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# Meta-analysis of urological complication between early vs late ureteric stent removal in kidney transplant recipient

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### Abstract

**Introduction:** The optimal timing of ureteric stent removal in kidney transplant recipients is still being debated. Therefore, meta-analysis is aimed to determine urological complications between early vs late ureteric stent removal in Kidney transplant recipients.

**Methods:** The analysis compared major urological complications with urinary tract infections between early vs late ureteric stent removal in kidney transplant recipients. It was conducted using PRISMA guidelines and the Cochrane Handbook for Systematic Review of interventions. Data were collected after literature research, and analyzed using Review Manager 5.3.

**Results:** 17 studies were conducted with various duration cut off points for stent removal. The incidence of urinary tract infections showed a significant decreased in the group with early ureteric stent removal. However, no difference of major urological complications was observed. Evidence showed the timing of stent removal should be determined early to reduce major urological complications and the incidence of urinary tract infections.

**Conclusion:** There was no difference in the prevention of major urological complications between early and late stent removal. The incidence of urinary tract infections increased significantly in the group with late ureteric stent removal, hence, the 2 weeks cut off point in early state was the best timing for ureteric stent removal.

Keywords: ureteric stent, early, late, kidney transplant recipients, urological complications, urinary tract infections

## Introduction

Kidney transplant is a complex procedure which interferes with the normal anatomical structure of the urinary tract system<sup>[1]</sup>. In addition, it can cause defect and urinary leakage which is more common <sup>[2]</sup>. Recently, the attempts to insert a ureteric stent in recipients were conducted to reduce ureteral strictures risks, obstruction, and urinary leakage [3]. It was considered successful as reported in many studies. However, the only problem was the risk of urinary tract infections, when the stent was placed for too long<sup>[4]</sup>. Subsequently, various centers have their consensus for stent placement, although early stent removal is more preferred, ranging from 1-2 weeks (some reported 6 weeks earlier) <sup>[5]</sup>. Regardless of this, some studies showed controversial evidence of placing ureteric stent for too long was found to yield good result. Therefore, meta-analysis aims to determine urological complications between 1-2 weeks early vs late ureteric stent removal in Kidney transplant recipients.

#### Methods

This analysis compared the major urological complications with urinary tract infections between 1-2 weeks early vs late ureteric stent removal in recipients. It was conducted using PRISMA guidelines and Cochrane Handbook for Systematic Review of interventions. Furthermore, a comprehensive literature search was performed by the authors on January 28th, 2020, in which relevant studies were obtained from Medline and SCOPUS. The eligible studies were searched with the keywords based on the meta-analysis titles, the duplicate journals were then managed using EndNote. After this, the titles and abstracts were reviewed. Finally, the full texts were examined for inclusion whether they contain original data from the group, clinical trials, and observational studies. English language journals and full texts were included. (Figure 1).

The author's years of study and subjects were collected. The parameter used was pooled proportion, in which data were solely analyzed by a Review Manager, and the significant limit was 0.05. While dichotomous analysis was conducted for those with high chance of survival, and dichotomous data were presented as odds ratios (ORs) with 95% confidence intervals (CI).

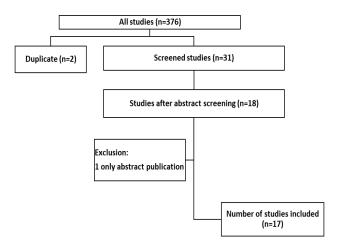


Fig 1: Flow chart PRISMA of this meta analysis

### Results

17 tests were conducted with various duration cut off points of stent removal (Table 1) <sup>[1, 6, 22]</sup>. The parameters used were major urological complications and the incidence of urinary tract infections. The incidence of urinary tract infections showed a

significant

decreased in the group with early ureteric stent removal. However, no difference of major urological complications was observed.

Table 1: Studies ad	dressing major uro	ological compli	ications and th	e incidences of	urinary tract infe	ction (UTI)	

~			Earl	v	Late	
Studies addressing major urological complications	Location	Duration			Number	-
1 w vs 4-6w						
Gunawansa 2015 <sup>[6]</sup>	Srilanka	1 w vs 4 w	0	203	2	179
Indu 2012 <sup>[7]</sup>	China	1 w vs 4 w	1	50	0	50
Lee 2013 <sup>[8]</sup>	China	1 w vs 6 w	6	26	3	26
Parapiboon 2012 <sup>[1]</sup>	Thailand	1 w vs 4 w	4	37	2	37
Patel 2017 <sup>[9]</sup>	UK	1 w vs 6 w	6	79	36	126
Soldano 2014 [10]	UK	1 w vs 6 w	0	47	3	47
Taghizadeh-Afshari 2014 [11]	India	1 w vs 4 w	2	45	5	45
2  w vs > 2  w						
Coskun 2011 <sup>[13]</sup>	Turkey	2 w vs 3 w	0	10	0	38
Dadkhah 2016 [14]	Iran	2 w vs 3 w	27	194	66	335
Soylu 2019 <sup>[15]</sup>	Turkey	$2 \le v \le 2 \le v$	1	44	2	72
Verma 2002 <sup>[16]</sup>	India	2 w vs 4 w	3	52	6	57
3 w vs 6 w						
Huang 2012 <sup>[17]</sup>	China	3 w vs 6 w	2	179	2	186
Studies addressing UTI incidences	Location	Derection	Earl	у	Late	9
Studies addressing UTT incidences	Location	Duration	Number	Total	Number	Total
1 w vs 4-6 w						
Gunawansa 2015 <sup>[6]</sup>	Srilanka	1 w vs 4 w	23	203	19	179
Indu 2012 <sup>[7]</sup>	India	1 w vs 4 w	5	50	50	150
Lee 2013 <sup>[8]</sup>	China	1 w vs 6 w	14	26	8	26
Liu 2017 <sup>[18]</sup>	UK	1 w vs 6 w	3	52	15	51
Parapiboon 2012 <sup>[1]</sup>	Thailand	1 w vs 4 w	15	37	27	37
Patel 2017 <sup>[9]</sup>	UK	1 w vs 6 w	6	79	31	126
Soldano 2014 [10]	UK	1 w vs 6 w	1	47	7	47
Taghizadeh-Afshari 2014 [11]	India	1 w vs 4 w	11	43	15	43
2  w vs > 2  w						
Asgari 2016 [19]	Iran	2 w vs 3 w	9	61	8	30
Coskun 2011 <sup>[15]</sup>	Turkey	2 w vs 4 w	1	10	17	38
Dadkhah 2016 [14]	Iran	2 w vs 3 w	35	194	24	335
Ramamoorthy 2018 <sup>[19]</sup>	India	2 w vs 6 w	6	24	10	24
Sarier 2017 <sup>[20]</sup>	Turkey	2 w vs 3 w	7	28	17	79
Soylu 2019 [15]	Turkey	$2 \le v \le 2 \le v$	6	44	12	72
Verma 2002 <sup>[16]</sup>	India	2 w vs 4 w	13	52	20	57
Wingate 2017 <sup>[21]</sup>	USA	2 w vs 3 w	23	143	32	161
Yuksel 2017 [22]	Turkey	$2 \le v \le 2 \le v$	5	601	7	217
3 w vs 6 w						
Huang 2012 <sup>[17]</sup>	China	3 w vs 6 w	4	179	15	186
<5 w vs >5 w						
Mannu 2014 [23]	UK	>5 w vs >5 w	7	31	34	372

This analysis included 7 tests conducted by comparing major urological complications between stent removal in 1 week vs 4-6 weeks, and 4 tests in <2 weeks vs >2 weeks. There was no significant difference of major urological complications between

stent removal in 1 week vs 4-6 weeks (OR 0.6; 95%CI 0.21-1.69; p=0.05; I<sup>2</sup> 53%; Figure 2), and also between <2 weeks vs >2 weeks (OR 0.65; 95%CI 0.41-1.02; p=0.06; I<sup>2</sup> 0%; Figure 3).

	Earl	y	Late	9		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Gunawansa 2015	0	203	2	179	8.3%	0.17 [0.01, 3.66]	· · · · · · · · · · · · · · · · · · ·
Indu 2012	1	50	0	50	7.6%	3.06 [0.12, 76.95]	
Lee 2013	6	26	3	26	18.4%	2.30 [0.51, 10.41]	
Parapiboon 2012	4	37	2	37	16.1%	2.12 [0.36, 12.36]	
Patel 2017	6	79	36	126	24.4%	0.21 [0.08, 0.51]	<b>_</b>
Soldano 2014	0	47	3	47	8.5%	0.13 [0.01, 2.66]	· · · · · · · · · · · · · · · · · · ·
Taghizadeh-Afshari 2014	2	45	5	45	16.7%	0.37 [0.07, 2.03]	
Total (95% CI)		487		510	100.0%	0.60 [0.21, 1.69]	
Total events	19		51				
Heterogeneity: Tau <sup>2</sup> = 0.91;	Chi <sup>2</sup> = 12	.67, df	= 6 (P = 0	).05); I <sup>z</sup>	= 53%		
Test for overall effect: Z = 0.	97 (P = 0	.33)					Favours (experimental) Favours (control)

Fig 2: Forest plot of meta-analysis comparing major urological complications between stent removal in 1 week vs 4-6 weeks.

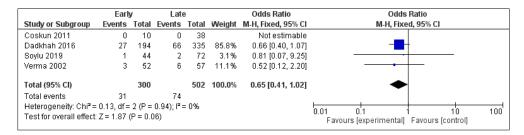


Fig 3: Forest plot of meta-analysis comparing major urological complications between stent removal in <2 weeks vs >2 weeks.

This analysis included 8 studies conducted by comparing the incidence of urinary tract infections between stent removal in 1 week vs 4-6 weeks, and 9 studies conducted by comparing major urological complication between stent removal in <2 weeks vs >2 weeks. There was significant difference in the incidence of

urinary tract infections between stent removal in 1 week vs 4-6 weeks (OR 0.47; 95% CI 0.34-0.65; p=0.0006; I<sup>2</sup> 73%; Figure 4), and also between <2 weeks vs >2 weeks (OR 0.71; 95% CI 0.39-1.27; p=0.0005; I<sup>2</sup> 71%; Figure 5). The cut-off point of 2 weeks showed better odd ratios than 1 week (OR 0.47 vs 0.71).

	Earl	y	Late	е		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Gunawansa 2015	23	203	19	179	15.6%	1.08 [0.57, 2.05]	
Indu 2012	5	50	50	150	19.6%	0.22 [0.08, 0.59]	<b>-</b>
Lee 2013	14	26	8	26	3.2%	2.63 [0.84, 8.17]	+
Liu 2017	3	52	15	51	12.5%	0.15 [0.04, 0.55]	
Parapiboon 2012	15	37	27	37	14.0%	0.25 [0.09, 0.67]	
Patel 2017	6	79	31	126	19.3%	0.25 [0.10, 0.64]	<b>_</b>
Soldano 2014	1	47	7	47	6.0%	0.12 [0.01, 1.05]	
Taghizadeh-Afshari 2014	11	43	15	43	9.7%	0.64 [0.25, 1.62]	
Total (95% CI)		537		659	100.0%	0.47 [0.34, 0.65]	•
Total events	78		172				
Heterogeneity: Chi <sup>2</sup> = 25.65	, df = 7 (P	= 0.00	06); I <b>²</b> = 7	73%			0.01 0.1 1 10 100
Test for overall effect: Z = 4.	62 (P < 0	00001	)				0.01 0.1 1 10 100 Favours [experimental] Favours [control]

Fig 4: Forest plot of meta-analysis comparing the incidence of urinary tract infections between stent removal in 1 week vs 4-6 weeks.

Early Late		9		Odds Ratio	Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI
Asgari 2016	9	61	8	30	10.8%	0.48 [0.16, 1.39]	
Coskun 2011	1	10	17	38	5.1%	0.14 [0.02, 1.19]	· · · · · · · · · · · · · · · · · · ·
Dadkhah 2016	35	194	24	335	14.8%	2.85 [1.64, 4.96]	
Ramamoorthy 2018	6	24	10	24	9.7%	0.47 [0.14, 1.60]	
Sarier 2017	7	28	17	79	11.3%	1.22 [0.44, 3.34]	
Soylu 2019	6	44	12	72	10.9%	0.79 [0.27, 2.28]	
Verma 2002	13	52	20	57	12.7%	0.62 [0.27, 1.42]	
Wingate 2017	23	143	32	161	14.5%	0.77 [0.43, 1.39]	
Yuksel 2017	5	601	7	217	10.2%	0.25 [0.08, 0.80]	
Total (95% CI)		1157		1013	100.0%	0.71 [0.39, 1.27]	•
Total events	105		147				
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:				(P = 0.0	0005); I² =	71%	0.01 0.1 1 10 100 Favours (experimental) Favours (control)

Fig 5: Forest plot of meta-analysis comparing the incidence of urinary tract infections between stent removal in <2 weeks vs >2 weeks.

#### Discussion

Evidence showed that the timing of stent removal should be determined early to reduce major urological complications and the incidence of urinary tract infections <sup>[9]</sup>. The theoretical benefit of ureteric stents in kidney stents was to generate a waterproof-

like uretero-neocystostomy and preventing anatomical tract tangles. After implantation, the manifestation of inflammation and oedema caused obstruction at the anastomosis <sup>[23]</sup>. In this case, the stent helped to drain urine from the kidney into the bladder, reducing intra-ureteric pressure. The stent also aids in

preventing Ischaemic-related distal ureter necrosis, and subsequent urine leakage <sup>[24]</sup>.

As predicted, recent tests demonstrated shorter stent durations. Many RCTs reported the benefit of early stent removal, except the best timing for the removal was still debated <sup>[7]</sup>. However, some tests showed controversial results. Dadkhah *et al* indicated remarkably high UTI incidences in the early stent removal group (10 days), which was two times higher than late stent removal group (30 days)<sup>[13]</sup>.

This analysis showed a significant decreased of urinary tract infections with early ureteric stent removal, and no difference of major urological complications was observed. Also, no difference was found in placing the stent in shorter or longer durations, therefore, making the attempt of early ureteric stent removal was preferred. In other aspects, early removal reduces either morbidity, costs, or both <sup>[5]</sup>.

As a foreign material in the recipient, ureteric stents were rapidly colonized with a biofilm of micro-organisms, which predisposed the bladder to UTI and pyelonephritis, due to backflow of urine into the kidney pelvis during bladder detrusor contraction <sup>[25]</sup>. Thus, early stent removal with urinary catheter may be considered a significant advantage, while no difference was observed in the prevention of major urological complications.

However, some limitations still exist, such as consensus differences in various centers, due to the diverse population's characteristics. Besides the usage of immunosuppressant drugs and the standard of prophylactic antibiotics were also different. And lastly many studies had different cut off points in determining early stent removal, making the analysis difficult when incorporating all the tests into analysis.

#### Conclusion

There was no difference in prevention of major urological complications between early and late stent removal. The incidence of urinary tract infection increased significantly in the group with late ureteric stent removal, hence, the 2 weeks cut-off point in early state was the best timing for ureteric stent removal.

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