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Long-term oncological outcomes of the Agarwal loop ligation technique for management of the distal ureter during laparoscopic radical nephroureterectomy

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Abstract

Objectives

To describe the Agarwal loop ligation technique for management of the distal ureter in laparoscopic radical nephroureterectomy (LNRU) for upper tract urothelial carcinoma (UTUC) and report on long-term oncological outcomes.

Materials and methods

In the Agarwal loop ligation technique, the distal ureteric stump is controlled using endoscopic Endoloop® or PolyLoop® ligation to ensure en bloc excision of the bladder cuff and prevent spillage of upper tract urine into the perivesical space. A retrospective review of the medical records of 76 patients who underwent the Agarwal loop ligation technique for UTUC at participating centres from July 2004 to December 2017 was performed. Data collected included demographics, peri-operative and long-term oncological outcomes. Survival was calculated using Kaplan Meier survival analyses.

Results and limitations

76 patients were included. Median age was 71.5 and median operative time was 4.3 hours. The intramural ureter and bladder cuff were completely excised in all patients. Distal surgical margins were clear in all, with only two patients found to have tumour extending to the circumferential surgical margin. There were no cases of perivesical recurrence or port site metastasis. Five-year bladder, local and contralateral recurrence-free survival was

59.6%, 89.0% and 93.5% respectively. Metastatic free survival at five-years was 73.5%. Five-year overall survival and cancer specific survival rates were 70.3% and 84.7% respectively.

Conclusions

We have described the Agarwal loop ligation technique for management of the distal ureter in LRNU. This technique complies with oncologic principles outlined in the European Association of Urology (EAU) guidelines, which minimizes tumour spillage. Long-term oncological outcomes are satisfactory, with no cases of perivesical recurrence detected in this series.

Introduction

Upper tract urothelial carcinoma (UTUC) accounts for 5-10% of all urothelial tumours(1). It is uncommon with an estimated annual incidence in Western countries of almost two cases in 100,000 people(1). Overall, 60% of UTUCs are invasive at diagnosis compared with 15-20% of bladder tumours(1). Open radical nephroureterectomy (ORNU) with bladder cuff excision (BCE) is the standard of care for high risk UTUC. Laparoscopic radical nephroureterectomy (LRNU) is less invasive compared with ORNU, whilst having comparable oncological outcomes.

Various surgical techniques have been described for the management of the distal ureter during radical nephroureterectomy (RNU), with no single method proven to be superior oncologically(2-5). Conventionally, the distal ureter is managed via an open approach(1). This requires a lower abdominal incision and open cystostomy, all of which confers additional morbidity and risk as well as a longer post-operative recovery. Several endoscopic techniques have been described to simplify the distal ureter resection, including transurethral resection or incision of the ureteric orifice(3, 6-9). Some of these methods do not involve ureteric orifice occlusion and run the risk of tumour spillage and increased risk of local recurrence(3, 10, 11). Complete laparoscopic or robot-assisted approaches to the management of the distal ureter have been described(12-14) but these may be technically demanding and long-term oncological safety is not yet established(1, 15).

The Agarwal loop ligation technique is a method of controlling the distal ureteric stump using endoscopic Endoloop® (Ethicon, Sommerville, NJ) or PolyLoop® (Olympus Medical System Corp., Tokyo, Japan) ligation to prevent potential spillage of upper tract urine into the perivesical space during en bloc BCE(8, 9). In a small case series of thirteen patients, this technique was found to be oncologically safe(8). This study aims to determine the long-term oncological outcomes of the Agarwal loop ligation technique for management of the distal ureter in LRNU.

Materials and methods

Between July 2004 to December 2017, 76 patients underwent LRNU with the Agarwal loop ligation technique for UTUC at multiple hospitals. The selection of the Agarwal loop ligation technique over other techniques for management of the distal ureter was based on surgeon preference. Following the encouraging results with loop ligation in earlier publications (8, 9), this technique was then widely used at our institutions by various urologists. For surgeons who have adopted the Agarwal loop ligation technique, they will preferentially use this technique for laparoscopic nephroureterectomy and not limit its use to upper ureteric and renal pelvis urothelial carcinomas. In the uncommon occurrence of distal ureteric urothelial carcinoma protruding into the bladder, surgeons preferentially employed an open management of the distal ureter to avoid seeding of tumour.

Clinicopathological data was extracted retrospectively from medical records and included: age; gender; body mass index; smoking history; history of bladder carcinoma; operative time; length of stay (LOS); conversion to open; if bladder closure was performed; rate and time to cystogram performed; length of catheterisation; post-operative complications within 30 days as defined by Clavien-Dindo classification; pathological grade and stage; location of tumour; surgical resection margins (distal ureteric and circumferential); follow-up duration; dates of bladder, contralateral (UTUC in contralateral upper urinary tract), local (lymph node or surgical bed recurrence within the retroperitoneal and/or pelvic field) and metastatic (lung, bone, liver, brain, or other) recurrences; date and cause of mortality.

Surgical technique

The patient is placed in a lithotomy position after induction of general anaesthesia. A thorough endoscopic examination of the bladder for concurrent bladder tumour is performed via a 30° lens 25-Fr cystoscopy. The presence of bladder tumour is contraindicated for endoscopic distal ureter management techniques due to risk of tumour seeding. A resectoscope mounted with a hot Collins knife is used to circumscribe the ureteric orifice with a 1cm bladder cuff. The depth of incision is carried up to partial thickness of the bladder and care is taken not to detach the ureter or expose the perivesical fat at this stage to avoid extravasation of urine which may result in tumour seeding.

The majority of cases in this series were performed using Endoloop® (Figure 1)(8). An 8-Fr ureteral dilator (Cook Urological, Inc., Bloomington, Ind) is cut to 34cm and passed through the cystoscopy working channel up to the tip. A preformed 0 PDS II Endoloop® is cut and released from its sheath and subsequently fed into the ureteral dilator in a retrograde fashion. The loop size is reduced to approximately 3cm and held against the ureteral dilator tip. This is then retracted into the cystoscopic sheath to allow the loop to be just visible. The cystoscope is passed into the bladder and the Endoloop® advanced over the mushroom-shaped ureteric stump. Ligation of the distal ureter is achieved by using the ureteral dilator to push and tighten the Endoloop® knot. An Albarran bridge can be used to assist in this manoeuvre.

The 9 most recent cases in this series were performed using a nylon PolyLoop® device (Figure 2)(9). This device requires a minimum working channel of 2.8mm and fits down a 25-Fr cystoscopic sheath. An Albarran deflecting bridge can be used in difficult cases. The device is passed through the working channel with the loop retracted back in its plastic sheath. Once the PolyLoop® device tip is in the bladder, the loop is pushed out of the plastic sheath and positioned over the ureteric stump. One advantage of the PolyLoop® device over Endoloop® is the ability to adjust the loop size by manoeuvring the outer plastic sheath using the yellow cylinder, therefore allowing for easier placement of the loop around the bladder cuff. Once in correct position, advancing the yellow cylinder pushes the outer plastic sheath forward to tighten the Polyloop® knot. The knot is then secured by deploying a silicone rubber stopper over the loop inside the plastic sheath by pulling the slider proximally. The loop is then detached by pushing the slider distally until it stops.

Once the ureteric stump is ligated, it is further dissected until perivesical fat is reached and the distal ureter is detached from the bladder. Extravasation of fluid is minimised by not over-distending the bladder and keeping the height of irrigation fluid to a minimum. The bladder is then drained with an 18-Fr Foley catheter. A laparoscopic transperitoneal nephroureterectomy is performed in a 45° semi-flank position allowing rotation of the table on either side if required. The kidney and ureter are dissected up to the pelvic brim. A small Gibson incision is made in the ipsilateral groin after rotating the table to make the patient as flat as possible. The distal ureter is dissected extraperitoneally and the specimen is retrieved en bloc. Closure of the bladder defect was dependent on surgeon preference. The senior author (DA) of this article closed the bladder defect under direct vision in two layers for all cases. The Foley catheter is kept in place for 7-14 days. Cystogram prior to catheter removal was performed based on surgeon preference.

Follow-up

Surveillance followed a standard protocol. For non-invasive disease, cystoscopy and urinary cytology was performed at 3-months post-operatively and repeated yearly with upper tract imaging for 10-years. For invasive disease, cystoscopy and urinary cytology was performed at 3-months post-operatively then yearly for 10-years. Upper tract imaging was performed 6-monthly for 2-years and then annually for 10-years.

Primary outcome

Primary outcome of this study was perivesical recurrence free survival (RFS).

Secondary outcome

Secondary outcomes include bladder, local and contralateral RFS, metastasis free survival (MFS), cancer specific survival (CSS), overall survival (OS), and complication rates.

Statistical analysis

Statistical analyses were performed using *Stata Statistical Software: Release 16* (StataCorp LLC, Texas, United States). Survival was calculated using Kaplan Meier survival analyses.

Results

Seventy-six patients were identified. There were 53 (69.7%) male and 23 (30.3%) female patients. Median age was 71.5 (IQR 65.0-78.0) years. Median operative time was 4.3 (IQR 3.5-5.0) hours and median LOS was 6.0 (IQR 4.0-7.0) days. There were no failures with the use of either Endoloop® or Polyloop® devices in this series. No patients required conversion to open surgery. Primary bladder closure was performed in 30 (39.5%) patients. Cystogram was performed in 36 (47.4%) patients. One patient was identified to have a urine leak on cystogram day-7 post-operatively and subsequently had a successful trial of void at day-10. This patient did not have formal bladder closure. Median time to cystogram was 10.0 (IQR 7.0-11.5) days. Median length of catheterisation was 10.0 (IQR 8.0-14.0) days. (Table 1).

Of the 30-day post-operative complications, three (3.9%) patients had major complications defined as Clavien Dindo grade ≥3 (Table 1). One patient developed type one respiratory failure secondary to exacerbation of known chronic obstructive pulmonary disease, requiring intensive care admission for non-invasive ventilation. One patient had post-operative haemorrhage requiring return to theatre for haemostatic control. The other patient had multiple cardiac risk factors and died due to acute myocardial infarction day-four post-surgery.

All patients had pathologically confirmed UTUC. Twenty (26.3%) patients had tumour involving mid or distal ureter, 55 (72.4%) involving proximal ureter or kidney and unspecified tumour location in one (1.3%). Distal ureteric margin was clear in all cases. Circumferential margin was positive in two patients who had extensive renal pelvis pT3 disease into perihilar fat and poorly differentiated high-grade tumour. (Table 1).

Median follow-up for bladder RFS, contralateral RFS, local RFS, MFS, OS and CSS was 24.3, 47.9, 49.8, 52.5, 47.9 and 49.8 months respectively. There were no cases of perivesical recurrence or port site metastasis. Bladder, local and contralateral RFS at five-years were 59.6%, 89.0% and 93.5% respectively. Five-year MFS was 73.5%. Five-year OS and CSS rates were 70.3% and 84.7% respectively (Figure 2).

Discussion

A variety of techniques for managing the distal ureter during RNU have been described. These techniques can largely be categorised into four groups: open, endoscopic, pure laparoscopic and pure robotic (Figure 3). Each has its own advantages and disadvantages. According to the European Association of Urology (EAU) guidelines, oncological principles involve removing the kidney and ureter en bloc with the bladder cuff, avoiding entering the urinary tract and avoiding tumour spillage(1). In cases of incomplete distal nephroureterectomy, tumour recurrence within the ureteric stump has been reported to be up to 30-64%, even in the absence of positive surgical margins(16, 17).

Open distal ureterectomy is considered the gold standard approach, allowing en bloc resection of the distal ureter with the least risk of tumour spillage(1). However, it is invasive, with associated morbidity of a large lower abdominal incision and cystostomy. This results in increased post-operative pain, prolonged LOS, and longer time before return to work(18). In addition, factors such as prior pelvic surgery or radiotherapy and obesity may render the open approach challenging(19). Tumour recurrence at the resection site and in local retroperitoneum have been reported with the open method(3, 4, 20)(Table 2). A recent large systematic review and meta-analysis reported the ORNU group as having the lowest 5-year CSS (proportion:0.77; CI 0.74,0.80)(15). These findings raise the question of whether ORNU should still be considered the gold standard approach.

Several less invasive endoscopic techniques for managing the distal ureter in RNU have been described. One of the oldest endoscopic methods of BCE is the pluck technique, which involves transurethral resection of the ureteric orifice (TURUO) down to perivesical fat, facilitating subsequent plucking of the distal ureter from above(6). As the distal ureter is not controlled early, there is risk of tumour seeding into the perivesical space, with perivesical tumour recurrence reported following this technique(10, 11, 21)(Table2). Another concern with the pluck technique is the risk of avulsion of the distal ureter and leaving the distal ureteric segment behind(22).

The variation of pluck technique consists of transurethral circumferential incision of the ureteric orifice (TCIUO) using a Collins knife(3). TCIUO without ureteric orifice ligation also carries the risk of local recurrence(3)(Table 2). To reduce the risk of perivesical tumour

spillage, various endoscopic methods of ureteral occlusion have been suggested. Gill *et al.* described their technique of ligating the ureter transvesically with Endoloop® ligature via two needlescopic ports placed into the bladder(7). This technique is technically demanding and time consuming with a reported mean cystoscopic procedure time of 90 minutes. Local pelvic recurrence and positive surgical margins have been reported with this technique(4, 20, 23)(Table 2). Of various distal ureter techniques, ureteral stripping is considered inferior to BCE(1) and is rarely practiced.

Pure laparoscopic approaches aim to replicate an open approach by maintaining an intact ureter during nephroureterectomy. This requires advanced technical skills to isolate the ureter down to the detrusor hiatus and suture the bladder defect close(12, 19). Inadequate dissection of ureter can result in leaving the distal ureteric stump behind. Furthermore, not all centres will have the expertise to perform this surgery. Laparoscopic extravesical stapling of the distal ureter is technically less demanding and may maintain a closed urinary tract. The potential for leaving viable urothelial tissue within the staple line is of concern, with cystoscopically appreciable remnants of the resected ureteric orifice described in up to 50% of cases in the literature(19).High incidence of positive surgical margins and local pelvic recurrence have been reported with the extravesical stapling technique(11, 19, 23)(Table 2).

Robotic nephroureterectomy is gaining increasing popularity. With wristed instrumentation and three-dimensional magnification, this approach facilitates the dissection of intracorporeal BCE and watertight bladder closure. Positive surgical margins, local pelvic recurrences and retained ureteric orifices have been reported with robotic techniques(13, 14)(Table 2). Urine from an open bladder may leak and seed into remote parts of the abdomen in Trendelenburg position. Long-term safety of robotic technique is yet to be established. A recent systematic review and meta-analysis comparing robotic to other nephroureterectomy techniques found higher risk of metastasis in the intracorporeal group, although the robotic group had more multifocal and higher-grade disease. Nevertheless, the authors recommend further scrutiny of this finding(15).

Bladder defect closure remains controversial. Oncological principles suggest closure, especially in patients with concurrent or past history of bladder tumour or contralateral

disease. For various reasons, the senior author (DA) suggests formal closure of the bladder. Firstly, cystogram may not be needed prior to catheter removal, and the catheter may be removed earlier. Secondly, bladder closure may reduce complications related to perivesical urine collection and may also allow instillation of adjuvant intravesical Mitomycin(24).

Bladder recurrence is common post radical nephroureterectomy, with a five-year RFS rate of 59.6% in this cohort. This is not dissimilar to findings from a Cochrane review which estimates the risk of intravesical recurrence following RNU to occur in 22-47% of patients within a two-year postoperative period(24). Previous bladder cancer and smoking are predictors of increased risk of intravesical recurrence(24); the proportion of patients in this cohort with these risk factors were 30.3% and 50.0% respectively. The impact of the method of distal ureter management during RNU on intravesical recurrence has been investigated by several authors with conflicting reports(2-5, 19, 20, 25, 26)(Table 3). Despite the controversy of whether incidence of bladder recurrence is related to the type of distal ureter management, bladder recurrence is not a prognostic factor for survival. The primary recognised prognostic factors are tumour stage and grade(1).

Locoregional and contralateral recurrences following nephroureterectomy are infrequently reported in the literature. Five-year contralateral RFS in this series was 93.5%, similar to other series (95.0%)(27). Rates of local recurrence was relatively low in this study with five-year local RFS rate of 89.0% comparable to that reported in the literature (80.5-94.2%)(28). None of the local recurrence were perivesical. Five-year MFS and OS of 73.5% and 70.3% does not differ from other series (67-91%, and 43-73%) respectively(29). Overall survival results also reflects the comorbidities of this patient group. Based on the American Society of Anaesthesiologists (ASA) physical status classification system, 43.4% of patients had a score of 3, indicative of severe systemic disease. Five-year CSS of 84.7% compares favourably to that reported in the literature (73.2-78.6%)(30). The proportion of patients with tumour stage ≥T2 disease in this series was 43.5%, a rate slightly lower to that published in the literature (55.9%)(31). This may contribute to the favourable OS and 5-year CSS results of this series. None of the patients in this series had suspicious lymph node metastasis on pre-operative imaging and this may also contribute to the favourable OS and 5-year CSS. Lymph node dissection (LND) was not performed in any patients. LND has not

been associated with improved oncological outcomes in patients with UTUC without suspicious lymph node metastasis on pre-operative imaging(32, 33).

Oncological outcomes following different approaches to the distal ureter and bladder cuff have been examined(2-5, 11, 19, 20, 25, 26)(Table 3). In a large retrospective analysis comparing open intravesical, extravesical and endoscopic methods by Xylinas *et al*, there was no difference in terms of RFS, CSS and OS(2). Li *et al* reported similar findings with no difference in RFS and CSS(3) amongst the three groups, although Kapoor *et al* reported lowest RFS with the open intravesical method(20). Comparing open to endoscopic techniques: Walton *et al* reported similar disease-specific mortality between the two groups(5), Allard *et al* concluded no association of MFS rates with either technique(4), and Fragkoulis *et al* reported no difference in 5-year CSS between both groups(26). Gkougkousis *et al* concluded insufficient evidence to support or refute endoscopic management of the distal ureter to open BCE(11). Ritch *et al* reported no difference in RFS between open, pure laparoscopic and extravesical laparoscopic stapling groups(19).

With no prospective, randomized comparisons that exist, the question remains as to the best technique to manage the distal ureter during RNU. Considering the low incidence of UTUC and multitude of techniques, such trials are difficult to conduct. In addition, outcomes may reflect other factors such as surgeon performance. Several studies have shown no difference in oncological outcomes between open and endoscopic approaches(2-5, 11, 19, 26) thus it may make sense that a surgeon should choose a technique that is oncologically sound and easy to perform with minimal complications.

With the Agarwal loop ligation technique, cystoscopic dissection is less time consuming with minimal learning curve. This study shows that complete excision of the distal ureter was achieved in all cases with no positive margin identified in the distal ureteric end, despite mid or distal tumour present in 26.3% of cases. The Endoloop® or PolyLoop® acts as a marker of the distal end of ureter and allows for reliable confirmation of complete excision. Furthermore, this technique allows the distal ureteric orifice to be ligated prior to detaching the ureter to prevent tumour seeding. Ensuring complete ureteric excision and avoiding tumour spillage is key to avoiding local tumour recurrence. This study demonstrates that the

Agarwal loop technique is able to achieve both of these and as a result there was no perivesical recurrence in this case series.

Due to the retrospective nature of this study, data collection was therefore reliant on accuracy and completeness of clinical records. For various reasons out of our control, some of the patients were lost to follow-up for various reasons. This is however reflective of real-life practice. Patients with missing survival data are censored at the last date of follow-up for survival analysis. The number of patients lost to follow-up can be determined from the "number at risk" at each stage of the survival curve (Figure 2). This is a case series with no comparison arms. For this reason, we cannot conclusively state that the Agarwal loop ligation technique is superior or inferior to other BCE techniques. There were no perivesical recurrence on follow-up with this technique which is favourable when qualitatively compared with other series in the literature. Lastly, single dose instillation of adjuvant Mitomycin was not administered in any patients post-operatively due to logistical reasons. There is evidence that the use of Mitomycin reduces the risk of bladder recurrence but no evidence of improved OS. Therefore, this is unlikely to have affected our OS rate and primary outcome of perivesical RFS.

Conclusion

We have described the Agarwal loop ligation technique for management of the distal ureter in LRNU. This technique complies with oncologic principles outlined in EAU guidelines, which minimises tumour spillage. Long-term oncological outcomes appear similar to other distal ureter management techniques during nephroureterectomy, with no cases of perivesical recurrence detected in this series. Further prospective studies with comparison arms are warranted.

Conflicts of Interest

None declared

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Table 1. Patient demographics, perioperative and pathological outcomes of patients who underwent Agarwal loop ligation method for management of distal ureter in laparoscopic radical nephroureterectomy.

Number of patients	76
Gender	
Male	53 (69.7)
Female	47 (30.3)
Age (years)	71.5 (44.0 – 91.0)
Body mass index	29.2 (18.0 - 48.7)
Smoking history	24 (38.7)
History of bladder urothelial carcinoma	23 (30.3)
Operative time (hours)	4.3 (2.5 - 7.0)
Length of stay (days)	6 (3 – 23)
Conversion to open	0 (0)
Bladder closure performed	30 (39.5)
Cystogram performed	36 (47.4)
Time to cystogram (days)	10 (5 – 16)
Length of catheterisation (days)	10 (3 - 20)
ASA physical status classification score	
ASA score 1	11 (14.5)
ASA score 2	32 (42.1)
ASA score 3	33 (43.4)
ASA score 4	0 (0)
30-day complication rates	23 (30.3)
No. of clavien dindo grade I	12 (15.8)
No. of clavien dindo grade II	8 (10.5)
No. of clavien dindo grade IIIa	0 (0)
No. of clavien dindo grade IIIb	1 (1.3)
No. of clavien dindo grade IVa	1 (1.3)
No. of clavien dindo grade IVb	0 (0)
No. of clavien dindo grade V	1 (1.3)
Pathological grade	
High grade	57 (75.0)
Low grade	19 (25.0)
Pathological T stage	
Tis	1 (1.3)
Ta	33 (43.4)

T1	9 (11.8)
T2	10 (13.2)
T3	23 (30.3)
Pathological N stage	
N0/X	73 (96.1)
N1	2 (2.6)
N2	1 (1.3)
Location of tumour	
Involves mid or distal ureter	20 (26.3)
Proximal ureter or kidney only	55 (72.4)
Unspecified	1 (1.3)
Positive surgical margin	
Distal ureteric margin	0 (0)
Circumferential margin	2 (2.6)

ASA = American Society of Anaesthesiologists

Table 2. Retained ureteric orifice, positive surgical margin and local pelvic recurrence of different distal ureter excision techniques as a part of radical nephroureterectomy for urothelial carcinoma

Distal ureteral technique	Authors	n	Retained ureteric orifice	Positive surgical margins (bladder cuff and circumferential)	Local pelvic recurrence (ipsilateral pelvis, perivesical, bladder cuff/resection site)
Open Intravesical	**Kapoor *et al*** (20)	406		39 (9.6%)	4 (0.01%)
	Li *et al* (3)	81			6 (7.4%)
	Allard *et al* (4)	20		4 (20.0%)	
Open Extravesical	**Kapoor *et al*** (20)	316		32 (10.1%)	4 (0.01%)
	Li *et al* (3)	129			10 (7.8%)
	Allard *et al* (4)	29		3 (10.3%)	
TURUO	**Laguna *et al*** (10)	129			9 (7.0%)
	Gkougkousis *et al* (11)	663		0/27 (0%)	13/342 (4.0%)
	Tseng *et al* (21)	118		7 (5.9%)	1 (0.8%)
TCIUO without occlusion of UO	**Li *et al*** (3)	91			5 (5.5%)
TCIUO with transvesical occlusion of UO with Endoloop®	**Matin *et al*** (23)	36			13.9%
	Kapoor *et al* (20)	98		10 (10.2%)	0
	Allard *et al* (4)	61		2 (3.3%)	
TCIUO with transurethral occlusion of UO with Endoloop®/ Polyloop®	**Agarwal *et al*** (8, 9)	13	0	0 (0%)	0 (0%)
		6	0	0 (0%)	0 (0%)
Laparoscopic extravesical stapling	**Matin *et al*** (23)	12		3 (25.0%)	5 (41.7%)
	Gkougkousis *et al* (11)	61		5/28 (18.0%)	2/14 (14.0%)
	Ritch et al (19)	14	7 (50%)	2 (14.0%)	
Robotic	**Tai *et al*** (14)	54	4 (7.4%)	3 (5.6%)	1 (1.9%)
	Aboumohamed *et al* (13)	60		5 (8.3%)	2 (3.3%)

TURUO - transurethral resection of the ureteric orifice

TCUIO - transurethral circumferential incision of the ureteric orifice

Table 3. Oncological outcomes of studies comparing different distal ureter excision techniques as a part of radical nephroureterectomy for urothelial carcinoma

Authors	Technique	n	Median follow up, months (range)	Oncological outcomes				
				Intravesical recurrence	Correlation of technique with IVR	Distant metastasis	Disease specific mortality	Correlation of technique with oncological outcome
Xylinas *et al* (2)	Open intravesical	1811	57.5 (1-271)	388 (21.4%)	Higher IVR in endoscopic group compared to open methods (p=0.02)		419 (23.1%)	2-year and 5-year CCS and OS similar in three groups
	Open extravesical	785		160 (20.3%)			175 (22.3%)	
	Endoscopic (TCIUO)	85		29 (34.1%)			11 (12.9%)	
Kapoor *et al* (20)	Open intravesical	406	24.6	77 (19.9%)	Lowest IVR in open intravesical method (p=0.0092)			Lowest RFS in open intravesical method (p<0.05)
	Open extravesical	316		66 (20.9%)				
	Endoscopic (TCIUO with transvesical loop ligation)	98		23 (23.5%)				
Li *et al* (3)	Open intravesical	81	33 (1-163)	23.5%	IVR not associated with ureteral technique (p=0.485)	7.4%		RFS and CSS was not associated with the three bladder cuff techniques (p=0.680 and p=0.502 respectively)
	Open extravesical	129		24.0%		10.1%		
	Endoscopic (TCIUO without occlusion of UO)	91		17.6%		5.5%		
Walton *et al* (5)	Mostly open intravesical	48	39 (14-204)	18 (78.3%)	IVR not associated with ureteral technique (p=0.465)			DSS similar in both groups (p=0.438)
	Endoscopic (Mostly TURUO)	90	46 (12-168)	39 (79.6%)				

Salvador-Bayarri *et al* (25)	Open method	87	22 (4-133)	34 (39.0%)	IVR not associated with ureteral technique			
	Endoscopic (TURUO)	58		20 (34.5%)				
Allard *et al* (4)	Open intravesical	20	22 (1-113)	7 (35.0%)	IVR not associated with ureteral technique (p=0.623)	2 (10.0%)		MFS not associated with technique (p=0.384)
	Open extravesical	29		8 (26.7%)		6 (20.6%)		
	Endoscopic (TCIUO with transvesical loop ligation	61		19 (31.1%)		10 (16.4%)		
Gkougkousis *et al* (11)	Open method	305	Not reported	83/228 (36.4%)		13/99 (13.1%)	23/177 (13.0%)	Insufficient evidence to support or refute endoscopic management of the distal ureter to open BCE
	Endoscopic (TURUO)	663		150/402 (37.3%)		15/218 (6.9%)	41/456 (9.0%)	
	Endoscopic (TCIUO with loop ligation/stapling)	114		14/70 (20.0%)		6/71 (8.5%)	1/38 (2.6%)	
	Extravesical lap stapling	61		5/12 (41.7%)		3/17 (17.6%)	0/9 (0%)	
	Ureteral stripping	169		28/135 (20.7%)		7/106 (6.6%)	7/77 (9.1%)	
Fragkoulis *et al* (26)	Open	192	80.4	46 (23.9%)	IVR not associated with ureteral technique (p=0.51)			No difference in 5-year CSS in both groups
	Endoscopic (TCIUO)	186		50 (26.8%)				
Ritch *et al* (19)	Open	10	16	2 (20.0%)		0 (0%)		No difference in RFS in 3 groups
	Pure laparoscopic	12	7	0 (0%)		0 (0%)		

	Extravesical laparosopic stapling	14	21	1 (7.1%)		2 (14.3%)	1 (7.1%)	

IVR - intravesical recurrence

TCIUO - transurethral circumferential incision of the ureteric orifice

TURUO - transurethral resection of the ureteric orifice

CSS - cancer specific survival

OS - overall survival

RFS - recurrence free survival

DSS - disease specific survival

MFS - metastatic free survival

BCE – bladder cuff excision

Figure 1[1]. Technique of cystoscopic loop ligation using Endoloop® and PolyLoop® and detachment of the distal ureter. (A) Ureteric orifice with a 1 cm bladder cuff is scored circumferentially and dissected through the partial detrusor thickness using a Collins knife. (Top B) The ureteric stump is ligated with PDS Endoloop®. (Top C) The ureteric stump, once ligated, is further dissected and detached from the bladder. (Bottom B) The PolyLoop® device is positioned over the ureteric stump, and the loop gently tightened by advancing the plastic sheath over the loop using the yellow cylinder. (Bottom C) The PolyLoop® is secured by sliding the silicone rubber stopper over the loop by pulling slider proximally. (Bottom D) The PolyLoop® is detached by pushing the slider distally. Ureteric stump is further dissected and detached from the bladder using a Collins knife.

[1] *Permission was granted by Elsevier Inc and S. Karger AG, Basel, for this figure to be reproduced. This figure was published in Urology, Vol 71, Agarwal DK, Khaira HS, Clarke D, Tong R. Modified transurethral technique for the management of distal ureter during laparoscopic assisted nephroureterectomy, 740-3, Copyright Elsevier (2008); and Current Urology, Vol 13, Agarwal DK. Agarwal PolyLoop Ligation Technique for the Management of the Distal Ureter during Laparoscopic Assisted Nephroureterectomy, 209-13, Copyright S. Karger AG (2019).*

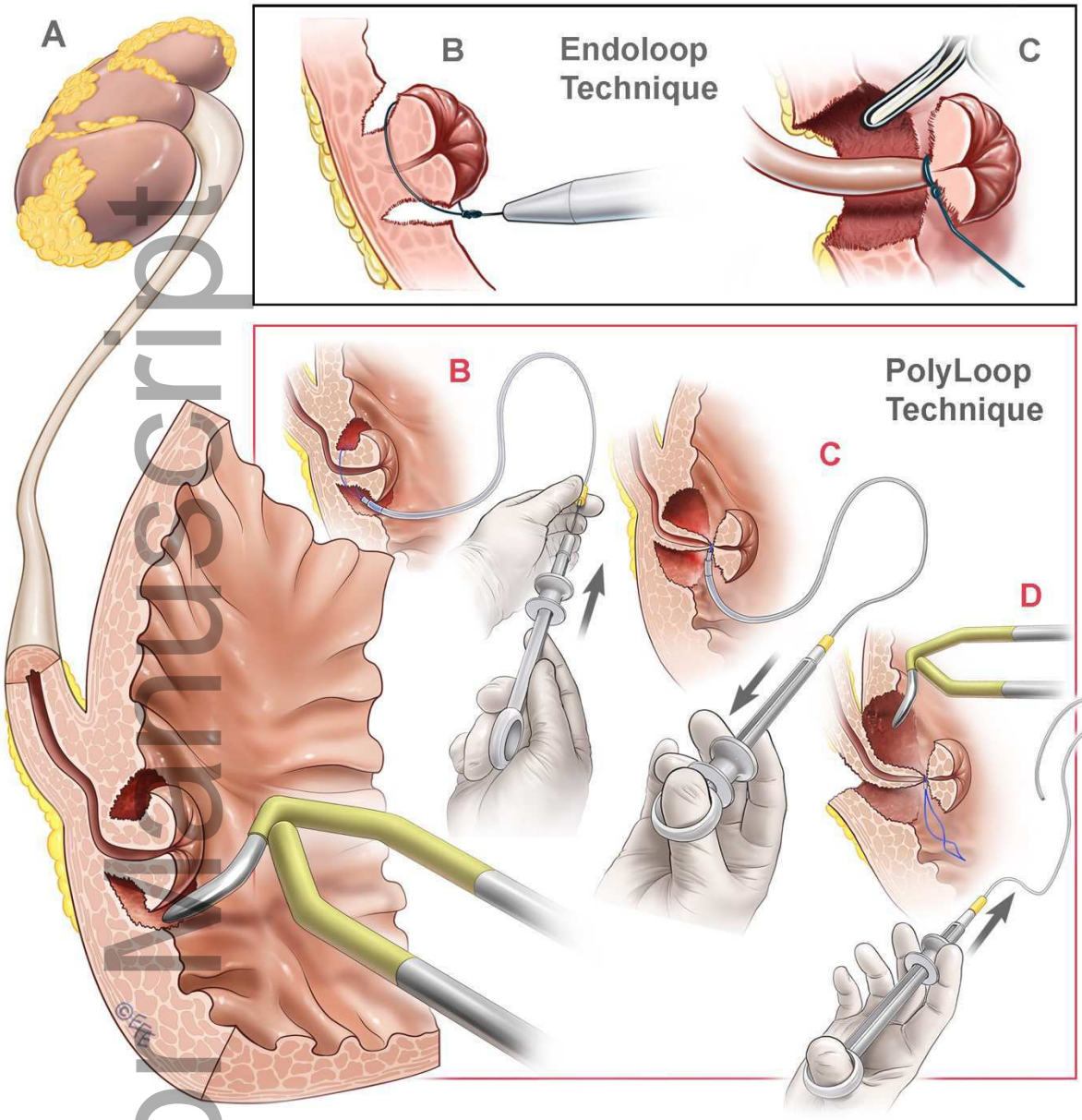


Figure 2. Kaplan Meier survival curves demonstrating the long-term survival rates for patients who underwent laparoscopic nephroureterectomy with Agarwal loop ligation technique. A) Overall survival. B) Cancer-specific survival. C) Metastasis-free survival. D) Local recurrence-free survival. E) Bladder recurrence-free survival. F) Cancer-specific survival by tumour stage

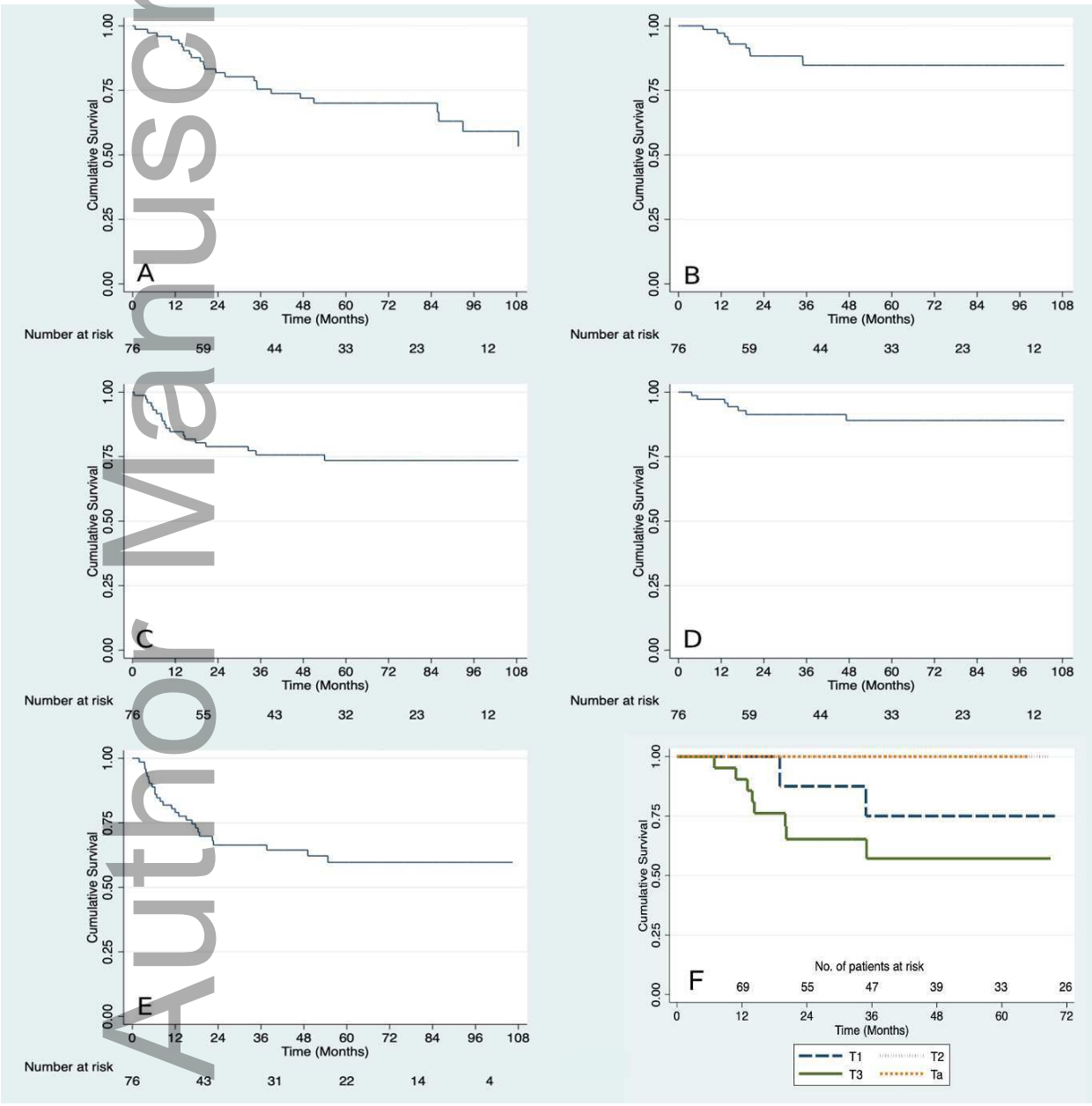
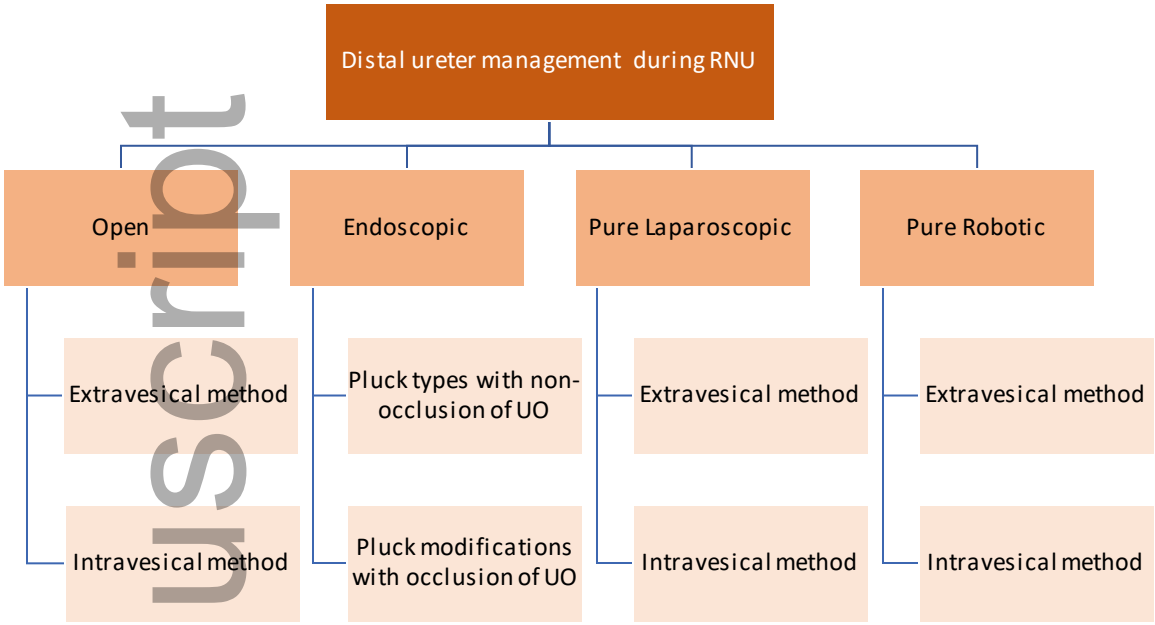


Figure 3. Techniques of distal ureter management during radical nephroureterectomy



Ureteral intussusception technique is rarely practiced nowadays and should be considered a historical approach

RNU - radical nephroureterectomy
UO - ureteric orifice