Pergamon

European Journal of Cancer Vol. 32A, No. 3, pp. 465–469, 1996

Printed in Great Britain
0959–8049/96 $15.00+0.00

0959-8049(95)00618-4

Original Paper

Renal Function after Unilateral Nephrectomy for Wilms' Tumour: the Influence of Radiation Therapy

S.S.N. de Graaf,[1] H. van Gent,[1] W.Ch.C. Reitsma-Bierens,[1] W.H.J. van Luyk,[1] W.V. Dolsma[2] and A. Postma[1]

[1]Beatrix Children's Hospital; and [2]Department of Radiation Therapy, University Hospital, P.O. Box 30.001, 9700 RB Groningen, The Netherlands

The effect of therapy on renal function after unilateral nephrectomy for Wilms' tumour was studied. In the second year following unilateral nephrectomy, glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) were estimated simultaneously by measuring ^{125}I-iothalamate clearance and ^{131}I-hippurate clearance. Of 41 evaluable patients, 29 received chemotherapy as sole treatment modality following nephrectomy (group 1); 12 patients additionally received radiation therapy to a field that included the remaining kidney (group 2). Results were expressed as standard deviation scores (*z*-scores). In group 1, mean *z*-score for GFR was −0.27 (94.6% of normal) and in group 2 mean *z*-score was −1.51 (72.7% of normal for two kidneys) ($P = 0.022$, Mann–Whitney *U*-test). Mean *z*-score for ERPF was −0.09 (97.0%) in group 1 and −1.53 (73.8%) in group 2 ($P = 0.039$). It was concluded that the combination of chemotherapy and radiation therapy, in contrast to chemotherapy alone, negatively affects the ability of the remaining kidney to adjust its function after the loss of its counterpart.

Key words: nephroblastoma, radiotherapy, glomerular filtration rate, effective renal plasma flow, nephrectomy

Eur J Cancer, Vol. 32A, No. 3, pp. 465–469, 1996

INTRODUCTION

WITH CURE rates for childhood malignancies increasing, the number of long-term survivors of cancer in the paediatric population grows. Therefore, information on late side-effects of treatment is of increasing interest. Information on long-term sequelae of therapy is also needed for the design of new treatment strategies that search for an optimal balance between anticancer efficacy and treatment-related toxicity. In children with Wilms' tumour, a high cure rate has been achieved with surgery, radiation therapy and chemotherapy [1–4]. Therefore, to further improve the outcome of treatment, we must evaluate each one of the specific treatment modalities not only with respect to their contributions to survival but also with respect to toxicity. Examples of treatment-specific long-term sequelae in Wilms' tumour patients include the loss of a kidney as a result of surgery, the risk of second malignant tumours associated with radiation therapy and a chance of cardiovascular problems due to chemotherapy (doxorubicin) [5].

Correspondence to S.S.N. de Graaf
Revised 11 Aug. 1995; accepted 17 Oct. 1995

This report deals with the impact of radiation therapy on renal function in Wilms' tumour patients. After unilateral nephrectomy in childhood, the remaining kidney generally adjusts its function and size to the new situation: this phenomenon is described as a compensatory hypertrophy of the kidney [6,7]. In children who have had a nephrectomy for Wilms' tumour, the ability of the remaining kidney to adjust to the increased demand might be impaired owing to antiproliferative agents and/or irradiation. Therefore, we studied glomerular filtration rate and effective renal plasma flow in Wilms' tumour patients who were treated by multimodality therapy; specifically, we were interested in the impact of irradiation on the remaining kidney.

PATIENTS AND METHODS

48 consecutive patients with newly diagnosed Wilms' tumour were considered for this study. Two children from overseas had to be excluded because they had returned to their home countries before the time of the renal evaluation. 5 patients relapsed before the tests were done and were also excluded. Thus, the subjects of this study are 41 unselected children, 16 boys and 25 girls. Median age at diagnosis was 3

years and 3 months, ranging from 5 months to 9 years and 9 months.

Patients were treated on institutional protocols that were similar to treatment protocols of the National Wilms' Tumor Study [1, 2]. All children received vincristine and actinomycin-D; 12 patients received doxorubicin as a third cytostatic agent (median cumulative dose 300 mg/m^2, range 150–480 mg/m^2). Radiation therapy to lungs and/or abdomen was given as indicated by tumour extension. Relevant for this study is that 12 patients received postoperative irradiation to a field that included the remaining kidney; actual radiation doses to the remaining kidney ranged from 1000 to 1500 cGy in daily fractions of 125–150 cGy. There was one exception who received 2250 cGy in 15 fractions because of bulky residual intraperitoneal disease. Of the 12 patients who were treated with irradiation on the remaining kidney, 8 also received doxorubicin. In 29 cases, no irradiation was given to the remaining kidney.

Two groups of patients were compared. Group 1 included the patients who received only chemotherapy as postoperative treatment ($n = 29$); group 2 included the patients who also received radiation therapy with the remaining kidney in the field ($n = 12$). The distribution of patient characteristics between the two groups is shown in Table 1.

Measurement of glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) at the Division of Paediatric Nephrology was part of the standard care for Wilms' tumour patients, and was scheduled early in the second year after nephrectomy, when chemotherapy had been discontinued for an ample period. GFR and ERPF were estimated simultaneously by measuring ^{125}I-iothalamate clearance and ^{131}I-hippurate clearance using a continuous infusion technique with an indwelling bladder catheter [8–10]. Briefly, GFR was calculated as the quotient of ^{125}I-iothalamate excretion rate and ^{125}I-iothalamate plasma concentration at steady state; ERPF was calculated as the quotient of ^{131}I-hippurate excretion rate and ^{131}I-hippurate plasma concentration at steady state.

Renal function varies with age. Therefore, measured values for GFR and ERPF were expressed as standard deviation scores. Data were transformed into standard deviation scores using the following formula:

$$z = (x - \mu)/\sigma,$$

where z represents the standard deviation score, x is a measured value for GFR or ERPF, μ is the mean and σ the standard deviation of the normal value for the age of the

Table 1. Patient characteristics

	Group 1	Group 2
Number of patients	29	12
Male/female ratio	10/19	6/6
Median (range) age in months		
At diagnosis	33 (5–117)	45 (14–112)
At renal function test	43 (18–139)	62 (25–125)
Median (range) interval in months between diagnosis and renal function test	13 (11–22)	13 (11–22)

patient. We used a chart with normal values for GFR and ERPF which is a routine reference at the Division of Paediatric Nephrology of the Beatrix Children's Hospital; this chart is based on data from the literature [11–14]. In addition to the standard deviation scores, measured GFR and ERPF are also presented as a percentage of mean normal values for children of the same age with two kidneys.

Differences in GFR and ERPF between the patients that did or did not receive irradiation to the remaining kidney (group 1 versus group 2) were tested by the Mann–Whitney U-test using the CSS statistical software package [15,16].

RESULTS

Estimated values of GFR and ERPF for each individual patient are listed in Table 2. A summary of the data, transformed to standard deviation scores, is shown in Table 3. Data are presented for the whole group of 41 evaluable patients and for the children that did or did not receive irradiation on the remaining kidney. There was a statistically significant difference in GFR between group 1 and group 2. In group 1, comprising the children that did not receive irradiation to the remaining kidney, the mean standard deviation score for GFR was −0.27 versus −1.51 in group 2 ($P = 0.022$). ERPF was also lower in the irradiated children: mean standard deviation score was −1.53 in group 2 versus −0.09 in group 1 ($P = 0.039$). The distributions of standard deviation scores for GFR in children who did or did not receive irradiation to the remaining kidney are graphically represented in Figure 1.

To facilitate the understanding of the order of magnitude of the differences, mean values of GFR and ERPF were calculated as a percentage of normal values for age-matched children with two kidneys. In the children that did not receive irradiation, mean GFR and ERPF were 94.6 and 97.0%, respectively. In the irradiated children, mean GFR was 72.7% of normal; mean ERPF was 73.8% of normal. For all patients, mean GFR was 88.1% and mean ERPF was 89.8%.

DISCUSSION

We evaluated renal function in Wilms' tumour patients, 1 year after nephrectomy. Overall, results seem to be satisfactory. Mean GFR and ERPF were almost 90% of normal values for age-matched children with two normal kidneys. Results are particularly reassuring in children who did not receive irradiation to the remaining kidney; their mean GFR and ERPF 1 year after nephrectomy were 94.6 and 97.0% of normal values for two kidneys, respectively. Thus, chemotherapy with vincristine, actinomycin-D and doxorubicin after nephrectomy does not affect the ability of the remaining kidney to adjust. This observation is consistent with the data of Bhisitkul and associates [17], who found normal values for renal functional reserve of the non-irradiated kidney, 9–23 years after unilateral nephrectomy for Wilms' tumour.

The addition of irradiation to chemotherapy, however, appears to result in a reduced potential of the kidney to adjust to the increased demand. In the children who received irradiation, mean GFR was 72.7% of normal; mean ERPF was 73.8%. Standard deviation score averaged −1.51 for GFR and −1.53 for ERPF. Although a renal function in the range of 75% may not pose an immediate threat to the patients, our study provides information only at one single time point 1 year after treatment. At that time, median age of the irradiated children was 5 years. Longer follow-up is needed to determine what happens to the kidney when these children grow up to

Table 2. Primary data per individual patient

Patient no.	Irradiation* (cGy)	Doxorubicin† (mg/m²)	Age‡ (months)	GFR ml/min	GFR z-score	ERPF ml/min	ERPF z-score
1			18	31.0	0.57	126.0	−0.08
2			20	34.0	0.84	153.0	0.62
3			22	25.6	−0.88	103.1	−1.14
4			24	36.0	0.67	189.0	1.39
5			25	23.9	−1.43	105.8	−1.29
6			26	23.9	−1.51	76.0	−2.28
7			28	22.3	−1.91	77.6	−2.36
8		150	28	24.8	−1.52	120.0	−1.07
9			29	32.3	−0.46	138.0	−0.61
10			29	45.8	1.59	221.0	1.89
11		270	30	29.0	−1.04	123.0	−1.13
12			32	34.8	−0.36	156.0	−0.30
13			36	31.8	−1.10	148.6	−0.82
14			43	40.1	−0.55	184.6	−0.31
15			43	27.5	−2.08	108.6	−2.39
16			50	36.9	−1.37	149.2	−1.72
17			51	42.7	−0.79	168.0	−1.29
18			53	71.9	2.18	541.0	8.17
19			55	43.1	−0.99	163.0	−1.66
20			55	66.0	1.38	277.0	1.23
21			65	55.5	−0.35	285.1	0.71
22			66	63.1	0.28	281.1	0.55
23			67	59.9	−0.03	317.2	1.32
24			67	32.3	−2.53	198.0	−1.51
25		480	93	62.9	−0.54	240.0	−1.41
26		300	104	63.1	−0.81	262.0	−1.29
27			112	56.4	−1.54	249.9	−1.78
28			125	67.7	−0.97	257.0	−2.00
29			139	187.0	7.41	803.8	7.99
30	1500		25	17.9	−2.41	101.5	−1.42
31	1500		27	32.9	−0.17	138.8	−0.42
32	1500	420	38	15.7	−3.34	79.9	−2.90
33	1500	400	57	30.9	−2.33	121.2	−2.82
34	1000	300	58	46.8	−0.78	197.0	−0.98
35	1500		60	33.1	−2.23	152.0	−2.22
36	1000	300	62	45.2	−1.15	172.0	−1.83
37	1000	270	63	47.0	−1.03	201.0	−1.19
38	1500	420	69	63.6	0.24	289.3	0.57
39	2250		74	36.2	−2.35	202.7	−1.64
40	1000	150	123	67.0	−0.98	301.0	−1.07
41	1200	150	125	60.5	−1.52	236.0	−2.41

*Total dose to the remaining kidney; †Total cumulative dose administered; ‡Age at the time of the measurements. GFR, glomerular filtration rate; ERPF, effective renal plasma flow; *z*-score, standard deviation score.

Table 3. Summary of glomerular filtration rate and effective renal plasma flow, transformed to standard deviation scores

	All patients	Group 1	Group 2	*P*-value*
GFR, mean ± S.D. (*z*-score)	−0.57 ± 1.74	−0.27 ± 1.82	−1.51 ± 1.05	0.022
ERPF, mean ± S.D. (*z*-score)	−0.51 ± 2.28	−0.09 ± 2.52	−1.53 ± 1.01	0.039

*Difference between group 1 and group 2; Mann–Whitney *U*-test. GFR, glomerular filtration rate; S.D., standard deviation; ERPF, effective renal plasma flow; *z*-score, standard deviation score.

adolescence and adulthood. Vascular effects of irradiation may become manifest in the course of time: chronic radiation nephropathy may not be diagnosed until 10–14 years following therapy [18].

The measurement of the ^{125}I-iothalamate clearance with the continuous infusion technique is an accurate method for the determinatin of GFR. Sigman and associates [9] compared 100 simultaneous clearances of inulin and radiolabelled iothalamate over a range from 2 to 167 ml/min and showed that inulin and iothalamate clearance are practically identical; the ratio of iothalamate to inulin clearance was 1.005. Thus, when inulin clearance is considered as the gold standard for GFR, we can estimate GFR accurately by measuring ^{125}I-iothalamate clearance. The estimation of ERPF using ^{131}I-hippurate is based on the same principles [8–10].

Some studies of renal function after treatment for Wilms' tumour used methods that lack sufficient precision. For

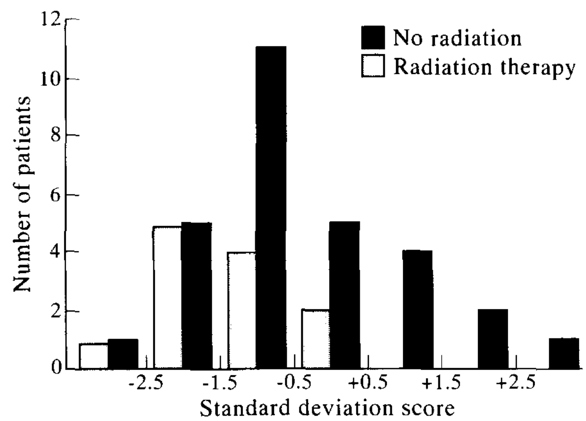

Figure 1. Distribution of standard deviation scores for glomerular filtration rate in irradiated and non-irradiated patients.

instance, serum creatinine concentration is a widely used measure of renal function, but it has been shown that a given level of creatinine in serum can be associated with a wide range of values for GFR [19]. The measurement of endogenous creatinine clearance for the estimation of GFR also has its limitations. An increasing tubular secretion of creatinine in case of a decreasing GFR, variability in dietary protein intake, strenuous exercise and the presence of non-creatinine chromatogens in the assay are all factors that can influence the reliability of the measured creatinine clearance [20]. Furthermore, the practical problems of collecting a reliable 24-h urine sample in young children for the calculation of creatinine clearance are obvious.

One of the early studies on renal function following nephrectomy for malignant disease in children was published in 1969 by Mitus and colleagues [21]. This was a retrospective study in which the interval between nephrectomy and renal evaluation ranged between 6 months and 18 years. Virtually all patients were irradiated. Urinalysis, creatinine clearance, serum urea and intravenous urograms were used as parameters for renal function. It was concluded that normal renal function could be preserved, if irradiation to the remaining kidney was kept below 1200 cGy (orthovoltage). The incidence of abnormal creatinine clearance in patients who received 1200–2400 cGy was 33%. Although the results of Mitus and associates [21] could be consistent with our observaltions, caution is needed in the interpretation because both the irradiation and chemotherapy used differed from current standards; also, parameters of renal function were different in our study.

Jereb and associates [22] investigated retrospectively whether the dose of radiation to the remaining kidney made a difference for renal function. These investigators used an accurate technique for the estimatation of GFR and ERPF and were unable to show a difference in renal function between patients that received 250 cGy orthovoltage versus 1700 gCy given by a cobalt-60 unit. A caveat in this study, indicated by the authors, was that the interval between treatment and renal studies was substantially longer in patients who received the lower dose of radiation. Jereb and associates did not study a group of children who did not receive irradiation.

Wikstad and colleagues [23] also used an accurate method for the measurement of renal function; they reported on 22 Wilms' tumour patients and 15 patients who had undergone a nephrectomy for hydronephrosis. In the Wilms' tumour patients, all of whom had received both radiation therapy and chemotherapy, GFR was significantly lower than in patients with hydronephrosis who obviously did not receive irradiation and chemotherapy. ERPF was the same in both groups. Mean GFR in the Wilms' tumour patients was 82% of GFR in children with two normal kidneys; this is in accordance with our findings in the irradiated children.

A comparison between two groups of Wilms' tumour patients that did or did not receive irradiation to the remaining kidney was carried out by Walker and associates [24]. In both groups, creatinine clearance was significantly lower than in normal controls; there was no difference between the groups. Barrera and colleagues [25] found a subnormal average creatinine clearance in 16 patients in whom 3000 cGy irradiation was directed to the tumour bed, not to the contralateral kidney. Our reservations about the accuracy of creatinine clearance have already been discussed. The influence of treatment modality on GFR was also investigated by Levitt and associates; follow-up time ranged from 7 to 19 years [26]. Their results were puzzling: patients who received radiation therapy between 130 and 1200 cGy to the remaining kidney had a GFR that was significantly higher than in patients who received either a higher dose of radiation therapy (1200–1720 cGy) or no irradiation at all.

Obviously, variability in follow-up time is a potential confounding factor when treatment groups are compared with respect to late side-effects. In each of the above retrospective studies on renal function, the interval between treatment and the assessment of renal function was extremely variable. In our study, the renal evaluation for each patient was done in the second year after nephrectomy. Interpatient variability in the interval between treatment and measurement of GFR and ERPF was small compared to previous studies. An interval of at least 1 year between nephrectomy and the measurement of renal function appears more than sufficient to achieve a new functional steady state: a few weeks after unilateral nephrectomy, an increase in GFR and ERPF of the remaining kidney occurs which remains stable thereafter [27, 28].

The size of the contralateral kidney after treatment for Wilms' tumour has been the subject of several retrospective studies with conflicting results. Cassady and associates [29] used urograms to measure growth rate of the remaining kidney in 11 children that received 1200 cGy to the kidney compared to 12 children that did not receive irradiation to the kidney. The difference in mean growth rates between the irradiated kidneys (0.50 cm/year) and non-irradiated kidneys (0.65 cm/year) suggested that 1200 cGy irradiation therapy has an impact on renal growth rate, although the difference was not statistically significant. Walker and colleagues [24] also reported on renal growth following nephrectomy for Wilms' tumour. They measured the ratio of lumbar vertebral length and renal length on serial X-rays, making the debatable assumption that vertebral growth was not affected by radiation therapy. Using this method, they were unable to show an influence of irradiation on the growth of the remaining kidney.

Mäkipernaa and associates [30] used ultrasound to measure the size of the remaining kidney in 30 cases, 11–28 years after nephrectomy for Wilms' tumour. All but 2 patients were treated with chemotherapy; none received irradiation directed to the remaining kidney. The mean length of the remaining kidney was 2.0 standard deviations larger than reference values for healthy children. This observation confirms the occurrence of a compensatory hypertrophy after chemotherapy; the investigators did not compare results with children who also received radiation therapy. Wikstad and associates [23] measured renal size by urography in patients who 5–30 years before had received a unilateral nephrectomy for either hydronephrosis or Wilms' tumour; all Wilms' tumour patients had received radiation therapy and most were also treated with chemotherapy. They found a compensatory hypertrophy in both groups, but the remaining kidney was significantly smaller in Wilms' tumour patients than in hydronephrosis patients.

Our study focused on function rather than size of the remaining kidney. Nevertheless, a reduced growth of the remaining kidney after unilateral nephrectomy, as has been reported by some investigators, might be the anatomical reflection of a compromised renal function as a result of therapy.

In conclusion, we have shown that, following unilateral nephrectomy for Wilms' tumour, both GFR and ERPF are significantly lower in patients who received radiation therapy to the remaining kidney in combination with chemotherapy, when compared to patients who received only chemotherapy. Although renal function in the irradiated children should still be sufficient to meet normal demands, adverse effects of radiation may increase over the years. Therefore, longer follow-up of renal function in these patients, including monitoring of blood pressure, proteinuria and microalbuminuria, will be needed to assess the ultimate sequelae of treatment.

We acknowledge that radiation therapy has made a major contribution to the improvement of cure rates in children with Wilms' tumour. The results of our study support the implementation of clinical trials that address the question of whether radiation therapy on the remaining kidney can be further reduced or avoided in selected groups of patients without compromising high survival rates.

1. D'Angio GJ, Evans A, Breslow N, *et al.* The treatment of Wilms' tumor: results of the Second National Wilms' Tumor Study. *Cancer* 1981, **47**, 2302–2311.
2. D'Angio GJ, Breslow N, Beckwith JB, *et al.* Treatment of Wilms' tumor: results of the Third National Wilms' Tumor Study. *Cancer* 1989, **64**, 349–360.
3. Tournade MF, Com Nougue C, Voute PA, *et al.* Results of the Sixth International Society of Pediatric Oncology Wilms' Tumor Trial and Study: a risk-adapted therapeutic approach in Wilms' tumor. *J Clin Oncol* 1993, **11**, 1014–1023.
4. Lukens JN. Progress resulting from clinical trials: solid tumors in childhood cancer. *Cancer* 1994, 74 (Suppl.), 2710–2718.
5. Evans AE, Norkool P, Evans I, Breslow N, D'Angio GJ. Late effects of treatment for Wilms' tumor: a report from the National Wilms' Tumor Study Group. *Cancer* 1991, **67**, 331–336.
6. Hayslett JP, Kashgarian M, Epstein FH. Functional correlates of compensatory renal hypertrophy. *J Clin Invest* 1968, **47**, 774–799.
7. Eklöf O, Ringertz H. Kidney size and growth in unilateral renal agenesis and in the remaining kidney following nephrectomy for Wilms' tumor. *Acta Radiol Diagn* 1976, **17**, 601–608.
8. Smith HW. Measurement of the filtration rate. In Smith HW, ed. *The Kidney Structure and Function in Health and Disease*. New York, Oxford University Press, 1951, 39–62.
9. Sigman EM, Elwood CM, Knox F. The measurement of glomerular filtration rate in man with sodium iothalamate I^{131}. *J Nucl Med* 1965, 7, 60–68.
10. Donker AJM, Van der Hem GK, Sluiter WJ, Beekhuis H. A radio-isotope method for simultaneous determination of the glomerular filtration rate and the effective renal plasma flow. *Neth J Med* 1977, **20**, 97–103.
11. McCrory WW. Quantitative measurement of renal function during growth in infancy and childhood. In *Developmental Nephrology*. Cambridge, Massachusetts, Harvard University Press, 1972, 79–122.
12. Barnett HL, McNamara H, Schultz S, Tompsett R. Renal clearances of sodium penicillen G, procaine penicillen G and inulin in infants and children. *Pediatrics* 1949, **3**, 418–422.
13. Richmond JB, Kravitz H, Segar W, Waisman HA. Renal clearance of endogenous phosphate in infants and children. *Proc Soc Exp Biol Med* 1951, **77**, 83–87.
14. Heilbron DC, Holliday MA, Al-Dawwi A, Kogan BA. Expressing glomerular filtration rate in children. *Pediatr Nephrol* 1991, **5**, 5–11.
15. Mann HB, Whitney DR. On a test of whether one of two random variables is stochastically larger than the other. *Ann Math Statist* 1947, **18**, 50–60.
16. Nonparametric statistics. In *CSS Complete Statistical System*. Tulsa, OK, StatSoft, Inc., 1988, 615–678.
17. Bhisitkul DM, Morgan ER, Vozar MA, Langman CB. Renal functional reserve in long-term survivors of unilateral Wilms tumor. *J Pediatr* 1991, **118**, 698—702.
18. Halperin EC, Kun LE, Constine LS, Tarbell NJ. Late effects of cancer treatment. In *Pediatric Radiation Oncology*. New York, Raven Press, 1989, 344–386.
19. Levey AS, Perrone RD, Madias NE. Serum creatinine and renal function. *Ann Rev Med* 1988, **39**, 465–490.
20. Wetzels JFM, Huysmans FThM, Koene RAP. Creatinine as a marker of glomerular filtration rate. *Neth J Med* 1988, **33**, 144–153.
21. Mitus A, Teft M, Fellers FX. Long-term follow-up of renal functions of 108 children who underwent nephrectomy for malignant disease. *Pediatrics* 1969, **44**, 912–921.
22. Jereb B, Aperia A, Berg U, Broberger O, Båryd I. Renal function in long-term survivors after treatment for nephroblastoma. *Acta Paediatr Scand* 1973, **62**, 577–584.
23. Wikstad I, Pettersson BA, Elinder G, Sokucu S, Aperia A. A comparative study of size and function of the remnant kidney in patients nephrectomized in childhood for Wilms' tumor and hydronephrosis. *Acta Paediatr Scand* 1986, **75**, 408–414.
24. Walker RD, Reid CF, Richard GA, Talbert JL, Rogers BM. Compensatory renal growth and function in postnephrectomized patients with Wilms' tumor. *Urology* 1982, **19**, 127–130.
25. Barrera M, Roy LP, Stevens M. Long-term follow-up after unilateral nephrectomy and radiotherapy for Wilms' tumor. *Pediatr Nephrol* 1989, **3**, 430–432.
26. Levitt GA, Yeomans E, Dicks Mireaux C, Breatnach F, Kingston J, Pritchard J. Renal size and function after cure of Wilms' tumour. *Br J Cancer* 1992, **66**, 877–882.
27. Pabico RC, McKenna BA, Freeman RB. Renal function before and after unilateral nephrectomy in renal donors. *Kidney Int* 1975, **8**, 166–175.
28. Fotino S. The solitary kidney, a model of chronic hyperfiltration in humans. *Am J Kidney Dis* 1989, **13**, 88–98.
29. Cassady JR, Lebowitz RL, Jaffe N, Hofman A. Effect of low dose irradation on renal enlargement in children following nephrectomy for Wilms' tumor. *Acta Radiol Oncol* 1981, **20**, 5–8.
30. Mäkipernaa A, Koskimies O, Jääskeläinen J, Teppo A-M, Siimes MA. Renal growth and function 11–28 years after treatment of Wilms' tumour. *Eur J Pediatr* 1991, **150**, 444–447.

Acknowledgements—We wish to thank Dr R.Y.J. Tamminga for his advice on the standard deviation scores, and the nursing staff of the Paediatric Function Centre of the Beatrix Children's Hospital for their assistance in the renal function tests.