Renal transplantation in patients with urinary diversion: a case-control study

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Abstract

Background. Renal transplantation in Sweden in patients with ileal conduits or continent reservoirs was investigated in order to compare the outcome with regard to graft and patient survival as compared to controls.

Methods. Patient data from the four transplantation centres in Sweden were collected on: treatment prior to transplantation, time needed for the operative procedure, and postoperative care and outcome in terms of renal function as well as graft and patient survival at 1 and 5 years. The pattern of urinary tract infection was also investigated. Each case with urinary diversion was matched with two non-diabetic controls.

Results. Ten male and 12 female cases were found who had received 27 grafts between 1982 and 1996. Five patients had a Kock reservoir and 17 had a Bricker conduit. The time needed for the transplant procedure was significantly longer in the case group. After matching the case group with 54 controls, we found that the renal function was similar in both groups. Graft and patient survival was about 70% after 5 years. Postoperative surgical complications in the case group were only seen in a few cases. The pattern of bacteria causing urinary tract infection was slightly different among the patients with ileal conduits or continent reservoirs.

Conclusion. Patients with ileal conduits or continent reservoirs have similar graft and patient survival rates as the general kidney transplant population. The presence of constant bacteriuria did not adversely affect survival. Prophylactic antibiotic treatment seems not to be warranted. There appears to be no indication for native nephrectomy, except in selected cases. The study did not show any advantage with regard to continent reservoirs vs ileal conduits.

Key words: Bricker; human; Kock; renal transplantation; survival; urinary diversion; urinary tract infection

Introduction

The pioneer work by Bricker in 1950 [1] and the continent urinary reservoir by Kock [2], as well as other methods of urinary diversion [3], have paved the way for alternative technical treatments for patients with severe outflow obstruction. A low-pressure reservoir [4,5] gives the patient a better quality of life than a urostomy [4]. Renal transplantation into the ileal conduit was first reported by Kelly et al. [6]. In some patients, one can perform an undiversion before the renal transplantation, if a urodynamic investigation shows that the native bladder can be used in renal transplantation [7]. In patients with a neuropathic bladder who want a continent urinary diversion, a reservoir remains the alternative. In this study, we aimed to identify all patients in Sweden with ileal conduits or continent reservoirs who had received renal transplants. We wished to compare this group with controls as regards renal function, graft, and patient survival. Another aim was to investigate the bacterial spectrum in urine cultures and the incidence of hospitalization because of urosepsicaemia.

Subjects and methods

Patients

Data on all kidney transplant patients in Sweden who had undergone urinary diversion procedures with an ileal conduit or a continent reservoir were collected.

Each patient was matched with two non-diabetic controls. Matching was carried out for age, sex, and year of transplantation. Dialysis mode and time on dialysis were noted for all patients. The time in the operating room for the transplantation was recorded as well as the number of days the patient remained in hospital after transplantation.

Urine samples were examined for bacteria after surgery and at regular intervals thereafter. After discharge, patients were usually seen every third month in the outpatient clinic. The bacteriological findings were evaluated for the presence of differences in bacteria species between cases and controls. Cultures were regarded as positive if > 10⁵ bacteria/ml were present [8].

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One-year and 5-year patient and graft survival rates were calculated. Patient survival in the case group was calculated from the date of the first transplantation. Graft function was estimated by the serum creatinine levels at 1, 3 and 5 years.

Statistical analyses

Median and ranges are presented unless otherwise stated. Statistical analysis was performed using a commercially available software package, Statistica, version 5.0 (StatSoft, Tulsa, OK, USA). Discrete variables were compared by the χ² test with Yate’s continuity correction. Group differences in continuous variables were assessed by Student’s t-test or Mann–Whitney U test as appropriate. Coefficients of skewness and kurtosis were used to test deviations from a normal distribution. Graft and patient survival according to Kaplan–Meier were calculated. The curves were compared using log-rank statistics. A P value <0.05 was considered statistically significant.

Results

Twenty-two patients, 10 males and 12 females (total 27 grafts), transplanted between 1982 and 1996 were identified. The total number of kidney transplantations in Sweden during these years was 4919. Thus, our cases represent less than 1% of the renal transplantations performed during this period.

All but two cases were on standard triple immunosuppression protocols consisting of cyclosporin (CsA), azathioprine (Aza), and prednisolone (Pred). One woman had Aza and Pred and one man was on tacrolimus and Pred. Most of the controls (40/54) were on CsA, Aza and Pred, 10 were taking CsA and Pred, three Aza and Pred, and one woman was on tacrolimus and Pred.

The cause of bladder dysfunction was malformation in four patients, neurogenic in nine, tuberculosis in three and recurrent urinary tract infections in two patients. One of the male patients injured his spine in an accident, and developed a neuropathic bladder. Another male injured his bladder severely in a car accident. One male patient had bladder lipomatosis and one female patient had phenacetin nephritis and nephrolithiasis.

All except two patients had their diversion procedure performed before the transplantation. One woman underwent a Bricker diversion procedure because of bladder contracture secondary to severe bladder infections. A man who had been transplanted three times underwent a Kock diversion procedure after the second graft was lost. This patient’s first two grafts are not included in the material.

The median age at the time of the diversion procedure was 32 years (range 3–67 years). The diversion procedure was a Bricker conduit in 17 patients and a Kock continent reservoir in five patients. One of the women underwent a Coffey diversion at age 14 and was reoperated with a Bricker conduit at age 32, prior to transplantation. Another woman had her first Bricker conduit operation when she was 3 years old. Because of a conduit stricture with resultant hydro-nephrosis, it was revised 2 years after transplantation. At the same operation, the patient underwent bilateral nephrectomy and removal of an asymptomatic calculus in the conduit.

Among the controls, five had malformations, 23 chronic glomerulonephritis, five chronic pyelonephritis, eight polycystic kidney disease and the remainder had miscellaneous diagnoses. Of the male cases, one had been regrafted once. Four of the female cases had been regrafted once. Each retransplantation was treated as a new event. Thus, the 22 cases comprised 27 grafts, eight living donor (LD) and 19 cadaveric donor (CD). These cases were matched with 54 non-diabetic controls, 16 LD, and 38 CD (Table 1).

No significant difference in the median time on dialysis was present between the cases, 14 months, and controls, 11 months. Of the cases, 25 (93%) were on haemodialysis while two (7%) were not on dialysis before grafting. Of the controls, 33 (57%) were on haemodialysis, 12 (21%) on peritoneal dialysis, and 9 (16%) were not on dialysis treatment.

The median age at transplantation was 40 years in the patients and 43 among the controls. The median donor age was 41 and 43 years.

The median time in the operating room was 235 min (range 135–510) in the case group and 185 min (range 115–305) in the control group, a significant difference (P < 0.001). In one male case, a reanastomosis between the ureter and ileal conduit was performed 2 months after transplantation. Another postoperative complication, conduit stricture and calculus formation, has been mentioned above.

The median number of days in hospital was 24 for the cases and 21 days in the control group, consistent with similar onset of function in both groups.

During the first 3 months postoperatively, two male and two female cases had an acute rejection episode. The routine treatment was 500 mg methylprednisolone i.v., followed by 250 mg for 2 days. One male case had three acute rejection episodes, all of which were treated with methylprednisolone. In both the cases and the control groups, the median number of acute rejection episodes was one.

The median serum creatinine levels were 119 μmol/l among the cases and 137 μmol/l in the control group after 1 year (reference value <120 μmol/l). The corresponding values at 5 years were 147 and 132 μmol/l. The mean difference between the serum creatinine values at 3 years and 1 year was significantly higher in the case group, 28 ± 55, CI (4.53) vs 0.2 ± 28 μmol/l, CI (−8.8); P = 0.008. The difference in serum creatinine levels between 5 and 1 years and 5 and 3 years respectively was not statistically significant. Among the cases, two females died within 5 years after transplantation. The cause of death was pneumonia and colon tumour with metastases respectively. One male case died of a myocardial infarction 6 years after transplantation. Two of the cases died with a functioning graft. In the control group, two females died within 5 years after transplantation, both from cardiovascular disease.
Four male cases required haemodialysis treatment again after chronic graft rejection, one after 2 years, one after 4 years and two patients after 6 years. The 1-year graft survival rates were 25/27 (93%) among the cases and 50/54 (93%) in the control group. The 5-year graft survival rates were 19/27 (70%) and 40/54 (74%) respectively. The patient survival was 21/22 (95%) for cases and 100% for controls at 1 year and 20/22 (91%) and 42/44 (95%) at 5 years respectively. The graft and patient survival rates were not significantly different, at either 1 year or 5 years.

Urine cultures showing >10⁵ colony-forming units/ml were regarded as positive. Virtually all urine cultures in the case group showed some degree of bacteriuria. No changes in the resistance pattern occurred after prescription of antibiotic treatment. Antibiotic prophylaxis was not generally used. One episode of urosepticaemia was found in the case group and one in the control group.

*Staphylococcus epidermidis* and *Enterococci* were the commonest species during the first 3 months post-transplantation. Alpha streptococci, *Klebsiella*, *Enterococci*, *Escherichia coli* and *Proteus* were detected in both patient groups. *Acinetobacter*, *Diphtheroids*, *Morganella*, *Providencia*, and *Xanthomonas* were found only among the cases.

### Discussion

This study shows that patients with ileal conduits or continent reservoirs do as well after renal transplantation as controls in terms of graft and patient survival rates. The presence of chronic bacteriuria did not affect renal function, as assessed by the serum creatinine level. Since Kelly et al. first reported successful renal transplantation in patients with ileal conduits [6], other studies [9] have shown that patients with conduits can safely undergo renal transplantation if they are carefully selected. After transplantation, some patients develop native bladder contracture or other disease necessitating cystectomy and construction of a conduit [10]. This was done in one of our female patients. A conduit, or reservoir procedure, is preferably done before the transplantation [11] to reduce the postoperative risks at transplantation. Some authors [12] recommend irrigation of the conduit in the anuric patient until a graft becomes available, while others consider this procedure unnecessary [13]. Undiversion is sometimes an option in patients having a diversion for reasons other than a neurogenic bladder. The undiversion can be performed before [14] or after [15] transplantation.

We recorded the time spent in the operating room for a transplantation because we thought that the transplantation procedure would be more complicated among the cases. The median time in the operating room was, indeed, longer among the cases, although the range varied greatly. Three main complications have been reported after renal transplantation in patients with conduits. They include calculus formation [9,11,16], urinary leakage [11], and conduit stricture [9,17] and they were also seen in two of the patients in the present study.

Urodynamic assessment of urinary diversions is recommended by some investigators [9,18]; however, urodynamic assessment was not done in the present material. When an outflow obstruction is suspected, our practice is to use ultrasound and isotope scans as diagnostic methods.

Bacteria are frequently found in urine samples from conduits [16]. Contaminated samples can be avoided by using a proper technique [16] when collecting urine from the conduit. In the present study, medical records indicated that cultures of urine samples taken from the conduit were routinely done without taking specific precautions to avoid contamination. The bacterial patterns in our cases and controls were similar to those seen in other studies [8]. Multiresistant strains did not develop as a result of the various antibiotics given. Since many kidney transplant recipients were being treated for urinary tract infections outside the trans-

### Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Cases</th>
<th>Controls</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Kock</td>
<td>Bricker</td>
<td>All</td>
</tr>
<tr>
<td>Age at tx (years)</td>
<td>28 (12–39)</td>
<td>6</td>
<td>39 (12–68)</td>
</tr>
<tr>
<td>Donor age (years)</td>
<td>30 (27–43)</td>
<td>6</td>
<td>43 (16–72)</td>
</tr>
<tr>
<td>LD/CD (n)</td>
<td>5/3</td>
<td>6</td>
<td>5/16</td>
</tr>
<tr>
<td>Retransplantations (n)</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>O.R. time (min)</td>
<td>260* (210–315)</td>
<td>5</td>
<td>235* (135–510)</td>
</tr>
<tr>
<td>S-creatinine at 1 year (µmol/l)</td>
<td>117 (79–161)</td>
<td>6</td>
<td>125 (73–195)</td>
</tr>
<tr>
<td>S-creatinine at 3 years (µmol/l)</td>
<td>134 (71–354)</td>
<td>6</td>
<td>132 (71–256)</td>
</tr>
<tr>
<td>S-creatinine at 5 years (µmol/l)</td>
<td>211 (91–382)</td>
<td>4</td>
<td>144 (93–318)</td>
</tr>
<tr>
<td>Patient survival (years)</td>
<td>6 (4–9)</td>
<td>3</td>
<td>9 (0–16)</td>
</tr>
</tbody>
</table>

Values are median (range).

*Tx, transplantation; LD, living donor; CD, cadaveric donor; O.R., operating room; S-creatinine, serum creatinine.

*P < 0.001; †P < 0.001 vs controls.
plant centres [8], the true number of urinary tract infections could not be estimated by collecting data from hospital records. Because standard triple immunosuppression with cyclosporin, prednisolone, and azathioprine can mask symptoms of urinary tract infection, it has been recommended to treat all bacteriuria in transplant recipients with conduits [16]. Recurrent urinary tract infections may also predispose to formation of calculi in the conduit [11].

The patients with conduits or reservoirs in the present study were given antibiotics on grounds of bacteriuria alone less frequently in recent years. This is due to the experience that many patients do well, despite chronic bacteriuria, and to a general trend to restrict the use of antibiotics to avoid superimposed infections, such as Pseudomonas [19]. At present, antibiotic treatment is not prescribed unless the patient has additional symptoms such as tenderness in the graft, fever, or an elevated C-reactive protein level. In this material, we found that chronic bacteriuria did not predispose to urosepsicaemia, as septicemia was only found in one patient and in one control. There appears to be a low risk of ascending infections, which is in accordance with findings by other investigators [20].

Graft survival rates were similar in both case and control groups. Thus, we found that the presence of chronic bacteriuria [11] did not affect graft survival in transplant recipients with conduits or reservoirs. Survival data are comparable to those of other studies [9,18,21]. The study included too few patients to detect group differences in survival with adequate statistical power.

The median serum creatinine levels did not differ between the groups and were similar to values reported by others [18,21]. However, the mean difference in serum creatinine levels between 3 and 1 year was significantly higher among the cases, but a marked reduction in graft function for a few cases can explain this finding. There was a larger decline in graft function in the group with Kock reservoirs, but this group only comprised four patients after 5 years, and no statistically significant difference was detected. The study group was too small to form a basis for a recommendation whether to choose a reservoir or a conduit for these patients. A continent reservoir appears to be the method of choice [3].

Based on the results in this study, we cannot recommend native nephrectomy in patients with urinary diversion, as this was only necessary in one patient.

In summary, this study shows that renal transplant recipients with a conduit or a continent reservoir do as well as non-diabetic control patients as regards renal function and graft and patient survival.

Acknowledgements. The authors are greatly indebted to Anders Christensen, Gudrun Nyberg, Nils Persson and Jan Wahlberg for their assistance in collecting patient data.

References

Received for publication: 2.12.98
Accepted in revised form: 13.7.99