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Changes in venous hemodynamics after renal transplantation

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Abstract To explain an occasionally observed transient swelling of the ipsilateral leg in renal transplant recipients in the absence of deep vein thrombosis, we took serial measurements of venous outflow resistance and duplex examinations of both legs. Fourteen recipients of a living related donor kidney graft were submitted to strain gauge plethysmography and duplex examination before transplantation and 1 and 6 weeks thereafter. Venous outflow resistance and venous flow were measured and the veins were assessed for thrombosis. Strain gauge plethysmography showed a significant increase in venous outflow resistance in the leg on the side of the renal transplant 1 week after transplantation [0.28 ± 0.13 vs 0.40 ± 0.15 mmHg.s (ml/100 ml)$^{-1}$; $P < 0.05$]. Six weeks later, the venous outflow resistance had returned to preoperative values [0.30 ± 0.11 mmHg.s (ml/100 ml)$^{-1}$; P = NS]. On the contralateral side, no significant differences were found. Duplex examinations showed no signs of thrombosis. Venous flow measurements in the common femoral vein showed no significant differences. We conclude that the additional blood supply to the iliac veins results in an increase in venous outflow resistance in the ipsilateral leg, which can explain the observed swelling of this leg and may have implications for the preferred method of diagnosis of venous thrombosis after renal transplantation.

Key words Kidney transplantation, venous blood flow · Venous blood flow, kidney transplantation · Duplex ultrasound, kidney transplantation

Introduction

Vascular complications are not uncommon after renal transplantation. Arterial thrombosis and stenosis of the arteries supplying the kidney allograft have been reported [14–16]. Moreover, venous complications, mostly thrombosis of the renal vein or of the iliofemoral veins, are not uncommon [1, 5, 9, 11]. In our experience, a transient swelling of the leg on the side of the renal transplant is occasionally noted, without (sonographic) evidence of a thrombosis. This is interpreted as the result of possible alterations in venous hemodynamics

due to the transplantation procedure. To investigate this alleged alteration, we performed consecutive physiological examinations in renal transplant recipients. Measurements of venous hemodynamics were taken before and after renal transplantation in a group of recipients of living related donor (LRD) organs.

Patients and methods

After informed consent was obtained, 14 patients who were to receive a LRD kidney transplant were submitted to plethysmographic and duplex ultrasound investigation. Measurements were taken on the day before transplantation and 1 and 6 weeks thereafter. Patients (eight male, six female; median age 28 years) had no history of thrombosis or previous pelvic surgery.

Plethysmography was performed with the strain gauge method [8, 9], in which a variation in circumference of the limb causes a variation in the length of a mercury-filled rubber tube (strain gauge). The corresponding percentage change in the electrical resistance of the mercury thread is converted into percentage limb volume change (ml/100 ml). Limb volume changes can be continuously recorded with the use of a personal computer. Pneumatic cuffs on both thighs are used to induce temporary venous congestion in the legs, resulting in an increased venous pressure (mmHg) and an increased venous volume in the leg. The instant decrease in limb volume [= venous outflow (ml/100 ml/s] after release of the pneumatic cuff is translated into venous outflow resistance of the leg and is expressed in mmHg.s $(ml/100\ ml)^{-1}$. This can be understood as an analog to Ohm's law ($V = I.R$ or $R = V/I$), where resistance is the result of "pressure/flow". The methodological aspects of the method have been described earlier [4, 13]. Duplex ultrasound measurements were performed with a Toshiba SSA-270 A. The common femoral vein was assessed for thrombosis [11, 12] and measurements of femoral venous diameter and blood velocity in the vein were taken. Venous flow calculations were made from these measurements [flow = area.mean velocity (ml/min)].

Transplantation was performed using standard surgical techniques. Arterial and venous end-to-side anastomoses were performed on the common or external iliac artery and vein. Anticoagulant or antiplatelet drugs were not administered. Immunosuppression was achieved with cyclosporin and prednisone. Cyclosporin was started 6 h after transplantation intravenously at 3 mg/kg body weight for 2 days and then continued orally after being adjusted to trough blood levels (target values 200–400 ng/ml).

All values are expressed as mean ± SD. Statistical analysis was done with the paired Student's *t*-test. Probability values below 0.05 were considered significant.

Results

In this group of patients, there was no ipsilateral leg swelling. The results of the plethysmographic measurements are shown in Table 1. The data for the ipsilateral and contralateral legs are shown separately. There were no differences between the two legs before transplantation. The first post-transplant measurement showed a significant rise in venous outflow resistance in the ipsilateral leg compared to the first pretransplant measurement. In the contralateral leg, no such rise was found. Compared to the contralateral leg, venous outflow resistance in the ipsilateral leg was significantly increased 1 week post-transplantation. Six weeks post-transplantation, venous outflow resistance measurements showed no significant difference with the preoperative measurement, nor were there differences between the ipsilateral and contralateral legs.

Table 1 Results of plethysmographic venous resistance measurements in 14 renal transplant recipients (28 legs). All values are given in mm Hg · s $(ml/100\ ml)^{-1}$; means ± SD

	Ipsilateral leg	Contralateral leg
Before transplantation	0.28 ± 0.13	0.33 ± 0.14
1 week post-transplantation	0.40 ± 0.15*	0.34 ± 0.13**
6 weeks post-transplantation	0.30 ± 0.11	0.37 ± 0.17

* $P < 0.05$ compared to pretransplant measurements; ** $P < 0.05$ compared to measurements in ipsilateral leg

Table 2 Results of duplex ultrasound venous flow measurements in the common femoral vein in 14 renal transplant recipients (28 legs). All values are given in ml/min; mean ± SD

	Ipsilateral leg	Contralateral leg
Before transplantation	80.4 ± 56.3	73.3 ± 51.6
1 week post-transplantation	90.3 ± 49.6	74.3 ± 78.9
6 weeks post-transplantation	86.4 ± 56.0	86.3 ± 75.6

Duplex ultrasound investigations were performed in all patients. None showed signs of venous thrombosis or peritransplant fluid collections (lymphocele) that could have been an external reason for increased venous ouflow resistance. Flow measurement results are shown in Table 2. There were no statistically significant differences in blood flow measurements before and after transplantation, or between the two legs after transplantation.

Discussion

Retrospective clinical studies have reported the incidence of deep venous thrombosis to be 8 %–10 % in kidney allograft recipients [1]. In most studies, diabetic patients have a three to six times higher risk of having thrombosis than those without diabetes [2, 3]. Allen et al. [1] showed that only 1.7 % of patients developed deep venous thrombosis within 1 month after transplantation and that the majority of the thrombotic events occurred in the 4th month after transplantation, which is later than in other patients undergoing major surgery. In their study, 38 % of the patients with thrombosis also suffered from pulmonary embolism. Prospective studies, using strain gauge plethysmography and thermography for diagnosis of deep venous thrombosis, have suggested that, after renal transplantation, venous

thrombosis occurs in up to 24% of allograft recipients within 3 weeks after transplantation [3, 5]. None of the patients in these studies actually had pulmonary embolism. The same number of abnormal plethysmographic and thermographic findings was observed in each leg, whether or not it was on the same side as the renal transplant.

The latter findings contradict the observations that most thrombotic events in renal allograft recipients occur relatively late after transplantation [2, 6]. This late occurrence has been attributed to the fact that hemostasis is disturbed in patients on dialysis [8] and that venous flow is enhanced in the deep veins as a result of the renal transplant blood flow added to these veins. It is, however, poorly understood why, unlike in other patients undergoing major surgery, this often occurs several months or even years after transplantation [1]. Hypercoagulability due to corticosteroids [10] and defective fibrinolysis [17] have been implicated as causes for this. The alteration in pelvic venous hemodynamics, with relatively low blood velocities in the distal external iliac vein, representing the risk factor stasis, may also play a role in this delayed occurrence of deep vein thrombosis.

It was our intention to evaluate the possible changes in pelvic venous hemodynamics following the clinical observation of leg swelling on the side of the transplant in the absence of ultrasound signs of venous thrombosis in renal transplant recipients. Renal blood flow studies have shown that blood flow through a kidney allograft can be as high as 600 ml/min [7], which is approximately twice the amount of blood flow to one leg at rest. Our hypothesis was that the pelvic venous system may become overloaded because of the increased blood supply from the the renal transplant. The venous supply from the renal allograft may result in a rise in venous pressure in the central pelvic veins, which subsequently causes an increased venous resistance for the outflow of the leg. In the current study, a significant increase in venous outflow resistance on the side of the renal transplant was found 1 week after transplantation. Six weeks later, this had disappeared. The venous system may have adapted itself to the increased blood supply of the renal transplant. Duplex examinations excluded thrombosis as the cause of increased venous outflow resistance. Although we did not perform duplex examinations at the popliteal fossa, distal thrombosis is not likely to increase venous outflow resistance as measured by plethysmography at the calf. Furthermore, none of the patients examined had symptoms of progressive thrombosis. A statistically significant alteration in venous blood flow in the femoral vein was not found. A slight increase was found 1 week after transplantation, but due to large individual varjation this did not reach the level of statistical significance.

Due to the increased venous outflow resistance after renal transplantation, conventional plethysmography is, in our view, unsuitable for making the diagnosis of postoperative venous thrombosis. Although it was not the subject of this study, it may be speculated that the increased venous outflow resistance of the leg causes delayed contrast filling of the femoral vein during contrast venography, suggesting venous thrombosis in an intact venous system.

We conclude that, after renal transplantation, an increase in venous outflow resistance occurs in the ipsilateral leg as a result of the additional venous inflow in the deep veins. Strain gauge plethysmographic diagnosis of deep vein thrombosis may thus be hampered by this physiological phenomenon after renal transplantation. It can even be speculated that contrast venography may suggest thrombosis due to delayed filling of the deep veins in the presence of increased venous outflow resistance. Direct echographic examination of vein compressibility and/or intraluminal visualization of thrombus is not hampered by these phenomena.

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