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[Intervention Review]

Early versus late ureteric stent removal after kidney transplantation

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ABSTRACT

Background

Kidney transplantation is the treatment of choice for patients with end-stage kidney disease. In a previous review we concluded that the routine use of ureteric stents in kidney transplantation reduces the incidence of major urological complications (MUC). Unfortunately, this reduction appears to lead to a concomitant rise in urinary tract infections (UTI). For kidney recipients UTI is now the commonest post-transplant complication. This represents a considerable risk to the immunosuppressed transplant recipient, particularly in the era of increased immunologically challenging transplants. There are a number of different approaches taken when considering ureteric stenting and these are associated with differing degrees of morbidity and hospital cost.

Objectives

This review aimed to look at the benefits and harms of early versus late removal of the ureteric stent in kidney transplant recipients.

Search methods

We searched the Cochrane Kidney and Transplant Specialised Register up to 27 March 2017 through contact with the Information Specialist using search terms relevant to this review. Studies contained in the Specialised Register are identified through search strategies specifically designed for CENTRAL, MEDLINE, and EMBASE; handsearching conference proceedings; and searching the International Clinical Trials Register Search Portal and ClinicalTrials.gov.

Selection criteria

All RCTs and quasi-RCTs were included in our meta-analysis. We included recipients of kidney transplants regardless of demography (adults or children) or the type of stent used.

Data collection and analysis

Two authors reviewed the identified studies to ascertain if they met inclusion criteria. We designated removal of a ureteric stent before the third postoperative week (< day 15) or during the index transplant admission as "early" removal. The studies were assessed for quality using the risk of bias tool. The primary outcome of interest was the incidence of MUC. Further outcomes of interest were the incidence of UTI, idiosyncratic stent-related complications, hospital-related costs and adverse events. A subgroup analysis was performed examining the difference in complications reported depending on the type of ureteric stent used; bladder indwelling (BI) versus per-urethral (PU). Statistical analyses were performed using the random effects model and results expressed as relative risk (RR) with 95% confidence intervals (CI).

Main results

Five studies (1127 patients) were included in our analysis. Generally the risk of bias of the included studies was judged low or unclear; they addressed the research question and utilised a prospective randomised design. It is uncertain whether early stent removal verus late stent removal improved the incidence of MUC (5 studies, 1127 participants: RR 1.87, 95% CI 0.61 to 5.71; I^2 = 21%; low certainty evidence). The incidence of UTI may be reduced in the early stent removal group (5 studies, 1127 participants: RR 0.49 95% CI 0.30 to 0.81; I^2 = 59%; moderate certainty evidence). This possible reduction in the UTI incidence was only apparent if a BI stent was used, (3 studies, 539 participants, RR 0.45 95% CI 0.29 to 0.70; I^2 = 13%; moderate certainty evidence). However, if an externalised PU stent was used there was no discernible difference in UTI incidence between the early and late group (2 studies, 588 participants: RR 0.60 95% CI 0.17, 2.03; I^2 = 83%; low certainty evidence). Data on health economics and quality of life outcomes were lacking.

Authors' conclusions

Early removal of ureteric stents following kidney transplantation may reduce the incidence of UTI while it uncertain if there is a higher risk of MUC. BI stents are the optimum method for achieving this benefit.

PLAIN LANGUAGE SUMMARY

Early versus late ureteric stent removal after kidney transplantation

What is the issue?
The ureter drains urine from the kidney into the bladder and has to be reconnected during kidney transplantation. To protect this new connection the operating surgeon places a plastic stent inside the ureter to help it heal. Routinely this stent would be left in place for up to three months. However, this is associated with an increased risk of urine infection which can be high-risk for transplant recipients whose immune system is suppressed through anti-rejection medication. If this stent could be removed earlier then the risk of infection may be reduced but would it be associated with major urological complications e.g. urine leak or obstruction.

What did we do?
This study was designed to review all the previously published research in this area to determine the answer to this question. Five studies including 1097 patients were identified.

What did we find?
It is uncertain whether the number of major urological complications were different in those patients whose stent was removed early (less than 15 days post-operatively), when compared with those removed later (more than 15 days post-operatively). The number of patients suffering from a urinary tract infection may be less in the early removal group - especially if the stent was not exposed to the external environment. The studies identified for this review were generally of poor quality.

Conclusions
It is uncertain whether a bladder indwelling ureteric stent that is removed early following kidney transplantation reduces the risk of complications, however it may prevent urine tract infections.

Summary of findings for the main comparison. Early versus late ureteric stent removal after kidney transplantation

Early versus late ureteric stent removal after kidney transplantation

Patient or population: kidney transplant recipients
Intervention: early ureteric stent removal
Comparison: late ureteric stent removal

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Risk with late removal	Risk with early removal			
Major urological complications: all stents follow-up range: 3 to 12 months	Study population		RR 1.87 (0.61 to 5.71)	1127 (5)	⊕⊕⊕⊕ LOW [1]
	12 per 1,000	23 per 1,000 (7 to 69)			
Major urological complications: bladder indwelling stents follow-up range: 3 months to 12 months	Study population		RR 1.67 (0.52 to 5.36)	539 (3)	⊕⊕⊕⊕ LOW [1]
	15 per 1,000	24 per 1,000 (8 to 79)			
Major urological complications: per-urethral stents follow-up range: 3 months to 12 months	Study population		RR 1.51 (0.03 to 74.45)	588 (2)	⊕⊕⊕⊕ LOW [1]
	10 per 1,000	15 per 1,000 (0 to 732)			
Urinary tract infection: all stents	Study population		RR 0.49 (0.30 to 0.81)	1126 (5)	⊕⊕⊕⊖ MODERATE [1 2]
	185 per 1,000	91 per 1,000 (56 to 150)			
Urinary tract infection: bladder indwelling stents	Study population		RR 0.45 (0.29 to 0.70)	539 (3)	⊕⊕⊕⊖ MODERATE [1 2]
	209 per 1,000	94 per 1,000 (61 to 146)			
Urinary tract infection: per-urethral stents	Study population		RR 0.60 (0.17 to 2.03)	587 (2)	⊕⊕⊖⊖ LOW [1 2]
	164 per 1,000	98 per 1,000			

		(28 to 333)			

*__The risk in the intervention group__ (and its 95% CI) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] All studies were unblinded, however, this was unavoidable given the nature of the intervention. The majority of studies provided minimal information on processes of randomisation and allocation
[2] Inconsistent definition and variable reporting of urinary tract infection across included studies

BACKGROUND

Description of the condition

Kidney transplantation is the treatment of choice for patients with end-stage kidney disease (ESKD). Over the last four decades, surgical techniques have been refined and the majority standardised. In current surgical practice there remains very little variation between centres and surgeons in most aspects of kidney transplant surgery. The anastomosis created between the donor transplant ureter and the bladder remains one aspect of surgical practice where techniques continue to evolve (Nicholson 1991). In a previous review we focused on the role of the ureteric stent and its function in reducing major urological complications (MUC), urinary leak or fistula and ureteric stenosis (Wilson 2013). We concluded that the universal use of stents reduces the incidence of MUC from between 7% and 9%, to 1.5%. Unfortunately, this reduction appears to lead to a concomitant rise in urinary tract infections (UTI) which is offset by the use of antibiotics. In addition, stents are associated with idiosyncratic complications (migration, malposition, haematuria, encrustation, irritative bladder symptoms, and may be forgotten) (Bardapure 2014). More recently there have also been some isolated reports of an association between the use of ureteric stents and the incidence of an opportunistic viral pathogen - BK virus (Siparsky 2011), consequent to its negative effects on distal ureteric motility.

Description of the intervention

Ureteric stents used in transplantation can be of different lengths (12 cm to 36 cm), calibres (5F to 7F) and designs (percutaneous (PC), per-urethral (PU), or bladder indwelling (BI)). Most centres have traditionally placed BI stents for a period of four weeks to three months before removal in an operating room using a flexible cystoscope under local anaesthetic, or if it is combined with another procedure such as haemodialysis fistula ligation, under general anaesthetic (Wilson 2013). This approach necessitates a further admission to hospital and hospital costs.

Several approaches have been suggested to maximise the benefit of stents and reduce morbidity, costs or both. One option is to remove the stent before the patient leaves hospital (a period of only one or two weeks) (Indu 2012; Thiyagarajan 2012), another is to use a PC or PU stent which can be removed in the ward or outpatient clinic (Olsburgh 2010). A further option is to tie the BI stent to the urinary catheter (Morris-Stiff 1998) and remove them simultaneously (week 1). On the basis of these descriptions and standard practices we arbitrarily designated removal of a ureteric stent before the third postoperative week (< day 15) or during the index transplant admission as "early" removal.

How the intervention might work

Ureteric stents seem to reduce MUC in two phases. At initial placement ureteric stents help the surgeon by reducing anatomical kinking and delineating the lumen to aid in suture placement. After implantation, inflammation and oedema can cause obstruction at the anastomosis, and the stent helps urine drain from the kidney into the bladder, reducing intra-ureteric pressure. This may also aid in preventing Ischaemic-related necrosis of the distal ureter and subsequent urine leak.

However, as a foreign body, ureteric stents rapidly become colonised with a biofilm of micro-organisms that may predispose to UTI in the recipient bladder and pyelonephritis due to back flow of urine into the kidney pelvis during bladder detrusor contraction (Waters 2008). In this respect, early removal with the urinary catheter may be considered a significant advantage. PC stents, or PU stents that run beside the urinary catheter, offer the advantage of being able to monitor transplant urine output independently of the native kidney output, thus differentiating between immediate and delayed graft function. This is certainly useful for research studies on ischaemic-reperfusion injury, but of dubious clinical significance in the short term.

Why it is important to do this review

Live donor kidney transplantation is becoming more widespread as the waiting time for cadaveric transplantation lengthens. As a result ABO-incompatible transplantation is more common and recipients treated with higher intensity immunosuppression are at increased risk of peri-operative complications. In one registry review of patients undergoing live donor kidney transplantation, UTI was the most common complication, with an incidence over 30% (Montgomery 2012). Some surgeons believe that the benefit of ureteric stents is only within the first one or two weeks after transplantation, and that leaving them in situ for longer leads to the potential for stent-related morbidity such as UTI, the possibility of being forgotten, and the risk of severe urosepsis on removing a late encrusted stent at four to six weeks (Bardapure 2014). Other clinicians believe that ischaemic necrosis or stenosis of the ureter is a delayed event and that an indwelling stent can prevent these complications only by being left for longer periods of time.

This review attempted to dissect differences in ureteric morbidity by meta-analysing data from studies differentiated by the length of time stents were left *in situ*.

OBJECTIVES

This review aimed to look at the benefits and harms of early (before the third postoperative week (< day 15) or during the index transplant admission as "early" removal) versus late removal of the ureteric stent in kidney transplant recipients.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) and quasi-RCTs (RCTs in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) looking at timing of ureteric stent removal in kidney transplantation.

Types of participants

Inclusion criteria

We included recipients of kidney transplants regardless of demography (adults or children) or the type of stent placed. To adequately assess studies the protocols should include data on the allocation and randomisation status of patients or kidneys with complex urinary tracts (bladder diversion, duplex ureters, en bloc transplants). Multivisceral recipients in whom a kidney is combined with other organs (e.g. liver or pancreas) are also included.

Exclusion criteria

Studies including patients with stenting of ileal conduits or continent urinary diversions were excluded.

Types of interventions

We investigated the timing of stent removal (early versus late) after kidney transplantation. Ureteric stents used in transplantation can be of different lengths (12 cm to 36 cm), calibres (5F to 7F) and designs (PC, PU, BI) (Wilson 2013). This review addressed the question of whether the stent can be removed sooner and reduce morbidity as well as associated hospital costs. We have also attempted to address the following questions.

1. PC versus BI stents
2. PU versus PC stents
3. BI versus PU stents

Types of outcome measures

MUC and UTI are the most important outcomes relevant to this review. MUC is a post-operative surgical complication usually associated with the vesicoureteric anastomosis. MUC is defined as any urological complication arising within the first 6 months following kidney transplantation that requires an intervention or re-operation e.g. urinary obstruction, leak, fistula or stenosis. This includes temporary placement of nephrostomy. We also considered:

1. Stent-related complications (e.g. irritation, migration, malposition, haematuria, encrustation, irritative bladder symptoms, forgotten stents)
2. Hospital-related costs including hospital stay, re-operation, surgical re-implantation
3. Adverse events related to stent removal (urosepsis, haematuria, rare graft loss, BK virus nephropathy)
4. Graft and patient survival.

Primary outcomes

The primary outcomes of importance were MUC and UTI incidence; and for all included studies, this was the minimum data set accepted.

Secondary outcomes

The secondary outcomes were stent-related complications, hospital-related costs and adverse events related to stent removal. The concept of treatment failure is also relevant, where an operatively placed PC or PU stent is replaced with a BI stent during the operation

Search methods for identification of studies

Electronic searches

We searched the Cochrane Kidney and Transplant Specialised Register up to 27 March 2017 through contact with the Information Specialist using search terms relevant to this review. The Cochrane Kidney and Transplant Specialised Register contains studies identified from several sources.

1. Monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL)
2. Weekly searches of MEDLINE OVID SP
3. Handsearching of kidney-related journals and the proceedings of major kidney conferences
4. Searching of the current year of EMBASE OVID SP
5. Weekly current awareness alerts for selected kidney and transplant journals
6. Searches of the International Clinical Trials Register (ICTRP) Search Portal and ClinicalTrials.gov.

Studies contained in the Specialised Register are identified through search strategies for CENTRAL, MEDLINE, and EMBASE based on the scope of Cochrane Kidney and Transplant. Details of these strategies, as well as a list of handsearched journals, conference proceedings and current awareness alerts, are available in the Specialised Register section of information about Cochrane Kidney and Transplant.

See Appendix 1 for search terms used in strategies for this review.

Searching other resources

1. Reference lists of review articles, relevant studies and clinical practice guidelines.
2. Letters seeking information about unpublished or incomplete studies to investigators known to be involved in previous studies.

Data collection and analysis

Selection of studies

The search strategy described was used to obtain titles and abstracts of studies that were relevant to the review. The titles and abstracts were screened independently by two authors, who discarded studies that were not applicable; however studies and reviews that included relevant data or information on studies were retained initially. Two authors independently assessed retrieved abstracts and, if necessary the full text, of these studies to determine which studies satisfied the inclusion criteria.

Data extraction and management

Data extraction was carried out independently by two authors using standard data extraction forms. There were no non-English language studies. Where more than one publication of one study existed, reports were grouped together and the publication with the most complete data used in the analyses. Where relevant outcomes were only published in earlier versions these data was used. Any discrepancy between published versions has been highlighted.

Assessment of risk of bias in included studies

The following items were independently assessed by two authors using the risk of bias assessment tool (Higgins 2011) (see Appendix 2) and depicted graphically using the RevMan "Risk of bias" tools.

- Was there adequate sequence generation (selection bias)?
- Was allocation adequately concealed (selection bias)?
- Was knowledge of the allocated interventions adequately prevented during the study?
  - Participants and personnel (performance bias)
  - Outcome assessors (detection bias)
- Were incomplete outcome data adequately addressed (attrition bias)?

- Are reports of the study free of suggestion of selective outcome reporting (reporting bias)?
- Was the study apparently free of other problems that could put it at a risk of bias?

Measures of treatment effect

For dichotomous outcomes (MUC, UTI) results are expressed as risk ratio (RR) with 95% confidence intervals (CI). There were no comparative meta-analysis data using continuous scales of measurement.

Unit of analysis issues

We did not encounter any specific unit of analysis issues; specifically no studies using cluster randomisation or cross-over allocation.

Dealing with missing data

Any further information required from the original author was requested by written correspondence (e.g. emailing corresponding author/s) and any relevant information obtained in this manner was to be included in the review. Evaluation of important numerical data such as screened, randomised patients as well as intention-to-treat, as-treated and per-protocol population was carefully performed. Attrition rates, for example drop-outs, losses to follow-up and withdrawals were investigated. Issues of missing data and imputation methods (for example, last-observation-carried-forward (LOCF)) was to be critically appraised (Higgins 2011). Due to the paucity of data across multiple comparisons "missing data" computations were not considered appropriate.

Assessment of heterogeneity

We first assessed the heterogeneity by visual inspection of the forest plot. Heterogeneity was then analysed using a Chi^2 test on N-1 degrees of freedom, with an alpha of 0.05 used for statistical significance and with the I^2 test (Higgins 2003). A guide to the interpretation of I^2 values is as follows.

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity.

The importance of the observed value of I^2 depends on the magnitude and direction of treatment effects and the strength of evidence for heterogeneity (e.g. P-value from the Chi^2 test, or a confidence interval for I^2) (Higgins 2011).

Assessment of reporting biases

Funnel plots were to be used to assess for the potential existence of small study bias, however there were insufficient studies identified to do this (Higgins 2011).

Data synthesis

Data were pooled using the random-effects model, but the fixed-effect model was also used to ensure robustness of the model chosen and susceptibility to outliers.

Subgroup analysis and investigation of heterogeneity

Subgroup analysis was used to explore possible sources of heterogeneity, for example, type of solid organ transplanted and study quality. Heterogeneity among participants could be related to age, gender, co-morbidities and underlying diseased organ pathology. Heterogeneity in treatments could be related to the type of stent, route of insertion, duration of placement, antibiotic regime, or mechanism of removal.

Adverse effects were tabulated and assessed with descriptive techniques, as they were likely to be different for the various techniques used. Where possible, the risk difference with 95% CI was to be calculated for each adverse effect, either compared to long term stent or to another stent technique. If enough studies were identified we planned to investigate the following clinically relevant subgroup analyses by technique:

- PC versus BI stents
- PU versus PC stents
- BI versus PU stents

Sensitivity analysis

We performed sensitivity analyses in order to explore the influence of the following factors on effect size.

- Repeating the analysis excluding unpublished studies;
- Repeating the analysis taking account of risk of bias, as specified above;
- Repeating the analysis excluding any very long or large studies to establish how much they dominate the results;
- Repeating the analysis excluding studies using the following filters: diagnostic criteria, language of publication and country.

'Summary of findings' tables

We have presented the main results of the review in 'Summary of findings' tables. These tables present key information concerning the quality of the evidence, the magnitude of the effects of the interventions examined, and the sum of the available data for the main outcomes (Schünemann 2011a). The 'Summary of findings' tables also include an overall grading of the evidence related to each of the main outcomes using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach GRADE 2008. The GRADE approach defines the quality of a body of evidence as the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest. The quality of a body of evidence involves consideration of within-trial risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias (Schünemann 2011b). We presented the following outcomes in the Summary of findings for the main comparison.

- Incidence of MUC
  - BI stents
  - PU stents
- Incidence of UTI
  - BI stents
  - PU stents

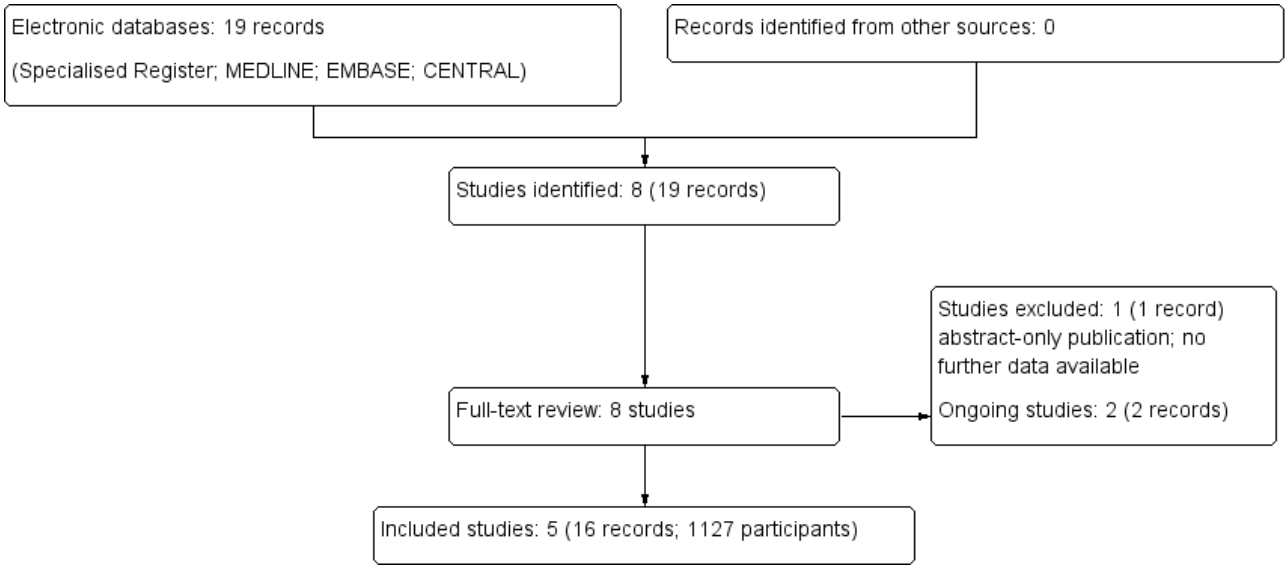
RESULTS

Description of studies

Results of the search

After searching the Specialised Register we identified 19 records. Five studies (16 records) were included (Gunawansa 2011; Huang 2012; Indu 2012; Parapiboon 2012; TrUST 2017), one study (one record) was excluded (Yari 2014), and two ongoing studies were identified (ACTRN12610000349044; ISRCTN51276329). These ongoing studies will be assessed in a future update of this review (Figure 1). Three of the five authors were contacted for further information regarding study design and results, one author responded to our enquiries.

Figure 1. Flow chart of study selection



Included studies

Five RCTs were included in the study with a total of 1127 patients. The studies were heterogeneous in nature, including living and deceased donors, adults and children, and varying definitions of what was defined as 'early' stent removal. This is summarised in detail in the Characteristics of included studies.

Participants

The 1127 patients in the analysis included adult and paediatric kidney transplant recipients. The majority of studies included only adults, while TrUST 2017 included both adults and children. The mean age was 40.4 years in the early removal group and 42.2 years in the late removal group. The type of donor varied: Indu 2012 and Gunawansa 2011 included only live donor recipients; Huang 2012 included only deceased donors; and Parapiboon 2012 and TrUST 2017 included both live and deceased donors. All live donor nephrectomies were laparoscopic.

Interventions

All studies utilised prophylactic double-J ureteric stents placed intraoperatively. Three studies (Indu 2012; Huang 2012; Parapiboon 2012) preferred the BI stent technique; the stent was removed by flexible cystoscopy at the defined post-operative date. Two studies (Gunawansa 2011; TrUST 2017) used the PU stent technique; the early removal participants had the stent anchored to the urinary catheter intraoperatively and removed simultaneously on day 7 post-operatively. The participants in the control arm of these studies received a standard BI stent. The definition of early removal varied considerable between studies; the majority of studies termed early removal at day 7 post-transplant. However, Huang 2012 study included early removal up to day 21. Unusually, the length of stay in this study was longer than routine, around 3 to 4 weeks. Equally, the author's definition of early removal was longer than our original, day 21 compared to day 15. Despite this discrepancy with our protocol we decided to include this study in the meta-analysis as the early stent removal time was comparable bearing in mind the relatively increased length of stay and the "intention to treat" fitted with our research question.

Outcomes

To investigate for MUC routine imaging (DTPA or ultrasound) was performed by two of the five studies (Indu 2012; TrUST 2017). The other studies investigated for the presence of a MUC if clinically indicated. A UTI was diagnosed based on the presence of bacteriuria on regular routine urine sampling in four studies (Indu 2012; Huang 2012; Parapiboon 2012; TrUST 2017) irrespective of symptoms. The remaining study (Gunawansa 2011) did not describe this approach and did not respond to our request for further information. The more idiosyncratic symptoms caused by ureteric stents (e.g. haematuria, encrustation, migration and irritation) were evaluated by two studies (Huang 2012; TrUST 2017). TrUST 2017 did a more in-depth analysis on participants quality of life and health status as a result of early stent removal using two separate validated questionnaires. The potential cost-effective benefits of early stent removal was analysed by Parapiboon 2012.

In summary, the study designs were heterogeneous with varying definitions of early or late stent removal. There was disparity in the type of donor, recipient and length of follow up. Overall studies were of an appropriate randomised controlled design comparing early with late ureteric stent removal. The nature

to which the studies focused on our primary outcome, major urological outcomes, varied but all identified this as an important factor for investigation.

Excluded studies

One study was excluded (Yari 2014). This study was excluded as only an abstract was available with very limited information regarding the number of patients in each of the three intervention arms therefore making analysis impossible. The authors did not respond to our attempts at contact for further information.

Risk of bias in included studies

There was a moderate degree of bias across all included studies attributed to varying sources. It is unclear how many studies made an attempt to formally randomise patients using appropriate computer programs and sealed allocation as most studies did not provide any information on these processes. As expected none of the studies attempted to blind participants or personnel to the intervention or to the outcome assessment. The majority of studies detailed complete follow-up of all participants involved in study, however, only one study include a CONSORT flow diagram (TrUST 2017). There were few published protocols of the studies available for comparison with published data therefore attributing the degree of reporting bias was problematic (Figure 2; Figure 3).

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

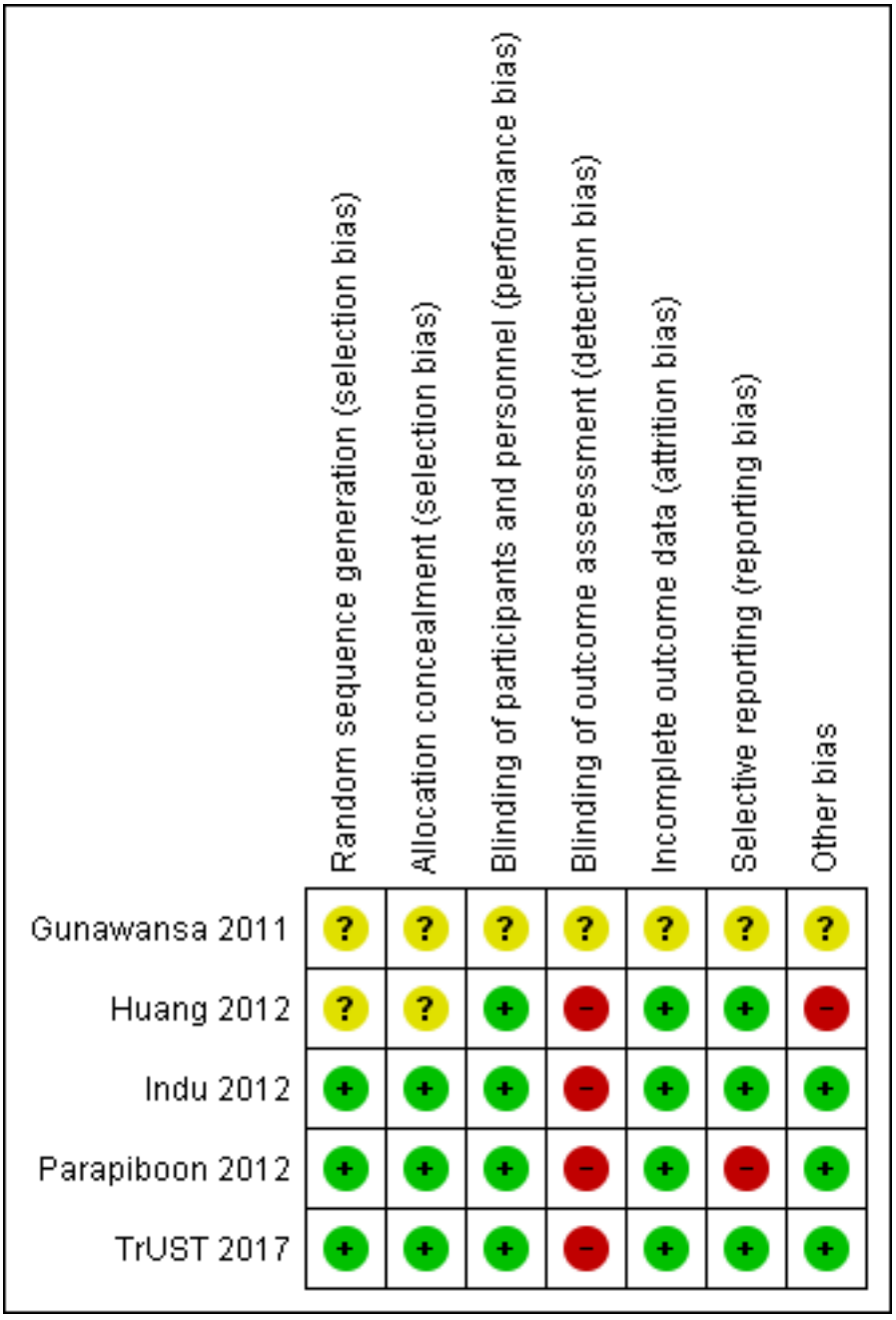
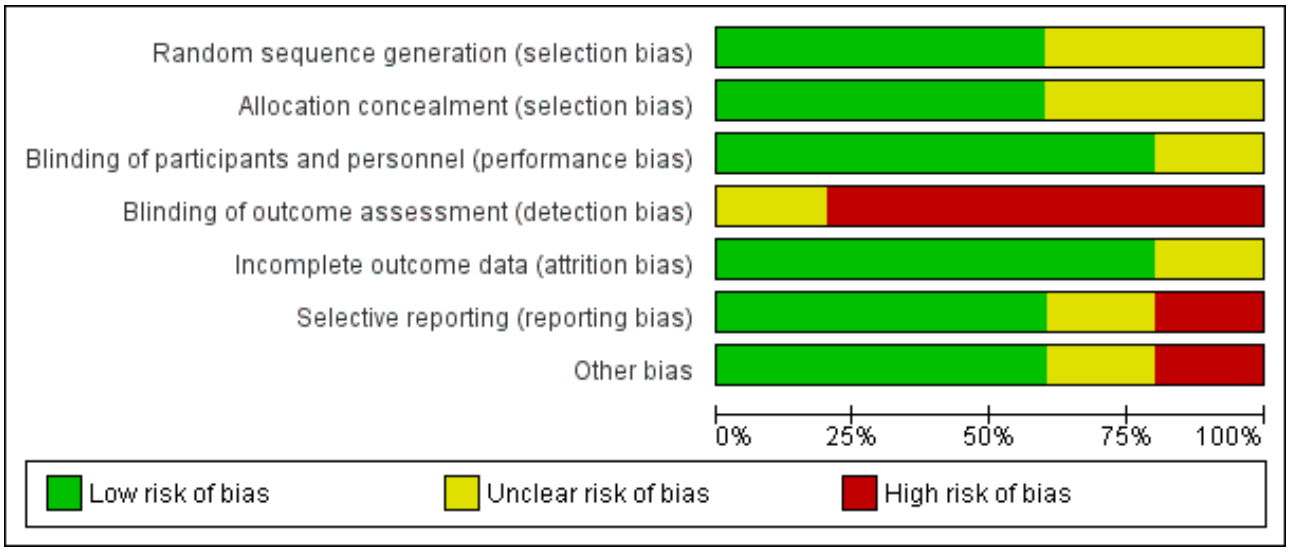


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

Gunawansa 2011 and Huang 2012 contained no information and did not respond to further requests for information regarding randomisation and allocation. Three studies (Indu 2012; Parapiboon 2012; TrUST 2017) describe a robust randomisation process.

- Indu 2012 randomised using computer-generated random numbers, placed into sealed opaque envelopes that were opened on day 7 after transplant by nurses on the ward and determined the allocation to either intervention arm. any participant who developed a leak, delayed graft function, or rejection prior to randomisation on day 7 was excluded. Both groups were receiving a BI stent and were not yet randomised to a particular arm therefore these exclusion criteria, although initially appearing unusual actually have no bias effect on outcome.
- Parapiboon 2012 described a computer-generated block of 4 randomisation process, with allocation concealment by sealed opaque envelopes.
- TrUST 2017 utilised an online randomisation program which was block stratified for age with randomly varying block sizes. Allocation was revealed to clinicians at the time of randomisation.

Blinding

As expected, none of the studies blinded participants or personnel to their allocated intervention. Equally, none of the studies attempted to blind personnel undertaking outcome assessments. This may represent a high risk area for detection bias as those clinicians caring for participants who were known to still have a ureteric stent in situ may have been more concerned about the risk of UTI and therefore sent urine samples more frequently leading to over diagnosis and treatment of asymptomatic bacteriuria.

Incomplete outcome data

Follow-up of participants in the included studies was complete for four studies (Huang 2012; Indu 2012; Parapiboon 2012; TrUST 2017). In these studies all patients were accounted for, however, only TrUST 2017 included a CONSORT diagram. Gunawansa 2011 had limited information available from the published abstracts and the authors did not respond to requests for further information.

Selective reporting

The majority of studies included did not have published study protocols available for comparison. TrUST 2017 published a protocol and it appears they have fully reported on all anticipated outcomes. Huang 2012 and Indu 2012 fully reported all outcomes. Gunawansa 2011 had limited information available based from the published abstracts and the author did not respond to requests for further information. Parapiboon 2012 did not report in detail the MUC encountered. These consisted of two patients in each intervention group, but there is no further detail as to the nature of this complication or what they deem to be a MUC. This study has published two papers; one focusing on the incidence of bacteriuria and the other a cost-benefit analysis. The incidence of UTI data is very detailed and well reported as this was their primary outcome of interest. MUC were not a priority in this study and as such there is very little detail reported on complications encountered potentially resulting in a degree of reporting bias.

Other potential sources of bias

Huang 2012 was judged to be at high risk of other potential bias due to the very long length of stay which may be associated with an increased risk of nosocomial infection. Three studies appeared to be free of other potential sources of bias (Indu 2012; Parapiboon 2012; TrUST 2017), and Gunawansa 2011 was judged unclear as there was insufficient information reported in the conference abstracts.

Effects of interventions

See: **Summary of findings for the main comparison** Early versus late ureteric stent removal after kidney transplantation

Major urological complications

It is uncertain whether early versus late stent removal makes any difference to MUC (Analysis 1.1 (5 studies, 1127 participants): RR 1.87, 95% CI 0.61 to 5.71; I^2 = 21%; low certainty evidence). Heterogeneity between studies was deemed to be low.

There was little or no difference in MUC when either BI stents (Analysis 1.1.1 (3 studies, 539 participants): RR 1.67, 95% CI 0.52 to 5.36; participants = 539; studies = 3; I^2 = 0%) or PU stents (Analysis 1.1.2 (2 studies, 588 participants): RR 1.51, 95% CI 0.03 to 74.45; participants = 588; studies = 2; I^2 = 78%) where used (test for subgroup differences: Chi^2 = 0.00, df = 1 (P = 0.96), I^2 = 0%).

Urinary tract infection

The incidence of UTI varied greatly between studies, ranging from 2.2% to 73%. Early stent removal may reduce the number of UTI compared to late removal (Analysis 2.1 (5 studies, 1126 participants, RR 0.49 95% CI 0.30 to 0.81; I^2 = 59%; moderate certainty evidence). These findings are within a markedly heterogeneous group, where the incidence and definition of UTI was very variable. The test for heterogeneity was moderate.

Patients were probably less likely to develop a UTI with early removal compared to late removal of a BI stent (Analysis 2.1.1 (3 studies, 539 participants): RR 0.45 95% CI 0.29 to 0.70; I^2 = 13%; moderate certainty evidence). There was little or no difference in UTI with early versus late PU stent removal (Analysis 2.1.2 (2 studies, 588 participants): RR 0.60, 95% CI 0.17 to 2.03; I^2 = 83%; low certainty evidence). Of note, there was substantial heterogeneity with PU stents.

Minor stent-related complications

Only Huang 2012, Indu 2012 and TrUST 2017 examined minor stent-related complications in more detail (e.g. haematuria, encrustation, migration). Huang 2012 found these complications were significantly more likely to occur in the late stent removal group. For example, irritative symptoms were experienced in 42/186 patients in the late group compared to 16/179 in the early group (P = 0.001). This study also reported 3 cases of 'forgotten stents' that resulted in removal at a much later date (12 weeks). Indu 2012 examined the incidence of stent migration, breakage and haematuria and found no cases in either the early or late stent removal group. In TrUST 2017, the late stent removal group experienced more pain (0/80 in early group versus 4/126 in late group; P = 0.259), more episodes of haematuria (0/80 early versus 2/126 in the late group; P = 0.666), and more episodes of migration (0/80 early versus 3/126 in the late group; P = 0.409). The TrUST 2017 investigators also evaluated participants health status and quality of life using FAIT-U and EQ-5D questionnaires. They found no difference at week one post-transplant, however, by week six the health status scores (FAIT-U) were significantly better in those patients who had their ureteric stent removed early (P = 0.012).

Cost-effectiveness

Only Parapiboon 2012 examined the cost effectiveness of early stent removal. In this study (intention-to-treat analysis) patients whose stent was removed at seven days were significantly less likely to develop a UTI (15/37, 40.5% versus 27/37, 72.9%; P = 0.004). According to figures from their centre, the mean hospital cost, including accommodation, investigations and treatment, for patients with a UTI was significantly higher than those without a UTI (11,890 USD versus 6897 USD, P < 0.001). The mean cost of early ureteric stent removal was lower than routine removal (8792 USD versus 11,182 USD; P = 0.06). With early ureteric stent removal the authors estimated a saving of 2390 USD per kidney transplant recipient.

DISCUSSION

Summary of main results

Universal use of ureteric stents in kidney transplantation has significantly reduced the incidence of MUC (Wilson 2013). However, they are associated with other risks such as UTI, haematuria, encrustation and irritative bladder symptoms. These risks are likely to increase in incidence the longer the stent is in place. It is uncertain whether ureteric stents can be safely removed at an earlier time point than traditionally accepted without any increase in risk of MUC (RR 1.87, 95% CI 0.61 to 5.71). There may be a reduction in the incidence of UTI with early stent removal (RR 0.49 95% CI 0.30 to 0.81). The incidence of UTI in the late stent removal group from this set of studies is directly comparable to the summative stented cohort from the meta-analysis by Wilson 2013.

Our analysis also identified that the associated reduction in UTI incidence was only seen BI stents (RR 0.45, 95% CI 0.29 to 0.70). In those studies where the ureteric stent was tied to the urinary catheter the benefit of early stent removal was lost (RR 0.60 95% CI 0.17 to 2.03). This may be due to the externalisation of the indwelling stent providing an easy track for antimicrobial colonisation. TrUST 2017, which utilised the PU stent method in their early removal arm, reported reasonably high treatment failure rate using this technique (15). This was reported as due to technical difficulties attaching the stent to catheter. This resulted in conversion of a PU stent to a BI stent and these stents were subsequently removed at the later time point six weeks post-operatively (Table 1).

One study reporting cost effectiveness estimated a saving of 2390 USD per patient with early stent removal.

Overall completeness and applicability of evidence

This review identified only a small number of studies for which limited information was available despite contacting the authors directly. All of the included studies provided information regarding our primary outcome of interest, MUC, and the secondary outcome UTI. Only three studies provided further information regarding other stent associated complications and, although not statistically significant, two of these studies noted a reduction in pain, haematuria, migration and encrustation of stents if they were removed early. Also of note, there are a number of ongoing studies which were not included and may provide more important information in the future (ACTRN12610000349044; ISRCTN51276329).

Our sensitivity analysis did not reveal any untoward influence on effect size when taking into account the filters described earlier in our methods section; excluding unpublished studies, excluding the largest studies, excluding studies with aberrant diagnostic criteria

and excluding studies with a different language of publication. We also examined the data using a "worst-case" scenario approach and this revealed that our conclusion is robust enough to withstand wide variations in data.

Quality of the evidence

The studies included in the review were generally of poor quality, with only three studies reporting a robust randomisation process (Indu 2012; Parapiboon 2012; TrUST 2017). With the limited information available it was difficult to assess to risk of bias for a few of the studies and these were assumed to be high risk. Due to the nature of the intervention blinding was not possible but this is unlikely to have affected outcome. Across included studies there is a relatively short follow-up period, median four months, but this is still likely to have captured the outcomes of concern, MUC and UTI.

There was a substantial degree of heterogeneity within the studies when examining UTI incidence, due to the differences in each individual study's definition of UTI. Some studies included all bacterial urinary colonisation irrespective of symptoms and others only included symptomatic patients. However, when investigating an immunosuppressed transplant recipient population any degree of bacteriuria is significant to warrant concern and therefore a change to practice, in this case earlier stent removal, which can minimise this risk, is of benefit.

Potential biases in the review process

In conducting a meta-analysis there is an inherent risk of publication bias due to the retrospective nature of the search. To minimise this risk we searched multiple databases without language restriction and utilised the Cochrane Kidney and Transplant Specialised Register to gain access to reports of studies only presented at conferences and meetings. The data presented is up to date as of March 2017 and the ongoing studies discovered in the search were still unpublished prior to our publication. However, in an attempt to minimise publication bias, we have included studies only published as a conference abstract which have not been through a robust peer review process. Four of the five studies included were published in peer reviewed journals. The studies included overall have a moderate degree of bias which we have attempted to minimise through developing a detailed protocol for analysis prior to commencing this study.

Agreements and disagreements with other studies or reviews

To our knowledge there are no other meta-analyses or systematic reviews addressing this issue.

AUTHORS' CONCLUSIONS

Implications for practice

It is uncertain whether early removal of ureteric stents following kidney transplantation is associated with a higher risk of MUC and may reduce the incidence of UTI in an immunosuppressed patient population. This benefit is only realised if the ureteric stent is BI as opposed to externalised and attached to the patient catheter.

Implications for research

A cost-benefit analysis would be valuable further research when considering early stent removal. It would interesting to include patient quality of life questionnaires as irritative bladder symptoms are a considerable source of patient complaint often ignored as a necessary evil by clinicians. Early removal would minimise this discomfort to patients and decrease the disruption and cost of a return appointment for stent removal at a later date. This has been addressed in TrUST 2017 but needs wider validation. We need more evidence to conclude exactly which early technique is better, BI versus PU versus PC, as there were a limited number of studies in each of these arms. It would also be beneficial to understand potential categories of patients in which early removal is not advised due to an inherent increased risk of MUC.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Gunawansa 2011

Methods	• Study design: parallel RCT

Gunawansa 2011 *(Continued)*

	• Study duration: January 2009 and August 2013 • Duration of follow-up: mean 16 (12 to 36) months
Participants	• Country: Sri Lanka • Setting: single-centre • Live donor kidney transplants for recipients with ESKD • Number: treatment group (203); control group (179) • Mean age ± SD (years): not reported • Sex (M/F): not reported • Exclusion criteria: not stated
Interventions	Treatment group • Early stent removal of PU stent tied to tip of urinary catheter intraoperatively and removed simultaneously with the catheter at the bedside at day 6 Control group • Late stent removal via flexible cystoscopy at day 28
Outcomes	• MUC (ureteric anastomotic stenoses) • UTI
Notes	• Abstract-only publications; no response from author regarding requests for further information • Prospectively followed up for MUC & UTI, no other detailed information available • Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Unclear risk	Insufficient information to permit judgement

Huang 2012

Methods	• Study design: parallel RCT • Study duration: January 2009 to December 2010 • Duration of follow-up: 3 months minimum
Participants	• Country: China • Setting: single centre • Deceased donor for adult ESKD recipients • Number: treatment group (179); control group (186) • Mean age ± SD (years): treatment group (42.8 ± 7.5); control group (43.5 ± 8.1) • Sex (M/F): treatment group (133/46); control group (137/49) • Exclusion criteria: not reported
Interventions	Treatment group • Early removal at week 3 post-op Control group • late removal at week 6 post-op Other information • Stent type: double-J stent, BI • Stent calibre: 5 Fr 15cm • Removed using flexible cystoscopy and local anaesthetic
Outcomes	• MUC: urological complications defined as any cause requiring PC nephrostomy or surgical revision (e.g. urinary fistula, leakage, ureteral obstruction) • UTI • Other stent related complications: duration of macroscopic haematuria, incident so of malposition or calculus formation
Notes	• Short follow-up • Definition of early removal is 3 weeks as opposed to < 15 days • Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement "...were randomly assigned to two groups"
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding but unlikely to affect outcome
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias)	Low risk	All patients accounted for:

Huang 2012 *(Continued)*

All outcomes		- 3 patients forgot to return for stent removal at 6 weeks and it was removed at 12 weeks - 4 patients removed from analysis (2 in each group) due to stent migration
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	High risk	Very long length of stay 3 to 4 weeks, maybe associated with increased risk of nosocomial infection

Indu 2012

Methods	• Study design: parallel RCT of 100 consecutive patients • Study duration: January 2007 and December 2009 • Duration of follow-up: 6 months minimum
Participants	• Country: India • Setting: single centre • Living donor kidney transplant (laparoscopic donor nephrectomy) for ESKD • Number: treatment group (50); control group (50) • Mean age ± SD (years): treatment group (34.4 ± 10.5); control group (33.8 ± 10.4) • Sex (M/F): treatment group (38/12); control group (40/10) • Exclusion criteria: if within 7 days patient developed urine leak, DGF or rejection prior to randomisation on day
Interventions	Treatment group • Early removal at day 7 post-op Control group • Late removal at day 28 post-op Other information • Stent calibre: 4Fr 16cm • Stent type: double J, BI • Removal: flexible cystoscopy, local anaesthetic and IV ceftazidime for antimicrobial cover • Urinary catheter removed day 6
Outcomes	• UTI • Asymptomatic bacteriuria • MUC • MSU sent routinely on day 7, at 3 weeks, 3 months and 6 months and at any other time if symptomatic • USS routinely performed on day 5, 4 weeks, 3 months and 6 months or if there was a rise in SCr • DTPA renogram routinely on day 5 and 6 months post-op
Notes	• Funding source: nil

Risk of bias

Bias	Authors' judgement	Support for judgement

Indu 2012 *(Continued)*

Random sequence generation (selection bias)	Low risk	Randomised by computer generated random numbers created by study coordinator
Allocation concealment (selection bias)	Low risk	Allocation kept in sealed opaque envelopes until opened on day 7 by ward nurses
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding but unlikely to impact outcome
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data, however CONSORT diagram not included
Selective reporting (reporting bias)	Low risk	No study protocol data but all reported outcomes are accounted for
Other bias	Low risk	The study appears to be free of other biases

Parapiboon 2012

Methods	• Study design: parallel RCT • Study duration: April 2010 to January 2011 • Study follow-up period: not reported
Participants	• Country: Thailand • Setting: single-centre • Living and deceased donors (58% living) for adult ESKD recipients • Number: treatment group (37); control group (37) • Mean age ± SD (years): treatment group (42.7 ± 12.4); control group (43.8 ± 14.1) • Sex (M/F): treatment group (24/13); control group (27/10) • Exclusion criteria: neurogenic lower urinary tract disease; abnormal anatomy; en bloc paediatric donors; CIT > 36 h
Interventions	Treatment group • Early removal day 7 post-op Control group • Late removal day 14 post-op Other information • Stent calibre: 6FR 26 cm • Stent type: double-J stent, BI • Removal: flexible cystoscopy with local anaesthetic • Bladder catheter for 7 days
Outcomes	• MUC

Parapiboon 2012 *(Continued)*

- UTI (defined as either asymptomatic, symptomatic or urosepsis)
- Routine MSU testing at day 0, 3, 7, 10, 14 and twice weekly until discharge
- Radioisotope scanning at 1 and 2 month post-op to detect urological complications

Notes	• No information on type of urological complication encountered • Includes cost-benefit analysis. • Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated block of 4
Allocation concealment (selection bias)	Low risk	Sealed opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinding not possible but unlikely to affect outcome
Blinding of outcome assessment (detection bias) All outcomes	High risk	No evidence of blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients accounted for but no CONSORT diagram
Selective reporting (reporting bias)	High risk	No information on what type of urological complications were encountered
Other bias	Low risk	The study appears to be free of other biases

TrUST 2017

Methods	• Study design: parallel RCT; block-stratified for age (2 to 16 years; 17 to 75 years) • Study duration: April 2010 to October 2013 • Duration of follow-up: minimum 6 months
Participants	• Country: UK • Setting: multicentre (6) • Living and deceased donors; adult and paediatric ESKD recipients • Number (analysed/PP population): treatment group (80/81); control group (126/131) • Median age, IQR (years): treatment group (47.5, 31.1 to 58.0); control group (41.7, 24.2 to 53.8) • Sex (M/F): treatment group (54/27); control group (93/37) • Exclusion criteria: increased risk of bleeding; abnormal urinary tract anatomy or function; planned early use of mTORi; stones
Interventions	Treatment group • Early removal group had a ureteric stent attached to the urethral catheter intraoperatively and then removed non-invasively on day 5 to 7

TrUST 2017 *(Continued)*

	Control group • Late removal group had a J-J stent placed routinely intraoperatively and it was removed at approximately 6 weeks cystoscopically Other information • Stent calibre: 6FR/16cm for adults, 4.8-6Fr/16cm for children • Stent Type: Double J stent • Bladder catheter for 75 days
Outcomes	• MUC (ureteric leaks, ureteric stenosis; "intermediate urological complications" i.e. oedema or clot causing obstruction that had to be managed by nephrostomy) (80 patients analysed in the early removal group) • UTI (79 patients in the early removal group analysed)
Notes	• Study not powered to assess MUC • 15 cases of failure to tie catheter to stent due to technical difficulty • 21 patients in the early group failed to receive the allocated treatment and were regarded as crossovers into the late group, undergoing late stent removal • Investigated effect of early removal on idiosyncratic stent complications and QoL • Funding source: NIHR and Guy's and St Thomas' Charity

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Online computer generated randomisation process, block stratified with randomly varying block sizes
Allocation concealment (selection bias)	Low risk	Allocation revealed to clinicians at time of randomisation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinding not possible but unlikely to affect outcome
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not possible
Incomplete outcome data (attrition bias) All outcomes	Low risk	CONSORT diagram included detailing full follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	The study appears to be free of other biases

BI - bladder indwelling; CIT - cold ischaemic time; DGF - delayed graft function; DPTA - diethylenetriaminepentaacetic acid; ESKD - end-stage kidney disease; IQR - interquartile range; IV - intravenous; M/F - male/female; MSU - midstream urine; mTORi - mammalian target of rapamycin inhibitor; MUC - major urological complications; PC - percutaneous; PU - per-urethral; PP - per protocol; RCT - randomised controlled trial; SCr - serum creatinine; SD - standard deviation; USS - urinary ultrasound; UTI - urinary tract infection

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Yari 2014	Not enough information included in abstract available regarding numbers of patients in intervention arms therefore unable to include in analysis. Authors did not respond to our contact for more information.

Characteristics of ongoing studies *[ordered by study ID]*

ACTRN12610000349044

Trial name or title	Pilot study: prospective randomised controlled trial of ureteric double J stenting with early vs standard stent removal to improve graft and patient outcome and reduce urological complications after renal transplantation
Methods	Prospective RCT comparing early removal of ureteric stent at day 4 (attached to catheter) compared to late removal 4-6 weeks post-op cystoscopically.
Participants	All patients > 16 years on the kidney transplant waiting list at a single centre Exclusion criteria: neurogenic bladder dysfunction or re-transplant
Interventions	Double J stent sutured to urinary catheter and removed simultaneously on day 4 post-transplant
Outcomes	Primary outcome (1): graft outcome assessed using histology from renal biopsy, SCr and eGFR Primary outcome (2): at 12 months post-transplant patient mortality data will be recorded Secondary outcome: MUC
Starting date	01/05/2010
Contact information	Dr Adam Bartlett, adamb@adhb.govt.nz
Notes	No outcome data to be obtained regarding UTI

ISRCTN51276329

Trial name or title	Randomised controlled trial of early versus late ureteric stent removal post kidney transplant
Methods	Parallel RCT
Participants	Sample size set at 350 based on power calculations. To include all adults receiving at kidney either living or deceased donor
Interventions	Group A - removal of ureteric stent on day 6-8 post-transplant Group B - removal of ureteric stent during week 4-6 post-transplant
Outcomes	Primary outcome: composite incidence of UTI and ureteric complications Secondary outcome: incidence of UTI, urine leak, stenosis, patient death, graft loss, surgical complications, immunological complications, readmission and length of stay, medical complications

ISRCTN51276329 *(Continued)*	
	Measure at 3 months post-transplant
Starting date	1/1/2014
Contact information	Dept of Surgery Addenbrookes
Notes	

eGFR - estimated glomerular filtration rate; MUC - major urological complications; RCT - randomised controlled trial; SCr - serum creatinine; UTI - urinary tract infection

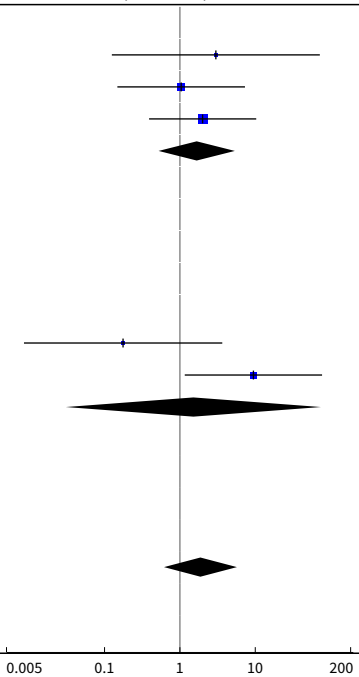
DATA AND ANALYSES

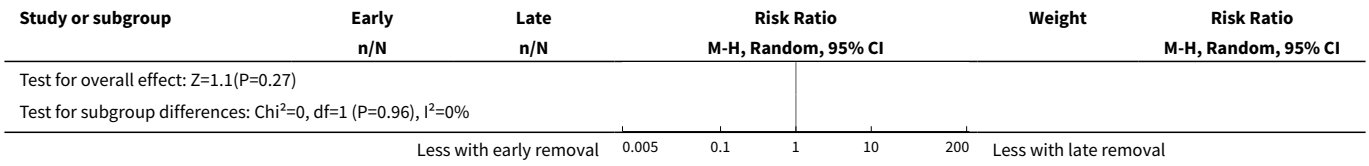
Comparison 1. Major urological complications

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Major urological complications	5	1127	Risk Ratio (M-H, Random, 95% CI)	1.87 [0.61, 5.71]
1.1 Bladder indwelling stents	3	539	Risk Ratio (M-H, Random, 95% CI)	1.67 [0.52, 5.36]
1.2 Per-urethral stents	2	588	Risk Ratio (M-H, Random, 95% CI)	1.51 [0.03, 74.45]

Analysis 1.1. Comparison 1 Major urological complications, Outcome 1 Major urological complications.

Study or subgroup	Early n/N	Late n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Bladder indwelling stents					
Indu 2012	1/50	0/50		10.9%	3[0.13,71.92]
Huang 2012	2/179	2/186		24.32%	1.04[0.15,7.3]
Parapiboon 2012	4/37	2/37		31.19%	2[0.39,10.26]
Subtotal (95% CI)	**266**	**273**		**66.41%**	**1.67[0.52,5.36]**
Total events: 7 (Early), 4 (Late)					
Heterogeneity: Tau^2=0; Chi^2=0.41, df=2(P=0.82); I^2=0%					
Test for overall effect: Z=0.86(P=0.39)					
1.1.2 Per-urethral stents					
Gunawansa 2011	0/203	2/179		11.85%	0.18[0.01,3.65]
TrUST 2017	6/80	1/126		21.75%	9.45[1.16,77.05]
Subtotal (95% CI)	**283**	**305**		**33.59%**	**1.51[0.03,74.45]**
Total events: 6 (Early), 3 (Late)					
Heterogeneity: Tau^2=6.2; Chi^2=4.5, df=1(P=0.03); I^2=77.8%					
Test for overall effect: Z=0.21(P=0.84)					
Total (95% CI)	**549**	**578**		**100%**	**1.87[0.61,5.71]**
Total events: 13 (Early), 7 (Late)					
Heterogeneity: Tau^2=0.34; Chi^2=5.06, df=4(P=0.28); I^2=20.95%					

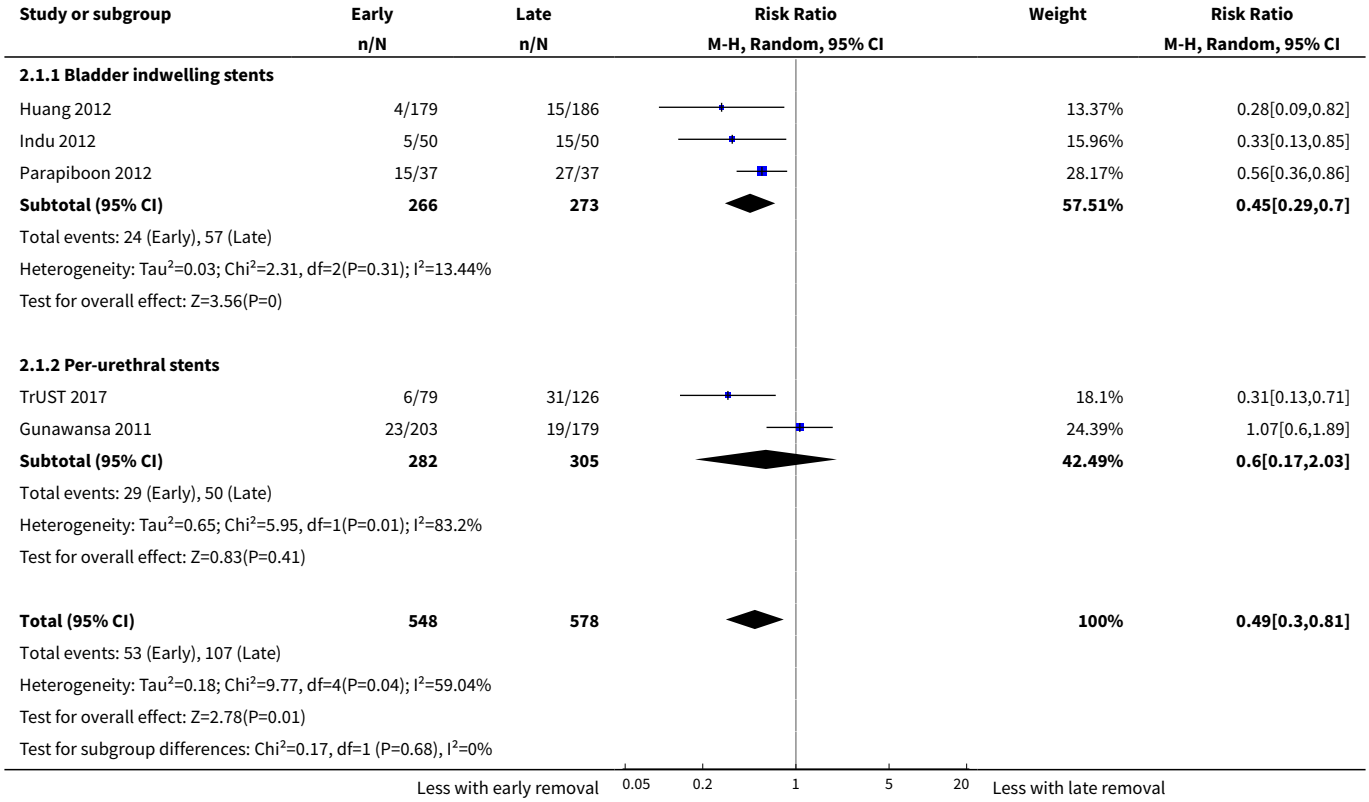




Comparison 2. Urinary tract infection

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Urinary tract infection	5	1126	Risk Ratio (M-H, Random, 95% CI)	0.49 [0.30, 0.81]
1.1 Bladder indwelling stents	3	539	Risk Ratio (M-H, Random, 95% CI)	0.45 [0.29, 0.70]
1.2 Per-urethral stents	2	587	Risk Ratio (M-H, Random, 95% CI)	0.60 [0.17, 2.03]

Analysis 2.1. Comparison 2 Urinary tract infection, Outcome 1 Urinary tract infection.



ADDITIONAL TABLES

Table 1. Reported adverse events

Study ID	Adverse events
Gunawansa 2011	Two patients in the late group required re-stenting due to ureteric stenosis
Huang 2012	Three patients in the late group had forgotten stents that were subsequently removed at 12 weeks
Indu 2012	Six patients in the early and 5 patients in the late group had acute rejection that required intervention
Parapiboon 2012	No adverse events reported
TrUST 2017	Sixteen patients did not receive their allocated treatment as there were technical difficulties attaching the stent to the catheter. In the early removal group, 1 patient's stent removal was delayed by 1 day because the urethral catheter balloon needed percutaneous needle puncture due to the stent suture There were 5 complications in patients who had early stent removal and these were all related to the percutaneous technique used in which the stent was tied to the catheter

APPENDICES

Appendix 1. Electronic search strategies

Database	Search terms
CENTRAL	1. MeSH descriptor: [Kidney Transplantation] this term only 2. kidney transplant*:ti,ab,kw (Word variations have been searched) 3. renal transplant*:ti,ab,kw (Word variations have been searched) 4. #1 or #2 or #3 5. MeSH descriptor: [Stents] explode all trees 6. stent*:ti,ab,kw in Trials (Word variations have been searched) 7. #5 or #6 8. #4 and #7
MEDLINE	1. Kidney Transplantation/ 2. exp Stents/ 3. stent$.tw. 4. or/2-3 5. and/1,4
EMBASE	1. exp kidney transplantation/ 2. exp stent/ 3. exp urologic stent/ 4. stent$.tw. 5. or/2-4 6. and/1,5

Appendix 2. Risk of bias assessment tool

Potential source of bias	Assessment criteria
Random sequence generation Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence	*Low risk of bias:* Random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random).
	High risk of bias: Sequence generated by odd or even date of birth; date (or day) of admission; sequence generated by hospital or clinic record number; allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory test or a series of tests; by availability of the intervention.
	Unclear: Insufficient information about the sequence generation process to permit judgement.
Allocation concealment Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment	*Low risk of bias:* Randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study (e.g. central allocation, including telephone, web-based, and pharmacy-controlled, randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes).
	High risk of bias: Using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.
	Unclear: Randomisation stated but no information on method used is available.
Blinding of participants and personnel Performance bias due to knowledge of the allocated interventions by participants and personnel during the study	*Low risk of bias*: No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
	High risk of bias: No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.
	Unclear: Insufficient information to permit judgement
Blinding of outcome assessment Detection bias due to knowledge of the allocated interventions by outcome assessors.	*Low risk of bias:* No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.
	High risk of bias: No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.
	Unclear: Insufficient information to permit judgement
Incomplete outcome data Attrition bias due to amount, nature or handling of incomplete outcome data.	*Low risk of bias:* No missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods.

(Continued)

	High risk of bias: Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation.
	Unclear: Insufficient information to permit judgement
Selective reporting Reporting bias due to selective outcome reporting	*Low risk of bias:* The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).
	High risk of bias: Not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study.
	Unclear: Insufficient information to permit judgement
Other bias Bias due to problems not covered elsewhere in the table	*Low risk of bias:* The study appears to be free of other sources of bias.
	High risk of bias: Had a potential source of bias related to the specific study design used; stopped early due to some data-dependent process (including a formal-stopping rule); had extreme baseline imbalance; has been claimed to have been fraudulent; had some other problem.
	Unclear: Insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias.

CONTRIBUTIONS OF AUTHORS

1. Draft the protocol: CHW, SAH, MLN
2. Study selection: CHW, SAH, ERT
3. Extract data from studies: CHW, SAH, ERT
4. Enter data into RevMan: CHW, SAH, ERT
5. Carry out the analysis: CHW, SAH, ERT
6. Interpret the analysis: CHW, SAH, ERT
7. Draft the final review: CHW, SAH, ERT
8. Disagreement resolution: MLN
9. Update the review: CHW, SAH

DECLARATIONS OF INTEREST

- Emily Thompson: none known
- Sarah Hosgood: none known
- Michael Nicholson: none known
- Colin Wilson: none known

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- National Institute for Health Research Blood and Transplant Research Unit (NIHR BTRU) in Organ Donation and Transplantation at the University of Cambridge, UK.
- Newcastle University, UK.
- NHS Blood and Transplant (NHSBT), UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There were no identified studies that utilised the PC method of stent placement and therefore this subgroup analysis that was included in the protocol could not be included. Only two studies included examined in any detail the incidence of idiosyncratic stent complications (e.g. bladder irritation, haematuria, encrustation) and therefore a robust meta-analysis could not be performed.

INDEX TERMS

Medical Subject Headings (MeSH)

*Ureter; Device Removal [*adverse effects]; Foreign Bodies [etiology]; Incidence; Kidney Transplantation [*adverse effects]; Postoperative Complications [epidemiology] [*etiology] [prevention & control]; Randomized Controlled Trials as Topic; Stents [*adverse effects]; Time Factors; Urinary Bladder; Urinary Tract Infections [epidemiology] [*etiology] [prevention & control]

MeSH check words

Adult; Child; Humans