Effect of ureteric stents on urological infection and graft function following renal transplantation

Jacob A Akoh, Tahawar Rana

Abstract

AIM: To compare urological infections in patients with or without stents following transplantation and to determine the effect of such infections on graft function.

METHODS: All 285 recipients of kidney transplantation at our centre between 2006 and 2010 were included in the study. Detailed information including stent use and transplant function was collected prospectively and analysed retrospectively. The diagnosis of urinary tract infection was made on the basis of compatible symptoms supported by urinalysis and/or microbiological culture. Graft function, estimated glomerular filtration rate and creatinine at 6 mo and 12 mo, immediate graft function and infection rates were compared between those with a stent or without a stent.

RESULTS: Overall, 196 (183 during initial procedure, 13 at reoperation) patients were stented following transplantation. The overall urine leak rate was 4.3% (12/277) with no difference between those with or without stents - 7/183 vs 5/102, \( P = 0.746 \). Overall, 54% (99/183) of stented patients developed a urological infection compared to 38.1% (32/84) of those without stents (\( P = 0.0151 \)). All 18 major urological infections occurred in those with stents. The use of stent (Wald \( \chi^2 = 5.505, P = 0.019 \)) and diabetes mellitus (Wald \( \chi^2 = 5.197, P = 0.023 \)) were found to have significant influence on urological infection rates on multivariate analysis. There were no deaths or graft losses due to infection. Stenting was associated with poorer transplant function at 12 mo.

CONCLUSION: Stents increase the risks of urological infections and have a detrimental effect on early to medium term renal transplant function.

INTRODUCTION

Stents are used to protect the ureter-bladder anastomosis when performing renal transplantation in order to avoid or reduce urological complications\(^1-8\). The insertion of a stent does not eliminate the risk of complications, particularly urinary leak but may alter the approach to managing them\(^6\). Due to immunosuppression, stenting in transplant patients increases the risk of urological or bloodstream infections\(^7,8\). As a result, opinion continues to be divided between those who routinely stent and those who only do so selectively on the basis of clear indications\(^2,9,10-13\). Proponents of selective stenting state that the associated risks are high enough to avoid rou-
tine stenting and advocate that careful surgical technique with selective stenting of problematic anastomoses yields similar results.4,12,13

The key question is to determine what effect the increased risk of urological infection with stenting has on the early and medium term outcome of renal transplantation. This study was carried out to compare the incidence of urological infection in patients with or without stents inserted at transplantation and to determine the effect of urinary tract infections (MUI) in the early post transplantation period on short and medium term graft function.

**MATERIALS AND METHODS**

All recipients of kidney transplantation at the South West Transplant Centre (SWTC), Derriford Hospital, Plymouth between January 2006 and December 2010 were included in the study. Patient data was entered prospectively into the renal computer database (PROTON Information System, Clinical Computing PLC, London, United Kingdom) that was also used for information on patients handed over to other centres for follow up. Patients who developed significant urological complications after hand back to their home units were referred back to the SWTC for management and included in this analysis. Transplant nurses at peripheral centres were contacted to provide information on those patients whose data were incomplete. The duration of follow up ranged from 12 mo to 72 mo.

Patients were managed according to the standard protocol of the SWTC. Immunosuppression comprised basiliximab (induction), tacrolimus (0.1 mg/kg per day), mycophenolic acid (2 g/d) and prednisolone. Antibiotic prophylaxis included a single intravenous dose of aminoglycosin 1.2 g at anaesthetic induction and a daily dose of co-trimoxazole 480 mg for 3 mo. At surgery, a 6-French, 12 cm, double pigtail ureteral stent (Cook Medical) was inserted at the discretion of the operating surgeon to establish internal drainage from the uretero-pelvic junction to the bladder. The transplant nurse practitioner would identify patients requiring stent removal and refer them to the urology nurse practitioners as soon as possible following transplantation. The stent was removed by flexible cystoscopy under local anaesthetic on a day case basis by a urologist. The duration of retention of routinely placed stents was progressively decreased from six weeks (initially) to two weeks in the latter phase of the study. Selectively inserted stents were removed after the duration advised by the transplant surgeon (usually 4-6 wk). In the latter part of the study period, a single intravenous prophylactic dose of antibiotics was administered prior to stent removal - usually gentamicin 3 mg/kg (rounded to the nearest convenient multiple of 40 and a maximum dose of 160 mg). If there were serious difficulties with venous access, the dose was given intramuscularly 30 min before the procedure. A mid stream specimen of urine was sent 48 h prior to removal of stent and this was repeated if blood or protein was present in urine or the patient was symptomatic.

The diagnosis of UTI was made on the basis of compatible symptoms supported by urinalysis and/or microbiological culture. Major urological infections (MUIs) included complicated UTI, pyelonephritis and urosepsis with or without bacteraemia. Delayed graft function (DGF) was defined as requirement for dialysis within the first week of transplantation. Primary non function (PNF) was defined as a graft that never worked or that never allowed the recipient to come off dialysis.

Relevant data including age, type and date of transplant, recognised risk factors for urological complications (stripped ureter, damaged renal arteries/bench surgery, multiple renal arteries, cold ischaemic time greater than 24 h, lower urinary tract obstruction and bladder abnormality) or risk factors for infection such as diabetes, reoperation and peritoneal dialysis associated peritonitis were entered into proforma sheets. This data was then transferred to an Microsoft Excel worksheet and analysed using SPSS 17® for Windows (SPSS Inc, Chicago, IL).

**Statistical analysis**

Early and late graft function, estimated glomerular filtration rate (eGFR) and creatinine (Cr) at 6 mo (Cr6, eGFR6) and 12 mo (Cr12, eGFR12), immediate graft function, graft outcome, infection rates, type of infection and urine leak were compared between those with a stent (ST) or without a stent (WST). Differences between groups were tested by the χ2 statistic. Correlation between duration of stenting, interval to infection after transplantation, number of infection episodes and Cr and eGFR at 6 mo and 12 mo were tested using Pearson’s correlation statistics. Also, the General Linear Modelling multivariate analysis of categorical variables [stent use; type of transplant - donation after circulatory death (DCD), donation after brain death (DBD) or living donation (LD); transplant number - whether first, second or third; diabetes; ureteric reflux; body mass index (BMI) > 30 kg/m²; and early transplant outcome - immediate function, DGF and PNF] affecting urological infection following transplantation was performed. A P value of < 0.05 was taken as significant.

**RESULTS**

A total of 285 renal transplants were performed during the period comprising 181 males (age, mean ± SE: 52.1 ± 1.0 years; median: 53.5 years) and 104 females (age, mean ± SE: 49.2 ± 1.2 years; median: 50.4 years) giving a male to female ratio of 1.7:1. The commonest causes of established renal failure were glomerulonephritis (14.7%), cystic kidney disease (14%), immunoglobulin A nephropathy (13.3%) and diabetic nephropathy (6.7%). The overwhelming majority of transplants (189, 66.3%) were from DCD donors, with living donors LD constituting 28%. Also, 240 of the 285 patients (84%) were undergoing their first transplants whereas 36 (13%) and 9 (3%) were having their second and third transplants respectively. Information about use of antibiotic prophylaxis prior to implantation was unavailable in 23 cases (8.1%)
but of the remaining 262, 86% (226) had appropriate prophylaxis. Ninety seven percent received prophylactic co-trimoxazole for 3 mo after transplantation.

One hundred and two patients (35.8%) did not have a ureteric stent inserted during their initial transplant operation. The indications for stenting in the remaining 183 (64.2%) are shown in Table 1. The demographic and other characteristics of the ST and WST groups are compared in Table 2. Thirteen of the WST group were stented at subsequent re-exploration and re-implantation of the transplant ureter (stenosis/stricture in ten, urine leak in two and negative exploration in one). Five patients in the ST group received a stent at subsequent re-operation for a urological complication. Overall, 196 (68.8%) patients received a stent following renal transplantation, with 159 (81%) of these inserted routinely. The proportion of patients receiving stents at transplantation (irrespective of whether inserted during the initial operation or at re-operation) varied with the type of organ donor (DCD 54.5%, DBD 58.8% and LD 70.9%), the differences were statistically significant - Pearson $\chi^2 = 6.202; df = 2; P = 0.045$. The mean ± SE duration of stenting was 46.99 ± 7.6 d, which was lower for routine than selective indication (39 ± 4.4 d vs 83.4 ± 33.2 d, respectively).

If eight patients with no data regarding urine leak were excluded from analysis, then the overall urine leak rate was 4.3% (12/277). Five of 100 patients (5%) not having a stent inserted during their initial transplant suffered urine leak whereas seven of 177 (4%) in the ST group leaked - the difference in leak rates between the two groups was not statistically significant (Table 2). Similarly, the difference in the distribution of ureteric stenosis or necrosis between groups was not statistically significant (Table 2).

Excluding 18 patients with missing information regarding infection, 49% (131/267) of the patients had infection after transplantation, with the majority (87%) being UTI. Five patients (1.9%) had miscellaneous (non urological) infections. Micro-organisms were isolated in 131 (46%) patients. Infection was caused by multiple organisms in 32% (42/131) but *Escherichia coli* (21%) was the commonest single isolate. Other coliforms amounted to 23%, whereas *Candida* was cultured in 1.5% cases. Overall, 54% (99/183) of ST patients developed a urological infection compared to 38.1% (32/84) of the WST group and the difference was statistically significant ($\chi^2 = 5.900; df = 1; P = 0.0151$). However, with respect to the initial transplant procedure, the difference in infection rates between ST and WST groups was not statistically significant (Table 2). The difference in the distribution of infection types (UTI or MUI) between the ST and WST groups was statistically significant (Yates $\chi^2 = 6.027; df = 1; P = 0.0141$). All 18 MUI (9 with urosepsis, 6 with pyelonephritis and 3 with bacteremia) occurred in those with stents. Ureteric stenting was associated with poorer allograft function at 6 mo and 12 mo (Table 3).

One hundred and eighty three (64.2%) patients achieved immediate allograft function whereas 90 (31.6%) had DGF and 12 (4.2%) had PNF. There was no difference in the rate of DGF between the ST and WST groups (Table 2). By the end of the follow up period, 17 patients had died with a functioning graft and 37 allografts had failed (Figure 1). Although the cause of death was undetermined in six, none of the deaths were directly related to urological infection (cardiac in four, cancer in three, bowel infarction in two, cytomegalovirus infection and trauma in one case respectively.

Infection was more likely to occur in ST patients with DGF (73.7%; 42/57) than in those with immediate allograft function (45%; 54/120) and the difference was statistically significant ($\chi^2 = 12.810; df = 1; P = 0.0003$). Irrespective of stenting, the association between infection and immediate allograft function [41% (71/173)] or DGF [65% (56/86)] was found to be statistically significant (Fisher's exact test, $P = 0.0003$). However, the distribution of UTI and MUI between patients with DGF

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**Table 1** Indications for stent placement during the initial transplant procedure $n$ (%)

| Reason                          | Comments             | n (%)       |
|---------------------------------|----------------------|-------------|
| Routine                         |                      | 159 (86.9)  |
| Ureter related                  | e.g., Stripped ureter| 9 (4.9)     |
| Poor kidney perfusion           |                      | 6 (3.3)     |
| Contracted/thin bladder         | Compliance mismatch  | 3 (1.6)     |
| Technical factors               | e.g., intra-abdominal implantation | 3 (1.6) |
| Ileal conduit                   |                     | 1 (0.5)     |
| Small kidney                    |                      | 1 (0.5)     |
| Long cold ischaemia time (> 24 h) | Concern about size of renal artery | 1 (0.5) |
| Total                           |                      | 183 (99.8)  |

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**Table 2** Comparison of groups with or without stent at initial transplant procedure $n$ (%)

| Parameter                        | Stented group ($n = 183$) | Without stent group ($n = 102$) | $P$ value |
|----------------------------------|---------------------------|----------------------------------|-----------|
| Gender (male)                    | 118 (65)                  | 63 (62)                          | 0.648     |
| Age (yr), mean ± SE              | 52.4 ± 1.0 (53.7)         | 49.1 ± 1.3 (50.6)                | 0.035     |
| Diabetes                         | 31 (17)                   | 13 (13)                          | 0.347     |
| BMI > 30 kg/m$^2$                 | 39 (21)                   | 21 (21)                          | 0.531     |
| Vesico-ureteric reflux           | 11 (6)                    | 14 (14)                          | 0.031     |
| First transplant                 | 151 (83)                  | 89 (87)                          | 0.315     |
| Type of transplant               |                           |                                  |           |
| DCD                              | 111 (61)                  | 78 (77)                          | 0.023     |
| DBD                              | 12 (7)                    | 5 (5)                            |           |
| LD                               | 60 (33)                   | 19 (19)                          |           |
| Delayed graft function           | 35 (20)                   | 35 (34)                          | 0.595     |
| Septin                           | 173 (99)                  | 91 (93)                          | 0.002     |
| Urine leak                       | 7 (4)                     | 5 (5)                            | 0.746     |
| Ureter stenosis                  | 6 (3)                     | 7 (7)                            | 0.359     |
| Ureter necrosis                  | 1 (0.5)                   | 0 (0)                            |           |
| Infection                        | 91 (53)                   | 40 (42)                          | 0.075     |
| Operation-infection interval (d) | mean ± SE                 | 28.1 ± 3.7                       | 0.451     |
| Median                           | 10.5                      | 11.0                             |           |

$^1$Median age in parenthesis. Figures in parenthesis indicate percentages (except for age), corrected for number with relevant data. BMI: Body mass index; DCD: Donation after circulatory death; DBD: Donation after brain death; LD: Living donation.
and immediate function were not statistically significant (Yate’s $\chi^2 = 0.054, df = 1, P = 0.8165$). Only the use of stent (Wald $\chi^2 = 5.505, df = 1, P = 0.019$), diabetes mellitus (Wald $\chi^2 = 5.197, df = 1, P = 0.023$), and a BMI > 30 kg/m² (Wald $\chi^2 = 3.801, df = 1, P = 0.051$) were shown to have significant influence on urological function rates on multivariate analysis.

Stents inserted for $\leq 30$ d were associated with a higher infection rate of 58.5% (49/84) compared to a rate of 48% (47/98) for those with stents longer than 30 d ($\chi^2 = 1.953, df = 1, P = 0.163$). The median time to infection in the ST group was 10.5 d (Table 2) with 75% of all infection episodes in their ST group. Though there were no graft losses or patient deaths secondary to MUIs and the rate of DGF was significantly lower than the 12% reported by Ashraf et al.[16] and Ranganathan et al.[17] not only showed a much higher infection rate in the stented group (76% vs 45% and 71% vs 39%, respectively), but also noted that patients who suffered a UTI while they had a stent in place were more likely to get further episodes of UTI after stent removal. In our study, all eighteen cases of MUI occurred in the stented group. This is similar to the finding by Branitz et al.[18] of all 10 episodes of severe infection in their ST group. Though there were no graft losses or patient deaths secondary to MUIs and the rate of DGF was significantly different to other UTIs, MUIs were associated with poorer transplant function at 12 mo (Table 3). In a Cochrane review of seven randomised controlled trials (1154 patients), Wilson et al.[19] found an increased risk of UTIs in stented patients (RR = 1.49, 95%CI: 1.04-2.15; with two kidneys lost to infections), but noted that this effect was neutralised by co-trimoxazole 480 mg daily. Argani et al.[20] also demonstrated the role of prophylactic cotrimoxazole in reducing the incidence of UTI in stented patients. Prophylaxis with co-trimoxazole is standard practice at the author’s centre (99% of the ST group received it) but the optimal duration of stenting was not statistically significant (Table 3).

**DISCUSSION**

This observational study demonstrates the higher risk of infection in patients with ureteric stenting compared to those without (54% vs 38%) during renal transplantation - rates that are similar to other reports[7,8,12,14] but much higher than the 12% reported by Ashraf et al.[16], Branitz et al.[18] and Ranganathan et al.[17] not only showed a much higher infection rate in the stented group (76% vs 45% and 71% vs 39%, respectively), but also noted that patients who suffered a UTI while they had a stent in place were more likely to get further episodes of UTI after stent removal. In our study, all eighteen cases of MUI occurred in the stented group. This is similar to the finding by Branitz et al.[18] of all 10 episodes of severe infection in their ST group. Though there were no graft losses or patient deaths secondary to MUIs and the rate of DGF was significantly lower than the 12% reported by Ashraf et al.[16] and Ranganathan et al.[17] not only showed a much higher infection rate in the stented group (76% vs 45% and 71% vs 39%, respectively), but also noted that patients who suffered a UTI while they had a stent in place were more likely to get further episodes of UTI after stent removal. In our study, all eighteen cases of MUI occurred in the stented group. This is similar to the finding by Branitz et al.[18] of all 10 episodes of severe infection in their ST group. Though there were no graft losses or patient deaths secondary to MUIs and the rate of DGF was significantly different to other UTIs, MUIs were associated with poorer transplant function at 12 mo (Table 3). In a Cochrane review of seven randomised controlled trials (1154 patients), Wilson et al.[19] found an increased risk of UTIs in stented patients (RR = 1.49, 95%CI: 1.04-2.15; with two kidneys lost to infections), but noted that this effect was neutralised by co-trimoxazole 480 mg daily. Argani et al.[20] also demonstrated the role of prophylactic cotrimoxazole in reducing the incidence of UTI in stented patients. Prophylaxis with co-trimoxazole is standard practice at the author’s centre (99% of the ST group received it) but the optimal duration of stenting was not statistically significant (Table 3).

The optimal duration of stenting in renal transplantation is not known. In this study the average duration for stenting over the period under consideration was 46 d. Although the duration of stenting did not significantly correlate with the risk of infection and had no statistically significant impact on Cr levels at 6 and 12 mo in our study, based on a median time to infection of 10.5 d, it would seem reasonable to remove all stents by 2 wk after insertion. This approach is similar to Verma et al.[21]...
A study of this nature has several limitations. The retrospective nature of this study limits its usefulness somewhat, but all the data were collected prospectively and recorded in a designated renal electronic database. In addition there were some gaps in the data, especially in the length of hospital stay, readmission rate, and the incidence of UTI prior to transplantation. This is partly due to the loss of patients to follow up and despite exhaustive efforts to individually chase all cases, data was unavailable from some of the outlying hospitals in the fairly large region covered by our centre. Also, it was not possible to determine the quantitative effect of infection on length of hospital stay or readmissions to hospital.

Notwithstanding the retrospective nature of this study, stents increase the risks of urological infections and appear to have a detrimental effect on early to medium term renal transplant function. Whether stents are used routinely or selectively, there is need to remove them early (<2 wk) in order to reduce the risk of infection.

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BACKGROUND

Stents are used to protect the joining between the transplant ureter and the recipient’s bladder when performing kidney transplantation in order to avoid or reduce complications. It is thought that using a stent in this way does not eliminate the risk of complications, particularly urinary leak may in fact increase the risk of urological or blood stream infections. As a result, opinion continues to be divided between those who routinely stent and those who only do so selectively on the basis of clear indications.

RESEARCH FRONTIERS

There are several reports on the effect of ureter stenting for kidney transplant recipients but the key issues such as how long it should be retained in the body before removal, its effect on kidney function remain unanswered. There are also no well conducted randomised controlled trials to assess the effect of stents.

INNOVATIONS AND BREAKTHROUGHS

Proponents of selective stenting state that the associated risks are high enough to avoid routine stenting and advocate that careful surgical technique with selective stenting of problematic anastomoses yields similar results. The key question is to determine what effect the increased risk of urological infection with stenting has on the early and medium term outcome of renal transplantation. In the present study, authors compared the incidence of urological infection in patients with or without stents inserted at transplantation and report the effect of urinary tract infections (UTIs) in the early post transplantation period on short and medium term graft function.

APPLICATIONS

This study suggests that stents increase the risks of urological infections and have a detrimental effect on early to medium term kidney transplant function. It calls for a controlled trial to determine the optimum duration of retaining stents following insertion.

TERMINOLOGY

A ureteric stent used for the purpose of kidney transplantation is a 6-French, 12 cm, double pigtail ureteral plastic tubing inserted to establish internal drainage from the ureter in to the bladder. The diagnosis of UTI was made on the basis of compatible symptoms such as discomfort during urination, urinary discharge, lower abdominal pain and fever supported by findings on urine strip test and/or microbiological culture. Major urological infections included complicated UTI.
pyelonephritis (infection extending to the kidneys) and urosepsis with or without bacteremia (bacteria multiplying in the blood stream).

**Peer review**

Although there are minor recommendations that would be good for the authors if they revise the manuscript accordingly, the manuscript can also be published in this original form as well given the nature of the study which is not randomized.

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