C. Thalhammer[1]
M. Aschwanden[1]
M. Mayr[2]
M. Koller[3]
J. Steiger[2]
K. A. Jaeger[1]

Duplex Sonography after Living Donor Kidney Transplantation: New Insights in the Early Postoperative Phase

Duplexsonographie nach Lebendnierentransplantation: Neue Erkenntnisse in der frühen postoperativen Phase

Original Article

Zusammenfassung

Ziel: Vaskuläre Komplikationen, unter anderem venöse Thrombosen, sind wichtige Ursachen für den frühen Verlust von Transplantatnieren. Duplexsonographische Flusscharakteristika nach Lebendnierentransplantation, insbesondere in der Vene, sind weitgehend unbekannt. Ziel der Studie war die Erfassung der renalen Perfusion in der postoperativen Phase unter spezieller Berücksichtigung der Transplantatvene. **Methoden:** 22 konsekutive Lebendnierenempfänger und ihre Spender wurden eingeschlossen und prospektiv beobachtet. Die folgenden Parameter wurden erfasst: der intrarenale Widerstandsindex (RI) der Spenderniere vor Transplantation sowie beim Empfänger der intrarenale RI, die Spitzenflussgeschwindigkeiten (PSV) und die „area under the curve" in der Nierenvene, die PSVs der Beckenarterie und der Nierenarterie direkt sowie ein und drei Monate nach Transplantation. **Ergebnisse:** Bei den 22 Lebendnierentransplantationen kam es zu keinem Organverlust wegen vaskulärer Komplikationen. Die höchsten venösen und arteriellen Flussgeschwindigkeiten (Median [Bereich] cm/s) wurden direkt postoperativ in der Nähe der Anastomosen gemessen (92 [22 – 211] und 271,5 [141,5 – 458]). Im Verlauf kam es zu einem signifikanten Abfall dieser Parameter (44,3 [13,3 – 156,9] und 186,8 [105,5 – 267,5]). Der RI fiel vom Spender zum Empfänger aufgrund einer postoperativen Tachykardie von 0,65 auf 0,60 ab (p = 0,06). Nach Herzfrequenzkorrektur zeigte sich ein stabiler Verlauf des RI über drei Monate. **Schlussfolgerung:** Initial hohe arterielle und venöse Spitzenflussgeschwindigkeiten bei stabilem Widerstandsindex und komplikationslosem Verlauf deuten auf ein postoperatives Adaptationsverhalten der Transplantat-

Abstract

Aim: Vascular complications of kidney transplantation, including transplant vein thrombosis, are relevant causes for graft loss in the early postoperative phase. However, duplex flow characteristics after living renal transplantation are widely unknown. Aim of the study was to assess renal perfusion in the postoperative period with special emphasis on the renal vein. **Methods:** 22 consecutive kidney graft recipients and their donors were included and prospectively followed up for three months. The following Doppler parameters were collected: in the donor before operation: the intrarenal resistive index (RI), in the recipient after transplantation and at one and three months: the intrarenal RI, peak flow velocities and area under the curve in the renal vein, as well as peak systolic velocities of the iliac and renal artery. **Results:** None of the 22 transplants failed due to vascular complications. Highest median venous (92 cm/s [range 22 – 211]) and arterial peak velocities (271.5 cm/s [141.5 – 458]) were observed close to the anastomosis immediately after transplantation. During follow-up, flow parameters significantly decreased at three months (44.3 cm/s [13.3 – 156.9] and 186.8 cm/s [105.5 – 267.5]). The RI decreased from donor to recipient at the day of operation due to tachycardia (0.65 to 0.60; P = 0.06). After correction for heart rate, the RI was stable during follow-up. **Conclusions:** Initial high peak velocities in conjunction with stable resistive indices in a cohort, free of vascular graft complications, suggest a postoperative physiologic adaptation process rather than a relevant stenosis requiring medical intervention.

affiliation
[1] Klinik für Angiologie, Universitätsspital Basel
[2] Klinik für Transplantationsimmunologie und Nephrologie, Universitätsspital Basel
[3] Institut für klinische Epidemiologie, Universitätsspital Basel

correspondence
Christoph Thalhammer, MD · University Hospital Basel, Department of Angiology · Petersgraben 4 · 4031 Basel · Switzerland · Tel.: ++ 41/61/2 65 51 57 · Fax: ++ 41/61/2 65 53 56 · E-mail: thalhammerc@uhbs.ch

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niere und nicht auf eine klinisch relevante, interventionsbedürftige vaskuläre Stenosierung hin.

Schlüsselwörter
Nierenvene · Sonographie · Doppler · Duplex · Nierentransplantation · Stenose · Venenthrombose

Key words
Renal vein · ultrasonography · Doppler · duplex · kidney transplantation · stenosis · venous thrombosis

Introduction

Colour coded duplex sonography is the first line diagnostic imaging tool of the transplant kidney, providing instantaneous assessment of intrarenal perfusion and identifying the feeding iliac artery as well as the transplant artery and vein [1, 2]. Although there has been a substantial increase in short- and long-term survival of kidney grafts [3], vascular complications, such as acute arterial or venous thrombosis, are still an important reason for failure after transplantation, especially in the early postoperative period [4, 5].

At our institution, a routine duplex sonography of renal perfusion in living donor transplants within the first hour after transplantation has been established. This procedure was introduced to detect vascular complications (e. g. renal ischaemia due to stenosis or kinking of the renal artery) as early as possible, and to obtain baseline perfusion parameters in case of further sonographic control examinations being required (e. g. decreasing diuresis, delayed graft function).

Venous thrombosis is a possible complication with an incidence between 0.1 % and 1.6 %, typically occurring in the first week after transplantation, usually leading to organ loss [3, 4, 6, 7]. Renal vein stenoses are rarely reported, but may be the initial stage of a complete renal vein thrombosis [8, 9]. To date, however, no generally accepted definition of a relevant renal vein stenosis, responsible for insufficient graft function or leading to renal vein thrombosis, exists in the literature. Some authors suggest a 3 to 4-fold increase in peak velocity in the renal vein, but an association with vascular complications has not been established [2, 10]. According to our own experience, strikingly high venous velocities in the renal transplant vein can be found in normally functioning kidneys.

The intrarenal arterial resistive index (RI) is a useful parameter for quantifying the alterations in renal blood flow. RI, however, is not specific for any kind of renal damage [11 – 16]. On the other hand, a RI of 0.80 or higher is associated with poor allograft performance and patients' death [17]. A continuously increasing intrarenal resistive index may also be a clue to imminent renal vein thrombosis, resulting in a biphasic "to-and-fro" signal, typical for complete venous thrombosis [8, 18, 19]. We therefore analysed the course of the intrarenal RI before and during the early course of transplantation as a parameter for overall renal perfusion and marker for intrarenal damage.

The main aim of our study was to report flow characteristics during 3 months follow-up in consecutive patients undergoing living donor kidney transplantation.

Methods

Between May 2004 and February 2005, all consecutive patients undergoing living kidney transplantation and their donors were asked to participate in the study. They were included up to a maximum of three days before transplantation and prospectively followed up for 3 months. The study was approved by the hospital ethics committee and informed consent was obtained from all subjects.

Colour coded duplex ultrasound measurements

Colour coded duplex ultrasound was performed by two experienced investigators (CT, MA), using a HDI 5000 duplex device (Philips, Best, Netherlands). For measurement of the donors' and recipients' RI, a curved 7 – 4 MHz transducer was used, the other parameters were collected with a phased 1 – 4 MHz transducer. All measurements were taken with great caution in order to avoid pain and local compression. Intrarenal RI of the donor kidney was measured up to a maximum of three days before transplantation. According to a standardised protocol, the following parameters were recorded within the first hour after transplantation, as well as after one and three months: intrarenal RI (upper, middle and lower part of the kidney), peak systolic flow velocities (PSV) in the renal artery at the site of the anastomosis, in the middle and in the hilus region, and peak flow velocities (PV) in the renal vein in the middle, just before and at the site of the venous anastomosis. The venous flow pattern can vary substantially, ranging from a monophasic signal with minimal undulations to widely oscillating patterns without difference in the PV. To take various flow patterns into account, the velocity time integral (VTI) of the Doppler curve was measured by calculating the area under the curve (HDI 5000 software, Philips, Best, Netherlands). The measuring points of the transplant vein are demonstrated in Fig. **1**. The RI was calculated as follows: (peak systolic velocity – end diastolic velocity)/ peak systolic velocity. Because of heart rate variations between different examinations, the heart rate corrected (standardised) RI was calculated (corrected RI = observed RI – 0.0026 × (80 – observed heart rate) [20]. All parameters were measured twice per visit, and the mean of the two values was used for further analysis. RI was calculated as the mean of the three measurement points, resulting in one value per kidney. Furthermore, the ratio of the PSVs in the renal artery anastomosis and the external iliac artery (renal/iliacal ratio; RIR) was calculated.

Statistical analysis

Descriptive analysis of flow data are given as median and range for all measurement occasions over time, separately. The influence of time on the development of the duplex measurements was assessed with random coefficient linear regression models with time-period as the fixed part, and we modelled between-patient variability as a random effect. The duplex response and the period variable was log transformed to linearise the time-outcome relation and to obtain normalisation of the outcome variable. "Problem cases" and "non-problem cases" were first analysed separately for each variable, and analyses of all cases was performed only if no significant difference was found between the two subsets. Differences between medians of the two subsets at different time points were assessed with the Mann-Whitney test. Analyses were done using procedure mixed of SAS 9.1.

Results

A total of 22 patients were included. Only one donor refused to give informed consent. Median age (range) was 53.2 (37 – 71) and 40.8 (18 – 67) years for donors and recipients, respectively. 68 % of the donors and 27 % of the recipients were female. Patients' body mass index was 22 (17 – 32) m^2/kg. Retroperitoneoscopic donor nephrectomy was performed in all subjects, the left kidney was transplanted in 20 of the 22 cases. In 18 subjects, transplantation and 3 months' follow-up was free of any complications, whereas complications occurred in 4 patients (kinking of the renal artery, detected in the first postoperative duplex examination; intraoperative sonographic detection of a renal artery dissection; relapse of primary focal segmental glomerulosclerosis; segmental renal infarction and vascular rejection). Separate analyses of the "problem-cases" and "non-problem cases" did not reveal significant differences, we therefore present the data for all 22 subjects.

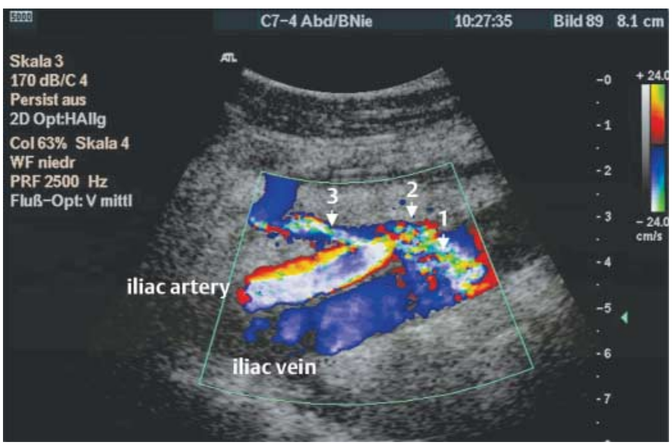

Fig. **1** Colour coded duplex sonography of the renal transplant vein: 1 anastomosis, 2 proximal to the anastomosis, 3 middle.
Abb. **1** Farbkodierte Duplexsonographie der Transplantatvene: 1 Anastomose, 2 vor der Anastomose, 3 Mitte.

PSVs of the different sections of the renal transplant artery are shown in Table **1**. The highest velocities were measured over the anastomosis throughout the whole course of the study with a significant time effect for all arterial parameters. The mean RIR was 1.51 ± 0.57 directly postoperatively and was lower than 3.0 in all cases. In contrast to the absolute values of arterial PSVs, the RIR remained stable in the course of time.

Median RI of the kidney at the donor site was 0.65. In the first hour after transplantation, the RI dropped to a median of 0.60 (P = 0.06). At follow-up, RI values turned back to levels observed within the donor (0.66). The decrease of the RI disappeared after correction for the elevated heart rates in the postoperative period. During follow-up, the corrected RI remained stable, but not the uncorrected RI's (Table **2**).

Median venous PVs were between 80.0 and 99.0 cm/s at the different sites after transplantation and decreased significantly over time (Table **3**). PVs were prevalently elevated at the site of the venous anastomosis directly postoperatively and proximal to the anastomosis at day 30 and day 90 (Fig. **2**). The same course is demonstrated analysing the velocity time integral (VTI) of the renal transplant vein (Table **4**). Overall, a great variation in all venous velocities was observed and finally seemed to diminish at the visit after three months. At the first postoperative examination, 7 pa-

Table **1** Renal transplant and external iliac artery peak systolic velocities of 22 kidney graft recipients during 3 months' follow-up

peak systolic velocity [cm/s]	*day 1 median (range)*	*day 30 median (range)*	*day 90 median (range)*
external iliac artery	161.5 (94.5 – 283.5)	154.2 (88.5 – 259.0) p = 0.006[1]	139.8 (97.0 – 217.0) p = 0.0004[1]
anastomosis	271.5 (141.5 – 458.0)	214.5 (142.5 – 442.5) n. s.[1]	186.8 (105.5 – 267.5) p = 0.0004[1]
middle of renal artery	190.5 (57.5 – 371)	162.5 (91.0 – 271.0) n. s.[1]	150.3 (64.5 – 325.0) n. s.[1]
hilus of renal artery	122.8 (46.5 – 199.5)	91.5 (37.0 – 337.0) n. s.[1]	94.5 (38.5 – 271.5) n. s.[1]

[1] Reference is day 1.

Table **2** Resistive index and heart rate of donor and kidney graft recipients during 3 months' follow-up

resitive index (RI)	*donor day – 3 median (range)*	*recipient day 1 median (range)*	*recipient day 30 median (range)*	*recipient day 90 median (range)*
median RI	0.65 (0.53 – 0.73)	0.60 (0.51 – 0.80) p = 0.06[1]	0.66 (0.57 – 0.86) p = 0.001[2]	0.66 (0.57 – 0.83) p = 0.001[2]
RI corrected for heart rate	0.65 (0.54 – 0.78)	0.66 (0.58 – 0.85) n.s.[1]	0.70 (0.61 – 0.90) n. s.[2]	0.68 (0.61 – 0.82) n. s. [2]
heart rate [beats/min]	83 (62 – 109)	110.5 (84 – 128)	95 (65 – 138)	92.5 (75 – 120)

[1] Reference is donor measurement.
[2] Reference is day of transplantation (day 1).

Table **3** Renal transplant vein peak velocities of 22 kidney graft recipients during 3 months' follow-up

peak velocity (cm/s)	*day 1 median (range)*	*day 30 median (range)*	*day 90 median (range)*
anastomosis	99 (23 – 187)	63 (20 – 245) n. s.[1]	49 (17 – 127) P = 0.0003[1]
before anastomosis	92 (22 – 211)	91.5 (27 – 301) n. s.[1]	63 (18 – 184) P = 0.0005[1]
middle of renal vein	80 (12 – 356)	59.5 (31 – 256) n. s.[1]	46 (16 – 184) P = 0.02[1]

[1] Reference is day 1.

Table **4** Renal transplant vein velocity time integral (VTI) of 22 kidney graft recipients during 3 months' follow-up

VTI (cm/s)	*day 1 median (range)*	*day 30 median (range)*	*day 90 median (range)*
anastomosis	82.0 (20.7 – 154.8)	50.1 (18.0 – 237.4) n. s.[1]	38.7 (13.2 – 103.3) P < 0.0001[1]
before anastomosis	74.5 (17.4 – 191.4)	70.1 (23.6 – 252.6) n. s.[1]	44.3 (13.3 – 156.9) P = 0.0001[1]
middle of renal vein	62.5 (9.2 – 311.9)	50.0 (25.6 – 207.1) n. s.[1]	39.8 (12.6 – 156.9) P = 0.02[1]

[1] Reference is day 1.

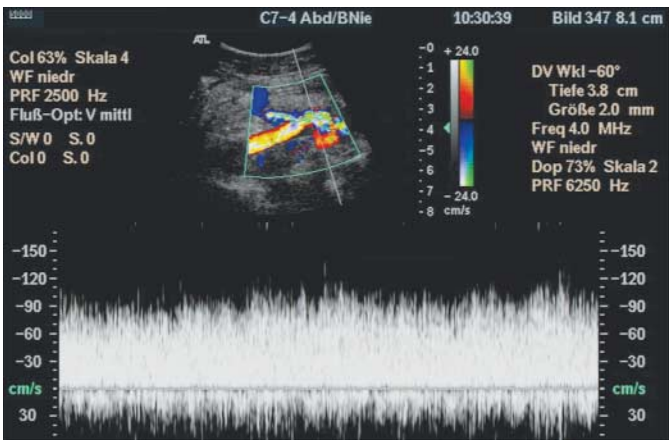

Fig. **2** Colour coded duplex sonography of the renal transplant vein: high flow velocities and turbulent flow in the vein in the area of the crossing with the iliac artery and at the site of the anastomosis with a peak velocity of 120 cm/s.
Abb. **2** Farbkodierte Duplexsonographie der Transplantatvene: schneller und turbulenter Fluss in der Vene im Kreuzungsbereich mit der Iliacalarterie und an der Anastomose mit einer Spitzenflussgeschwindigkeit von 120 cm/s.

tients presented with PV above 150 cm/s, decreasing in 5 patients after one month and in one patient after three months.

The use of linear mixed models was significantly superior to simple linear models, indicating that subjects with high initial velocities remain on high velocities during follow-up.

Discussion

High arterial flow velocity

Different peak systolic velocities to define a significant stenosis of the renal transplant artery have been published. Absolute cut-off values have been set between 180 cm/s and 300 cm/s [2, 21 – 23]. This wide range may be partly explained by a suggested inhomogeneity in technique and hardware used in the different studies, e. g. different transducers and calculation software. Velocity ratios overcome these problems and are suggested to be more reliable for quantifying stenoses [24]. The definition of significant renal transplant artery stenosis is still discussed, and "normal values" are not available. Using suggested absolute criteria, a significant renal artery stenosis would have been present in 36 % (cut off 300 cm/s) to 77 % (cut off 180 cm/s) of the patients in this study. Thus, at least in the immediate postoperative phase, these absolute values seem not to be useful. This is concluded from the fact that we did not observe any related problems of renal function or aggravation of arterial hypertension. Furthermore, the peak systolic velocity ratio of the external iliac artery and the renal artery anastomosis (RIR < 3.0) was within normal ranges in all patients during the whole study period.

Course of resistive index RI

In a prospective study, the normal RI was assessed in healthy subjects with a mean age of 42.1 years who were potential donors for renal transplantation and underwent intraarterial renal angiography [25]. In this study, the mean RI of 118 kidneys was 0.60 ± 0.01, only dependent of the donor's age. We observed a slightly higher median RI of 0.64 ± 0.06 of the donors' kidneys, consistent with the higher age of the donors of 53.2 years. In stable renal allografts, an intrarenal RI of 0.67 to 0.70 is accepted to be normal [1, 26 – 29]. In our study, the RI was 0.66 in the follow-up, which can be considered as normal.

In our study, the first duplex sonography in the recipient was performed within one hour after renal transplantation. We found a distinct decrease of the RI compared to the donor in this early postoperative phase and a significant increase one month after transplantation. We explain these findings with two possible mechanisms. Firstly, the RI is dependent on the heart rate [20]. Mostbeck et al. found a statistically significant decrease in RI with increasing heart rate (RI = 0.70 ± 0.06 at a heart rate of 70/min and RI 0.57 ± 0.06 at a heart rate of 120/min) and suggested a correction factor [20]. After adjustment for heart rate with this formula, the RI did not differ any more before and the first three months after transplantation. Thus, the lower RI in the early postoperative phase can be mainly explained by tachycardia. In addition, a decrease in the RI may be caused by reactive vasodilatation in reaction to perioperative ischaemia.

High venous flow velocity

A generally accepted definition of a relevant transplant vein stenosis is missing. In the literature, normal velocity values of renal transplant veins have not even been published. Frauchiger et al. arbitrarily defined a venous stenosis by a maximal venous velocity of 50 cm/s in combination with turbulences [30]. Using this definition, seven venous stenoses in 13 patients (54 %) with normal functioning kidney grafts were identified. The severity of all these "stenoses" decreased during follow-up. The median venous velocity in their study was 83 ± 75 cm/s on day 3; 84 ± 57 cm/s on day 7; and 61 ± 45 cm/s on day 17, respectively [30]. We observed even higher median peak velocities of about 100 cm/s in the transplant vein proximal to and at the level of the venous anastomosis. These velocities decreased after three months to a median value of 60 cm/s in our study. Using the definition of Frauchiger, we would have to state a venous stenosis in almost 70 % of our study population. Supported by the observation that venous flow patterns did not show a relevant inter-individual difference, the course of VTI was identical to PV in our population. Fortunately, no renal vein thrombosis occurred, and graft function was stable during follow-up. We suggest that high venous velocities and the decreasing course of the velocities may represent a "normal" development in stable renal grafts. Increased venous velocities in the early postoperative phase may be caused by postoperative oedema, haematoma, compression by the iliac artery, and a postischaemic vasodilatation after nephrectomy.

The study presents three important findings:

- High peak systolic velocities in the renal transplant artery are a common finding in the early postoperative phase, and absolute values seem not to be discriminative for the diagnosis of a significant stenosis. We suggest to use the peak systolic velocity ratio of the iliac and renal artery with a cut-off of 2.5 to 3.0, also under the condition that the resistive index remains normal.
- The resistive index is strongly influenced by changes in heart rate. Thus, tachycardia in the postoperative phase may cause a falsely low resistive index, and correction for heart rate should be considered.
- High peak velocities in the renal transplant vein are a common observation in the early postoperative phase and may be of no clinical relevance, on the condition that the resistive index remains normal and the clinical course is stable.

In conclusion, we found high blood flow velocities in renal transplant arteries and veins in stable renal grafts in the early postoperative phase. Therefore, high flow velocities seem to be a normal phenomenon in the early phase of transplantation and per se not sufficient to define a clinically relevant stenosis in this setting. Further investigations are needed to achieve reliable cut-off values especially for stenoses of renal transplant veins.

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