Microvascular Polytetrafluoroethylene Graft in the Rat

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With the recent advancement in the field of microvascular surgery, the demand for a microvascular prosthesis of 1-2 mm diameter has been increasing.

The authors attempted to insert a Gore-tex graft of 1 mm inner diameter to the rat aorta and renal artery with different techniques and different suture materials.

The telescoped technique was utilized for the anastomosis of the proximal part of the artery. They showed 80% patency of grafts up to 116 days with 10-0 ethilon and 83% patency up to 96 days with 7-0 silk in the rat aorta. In the rat renal artery, they showed 53.3% patency with 10-0 ethilon.

These results showed that Gore-tex grafts of a 1 mm inner diameter could be used for microvascular reconstructions but further laboratory experimentation is needed before clinical application.

Key Words: Microvascular surgery, Microvascular Gore-tex prosthesis, Telescoped anastomosis.

Recent advances in microvascular reconstructive technique combined occasionally with an extracorporeal approach now enable successful branched renal artery revascularization in many patients with renovascular hypertension who previously would have been considered either inoperable or candidates for nephrectomy by standard in situ technique (Novick and Pohl, 1979; Salvatierra et al., 1978).

Although autologous hypogastric artery and saphenous vein graft has been used for branched renal artery bypass with excellent clinical results, (Novick et al., 1977; Novick and Pohl, 1979) there are recent discouraging reports (Acland, 1972; Acland et al., 1977; Caffee, 1980; Ernst et al., 1972; Stanley et al., 1973) on the long-term follow-up of the saphenous vein in aortorenal bypass and also there are situations in which the hypogastric artery is not available due to extensive atherosclerotic involvement in which situation a readily available synthetic graft would be most advantageous.

The most widely used and well established synthetic vascular graft seems to be expanded polytetrafluoroethylene (PTFE). The smallest graft in clinical use is one with a 4 mm inner diameter. The reason for this limitation was due to the frequent formation of thrombosis and it has been generally accepted that 1-2 mm sized prosthesis are almost impossible for success
(Parsa and Spira, 1979). Multiple factors seem to be related to the early thrombosis.

It would be greatly advantageous if the 1 or 2 mm sized synthetic vascular grafts could work in the branched renal artery bypass. The authors attempted to test the different techniques with different suture materials in the rat aorta and then attempted to insert a 1 mm PTFE graft for the main rat renal artery.

**MATERIALS AND METHODS**

**Group A. 1 mm inner diameter PTFE (Gore-tex) graft for rat aorta.**

The 14 Sprague-Dawley rats weighing 300-350 gm were anesthetized by intraperitoneal injection of pentobarbital (3.5mg/100gm). A midline incision was made and the infrarenal part of the aorta was exposed. A portion of the infrarenal aorta was prepared and simple division was made between two vascular clamps. Gore-tex grafts 5 mm in length (1 mm inner diameter, fibril length 20 um) were inserted after flushing with heparinized Ringer-lactate solution. Telescoping technique (figure 1) was utilized for the anastomosis of the proximal portion of the aorta.

In the following 3 subgroups, different techniques with different suture materials were used.

1. In this subgroup, 5 PTFE grafts were inserted with 10-0 ethlon suture material with telescoping in the proximal end and end to end anastomosis in the distal end by continuous suture.

   II. In this subgroup, 6 PTFE grafts were inserted with 7-0 silk by telescoping at the proximal end and end to end method in the distal part of the aorta.

   III. In this subgroup, 3 PTFE grafts were inserted with 7-0 silk by telescoping at both ends.

   The patency of the grafts were checked by angiography.

**Group B. 1 mm PTFE graft for the rat renal artery.**

Seven Sprague-Dawley rats (300-350gm) were used in this group. After anesthetizing the rat with 3.5mg/100gm pentobarbital intraperitoneal injection, a midline incision was made and right nephrectomy was done. Left renal artery was dissected carefully from the renal vein. After careful dissection and preventing spasm by spraying 2% procaine on the renal artery, the renal artery was clamped with two separate clamps and was divided. The both ends were trimmed and flushed with heparinized Ringer-lactate solution. 1 mm inner diameter PTFE grafts 3 mm in length were inserted by telescoping in the proximal end and end to end anastomosis for the distal end with spation of the artery. The ischemic time was less for the distal end with spation of the artery. The ischemic time was less than 30 minutes. The patency of the grafts were checked by the survival of the rat and by angiography.

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Fig. 1. Diagram of the telescoped technique for PTFE graft for the proximal aortic anastomosis.
RESULTS

Group A-I.

Among 5 rats, one expired on the first day of operation due to technical failure. Four rats lived until they were sacrificed and all the vascular grafts were patent by angiographic study (Figure 2).

<table>
<thead>
<tr>
<th>Rat No.</th>
<th>Suture</th>
<th>Method</th>
<th>Days of sacrifice</th>
<th>Patency</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10–0</td>
<td>Tel + E-E</td>
<td>1</td>
<td>Expired</td>
</tr>
<tr>
<td>2</td>
<td>10–0</td>
<td>Tel + E-E</td>
<td>116</td>
<td>OK by angiography</td>
</tr>
<tr>
<td>3</td>
<td>10–0</td>
<td>Tel + E-E</td>
<td>115</td>
<td>OK by angiography</td>
</tr>
<tr>
<td>4</td>
<td>10–0</td>
<td>Tel + E-E</td>
<td>110</td>
<td>OK by angiography</td>
</tr>
<tr>
<td>5</td>
<td>10–0</td>
<td>Tel + E-E</td>
<td>12</td>
<td>OK by angiography</td>
</tr>
</tbody>
</table>

In this group there was 80% patency up to 116 days.

Group A-II.

Among rats, one expired early due to technical problems, the others were all living up to the day of sacrifice.

<table>
<thead>
<tr>
<th>Rat No.</th>
<th>Suture</th>
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<th>Patency</th>
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<tbody>
<tr>
<td>6</td>
<td>7–0</td>
<td>Tel + E-E</td>
<td>96</td>
<td>OK by angiography</td>
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<tr>
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<td>7–0</td>
<td>Tel + E-E</td>
<td>92</td>
<td>OK by angiography</td>
</tr>
<tr>
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<td>7–0</td>
<td>Tel + E-E</td>
<td>89</td>
<td>OK by angiography</td>
</tr>
<tr>
<td>9</td>
<td>7–0</td>
<td>Tel + E-E</td>
<td>67</td>
<td>OK by angiography</td>
</tr>
<tr>
<td>10</td>
<td>7–0</td>
<td>Tel + E-E</td>
<td>66</td>
<td>OK by angiography</td>
</tr>
<tr>
<td>11</td>
<td>7–0</td>
<td>Tel + E-E</td>
<td>1</td>
<td>Expired</td>
</tr>
</tbody>
</table>

In this group there was 83.3% patency up to 96 days.

The angiographic studies also confirmed functioning vascular grafts. (Figure 3).

Group A-III.

Among 3 rats, one expired on the second day of operation, the others were living up to the day of sacrifice.

<table>
<thead>
<tr>
<th>Rat No.</th>
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<th>Days of sacrifice</th>
<th>Patency</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>7–0</td>
<td>Tel + Tel</td>
<td>2</td>
<td>Obst. (expired)</td>
</tr>
<tr>
<td>13</td>
<td>7–0</td>
<td>Tel + Tel</td>
<td>82</td>
<td>Obst. by angiography</td>
</tr>
<tr>
<td>14</td>
<td>7–0</td>
<td>Tel + Tel</td>
<td>78</td>
<td>Obst. by angiography</td>
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</table>
All grafts turned out to be obstructed by angiographic study. (Figure 4). They showed non-functioning of all the grafts using the distal telescoping anastomosis. Even though the grafts were obstructed, they were living by intestinal collateral vessels.

Group B.

Among 7 rats, 3 expired within 7 hrs, others were living until the day of sacrifice.

<table>
<thead>
<tr>
<th>Rat No.</th>
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<th>Patency</th>
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<tr>
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<td>10–0</td>
<td>Tel + E-E</td>
<td>2</td>
<td>No (expired)</td>
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<tr>
<td>16</td>
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<td>Tel + E-E</td>
<td>2</td>
<td>No (expired)</td>
</tr>
<tr>
<td>17</td>
<td>10–0</td>
<td>Tel + E-E</td>
<td>3</td>
<td>No (expired)</td>
</tr>
<tr>
<td>18</td>
<td>10–0</td>
<td>Tel + E-E</td>
<td>67</td>
<td>OK by angiography</td>
</tr>
<tr>
<td>19</td>
<td>10–0</td>
<td>Tel + E-E</td>
<td>53</td>
<td>OK by angiography</td>
</tr>
<tr>
<td>20</td>
<td>10–0</td>
<td>Tel + E-E</td>
<td>49</td>
<td>OK by angiography</td>
</tr>
<tr>
<td>21</td>
<td>10–0</td>
<td>Tel + E-E</td>
<td>38</td>
<td>OK by angiography</td>
</tr>
</tbody>
</table>

Due to the big discrepancy in the size of the prosthesis and renal artery, the distal renal artery was spatulated and anastomosed to the prosthesis by the end to end method.

They showed a 53.3% patency rate.

The angiographic studies confirmed functioning grafts (Figure 5). Histologically, all the patent grafts were lined by a continuous neointima, consisting of a connective tissue layer covered by a thin endothelium 1-3 months after implantation. In this way the neo-intima became firmly attached to the prosthetic wall (Figure 6).

**DISCUSSION**

Controversy still continues concerning selection of the optimal material for branched renal artery replacement in conjunction with aortorenal bypass.

The autologous hypogastric artery may be procured with its branches and when available represents the optimum means of achieving renal revascularization of a branched renal artery.

Unfortunately the use of the hypogastric artery often is not suitable because of inadequate length or by extensive involvement with atherosclerosis (Novick et al, 1977).

Although the saphenous vein has been well established and used to replace or bypass on arterial lesion over the last 20 years, there are recent long-term studies revealing a distressingly large number of unsatisfactory appearing vein grafts on following-up angiography.

The incidence of thrombosis or stenosis was 14-18% but of great concern 5-25% of these venous grafts were found to have undergone dilation or frank aneurysm formation (Ernst et al, 1972; Stanley et al, 1973).

The clinical significance of these abnormal appearing vein grafts is as yet uncertain, however, doubts have been raised concerning the long-term durability of these sapheous vein grafts as renal artery substitutes. Search for an ideal arterial substitute continues and much attention has
been focused on the synthetic vascular prosthesis. The use of synthetic vascular grafts in large vessel is now well established in peripheral vascular surgery.

Synthetic vascular grafts have improved significantly with the introduction of the expanded PTFE. PTFE, better known by its trade name, Teflon, is an inert polymer of carbon and fluorine. PTFE is produced by mechanical expansion process that forms a porous structure characterized by solid nodes interconnected by fine fibrils.

The porous structure allows for fibrous tissue ingrowth and the formation of neointima.

The surface of the graft is highly electronegative and is hydrophobic, which enables it to be watertight so that no preclotting is necessary.

Clinical experiences with femoropopliteal bypass and even more distal bypass procedures by using 8 down to 4 mm sized PTFE have yielded patency rates that are, in some reports, comparable to those obtained with saphenous vein grafts (Veith et al, 1978 a; Veith et al, 1978 b). At the Cleveland Clinic 6 mm PTFE grafts have been used on occasion for aortorenal bypass. The smallest graft in clinical use 4 mm in size. The major reason of this limitation was due to the frequent formation of thrombosis after anastomosis.

Jacobson et al (1963) even declared that prosthetic grafts less than 4 mm in diameter should not be used.

It was with the introduction of expanded PTFE grafts that it became possible to maintain an open artificial prosthesis of 3 mm in inner diameter experimentally (Matsumoto et al, 1973). Since that time PTFE has gained acceptance for use in medium and smaller caliber artery substitution (Florian et al, 1976; Watanabe, 1980).

The extensive trials of PTFE, both clinically and experimentally have resulted in multifarious results. Some have found PTFE to be comparable to an autologous vein, while others have found the prosthesis to be less satisfactory (Florian et al, 1976; Matsumoto et al, 1973).

The application of synthetic grafts to arteries of 1-2 mm diameter has many problems and Parsa and Spira (1979) reported that PTFE grafts with a diameter 1 mm, perhaps have no place in microsurgery at the present time.

With the recent advancement in the field of microvascular bench surgery, the demand for a 1-2 mm sized synthetic microvascular prosthesis has been increasing.

It has been generally accepted up to now that the synthetic graft of 1-2 mm in diameter can not work for vascular prosthesis due to early thrombosis and obstruction.

Though the ideal microvascular prosthesis that will be equal to a suitable autologous vascular grafts has as yet not been developed and may never be developed, certainly one will be found that will be superior to inadequate autologous vessels.

It would be greatly advantageous if readily available 1-2 mm sized expanded PTFE graft could work in the branched renal artery substitution. Multiple factors seem to be related to the patency of the microvascular prosthesis. The physical property of the prosthesis, the suture material, the surgeon's skill and technique, method of anastomosis, the relative size of host artery and prosthesis, and the blood pressure influence the patency of the prosthesis after microsurgical anastomosis (Hayhurst and O'Brien, 1975; Jacobson et al, 1963).

In regard to the physical property of the synthetic PTFE graft, the pore size, density and the thickness of the wall seems to play an important role in long-term patency.

Campbell et al (1975) stressed that the pore size is the primary determinant of tissue ingrowth and as the porosity of the PTFE
becomes greater than 22 um, the patency rate falls precipitously and also the smaller the pore, the thinner is the neointima produced, which is thought to be more favorable for long-term patency.

The average pore size of the PTFE in current use is 10-30 um. The 1 mm PTFE that we used has 20 um pores. Graft thickness also affects the patency of the PTFE graft and recently Caffed (1980) reported multifarious results with various graft thickness of 1-2 mm inner diameter PTFE.

Selection of the proper sized PTFE graft compared to the vessel it replaces seems to be also important. Jacobson (1963) stressed that the diameter of the prosthesis should be 2 or 3 times the diameter of the vessel it replaces but Watanabe (1980) chose the PTFE graft 1.2-1.5 times the size of the host vessel in anastomosing with telescoped method.

In our experiments the relative ratio of rat renal artery and aorta to 1 mm inner diameter PTFE graft was 1:2 and 1:1. Due to the big discrepancy of the size between the rat's renal artery and the prosthesis, the proximal telescoping method was easier but needed more stitches to prevent backflow. At the distal end, we spatulated the renal artery and anastomosed with end to end suturing. With the almost equal size between rat aorta and 1 mm PTFE, the proximal telescoping method was a little bit difficult but the distal end to end anastomosis was easy due to the almost equal size. The authors agree that 1.2-1.5:1 ratio is ideal for the prosthesis to be anastomosed by the telescoped method.

Since the first report of end to end microvascular anastomosis by Jacobson and Suarez (1960), many investigators tried to find a better anastomotic method. For the micro-anastomosis, if possible, less stitches are desirable. Several investigators (Cobbett, 1967; Holt and Lewis, 1962; Yamagata et al, 1979) tried to do sureless techniques by teflon ring, glue, and by a soluble tube stent, and also several investigators (Eisenhardt, 1980; Harishiba, 1977; Dopov and Trich-kowa, 1975) attempted various technical methods.

Recently Lauritzen (1978) introduced the new telescoped method (sleeve or end in end) in anastomosing of the microvessels. This method has some theoretical disadvantages such as narrowing of the lumen, turbulence, and intraluminal exposure of the inserted cut end may possibly cause thrombosis. Despite these theoretical disadvantages and recent discouraging reports on the diminished blood flow, they turned out to be easier, faster, and functionally as reliable as the conventional end to end anastomosis. Karg and Holck (1980) reported a significantly lower frequency of late thrombotic deposition (13%) than the arterial end to end anastomosis (41%) and explained that this might be due to the theoretical advantages of the telescoped method because of the avoidance of intraluminal sutures, the more atraumatic handling, the rapid endothelial healing potential of the telescoped vessels. Watanabe ('1980) applied this telescoped technique to the 1.5 mm sized PTFE graft anastomosis and reported a 90% patency rate. He used the telescoped technique on both sides but we used telescoped method proximally and end to end method distally, which showed more satisfactory results. We had an 80% patency using 10-0 nylon and the telescoped technique in the rat aorta. Tizian et al (1980) inserted a 1 mm inner diameter PTFE graft in rat aortas with an evertting suture technique and reported an early patency rate of 77.7%.

Selection of good suture material seems to play an important role in the success of PTFE grafts. If the anastomosis can be done with fewer stitches, the better. Several investigators at-
tempted to do sutureless technique by teflon ring, glue and by soluble tube stent and also several investigators tried various technical methods. One author felt that dacron and nylon were preferable to silk with respect to durability and tissue response but Matsumato et al (1973) reported same results with 6-0 Tevdek and 6-0 silk.

Thiede (1979) reported concerning absorbable suture. Our result showed no differences between 10-0 nylon compared to 7-0 silk. So long as the tensile strength permits, the more fine the suture material, the better it looked.

The other factors affecting the patency of grafts seem to be the surgeon's skill and technique and good blood flow after anastomosis. As several investigators stressed, the surgeon's skill and adequacy of the microanastomosis using high magnification is the most important factor in ensuring final patency. For the rat's renal artery reconstruction with 1 mm PTFE graft, we could estimate the success of the graft by the immediate change of the kidney color after anastomosis. No rats that demonstrated a perfect kidney color immediately, were subsequently found to be thrombosed up to 83 days. Therefore, it is likely that almost all thrombosis occur in the immediate postoperative period as observed by other investigators and were the result of technical error in the arterial reconstruction.

For the topical irrigating solution, Acland (1972) has demonstrated that magnesium sulfate helps prevent small vessel thrombosis by its strong antiplatelet agglutination and vasodilatation effect. Nomoto et al (1974) also demonstrated a 100% patency rate with mag-sulfate and silicon rubber tube as a splint. Recently Acland (1980) reported that Ringer-lactate solution is much better than saline for the microvascular irrigating solution. We used heparinized Ringer-lactate for topical irrigation of the microvessels. Patency assessment is not easy and remains a major problem in microvascular surgery. There are several methods to check the patency such as the Hyhurst and O'Brien test, the cut test, angiograms, observing "longitudinal and expansile pulsation and wriggling" in the distal part as described by Acland (1972). Recently Freed et al (1979) presented anatraumatic quantitative method by using a high-frequency pulsed Doppler ultrasound. In the rats, even though the infrarenal aorta was completely obstructed by thrombosis in the PTFE graft, the rats were still living because of intestinal collateral circulations as already observed on hypertensive rats. So far as we reviewed, there are no reports available regarding the microvascular prosthesis for the branched renal artery. PTFE graft for the rat's main renal artery to a solitary kidney seems to be a unique and recommendable way to test the patency of a prosthesis and can check for possible late thrombosis by only observing the death of the rat. Tizian et al (1980) reported a 77.7% patency rate and recently Derman and Reichman (1979) reported a 90% patency rate with the 1 mm inner diameter PTFE graft. Our result was 80% with 10-0 nylon in the rat aorta and 83.3% with the 7-0 silk using proximal telescoping and distal end to end suturing. Contrary to these findings, in cases where both ends were telescoped, every graft was obstructed, which tells us that the end to end method is preferable at the distal anastomosis.

As many other investigators discovered, we also found that occlusion occurred within the first 72 hrs were mostly due to technical problems. Hyhurst and O'Brien reported late thrombosis in the 1st week and also Lauritzen and Hansson (1980) reported that neointima takes place in 2 stages. The initial fibrin platelet layer was reduced after a month and replaced by a neointima with mononuclear cells and
connected with interstitial cells. Our histologic slides of 116 day PTFE graft, showed well established permanent neointima attached to the prosthetic wall.

CONCLUSION

The results obtained in this study showed that PTFE grafts having an inner diameter of 1 mm were working in the aorta and renal arteries of rats. In the near future, branched renal arteries could be reconstructed by a small caliber prosthesis, but further laboratory experimentation is needed before the clinical application.

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**Fig. 6.** 116 days post implantation, permanent neointima was firmly attached to the prosthesis (HE, x400)
g. 2. Angiogram taken 116 days after PTFE implantation in the aorta and showing a patent graft.

g. 3. Angiogram taken 96 days after PTFE implantation in the aorta showing a patent graft.

g. 4. Angiogram taken 82 days after PTFE implantation in the aorta and showing an obstructed graft.

g. 5. Angiogram taken 67 days after PTFE implantation into the main renal artery shows a patent graft.