomosis. Thrombosis occurs more frequently when there are changes in the vessel wall.[19] It has also been shown that pulsatile arterial blood flow may promote apoptosis of vascular smooth muscle cells.[12]

Dysfunction of the overlying endothelium will result in aggregation and adhesion of thrombocytes to the subintimal layer. Prevention of injury within the first hour following anastomosis has a favorable effect on the integrity of the graft wall and, ultimately, on vessel patency. It is well-known that the most critical time of microvascular repair is the first few minutes after surgery. If the repair appears successful at this time, it is most likely that it will not end with failure.

In conclusion, relatively large increases in blood pressure cause ballooning of vein grafts, which in turn triggers thrombus formation resulting in decreased patency of grafted vessels. External support of a vein graft can protect a repair from early and late thrombosis.

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