*Available online*www.ijpras.com

International Journal of Pharmaceutical Research&Allied Sciences, 2017, 6(3):21-28

Research Article

ISSN : 2277-3657
CODEN(USA) : IJPRPM

Inside Out (Inverted) Autogenous Vein as an Arterial Substitute: An Animal Experimental Study

Abdollah Amirfarhangi[1], Sam Zeraatian[2*], Marjan Hajahmadi[3]

1-Assistant Professor of Cardiology, Department of Cardiology, Rasoul-e-Akram Medical Center, Iran University of Medical Sciences, Tehran, Iran.

2-Assistant professor of Cardiac Surgery, Department of Cardiac Surgery, Rasoul-e-Akram Medical Center, Iran University of Medical Sciences, Tehran, Iran.

3- Assistant Professor of Cardiology, Department of cardiology, Rasoul-e-Akram Medical Center, Iran University of Medical Sciences, Tehran, Iran.

[*]Corresponding authors

ABSTRACT

Background/Objectives: *The inside-out (inverted) vein graft is a venous tube, that pulled through itself to invert the normal orientation and place the outer adventitial layer inside the lumen of the graft. Our goal of this study was to assess the efficacy of inverted autogenous graft and compare its results with not inverted previously used vein grafts.*

Materials and Method: *In this experimental and pilot study, 12 dogs underwent general anesthesia and 10cm of their external jugular vein was separated. The excised segment was divided in two 5cm equal parts. One of them was inverted and the other one was left intact. Afterwards, 5cm of the right and left femoral arteries were removed and the inverted vein, along with the non-invaginated portion were grafted to the right and left femoral arteries, respectively. Patency of the grafts was evaluated by Doppler sonography at immediate post-operation and 3 and 6 months afterwards.*

Results*: All of the 12 inverted vein grafts were completely closed by thrombosis at 3 and 6 months follow up with Doppler sonography and none of them was patent. However, 11 (92%) of the non-inverted venous grafts were patent both at 3 and 6 months follow up. One of the non-inverted grafts was near total cut with thrombosis (8%) and the other two grafts were partially obstructed with intimal thickening.*

Conclusion: Using of the inverted vein graft as an arterial conduit was not safe and successful procedure and therefore cannot be recommended as a substitute to the conventional method.

Keywords: *Venous graft, Arterial graft, Inverted Venous Graft*

INTRODUCTION

Autogenous venous graft from saphenous vein and other site, has been frequently used and seems to be an ideal graft for the small and medium sized vessels. However, long term studies revealed some concern about usefulness and durability of these grafts such as size mismatch, intimal thickening and hyperplasia, thickening of the venous valves and long term aneurysmal formation of venous grafts [1]. Additionally, it is usually abandoned to use a

thrombosed or phlebitis venous graft. Synthetic grafts that have been used more frequently recently, have been shown to have multiple limitations such as high thrombogenicity and size discrepancy when used in small sized vessels. For these reasons, recent experimental studies have been designed and performed in order to evaluate inverted (inside out) autogenous veins as arterial graft [1-5]. As the vein is turned inside out, the previously internal and now external intimal layer would not be in direct contact with high pressure of the systemic arterial flow. In contrast, it is the adventitia, strong vessel layer, that will be in direct contact with the intravascular high pressure and thereby it is assumed that the disadvantages of the usual venous graft would be decreased or eliminated.

Our goal of this study was to assess the usefulness of inverted autogenous graft and compare its results with native and non-inverted grafts that used in classic method, in an experimental and pilot study.

MATERIAL AND METHODS

Animal study

Twelve dogs weighting 10-18 kg were maintained at the Animal Research Facility of Shiraz University of Medical Sciences (SUMS). They were housed under identical conditions. They all received the same diet through the experiment. The study protocol and animal using related ethical issues was approved by the ethical committee of Shiraz university of Medical Sciences (SUMS).

Experimental Design

The dogs underwent general anesthesia and operated in sterile condition. They were intubated and connected to the mechanical ventilator. 10 cm of the dogs' external jugular vein was excised for use as a conduit for grafting. The removed vein was divided in two equal segments. In one of the segments, the external adipose tissue was removed carefully from the surface of the adventitia and the vein was inverted and placed in heparin saline. The second segment was used as it was, and placed into heparin saline at room temperature.

Immediately after vein harvesting, and with bilateral inguinal incisions, approximately 5 cm of the right and left femoral arteries of the same dogs were excised. The inverted (inside-out) vein that stored in heparin saline was anastomosed to the right femoral artery by the 6-0 prolene suture as continuous method in an end-to-end fashion. Both sides of the arteries were spatulated. On the left side of the same dog, the second and intact vein segment of the jugular vein, which was not inverted, was anastomosed to the left femoral artery with the same method applied on the right side. All the procedure was completed within two hours after the vein grafts.

Post operatively anticoagulant therapy was applied and antibiotics were given for 3 days.

Patency of the femoral grafts was evaluated by Doppler sonography (Schiller AG, Germany) with 4 MHz probe, immediately post-operation, after 3 and after 6 months after operation.

After 6 months, the anastomosed venous grafts were removed surgically and all the specimens were analyzed with gross inspection then placed in buffered formalin. They were processed after 24 hours for paraffin embedding. A fire micro-thick slide was prepared from each block and stained by H&E and examined by light microscopy and histopathological assessment.

Data Analysis

Minimum sample size was estimated using an a priori power analysis based on a confidence level of 0.95 and a power of 0.90. Variance of the paired differences was based on previous data. The student's t-test and Mann-Whitney U tests were used to identify statistical differences between the characteristic of the right and left side anastomosis and other parameters. Statistical analysis was done with SPSS software (version 16 SPSS, Inc, Chicago, IL). Statistical significance was accepted when $P<0.05$

RESULTS

None of the dogs died and all of them completed the surgery without infection and other complications. Also all of them participated in follow up phase. The length of the used inverted venous grafts for the right side ranged from 3.2cm to 4.2cm (3.7 ± 0.5 cm). For the left side the length of the used intact grafts ranged from 3.3 cm to 4.0 cm (3.6 ± .4cm). The diameter of the venous grafts ranged from 8-12mm (10±2 mm) on both sides and diameter of the excised femoral arteries ranged from 5-8mm (6±2mm) on both sides.

Doppler Evaluation

At end of the examination, all of the inverted vein grafts were occluded. However, 11 of the 12 (92%) of the intact and conventional method anastomosis were patent; both at 3 months and 6 months follow up Doppler sonography (Table1).

Pathological assessment

Pathological analysis showed that all of the inverted grafts were completely thrombosed. The grafts were completely occluded and filled with large amounts of fibroblast. At the site of the anastomosis only a strand of fibrous tissue was present and no epithelialized canal was observed (Figure1).

However, on the left side grafts (conventional vein graft), only one specimen was completely obstructed with thrombosis (8.3%). The thrombosis was chronic type, with organized thrombosis (Figure3) and re-canalization of thrombi was evident (Figure4). In two other cases, the lumen was partially (50% of the lumen) obstructed with thrombosis and intimal thickening and hyperplasia (Figure 2). The other 9 samples (75%) were patent with acceptable amount of intimal thickening. The grafts wall were thin and regular (Figures 5,6) and the external elastic membranes were easily detectable (Figure6)

DISCUSSION

Autogenous vein first was used clinically as arterial graft by Jose Goyanes in 1906 and Erich Lexer in 1907 independently [6]. Through the experimental and clinical long term studies result, these vein grafting has been pointed out that several disadvantages such as early and late thrombosis, intimal thickening and hyperplasia, aneurysmal formation or valvular hypertrophy would be encountered. Another choice is the prosthetic graft but it has been well known that synthetic grafts have many limitations also, such as size mis-match for use in the small sized vessels such as the superficial femoral, renal or coronary arteries. During these early years of vascular grafts development, the characteristics of the ideal graft were defined [7]. The ideal graft must be readily available in a variety of sizes and lengths and suitable for use throughout the body.

It must be durable upon long-term implantation in humans, nonreactive, and free of toxic or allergic side effects. It must also be appropriately elastic, conformable to body surfaces, pliable, and easy to suture. Its cut ends should not fray, and it should not kink at flexion points. The inner surface must be smooth, with minimal trauma induction to blood elements, resistant to infection, and thrombosis. Availability, cost, and ability for frequent sterilization are other properties of the good graft.

First time, due to these limitations, Iwai et al. investigated the efficacy of the inverted (inside-out) venous graft in both humans and canine [1]. They applied inverted vein grafts in 9 patients and on 25 mongrel dogs. In the 9 patients, five cases were arterio-venous shunting for hemodialysis, one for replacement of femoral artery and three for inverted vein patch to the iliac or femoral arteries. They followed the patients from one month to one year. They observed more than 90% patency rate and all the clinical experiences were satisfactory. Therefore, they concluded that inverted autogenous vein grafting is a safe graft and should be considered as another option to widen the indication of the venous grafts. On the contrary, in our study we observed that all the inverted grafts failed and thrombosis occluded the grafts on the 3rd and 6th month of follow up.

Stenosis can increase the incidence of thrombosis and occlusion of the grafts. In this study, the internal diameter of the used jugular vein grafts was between 8-12 mm. On the other hand, the diameter of the femoral arteries was between 5 to 8 mm. Therefore, stenosis was eliminated and so the graft failure could not be attributed to the stenosis.

Because most grafts are initially tested in various experimental animal models, there are wide interspecies variations in the host response to an implanted vascular graft that influence its biologic behavior. In humans, spread of the endothelial pannus that originates at the anastomoses is very limited when compared with its extent in the pig, calf, or baboon. Furthermore, the in-growth of fibroblast through the wall of the prosthesis and the ability to "heal" the inner, lining is rudimentary compared with healing in various other species in which it occurs rapidly and may be complete in 4 to 8 weeks [8]. The properties of the prostheses in dogs are similar with humans, thus explaining the usefulness of the dog as the favorite animal model for studying vascular grafts. This was the reason that we used dogs in our study.

In another study performed by Szilagyi et al., long term patency rate of intact and non-inverted venous graft in femoro-popliteal artery bypass was evaluated [9, 10]. They reported a 64% patency rate after 5 years and 44% patency after 10 years. Failed cases developed progressive stenosis or dilation of the grafts wall. We obtained a 92% patency rate after 6 months' period. This rate is similar to Szilagyi results.

It seems that elimination of the inverted type venous graft needs further studies with properly designed and randomized studies.

CONCLUSION

In summary, our study findings suggest that an inverted (inside-out) vein cannot be safely used as an arterial graft. In our experimental study, inverted type vein graft was accompanied with Zero patency rate and the clinical experience was not satisfactory. Thus, we conclude that this way is not a safe procedure and more studies should be performed before considering it as vein conduit.

REFERENCES:

1. Iwai T, Nakamura H, Hatano R, Okamura K, Murakami T: Experimental and clinical studies of the inverted autogenous vein grafts. *J Cardiovas Surg* 1979; 20: 565-576.

2. Wang KK, Costas PD, Bryan DJ, Eby PL, Seckel BR: Inside-out vein graft repair compared with nerve grafting for nerve regeneration in rats. *Microsurg* 1995; 16: 65-70.

3. Benito-Ruiz J, Navarro-Monzonis A, Piqueras A, Baena-Montilla P: Invaginated vein graft as nerve conduit: An experimental study. *Mircrosurg* 1994; 15: 105- 115.

4. Iwai T, *et al*: Electron microscopic study of the inverted (inside-out) auto-vein graft. *Euro Surg Research* 1977; 9: 277.

5. Iwai T, *et al*: New vascular graft: Inverted (inside-out) vein graft. Proceedings X International Congress of Angiology, 1976: 495.

6. Kempczinski RF. Vascular Conduits: An Overview. In: Rutherford RB. Vascular Surgery, 5th edition. Philadelphia, 2000 p: 527.

7. Scales JT: Tissue reactions to synthetic materials. *Proc R Soc Med* 1953; 46: 647

8. Sauvage LR, Berger K, Wood SJ, *et al*: Interspecies healing of porus arterial prostheses: Observations, 1960-1974. *Arch Surg* 1974; 109:698.

9. Wylie EJ: Vascular replacement with arterial autografts. *Surgery* 1965; 57:14.

10. Szilagyi D.E. *et al*. Biological fate of autogenous vein implants as arterial substitutes. *Ann Surg* 1973; 178: 232.

Figure 1. Low power view of the site of anastomosis of inside out vein. Area has been totally replaced by fibrous tissue, with no vascular structure. Arrow shows suture material (H&E x 40).

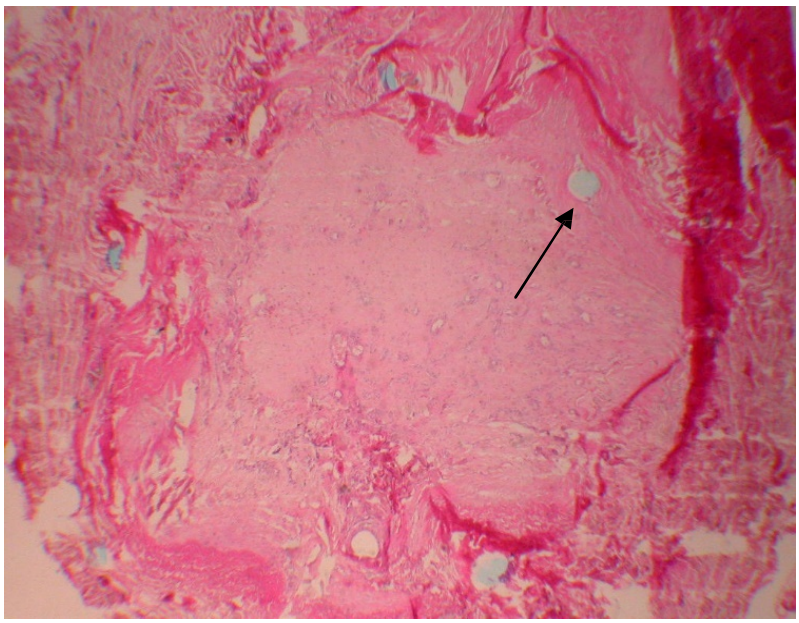

Figure 2. Low power view of an intact vein with asymmetric thickening of wall (partial thrombosis). Lower part of the picture shows normal thin layer of vein. Upper part shows intimal thickening (H&E x 40).

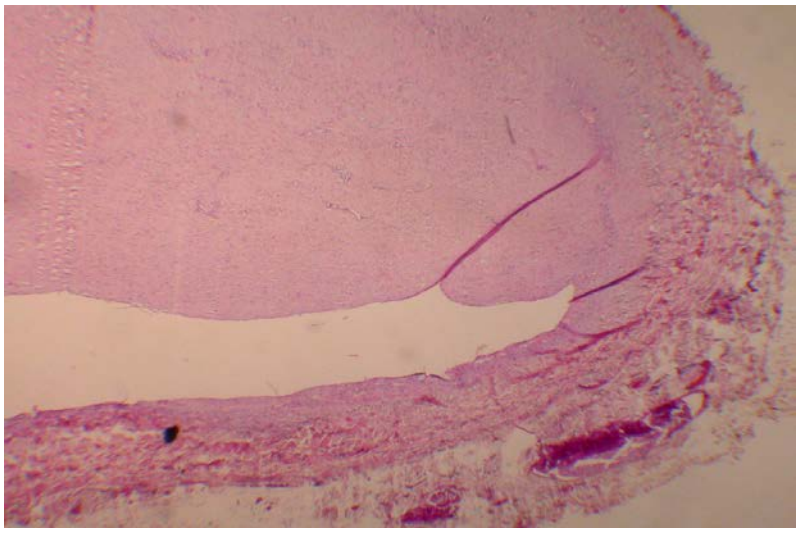

Figure 3. Near Total (90%) obliteration of lumen by thrombosis (H&E x 40)

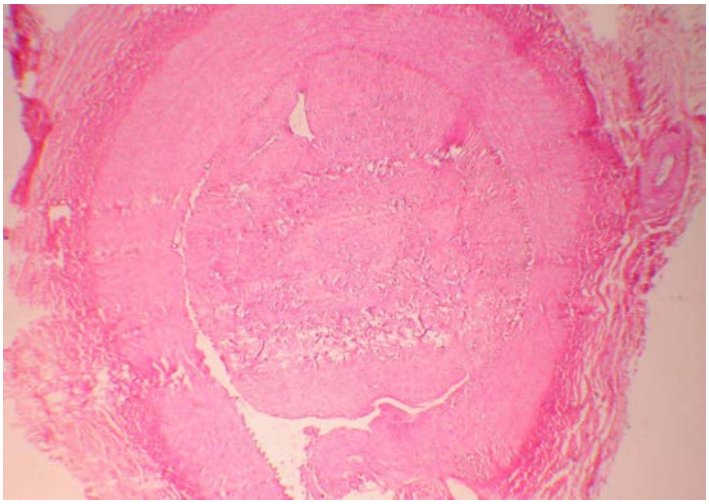

Figure 4. Higher view of the same field in the above figure. Small capillaries with endothelialization in the organized thrombosis. (H&E x 200.)

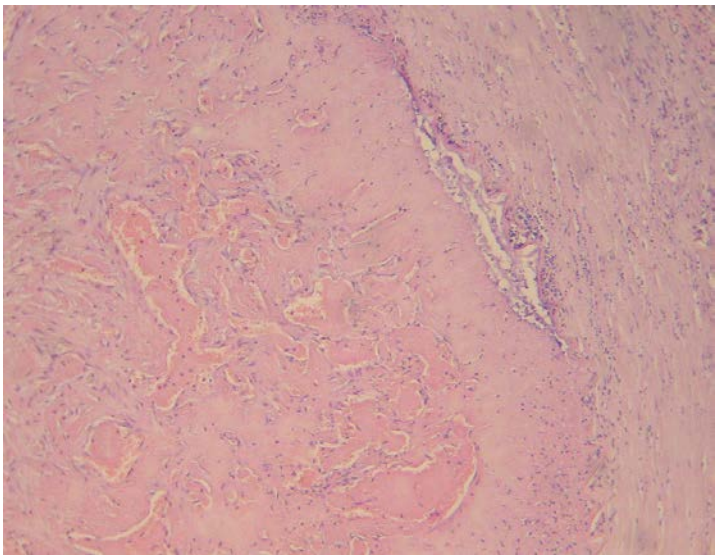

Figure 6. Higher view of the above figure. External elastic membrane is detectable (arrow). (H&E x 150).

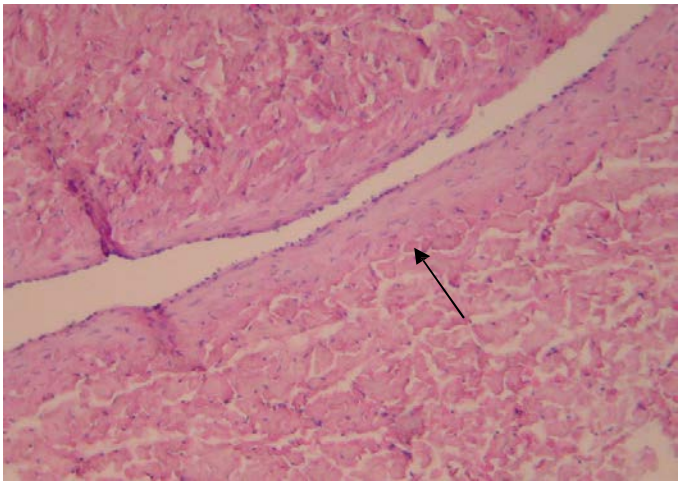

Table 1 Results of the experimental study

No. Dog	Doppler‡		Pathologic Study		Length (Rt/Lt) (cm)	Graft Diameter (Rt/Lt) (mm)
	Rt †	Lt	Rt	Lt		
1	Occluded	Patent	Thrombosed	50% occluded	3.5/3.5	8/9
2	Occluded	Occluded	Thrombosed	Thrombosed	4/3.5	9/9
3	Occluded	Patent	Thrombosed	Normal	3.2/3.3	10/12
4	Occluded	Patent	Thrombosed	Normal	4/4	12/12
5	Occluded	Patent	Thrombosed	Normal	4.2/4	12/12
6	Occluded	Patent	Thrombosed	Normal	3.5/4	11/11
7	Occluded	Patent	Thrombosed	Normal	4/4	10/11
8	Occluded	Patent	Thrombosed	50% occluded	3.5/4	11/11
9	Occluded	Patent	Thrombosed	Normal	4/4	12/11
10	Occluded	Patent	Thrombosed	Normal	4/4	8/8
11	Occluded	Patent	Thrombosed	Normal	3.5/3.3	9/9
12	Occluded	Patent	Thrombosed	Normal	3.2/3.4	9/10

† On the right side the inverted vein graft was used and on the left side simple non- inverted vein graft; ‡ Doppler results at 3 and 6 months follow up.