Transpl Int (2000) 13 [Suppl 1]: S84–S89

A. Elli
F. Quarto di Palo
R. Rivolta
A. Tarantino
G. Montagnino
A. Aroldi
C. Ponticelli

Effect of increased arterial resistance index on long-term outcome of well-functioning kidney grafts

A. Elli · F. Quarto di Palo · A. Tarantino · G. Montagnino · A. Aroldi · C. Ponticelli
Divisione di Nefrologia e Dialisi, IRCCS Ospedale Maggiore di Milano, Via Commenda, 15, Italy

R. Rivolta
I Servizio di Radiologia, Ospedale Maggiore IRCCS, Via Commenda, 15, Milano, Italy

Abstract An abnormal vascular status is present in the transplanted kidney. To define whether vascular factors might influence kidney function of the graft, the renal volume, blood flow and vascular resistance of a group of healthy subjects were compared with those of a group of well functioning renal transplants by color Doppler ultrasonography. Sixty healthy subjects and 75 well functioning cadaver renal transplant recipients were compared by color Doppler ultrasonography. Subsequently, 15 couples of donors and recipients of a living related renal graft were compared to observe the differences between the two organs of the same subject in a different environment. The variables studied were: the diameters and the volume of the kindey, renal blood flow and renal resistance index (RI). The group of cadaver renal transplant patients showed higher mean blood pressure ($P = 0.009$), higher serum creatinine levels ($P = 0.0001$) and lower endogenous creatinine clearance ($P < 0.0001$) than healthy controls. The length ($P < 0.00001$) and volume ($P < 0.001$) of the kidneys of cadaver transplanted patients were significantly greater than those of healthy subjects, while the length and volume of the living donors kidneys were identical to those of the recipients. RI, measured on renal vessels, showed lower values in healthy subjects and in kidney donors than in transplantated patients ($P < 0.00001$). Well functioning transplanted kidneys showed increased renal arterial RI. This non-immunologic factor did not appear to be detrimental with renal function in time, at least until 50 months after successful grafting.

Key words Color Doppler ultrasonography · Donor nephrectomy · Renal transplantation · Renal resistance index · Renal volume

Introduction

Despite progress in treatment, the transplanted kidney has a shorter half-life [22] than a native kidney after contralateral nephrectomy [34].

The main cause of the late loss of the transplanted kidney is "chronic graft dysfunction", a complex picture of multifactorial origin in which immunologic and non-immunologic factors play a yet undefined role [7, 19, 46, 47].

Among non-immunologic factors involved in graft damage, the reduced amount of transplanted nephrons has recently been emphasized [5, 7, 8, 17, 18, 20, 23, 45]: renal survival seems to be shortened when less than 50% of the required nephrons are allocated in the recipient [2, 13, 14, 31, 38, 43].

Other non-immunologic differences between the native and the transplanted kidney might be the presence of hypertension and of an abnormal vascular status in the recipient of the graft related [26] to the duration of

Table 1 Characteristics of the groups of normal subjects, cadaver transplants, living donors and living-related transplants. Values are means ± 1 SD

	Normal	Cadaver transplants		Living-related transplants		P*
		CSA[a]	AZA[a]	Donors	Recipients	
N. of cases	60	60	15	15	15	
Age (years)	40 ± 9	43 ± 9	48 ± 9°	51 ± 12°	39 ± 10	< 0.01
Gender (M/F)	30/30	32/28	8/7	6/9	7/8	NS[b]
Weight (kg)	69 ± 12	60 ± 13°	62 ± 10°	69 ± 12	61 ± 11°	< 0.01
Height (cm)	169 ± 10	162 ± 9°	160 ± 7°	165 ± 9	160 ± 8°	< 0.0005
Body surface area (m^2)	1.74 ± 0.21	1.62 ± 0.19°	1.65 ± 0.16°	1.74 ± 0.16	1.63 ± 0.18°	< 0.003
Mean arterial pressure (mm Hg)	91.2 ± 6.1	97.8 ± 8.5°	93.1 ± 8.2	96.8 ± 9.1°	98.4 ± 10.4°	< 0.009
Serum creatinine (μM/l)	80.0 ± 9.7	97.4 ± 11.8°	89.5 ± 12.3	101.2 ± 10.8°	106.5 ± 12.9°	< 0.0001
Creatinine clearance (ml/min)	94 ± 16	76 ± 17°	78 ± 18°	77 ± 13°	74 ± 16°	< 0.0001

[a] *CSA:* patients treated with triple therapy (cyclosporine, azathioprine and steroids), *AZA:* patients treated only with azathioprine and steroids

[b] Chi-square analysis

* One-way analysis of variance, statistical difference (Tukey's test) with respect to normal values indicated by ° (< 0.05)

uremia and to dialysis treatment [9]. Moreover, renal denervation, caused by the surgical procedure, and the heterotopic placement of the graft in the iliac fossa, might also play a role.

To define whether vascular factors might influence graft function, the renal volume, blood flow and vascular resistance of a group of healthy subjects were compared with those of a group of well functioning cadaver renal transplants by color Doppler ultrasonography.

A selected group of living donors and of their recipients was also compared in the same way to observe the differences between the twin organs of the same subject when located in a different environment.

Materials and methods

This study consisted of two parts. In the first part, 60 healthy subjects, 30 males and 30 females, with a mean age of 40 ± 9 years, and 60 cadaver renal transplant patients, 32 males and 28 females, with a mean age of 43 ± 9 years and a median transplant duration of 50 months (range 6–106), were studied by color Doppler ultrasonography between January 1996 and March 1997. At the time of investigation, mean serum creatinine levels in transplanted patients were 97.4 ± 11.8 μM/l and mean immunosuppressive treatment was cyclosporine 4.2 ± 0.7 mg/kg per day, azathioprine 70 ± 21 mg/day and 6-methylprednisolone 5.0 ± 1.2 mg/day. Cyclosporine mean trough blood levels were 206 ± 21 ng/ml.

To reduce pharmacologic interference with the vascular variables studied, tests were carried out in the morning, 12 h after cyclosporine and 24 h after 6-methyl prednisolone were taken. Moreover, to evaluate the potential importance of the treatment with cyclosporine on the observed data, a second group of 15 well functioning cadaver renal transplants treated only with azathioprine (82.5 ± 12.5 mg/day) and 6-methylprednisolone (7.5 ± 1.5 mg/day) and with a transplant duration of 136 months (range 76–184) was also studied (Table 1).

In the second part of this study, 15 couples of living kidney donors and their recipients were investigated. Donors were, six men and nine women, with mean age of 51 ± 12 years. Recipients were seven males and eight females, with a mean age of 39 ± 10 years. Transplant duration was 53 months (range 7–97). Mean serum creatinine levels were 106.5 ± 12.9 μM/l. We selected a group of living related transplants in which the immunologic compatibility was elevated (mean: 1.9 ± 0.1 mismatch HLA A, B and Dr), the warm and cold ischemia times were short (warm ischemia less than 1 min and cold ischemia less than 3 h), the number of rejection episodes was small (one fully reversible episode in 5/15 recipients) and the clinical course was favorable. Their mean immunosuppressive treatment was cyclosporine (CSA) 4.5 ± 0.6 mg/kg per day, azathioprine 75 ± 25 mg/day and 6-methylprednisolone 6.0 ± 2.2 mg/day. Cyclosporine mean trough blood levels were 235 ± 32 ng/ml. Body weight, height and body surface area of the donors and recipients were also considered.

All transplants showed stable renal function before and after the Doppler test. Criteria for exclusion were presence of a 24-h proteinuria exceeding 500 mg/day and/or abnormal urinary sediment, presence of diabetes and of hypertension at the moment of the ultrasound investigation. In all grey scale ultrasonography, anatomic abnormalities of the kidney or of the urinary tract were absent.

Cyclosporine trough blood levels were measured with a monoclonal antibody by FPIA analysis.

All patients gave their informed consent to the study.

Assessment of renal volume, blood flow and resistance index

On the morning of the day of ultrasound test, after a 24-h urine collection, a blood sample was collected from the fasting subjects to determine serum creatinine and trough blood cyclosporine level in patients treated with this drug. Endogenous creatinine clearance was calculated from serum and urine creatinine concentration levels. In all cases, body weight and height were also measured.

After 1 h of rest in the supine position in a suitable environment (20–23° C) to obtain basal conditions, brachial arterial pressure was measured and mean arterial pressure (MAP) was calculated. The color flow Doppler scan of the kidney was subsequently performed with an ATL Ultramark-9 HDI scanner (Bothell, Washington, USA), using a 2–4 MHz broadband convex probe. The same sonologist (R. R.) performed all the Doppler scans.

The outcome variables studied were the diameters and the volume of the kidney, renal blood flow and RI measured on renal, interlobar and cortical arteries.

Variables were determined in this order:

Table 2 Ultrasonographic variables of normal subjects, cadaveric transplants, living donors and living-related transplants. Values are mean ± 1 SD

	Normal		Cadaver transplants		Living-related transplants		*P*
	Right kidney ($n = 60$)	Left Kidney	CsA §[a] ($n = 60$)	Aza §[a] ($n = 15$)	Donors ($n = 15$)	Recipients ($n = 15$)	
Renal length (mm)	105.2 ± 8.1	108.4 ± 9.2	123 ± 10.5°	125 ± 9.3°	118 ± 8°	117 ± 8°	< 0.00001
Renal volume (ml)	125 ± 47	127 ± 25	183 ± 49°	195 ± 51°	164 ± 28°	157 ± 35°	< 0.001
Renal blood flow (ml/min)	258 ± 166	263 ± 90	277 ± 120	260 ± 105	250 ± 87	228 ± 95	NS
Renal resistance index	56.4 ± 4.8	57.8 ± 5.1	70.4 ± 6.7°	66.6 ± 5.1°	57.5 ± 9.5	66.4 ± 8.8°	< 0.00001
Interlobar resistance index	54.3 ± 4.8	55.5 ± 4.9	64.8 ± 8.1°	61.0 ± 5.9°	56.4 ± 8.1	60.3 ± 7.2°	< 0.00001
Cortical resistance index	50.5 ± 4.9	50.7 ± 4.7	56.5 ± 6.4°	54.1 ± 3.8°	52.0 ± 5.0	55.9 ± 4.7°	< 0.00001

[a] *CsA:* patients treated with triple therapy (cyclosporine, azathioprine and steroids), *Aza:* patients treated only with azathioprine and steroids

* One-way analysis of variance, statistical difference (Turkey's test) respect to normal values is indicated by ° (< 0.05)

1. The length, width, and thickness of the graft in mm. The kidney volume was calculated in cm^3 by the formula (0.49 × length × width × thickness) [1, 6, 12, 21, 30, 40]. With the probe used, Doppler sample width was 1.5 mm and, at depth of 6 cm, axial and lateral resolution were respectively 0.5 and 0.8 mm.
2. Renal blood flow (RBF) was measured from Doppler spectrum time-averaged mean velocity and vessel diameter as previously described [3, 4, 11, 15, 16, 36]. Every measure represented the mean of five subsequent determinations.
3. Resistance index (RI) was determined from the analysis of the spectral waveform as follows: the peak systolic frequency shift minus the lowest diastolic frequency shift divided by the peak systolic frequency shift [24, 32, 33, 36, 37, 39]. Doppler sample width was set at 2.5 mm. RI was calculated as an average value obtained for five waveforms of the main renal and interlobar artery. The measurement of RI on cortical vessels was obtained by color imaging, positioning the exploration probe externally to the visualized arcuate vessels. The mean of six waveforms was measured: two on the upper, two on the medium and two on the lower pole of the organ.

In our experience, the mean intraexamination coefficient of RI variation was 3.5 ± 2.1% at the cortical and 3.0 ± 1.9% at the renal and interlobar level [39]. Doppler waveforms were made at the lowest pulse repetition frequency possible to avoid artifacts [24, 44]. This maximized the size of the Doppler spectrum and decreased the percentage of error in the measurements. All RI values reported are multiplied by 100.

Statistical analysis

The data were analyzed with SPSS software (SPSS Inc., Chicago, USA). Categorical data were examined by chi-square analysis. Student's *t*-test for independent or dependent groups was used when appropriate. One-way analysis of variance was used to examine outcome variables in more than two groups. Tukey's multiple comparison procedure was chosen to identify significant differences among the groups.

Two-factor ANOVA was used to analyze RI with respect to the two selected factors: site of sampling (i.e. renal, interlobar or cortical artery) and different groups (healthy subjects, cadaver transplant, living donors and related recipients).

Linear regression analysis was used to assess the effects of transplant duration on the examined variables. Data are shown as means ± 1 SD unless otherwise indicated. $P < 0.05$ was considered significant.

Results

Compared with healthy subjects, the group or renal transplants showed lower body weight, height and body surface area (Table 1).

Mean blood pressure ($P < 0.009$) and serum creatinine levels ($P < 0.0001$) were higher, while endogenous creatinine clearance was lower ($P < 0.0001$) in the subjects with a single kidney, either donors or transplanted patients.

Living donors and cadaver transplants, treated with azathioprine and steroids, were older than living kidney recipients and CSA treated patients ($P < 0.01$) (Table 1). The median transplant duration was not different in the two groups of CSA-treated patients (50 months, range 6–106 for cadaver and 53 months, range 7–97 for living transplant recipients) and their age distribution was fully comparable.

The only difference observed between the two groups of kidney recipients treated with or without cyclosporine was transplant duration, which was longer in patients treated with azathioprine and steroids (median 136, range 76–184 months; $P < 0.001$).

The length ($P < 0.00001$) and volume ($P < 0.001$) of the transplanted kidney were significantly greater than those of the healthy subjects (Table 2), while the length and volume of the living donor kidney were identical to the recipients' ones. In the three types of grafted kidneys, renal blood flow was not statistically different from the living donor one and from the right or left kidney of a healthy subject (Table 2). Resistance index, measured on kidney vessels, showed lower values in healthy subjects and in kidney donors than in transplanted patients ($P < 0.00001$) (Table 2).

In renal grafts, RI was significantly increased in the main renal artery; the difference decreased at the interlobar level and was still present at the cortical level. The slope of decay of RI values in transplanted patients was steeper than in healthy subjects (Fig. 1). RI values were comparable between healthy subjects and donors

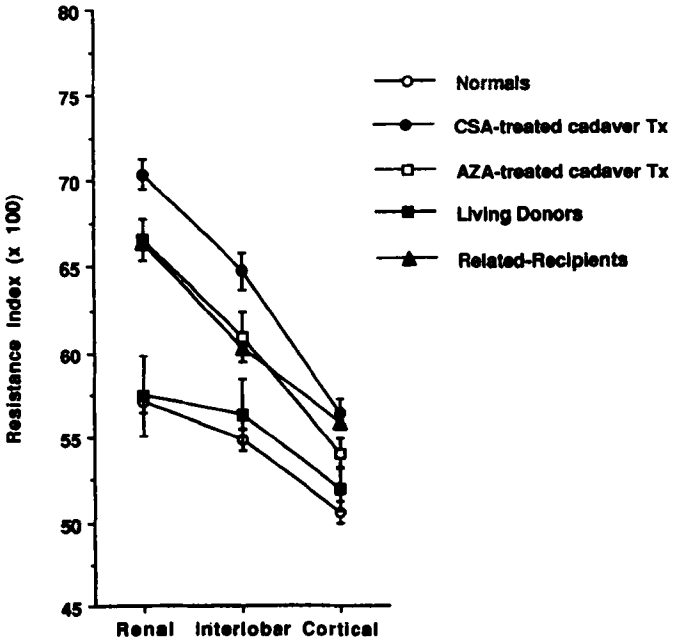

Fig. 1 Relationship among RI, measured in three different sites of renal vasculature, in the five groups examined. No statistical differences were observed between values of RI of normal subjects and living donors. Statistically increased RI was observed in cadaver and in living related grafts ($P < 0.0001$). In the three groups of renal transplants, a statistical difference was observed between main renal and interlobar artery ($P < 0.01$) and between cortical versus interlobar vessels ($P < 0.001$). *Vertical bars* are ± 1 SE

and between the three groups of transplanted patients (Table 2). Analysis of regression did not demonstrate any relationship among all the reported variables and graft duration.

Discussion

In the first part of this study, we compared normal subjects with renal transplant recipients. As expected, transplanted patients had a smaller body size, higher MAP and serum creatinine and lower creatinine clearances than normal controls. Renal length and volume were also increased in the transplanted kidneys and were similar to those observed in donors after nephrectomy.

In donors, mean values of creatinine were higher while blood flow and RI were similar to those found in normal subjects. These data show that nephrectomy in the adult is accompanied by parenchymal hypertrophy of the residual organ without important changes in blood flow.

Resistance index of the transplanted kidney vessels showed a specific difference from the healthy ones. RI measures the arterial impedance and influences the arterial compliance [29]. The transplanted kidney showed increased RI values when compared to donors in all the explored vascular areas, the donor RI was identical to that of healthy subjects. The observed differences were maximal at the level of main renal artery and slowly decreased at the interlobar and cortical level, so the slope of decay of RI values was steeper than in donors and healthy subjects.

Donors and recipients of a living related renal transplant enabled the selection of two groups of twin kidneys, differing only in the anatomic placement and immunosuppressive therapy. The differences observed in renal length, volume, and flow fall in the range of variability between right and left kidney of a healthy subject [16, 25, 49]. Also in this particular condition, RI was increased in transplanted recipients and normal in their donor partners.

In order to investigate whether immunosuppressive treatment could be the cause of the RI difference between transplanted patients and healthy subjects, we studied both patients treated with or without cyclosporine. Azathioprine does not appear to have vascular effects, while steroids tend to produce hypertension. It is well known that cyclosporine exerts different vascular effects: this drug has been shown to increase sympathetic activity and vascular resistance in skeletal muscle [27, 41, 42]. The infusion of cyclosporine increases blood pressure and reduces renal blood flow [48]. At the renal level, cyclosporine gives rise to specific vasoconstriction of the afferent arteriole [28], vessel located in the kidney cortex. Our tests were carried out in the morning before the drug was taken, in order to reduce its pharmocologic interference on the studied vascular variables. In these conditions, RI of renal vessels was similar when azathioprine and steroids or cyclosporine and steroids were used. In the transplanted kidney, cyclosporine increases pulsatility and RI of cortical vessels, but this effect was not evident with main renal artery [35]. The observed RI difference between donor and recipient seemed to be without negative effect on transplant function because regression analysis did not show any variation in renal volume, blood flow and RI related to transplant duration.

In conclusion, a well functioning transplanted kidney shows, in comparison with the healthy one, increased renal arterial RI. In patients without rejection or other complications, this non-immunologic factor does not appear to be detrimental to renal function at least until 50 months. An increase in RI, reducing the compliance of the smaller vessels, might influence vessel structure and accelerate vascular damage [10, 29]. Therefore it is not possible to exclude that, in the presence of other conditions of renal damage, such as arterial hypertension, diabetes or cyclosporine toxicity, this vascular abnormality might also play a role in chronic graft dysfunction.

References

1. Ablett MJ, Coulthard A, Lee REJ, Richardson DL, Bella T, Owen JP, Keir MJ, Butler TJ (1995) How reliable are ultrasound measurements of renal length in adults? Br J Radiol 68: 1087–1089
2. Alexander JW, Vaughn WK, Carey MA (1991) The use of marginal donors for organ transplantation: the older and younger donors. Transplant Proc 23: 905–909
3. Avasthi PS, Greene ER, Voyles WF (1987) Noninvasive doppler assessment of human postprandial renal blood flow and cardiac output. Am J Physiol 252: F1167–F1174
4. Avasthi PS, Tawney KW, Greene ER (1992) Noninvasive assessment of human renal blood flow by ultrasonic Doppler flowmetry. In: Lüscer TF, Kaplan NM (eds) Renovascular and renal parenchymatous hypertension. Springer, Berlin, pp 207–227
5. Barrientos A, Portoles J, Herrero JA, Torralbo A, Prats D, Gutierres-Millet V, Blanco J (1994) Glomerular hyperfiltration as a nonimmunologic mechanism of progression of chronic renal rejection. Transplantation 57: 753–755
6. Brandt TD, Neiman HL, Dragowski MJ, Bulawa W, Claykamp G (1982) Ultrasound assessment of normal renal dimensions. J Ultrasound Med 1: 49–52
7. Brenner BM (1985) Nephron adaptation to renal injury or ablation. Am J Physiol 249: F324–F337
8. Brenner BM, Milford MD (1993) Nephron underdosing: a programmed cause of chronic renal failure. Am J Kidney Dis 21: 66–72
9. Capron L, Grateau G (1998) Accelerated arterial disease in renal transplant recipients. Nephrol Dial Transplant 13: 49–50
10. Christensen K (1991) Reducing pulse pressure in hypertension may normalize small artery structure. Hypertension 18: 722–727
11. Dähnert WF, Dubbins PA (1990) Vascular ultrasound measurements. In: Goldberg BB, Kurtz AB (eds) Atlas of ultrasound measurements. Year Book Medical Publishers, Chicago, pp 72–96
12. Edell SL, Kurtz AB, Rifkin MD (1990) Normal renal ultrasound measurements. In: Goldberg BB, Kurtz AB (eds) Atlas of ultrasound measurements. Year Book Medical Publishers, Chicago, pp 146–160
13. Feldman HI, Fazio I, Roth D, Berlin JA, Brayman K, Burns JE, Grossman A (1996) Recipient body size and cadaveric renal allograft survival. J Am Soc Nephrol 7: 151–157
14. Gill IS, Hodge EE, Nowick AC, Steinmuller DR, Garred D (1993) Impact of obesity on renal transplantation. Transplant Proc 25: 1047–1048
15. Greene ER, Avasthi PS (1989) Effect of a high-protein meal on blood flow to transplanted human kidneys. Transplantation 48: 584–587
16. Greene ER, Venters MD, Avasthi PS, Conn R, Janke RW (1981) Noninvasive characterization of renal artery blood flow. Kidney Int 20: 523–529
17. Heeman UW, Azuma H, Tullius SG, Mackenzie H, Brenner BM, Tilney NL (1994) The contribution of reduced functioning mass to chronic kidney allograft dysfunction in rats. Transplantation 58: 1317–1322
18. Heeman UW, Azuma H, Tullius SG, Mackenzie HS, Schmid C, Brenner BM, Tinley NL (1995) Influence of renal mass on chronic kidney allograft rejection in rats. Transplant Proc 27: 549
19. Hostetter TH (1994) Chronic transplant rejection. Kidney Int 46: 266–279
20. Hostetter TH, Olson JL, Rennke HG, Venkatachalam MA, Brenner BM (1981) Hyperfiltration in remnant nephrons: a potentially adverse response in renal ablation. Am J Physiol 241: F85–F93
21. Hriack H, Lieto RP (1983) Sonographic determination of renal volume. Radiology 148: 311–331
22. Kasiske BL, Heim-Duthoy KL, Tortorice KL, Venkateswara K (1991) The variable nature of chronic declines in renal allograft function. Transplantation 51: 330–334
23. Kasiske BL, Ma JZ, Louis TA, Swan SK (1995) Long-term effects of reduced renal mass in humans. Kidney Int 48: 814–819
24. Kim SH, Kim WH, Choi BI, Kim CW (1992) Duplex Doppler US in patients with medical renal disease: resistive index vs serum creatinine level. Clin Radiol 45: 85–87
25. Krumme B, Blum U, Schwertfeger E, Flügel P, Höllstin F, Schollmeyer P, Rump LC (1996) Diagnosis of renovascular disease by intra- and extrarenal Doppler scanning. Kidney Int 50: 1288–1292
26. Krumme B, Grotz F, Kirste G, Schollmeyer P, Rump LC (1997) Determinants of intrarenal Doppler indices in stable renal allografts. J Am Soc Nephrol 8: 813–816
27. Mark AL (1990) Cyclosporine, sympathetic activity and hypertension. N Engl J Med 323: 748–750
28. Mason J (1990) Renal side effects of cyclosporine. Transplant Proc 22: 1280–1283
29. McVeigh GE, Finkelstein SM, Cohn JN (1993) Assessment of arterial compliance in hypertension. Curr Opin Nephrol Hypertens 2: 82–86
30. Ninan VT, Thomas Koshi K, Niyamthullah MM, Jacob CK, Gopalakrishnan G, Pandey AP, Shastry JCM (1990) A comparative study of methods of estimating renal size in normal adults. Nephrol Dial Transplant 5: 851–854
31. Odland MD, Kasiske BL (1993) Kidneys from female donors are at increased risk for chronic allograft rejection. Transplant Proc 25: 912
32. Petersen LJ, Petersen JR, Ladefoged SD, Mehlsen J, Jensen HE (1995) The pulsatility index and the resistive index in renal arteries in patients with hypertension and chronic renal failure. Nephrol Dial Transplant 10: 2060–2064
33. Platt JF, Rubin J, Ellis JH (1994) Diabetic nephropathy: evaluation with renal duplex Doppler US. Radiology 190: 343–346
34. Provoost AP, Brenner BM (1993) Commentary. Long-term follow-up of humans with single kidneys: the need for longitudinal studies to assess true changes in renal function. Curr Opin Nephrol Hypertens 2: 521–526
35. Quarto di Palo F, Rivolta R, Elli A, Castagnone D, Palazzi P, Abelli P, Zafiropulu S, Zanussi C (1993) Effect of cyclosporin A on renal cortical resistances measured by color Doppler flowmetry on renal grafts. Nephron 65: 240–244
36. Quarto di Palo F, Rivolta R, Elli A, Castagnone D (1995) The well-functioning renal graft evaluated by color-Doppler flowmetry. Nephron 70: 314–318
37. Quarto di Palo F, Rivolta R, Elli A, Castagnone D (1996) Relevance of resistive index ultrasonographic measurement in renal transplantation. Nephron 73: 195–200

38. Quarto di Palo F, Rivolta R, Elli A, Castagnone D (1997) The transplanted nephronic mass influences renal vascular resistance and blood flow in kidney grafts. Nephron 76: 43–48
39. Rivolta R, Castagnone D, Elli A, Quarto di Palo F (1996) Evaluation of kidney graft functional status by colour flow Doppler ultrasonography. Eur J Ultrasound 3: 223–229
40. Roger SD, Beale AM, Cattell WR, Webb JAW (1994) What is the value of measuring renal parenchymal thickness before renal biopsy? Clin Radiol 49: 45–49
41. Scherrer U, Vissing SF, Morgan BJ, Rollins JA, Tindall RSA, Ring A, Hanson P, Mohanty PK, Victor RG (1990) Cyclosporine-induced sympatetic activation and hypertension after heart transplantation. N Engl J Med 323: 693–699
42. Somers VK, Anderson EA, Mark AL (1993) Sympathetic neural mechanism in human hypertension. Curr Opin Nephrol Hypertens 2: 96–105
43. Sunrain N, Delaney V, Ding Z, Davis R, Daskalalkis P, Tejam A, Butt K, Hong J (1991) Renal transplantation from elderly living donors. Transplantation 51: 305–310
44. Taylor KJW, Holland S (1990) Doppler US. Part 1. Basic principles, instrumentation and pitfalls. Radiology 174: 297–307
45. Terasaki PI, Koyama H, Cacka JM, Gjertson DW (1994) The hyperfiltration hypothesis in human renal transplantation. Transplantation 57: 1450–1454
46. Tilney NL, Whitley WD, Diamond JR, Kupiec-Weglinski JW, Adams DH (1991) Chronic Rejection: an undefined conundrum. Transplantation 52: 389–398
47. Tullius SG, Tilney NL (1995) Both alloantigen-dependent and independent factors influence chronic allograft rejection. Transplantation 59: 313–318
48. Weir MR, Klassen DK, Shen SY, Sullivan D, Buddemeyer UE, Handwerger BS (1990) Acute effects of intravenous cyclosporine on blood pressure, renal hemodynamics and urine prostaglandin production of healthy humans. Transplantation 49: 41–47
49. Yura T, Takamitsu Y, Yuasa S, Shigehiro M, Takahashi N, Bandai H, Sumikura T, Uchida K, Tamai T, Matsuo H (1991) Total and split renal function assessed by ultrasound Doppler technique. Nephron 58: 37–41