Surgical aspects of renal transplantation
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Citation for published version (APA):

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Download date: 15 Oct 2018
CHAPTER 7

Is a selective splinted ureterocystostomy protocol feasible in renal transplantations? An analysis of 475 renal transplantations.

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Transpl Int. 2006; 19: 558-62

Routine splinting of the ureterocystostomy during renal transplantation lowers the urological complication rate but increases patient’s morbidity. The number needed to treat to prevent one urological complication is high. The aim of this study was to identify risk factors, which can be used in the implementation of a selective splinting ureterocystostomy protocol. Retrospective analysis of 475 consecutive renal transplantations performed between January 1999 and December 2004. Donor, surgical-technical and recipient factors were assessed.

Urological complications occurred in 62 (13%) patients. In 29 of these 62 patients (6.1%), only a temporary percutaneous nephrostomy catheter was necessary and in 33 (6.9%) surgical revision was required. Episodes of acute rejection and delayed graft function were identified as the only independent risk factors for a urological complication: odds ratio 2.62 [95% confidence interval: (CI) 1.38–4.97] and 2.22 (95% CI: 1.14–4.33), respectively. None of the risk factors for urological complications after renal transplantation that are known at the time of performing the ureterocystostomy are useful for the implementation of a selective splinting protocol.
INTRODUCTION

Despite meticulous surgical technique and improved immunosuppression therapy, urological complications continue to result in morbidity and occasional mortality after renal transplantation. The incidence of urological complications ranges from 2.5% to 30%\(^1\)\(^-\)\(^7\). The two major urological complications after renal transplantation are urinary leakage and obstruction often located at the ureterovesical junction or in the distal transplant ureter. Urological complications increase the length of hospitalization as well as costs, and may threaten transplant outcome. Over recent years, there has been debate as to whether splinting the ureterocystostomy results in a reduced postoperative urological complication rate. Two recent meta-analyses have demonstrated that splinting a ureterocystostomy leads to a significantly lower urological complication rate on comparison with non-splinted ureterocystostomy. However, the number needed to treat (NNT) with a routine splinting protocol in order to prevent one urological complication was high, ranging from 10 to 30. In addition, routine splinting leads to a higher urinary tract infection rate\(^8\)\(^,\)\(^9\).

We performed a retrospective analysis to investigate the frequency and occurrence of urological complications after renal transplantation using a non-splinted ureterocystostomy policy. The aim of our study was to identify potential risk factors, which at the time of performing the ureterocystostomy could be used to effectively identify patients at high risk of urological complications. These data could then be used to introduce a protocol of selective splinting of the ureterocystostomy intended to lower the NNT.

PATIENTS AND METHODS

Between January 1999 and December 2004, 475 consecutive renal transplantations (339 cadaveric- and 136 living donors) were performed at the Academic Medical Center, Amsterdam. Recipient median age was 44 years (range 4–75 years). All transplants were single renal transplantations and were performed by a group of seven surgeons using the extraperitoneal approach in the iliac fossa. The method used to establish urinary continuity was either the extravesical ureterocystostomy (Lich-Gregoir technique in 352 patients) or the intravesical ureterocystostomy (Politano-Leadbetter technique in 123 patients). The type of ureterocystostomy depended on the personal preference of the surgeon. All patients had an indwelling bladder catheter for 5–7 days postoperatively, which was removed after cystography had excluded urinary leakage. All patients were followed up at our center for at least 1 year after successful transplantation. Immunosuppressive therapy consisted of prednisone, a calcineurin inhibitor and mycophenolate mofetil. Recipients of a living donor kidney also received prophylactic anti-CD25 monoclonal antibody (basiliximab, Novartis BV, Arnhem, The Netherlands). From 2003, all patients were treated with prednisone, a
Is selective splinting ureterocystostomy feasible in renal transplantation?

calcineurin inhibitor, mycophenolate mofetil and basiliximab. Episodes of acute rejection were treated with pulsed doses of methylprednisolone. Renal transplant function was monitored by serial measurement of serum and urine creatinine, urinary output and renography. Delayed graft function was defined as the need for dialysis within the first postoperative week.

A urological complication was defined as any urinary fistula (leakage), ureteral obstruction and clots in the ureter or bladder requiring treatment. Urinary tract infections and vesicoureteral reflux were not counted as urological complications. If indicated, a percutaneous nephrostomy catheter was inserted and an antegrade pyelography was performed. The nephrostomy catheter was left in place to maintain renal excretory function. If urinary obstruction persisted despite the percutaneous nephrostomy catheter, an operative reconstruction was usually performed 3–6 months later. If there was dehiscence of the ureterocystostomy during the first few postoperative days, an operative revision of the urinary anastomosis was performed without delay.

Statistical analysis

Univariate and multivariate logistic regression analysis was performed to identify independent risk factors for urological complication. Multivariate logistic regression analysis was performed on all factors with a P-value of <0.20 in the univariate analysis. The chi-squared test was used to analyze discrete data between groups. Survival analysis was performed by the Kaplan–Meier technique and the log-rank test. A P-value of <0.05 was considered statistically significant. Statistical analysis was done using SPSS® version 11.5 (SPSS, Chicago, IL, USA).

RESULTS

Of the 475 consecutive renal transplantation procedures, 62 developed a urological complication (13.1%). These included 34 ureteral strictures, 16 ureteral strictures and leakage, 11 ureteral leaks and one blood clot in the bladder. In 29 of these 62 (6.1%) patients, the urological complication was managed with a temporary percutaneous nephrostomy catheter only. In the remaining 33 patients (6.9%), surgical revision was necessary to correct the urological complication. Of this surgical group of 33 patients, 26 patients (79%) had a percutaneous nephrostomy catheter in place prior to revision.

The time to onset of the urological complication is shown in Figure 1. Fifty percent of all urological complications occurred within the first two postoperative weeks and 73% within the first postoperative month.

The occurrence of urological complications was correlated with several donor, surgical-technical and recipient risk factors (Table 1). Donor age, episodes of acute rejection, and
delayed graft function were significantly correlated with the occurrence of a urological complication on univariate analysis. Multivariate analysis (Table 1) identified acute rejection (odds ratio 2.62, 95% CI: 1.38–4.94, P = 0.003) and delayed graft function (odds ratio 2.22, 95% CI: 1.14–4.33, P = 0.02) as the only significant independent risk factors for urological complications. There was no significant difference in the urological complication rate between cadaveric (13.6%) and living donor (11.8%) renal transplantation (P = 0.71). Although the urological complication rate between surgeons varied from 6.1% to 19.4%, there was no statistical significance (P = 0.29). The urological complication rates of the intra- or extravesical ureterocystostomy were 14.6% and 12.5%, respectively, which was not statistically significant (P = 0.65). Concomitant vascular reconstruction performed during the implantation had no significant effect on the occurrence of urological complications. The presence of a lower pole artery in the donor kidney was shown to lead to an increased incidence of urological complications especially if revascularization was not possible. However, multivariate analyses did not show it to be an independent risk-factor for urological complications.

Figure 1. Time interval between the operation and occurrence of the urological complication in the postoperative period.

Of the 62 grafts with an accompanying urological complication, seven were lost within the first postoperative year. The causes of graft loss were: two acute rejections, two instances of sepsis, one infected hematoma, one renal artery thrombus and one of unknown origin. The 1-month and 1-year graft survival rates in patients without urological complications were 98% and 92%, respectively, compared with 92% and 86% in patients with urological complications. The 1-year survival rate of patients with and without urological complications was 95% and 97%, respectively. The occurrence of a urological complication had no significant effect on the graft (P = 0.23) or patient (P = 0.87) 1-year survival rate.
Is selective splinting ureterocystostomy feasible in renal transplantation?

Table 1. Univariate and multivariate analysis of risk factors for urological complications.

<table>
<thead>
<tr>
<th>Factor</th>
<th>No of patients (n=475)</th>
<th>Urological complication (n=62)*</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Odds ratio¹</td>
<td>p</td>
</tr>
<tr>
<td>Recipient female sex</td>
<td>190</td>
<td>21 (11.1)</td>
<td>0.74 (0.42-1.30)</td>
<td>0.36</td>
</tr>
<tr>
<td>Living donor</td>
<td>136</td>
<td>16 (11.8)</td>
<td>0.85 (0.46-1.56)</td>
<td>0.71</td>
</tr>
<tr>
<td>Donor age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 18 yr</td>
<td>27</td>
<td>2 (4.0)</td>
<td>0.54 (0.12-2.34)</td>
<td>0.59</td>
</tr>
<tr>
<td>18-50 yr</td>
<td>200</td>
<td>13 (6.5)</td>
<td>0.30 (0.15-0.58)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt; 50 yr</td>
<td>162</td>
<td>34 (21.0)</td>
<td>3.75 (1.97-7.16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recipient age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 18 yr</td>
<td>35</td>
<td>5 (14.3)</td>
<td>1.12 (0.42-3.00)</td>
<td>0.82</td>
</tr>
<tr>
<td>18-50 yr</td>
<td>244</td>
<td>34 (13.9)</td>
<td>1.17 (0.69-2.01)</td>
<td>0.65</td>
</tr>
<tr>
<td>&gt; 50 yr</td>
<td>196</td>
<td>23 (11.7)</td>
<td>0.82 (0.47-1.42)</td>
<td>0.56</td>
</tr>
<tr>
<td>Recipient with diabetes</td>
<td>36</td>
<td>3 (8.3)</td>
<td>0.59 (0.17-1.97)</td>
<td>0.39</td>
</tr>
<tr>
<td>Vascular anastomosis &gt; 45 min</td>
<td>42</td>
<td>7 (16.7)</td>
<td>1.45 (0.60-3.51)</td>
<td>0.57</td>
</tr>
<tr>
<td>Cold Ischimic period &gt;24 hours</td>
<td>90</td>
<td>12 (13.3)</td>
<td>1.10 (0.55-2.21)</td>
<td>0.94</td>
</tr>
<tr>
<td>Concomitant vascular reconstruction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial and/or venous</td>
<td>115</td>
<td>15 (13.0)</td>
<td>1.00 (0.54-1.86)</td>
<td>0.99</td>
</tr>
<tr>
<td>Arterial</td>
<td>68</td>
<td>7 (10.3)</td>
<td>0.73 (0.32-1.69)</td>
<td>0.47</td>
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<tr>
<td>Venous</td>
<td>54</td>
<td>9 (16.7)</td>
<td>1.39 (0.64-3.00)</td>
<td>0.4</td>
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<tr>
<td>Lower pole art.²</td>
<td>38</td>
<td>8 (21.1)</td>
<td>1.90 (0.82-4.34)</td>
<td>0.13</td>
</tr>
<tr>
<td>Ligation lower pole art.³</td>
<td>8</td>
<td>3 (37.5)</td>
<td>4.15 (0.97-17.82)</td>
<td>0.06</td>
</tr>
<tr>
<td>Extravesical ureterocystostomy</td>
<td>352</td>
<td>44 (12.5)</td>
<td>0.83 (0.46-1.51)</td>
<td>0.65</td>
</tr>
<tr>
<td>Intravesical ureterocystomy</td>
<td>123</td>
<td>18 (14.6)</td>
<td>1.20 (0.67-2.17)</td>
<td>0.55</td>
</tr>
<tr>
<td>Surgeon</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>67</td>
<td>12 (17.9)</td>
<td>1.56 (0.78-3.12)</td>
<td>0.21</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
<td>7 (14.9)</td>
<td>1.19 (0.51-2.78)</td>
<td>0.69</td>
</tr>
<tr>
<td>3</td>
<td>31</td>
<td>6 (19.4)</td>
<td>1.67 (0.65-4.23)</td>
<td>0.29</td>
</tr>
<tr>
<td>4</td>
<td>113</td>
<td>10 (8.8)</td>
<td>0.58 (0.28-1.18)</td>
<td>0.13</td>
</tr>
<tr>
<td>5</td>
<td>96</td>
<td>12 (12.5)</td>
<td>0.94 (0.48-1.84)</td>
<td>0.86</td>
</tr>
<tr>
<td>6</td>
<td>49</td>
<td>3 (6.1)</td>
<td>0.41 (0.12-1.35)</td>
<td>0.14</td>
</tr>
<tr>
<td>7</td>
<td>72</td>
<td>12 (16.7)</td>
<td>1.41 (0.71-2.81)</td>
<td>0.33</td>
</tr>
<tr>
<td>Acute rejection</td>
<td>158</td>
<td>30 (19.0)</td>
<td>2.09 (1.22-3.58)</td>
<td>0.01</td>
</tr>
<tr>
<td>Delayed graft function</td>
<td>114</td>
<td>23 (20.2)</td>
<td>2.09 (1.19-3.67)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Values in parentheses are * percentages or ¹ 95 per cent confidence intervals.
²: A lower pole artery was present (30 revascularized and 8 ligated).
³: Ligation of a lower pole artery which could not be revascularized.
Of all the pre-, peri- and postoperative factors analyzed in our study, only acute rejection and delayed graft function were significantly correlated with the occurrence of a urological complication. Our overall urological complication rate was 13%, and our surgical revision rate for urological complications was 6.1%. These results are consistent with recent and larger series10-13. Classically, the two major etiological factors for urological complications after renal transplantation are surgical-technical factors and distal transplant ureteric ischemia. Surgical-technical factors include poor harvesting and ureterocystostomy techniques. The preservation of the periureteral vessels and fat, the reduction of ureteral length, avoiding large incisions in the bladder, avoiding external ureteral compression by the vas deferens, and creating a water-tight urinary anastomosis all decrease the incidence of urological complications14.

In addition, high-dose steroids as were used in the precyclosporine period are associated with an increased urological complication rate15.

Periureteral fat, ureter length, intraoperative problems and various bladder characteristics also influence the occurrence of urological complications. However, as these variables are difficult to quantify consistently in a retrospective study, we were unable to include them in our retrospective analysis as reliable quantification was not possible.

Diabetes was present in 8.3% of our recipients, but it was not correlated with the occurrence of urological complications.

Distal transplant ureter ischemia can occur if circulation to the lower pole is compromised. Our study showed that the presence of a lower pole artery, especially if it could not be revascularized, led to an increased urological complication rate. Because of the small numbers, the lower pole artery failed to reach statistical significance in the multivariate analysis. Despite this, every effort should be made to revascularize the lower pole artery when present.

Ultrasonography and radioisotope scanning are usually the first imaging modalities to be employed in renal transplant dysfunction16,17. If these studies reveal a ureteral leak or obstruction, the insertion of a percutaneous nephrostomy catheter and subsequent antegrade pyelography is a practical way of managing this problem18-20. Although introducing a percutaneous nephrostomy catheter is an important step in this situation, some authors assert that it rarely cures the problem on its own18-20. Our results contradict this, as, in 29 of the 62 patients (47%) with a urological complication, the temporary placement of a percutaneous nephrostomy catheter alone was sufficient to treat it successfully. These stenoses were probably caused by postoperative edema or were a temporary effect of an acute rejection on the ureter. If antegrade pyelography showed the obstruction to be persistent, then we chose to perform the necessary surgical revision. The majority of urological complications occur soon after transplantation. Previous reports have indicated that all urine leakages and
Is selective splinting ureterocystostomy feasible in renal transplantation?

most ureter strictures occur within 1 year after transplantation\textsuperscript{21,22}. In our study, 50\% of all urological complications occurred within 2 weeks and 73\% at 1 month after transplantation.

Some studies have emphasized the role of acute rejection in causing urological complications\textsuperscript{23,24}. Our findings support these results, as acute rejection was also shown to be an independent risk factor for urological complications in our study. It can be speculated that our study shows a correlation between acute rejection and the presence of a delayed graft function, as it is known that the presence of delayed graft function increases the risk of acute rejection\textsuperscript{25}.

Although the presence of a urological complication resulted in considerable morbidity, it had no significant effect on the 1-year graft or patient survival in our study. Van Roijen et al. reported that patients presenting with urological complications may have a higher probability of long-term graft survival because diagnosis of the complication is in itself an indication that they have a functioning graft\textsuperscript{26}.

The proposed benefits of a splinted anastomosis include continuous decompression of the ureter to avoid anastomotic tension, maintenance of the ureter in a more linear alignment to avoid kinking, and protection from ureteral narrowing or postoperative luminal obstruction because of edema or external compression. Disadvantages of the splint are obstruction and migration, stricture of the anastomosis, mucosal erosion causing hematuria, increased postoperative infection risk, ureteral calcification, postoperative pain and the need for an additional intervention necessary to remove a double-J stent. In two recently published meta-analyses of splinted versus nonsplinted ureterocystostomy, the use of a splint significantly reduced the incidence of urological complications\textsuperscript{8,9}. In the meta-analysis of Wilson et al. the data from seven published randomized controlled trials were pooled (total 1154 patients). Routine splinting of the ureterocystostomy reduced the incidence of urological complications significantly (relative risk 0.24, 95\% CI: 0.07–0.77, \(P = 0.02\)) from a median of 7\% of unsplinted anastomosis to 1\% of splinted anastomosis\textsuperscript{8}. The NNT varies between 10 and 30 depending on the experience of the surgeon. However, the use of a splint results in a significantly increased risk of a urinary tract infection when compared with the nonsplinted ureterocystostomy (relative risk 1.49, 95\% CI: 1.04–2.15, \(P = 0.03\)).

As we found the NNT too high to justify a routine splinting policy, we were particularly interested in developing a selective splinting policy to reduce the high NNT to prevent one urological complication. However, our analysis showed that it was not possible to use those risk factors known at the time of performing the ureterocystostomy to introduce a selective splinting policy.

In conclusion, acute rejection and delayed graft function are important risk factors for urological complications after renal transplantation, but other risk factors known at the time of performing the ureterocystostomy cannot be used for implementing a selective splinting ureterocystostomy protocol.
Acknowledgements

The authors thank Prof. D.A. Legemate and Dr M.P. Laguna Pes for comments on the draft manuscript. The following surgeons also performed the operations in this study: Prof. T.M. van Gulik, Dr R. Balm, Dr M.J. Lubbers and Dr H. Garibyan.

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Is selective splinting ureterocystostomy feasible in renal transplantation?


