

Early vs. standard unclamping technique in minimal access partial nephrectomy: a meta-analysis of observational cohort studies and the Lister cohort

Thomas Stonier^{1,2} · Bhavan Prasad Rai³ · Mariele Trimboli² · Ahmed Abroaf² · Amit Patel⁴ · S. Gowrie-Mohan² · Venkat Prasad² · Nikhil Vasdev² · Jim Adshead²

Received: 9 May 2017 / Accepted: 1 August 2017 / Published online: 10 August 2017
© Springer-Verlag London Ltd. 2017

Abstract To evaluate if early unclamping (EUC) of the renal pedicle compromises perioperative outcomes in minimally invasive partial nephrectomy (PN). The cohort study includes all robot-assisted PN performed between September 2012 and September 2015 by a single surgeon at the Lister Hospital, Stevenage, UK. The systematic review and meta-analysis was performed according to the PRISMA guidelines identifying studies comparing EUC and standard unclamping (SUC) in either laparoscopic or robot-assisted PN. The Lister cohort prospectively reported 84 cases of robot-assisted PN (SUC = 22, EUC = 62) with a mean age of 58 years (SD = 11). The operative time (OT), estimated blood loss (EBL) and warm ischaemia time (WIT) were 186.5 min (SD = 33.8), 125.5 mls (SD = 188.91) and 16.7 min (SD = 5.6), respectively. The data from the Lister cohort were included in the meta-analysis. The systematic review identified four studies, encompassing 666 cases (313 SUC, 353 EUC), for inclusion in the final analysis. There was a statistically

significant difference in WIT in favour of the EUC group [−10.59 min (95% CI −16.58, −4.60)]. Specifically, the reduction in WIT was more pronounced in laparoscopic PN (−15.43 min (95% CI −19.05, −11.81)), when compared with the robotic PN [−5.60 min (95% CI −5.70, −5.50)]. There was no statistical difference in OT [−3.97 min (95% CI −14.22, 6.28)]. EBL was found to be increased in the EUC group [71.39 ml (95% CI −0.78, 143.56)]. There was no statistically significant difference in transfusion rates or complications between the two groups. The EUC technique for robot-assisted PN appears to offer a safe limited period of WIT without compromising perioperative outcomes and morbidity.

Keywords Unclamping · Declamping · Partial nephrectomy · Laparoscopic · Robotic · Warm ischaemia time

✉ Thomas Stonier
tomstonier@gmail.com

Bhavan Prasad Rai
urobhavan@gmail.com

Mariele Trimboli
mariele.trimboli@nhs.net

Ahmed Abroaf
abroaf@gmail.com

Amit Patel
drapatel@gmail.com

S. Gowrie-Mohan
s.gowrie@ntlworld.com

Venkat Prasad
venkat.prasad@nhs.net

Nikhil Vasdev
nikhilvasdev@doctors.org.uk

Jim Adshead
j.adshead@nhs.net

¹ Department of Urology, Princess Alexandra Hospital, Harlow, UK

² Department of Urology, Hertfordshire and South Bedfordshire Urological Cancer Centre, Lister Hospital, Stevenage, UK

³ Department of Urology, James Cook University Hospital, Middlesbrough, UK

⁴ Department of Radiology, Lister Hospital, Stevenage, UK

Introduction

Nephron sparing surgery is increasingly becoming the approach of choice when feasible in patients with renal tumours [1]. Although non-clamping techniques have been described, most surgeons would employ a transient period of renal pedicle clamping whilst excising the renal tumour during a partial nephrectomy. The duration of ischemic time during the clamp time is a key modifiable factor that could impact long-term renal function [2]. With the traditional open partial nephrectomy, cooling methods were employed to prolong ischemia time [3]. However, with contemporary minimally access surgery, such as conventional laparoscopy or robotic assisted partial nephrectomy, there is no robust cooling strategy. Hence surgeons are reliant on efficient renorrhaphy techniques to ensure minimal warm ischemic time. In the standard unclamping (SUC) technique, the renal artery is clamped until completion of inner and outer layer parenchymal renorrhaphy. Baumert et al. first described the early unclamping (EUC) technique in laparoscopic assisted partial nephrectomy (LAPN) [4]. They reported a reduction in Warm Ischemia Time (WIT) by 50% with EUC. EUC involves early unclamping of the renal pedicle following the inner layer non-parenchymal renorrhaphy [5]. However, there is concern over the risks involved such as greater blood loss, poorer renorrhaphy as a result of compromised reconstruction in a bleeding field and consequent morbidity associated with it [6].

In this study, we systematically review the literature comparing early outcomes of EUC and SUC in both laparoscopic and robotic assisted partial nephrectomy. The study also included the Lister Hospital experience of robot-assisted partial nephrectomy using both techniques.

Methods

Lister cohort

Study population and data source

All demographic and clinical data of patients who underwent a Robotic Assisted Partial Nephrectomy have been recorded in a prospectively maintained database at the Lister Hospital, Stevenage, UK since September 2012. The procedure was performed by a single surgeon (JA) with a transperitoneal approach. The following parameters were recorded in the database: patient age, gender, laterality, size, number four nephrometry scores (retrospectively recorded), operating time, estimated blood loss, warm Ischemia time (measured as time from clamping of the renal artery to unclamping), complications graded by

Clavien Dindo, transfusion rates and postoperative histology.

Non-lister cohort studies

Evidence acquisition

Criteria for considering studies for this review All randomised trials and observational studies comparing SUC and EUC with either Laparoscopic assisted partial nephrectomy (LAPN) or Robotic Assisted Partial Nephrectomy (RAPN) were considered.

Search strategy and study selection

The systematic review was performed according to the Cochrane guidelines. Databases searched were MEDLINE (2000–September 2016), EMBASE (2000–September 2016), Cochrane Central Register of Controlled Trials—CENTRAL (in The Cochrane Library—Issue 1, 2016), CINAHL (2000–September 2016 and Individual urological journals). The search was conducted on 24/09/2016. References of searched papers were also evaluated for potential inclusion. All studies comparing SUC and EUC with either LAPN or RAPN were evaluated.

Outcomes measures

1. Warm ischemia time (WIT)
2. Operative time (OT)
3. Estimated blood loss (EBL)
4. Transfusion rates
5. Overall complication rates
6. Clavien 3 and higher complication rates

Quality assessment of studies

Studies were rated for level of evidence according to the criteria provided by the Centre of Evidence Based Medicine in Oxford, UK [7].

Data extraction and analysis

Three reviewers (TS, B and MT) independently identified all studies that appeared to fit the inclusion criteria for full review. Disagreement was resolved by consensus. Comparable data from each study was combined in a meta-analysis where possible. The Lister cohort (LC) was also included in the meta-analysis. A Mantel–Haenszel Chi-square test was used for continuous data and expressed as the mean difference (MD) with 95% CI and for dichotomous data an Inverse Variance was used and expressed as

odds ratio (OR) or risk difference (RD) with 95% CI. *p* value was considered significant if <0.05. Heterogeneity was analysed using a χ^2 test on N-1 degrees of freedom, with an alpha of 0.05 used for statistical significance and with the I^2 test [8]. I^2 values of 25, 50 and 75% correspond to low, medium and high levels of heterogeneity. A fixed-effect model was used unless statistically significant high heterogeneity ($I^2 > 75\%$ was considered as significantly high heterogeneity) existed between studies. A random effects model was employed if heterogeneity existed. If the data available were deemed not suitable for a meta-analysis it was described in a narrative fashion.

Results

Lister cohort

A total of 84 cases (SUC = 22, EUC = 62) were performed for suspected renal malignancies. The mean age, and tumour size were 58 years (SD = 11) and 25.9 mm (SD = 9.8), respectively. The male:female ratio was 3:1. The mean operative time (OT), estimated blood loss (EBL) and warm ischaemia time (WIT) were 186.5 min (SD = 33.8), 125.5 mls (SD = 188.91) and 16.7 min (SD = 5.6). The Mean PADUA Score for the two cohorts were similar SUC -7.03 (2.01), EUC -7.44 (1.32), *p* -0.177. There was no significant difference in operation time and overall complications as shown in Table 1. The overall complication rate for the series was 27% (23/84). Twenty one of these cases were Clavien-2 or lower complications. There were 2 cases with Clavien-3a complications, both from the EUC group (Selective embolization of left renal artery, Pneumothorax). The mean WIT was significantly shorter in the EUC cohort (21.36 vs. 15.11 min, *p* < 0.05), as well as the mean EBL (161.82 vs. 89.44 mls *p* < 0.05). No patients required radical nephrectomy or

conversion to open surgery. One patient in the EUC cohort required a blood transfusion.

Systematic review

Literature search

The literature search yielded 200 publications, of which all but 15 were excluded due to non-relevance and repetition based on the titles and abstracts. Full manuscripts were evaluated in 15 publications, of which 4 were included into the systematic review, as shown in Fig. 1.

Included studies

Four studies that included 666 cases (313 SUC, 353 EUC) were used in the final analysis. Characteristics of the included studies are shown in Table 2. All of the studies were published since 2007. There were no randomised control trials. Two were prospective observational cohort studies [4, 5] and two were retrospective observational cohort studies [9, 10]. Peyronnet et al. was multi-centre study with surgeons of variable experience. In Nguyen et al., the surgeon had experience with SUC before changing their technique to a EUC technique. Baumert et al. was performed by a single very experienced surgeon (had performed many LPNs and over 400 laparoscopic procedures in total). Francisco et al. adopted the EUC technique after experience with >100 LPN, >150 laparoscopic radical nephrectomies, 5 robotic radical nephrectomies, and 5 RAPN performed using the standard clamping technique where the entire reconstruction was performed during WIT.

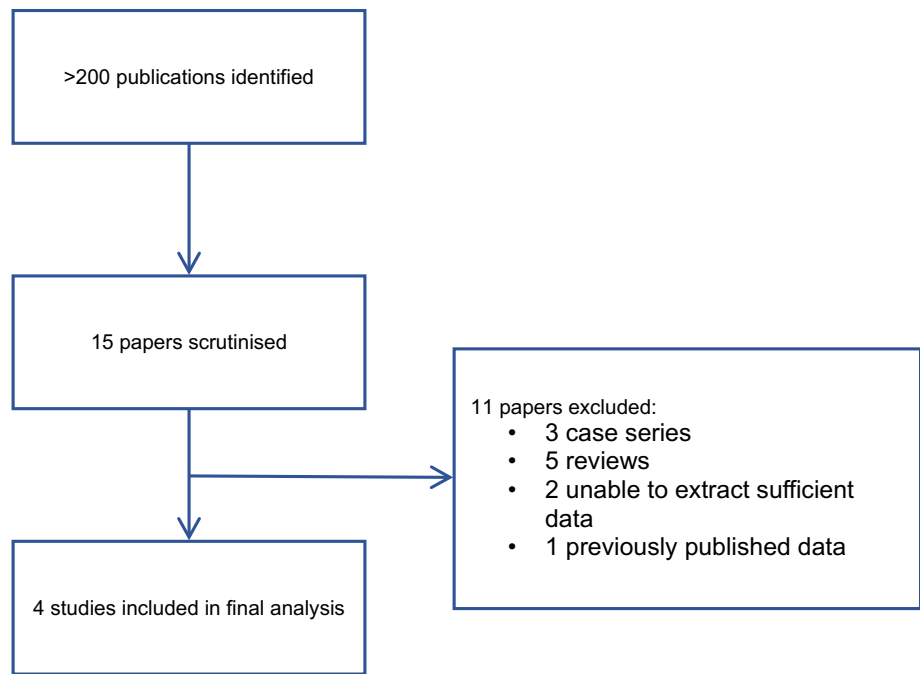
Excluded studies

Of the 11 studies excluded five were review papers. One publication included data which overlapped with another publication from the same group [11]. Two publications

Table 1 The demographic, perioperative and postoperative details of patients in the Lister cohort

	SUC <i>n</i> = 22	Early <i>n</i> = 62	<i>p</i> value
Mean age (SD)	58.86 (13.51)	57.81 (9.62)	0.69
Mean tumour size (SD)	24.45 (9.53)	26.12 (9.38)	0.4819
Mean PADUA Score (SD)	7.03 (2.01)	7.44 (1.32)	0.177
Operative time	199 (SD -44.75)	182.55 (SD -39.14)	0.13
WIT	21.36 (SD 6.31)	15.11 (SD -3.85)	<0.05
EBL	161.82 (SD 303.78)	89.44 (SD -105.5)	<0.05
Overall complication rates	5 (22.7%)	18(29%)	0.6
Clavien 1	7	9	
Clavien 2	9	16	
Clavien 3a	0	2	
Transfusion rates	0	1 (1.4%)	0.03

Fig. 1 PRISMA flowchart of studies identified for review



included patients who had undergone SUC and EUC but outcomes were presented as a combined group and so individual data required for this meta-analysis could not be extracted [12, 13]. Finally, three case series of EUC were excluded as there was no SUC comparison group. These studies included 16, 11 and 2 patients, respectively [14–16].

Outcomes

Warm ischaemia time (WIT) (Fig. 2)

Three studies from the literature and the LC were considered suitable for meta-analysis [4, 5, 10]. Kondo et al. was excluded from the meta-analysis as the standard deviation was not reported [9]. Two studies used a laparoscopic approach [5, 10] and two used a robotic approach [9]. Within the laparoscopic cohort there was high degree of heterogeneity hence a random effect model was used.

There was statistically significant difference in WIT favouring the EUC cohort across all subgroups:

Overall: mean difference (IV, Random, 95% CI) -10.59 [$-16.58, -4.60$]

Laparoscopic: mean difference (IV, Random, 95% CI) -15.43 [$-19.05, -11.81$]

Robotic: mean difference (IV, Random, 95% CI) -5.60 [$-5.70, -5.50$]

Operative time (OT) (Fig. 3)

Three studies from the literature and the LC were considered suitable for meta-analysis [4, 5, 10]. Kondo et al. was

excluded from the meta-analysis as the standard deviation was not reported [9]. Two studies used a laparoscopic approach [5, 10] and two used a robotic approach [9]. Within the laparoscopic cohort there was high degree of heterogeneity hence a random effect model was used.

There was no statistically significant difference in operative time across all the subgroups between the two techniques:

Overall: mean difference (IV, Random, 95% CI) -3.97 [$-14.22, 6.28$]

Laparoscopic: mean difference (IV, Random, 95% CI) -6.71 [$-36.88, 23.47$]

Robotic: mean difference (IV, Random, 95% CI) -4.77 [$-19.09, 9.55$]

Estimated blood loss (EBL) (Fig. 4)

Three studies from the literature and the LC were considered suitable for meta-analysis [4, 5, 10]. Kondo et al. was excluded from the meta-analysis as the standard deviation was not reported [9]. Two studies used a laparoscopic approach [5, 10] and two used a robotic approach [9]. In the robotic subgroup there was significant degree of heterogeneity in the results ($I^2 = 89\%$). Peyronnet et al. reported a trend towards increased EBL in the EUC group [10], while the LC showed a trend towards increased EBL in the SUC group. In view of the heterogeneity a random effect model was used. There was a significant difference in EBL between the two technique favouring the SUC technique overall (mean difference (IV, Random, 95% CI) 71.39 [$-0.78, 143.56$]) and in the laparoscopic subgroup

Table 2 The baseline demographic, perioperative and postoperative details the studies identified in the systematic review

Author	Cohort	No. pts.	Mean age years (SD)	Mean tumour size mm (SD)	Nephrometry score	LPN/ RAPN	Approach (transperitoneal/retroperitoneal)	OT mins (SD)	EBL ml (SD)	WIT mins (SD)	Overall complications	>3a Clavien complications
Baumert [4]	SUC	20	63 ± 15	-	-	LPN	-	111 ± 19	152 ± 194	27.2 ± 5	6	3
	EUC	20	58 ± 15	-	-	LPN	-	118 (± 30) <i>p</i> = 0.4	237 (±30) <i>p</i> = 0.17	13.7 (±4) <i>p</i> < 0.01	5	1
Nguyen [5]	SUC	50	58.8 (13.9)	28 (22)	-	LPN	Trans	246 (66)	231 (134)	31.1 (7.1)	11	7
	EUC	50	59.9 (12.9)	33 (14)	-	LPN	Trans	222 (66)	301 (304)	13.9 (4.8)	8	3
Peyronnet [10]	SUC	208	59.8 (0.8)	32.3 (1)	6.1 (RENAL)	RAPN	Trans	<i>p</i> = 0.15 174.5 (4.1)	<i>p</i> = 0.62 240 (28.1)	<i>p</i> < 0.0001 22.3 (0.55)	<i>p</i> = 0.61 44	22
	EUC	222	59.5 (0.77)	35.8 (1)	6.9 (RENAL)	RAPN	Trans	174.3 (4)	369.5 (27.6)	16.7 (0.53)	61	21
Kondo [9]	SUC	35	57.8 (range 36–81)	24.4 (range 9–43)	RENAL core range (4-6/7-9/10-12) <i>n</i> = 15/19/1	RAPN	Trans/retro <i>n</i> = 33/2	<i>p</i> = 0.97 190 (range 139–342)	<i>p</i> = 0.001 40 (range 5–150)	<i>p</i> < 0.001 23.3 (range 10–37)	<i>p</i> = 0.12 4	<i>p</i> = 0.07 1
	EUC	61	59.4 (range 36–82)	28.3 (range 9–71)	RENAL Score range (4-6/7-9/10-12) <i>n</i> = 23/32/6	RAPN	Trans/retro <i>n</i> = 56/5	190 (range 125–277)	30 (range 5–200)	16.3 (range 7–29)	3	0
			<i>p</i> = 0.73	<i>p</i> = 0.06	<i>p</i> = 0.39		<i>p</i> = 0.64	<i>p</i> = 0.61	<i>p</i> = 0.27	<i>p</i> < 0.001		

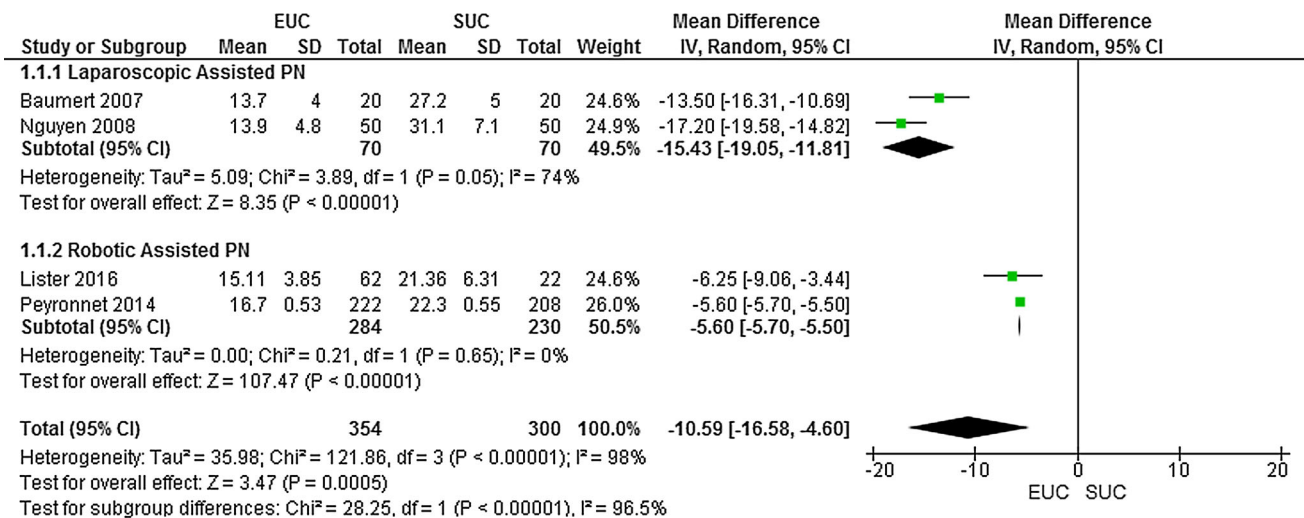


Fig. 2 Meta-analysis of observational studies reporting on warm ischaemia time (WIT)

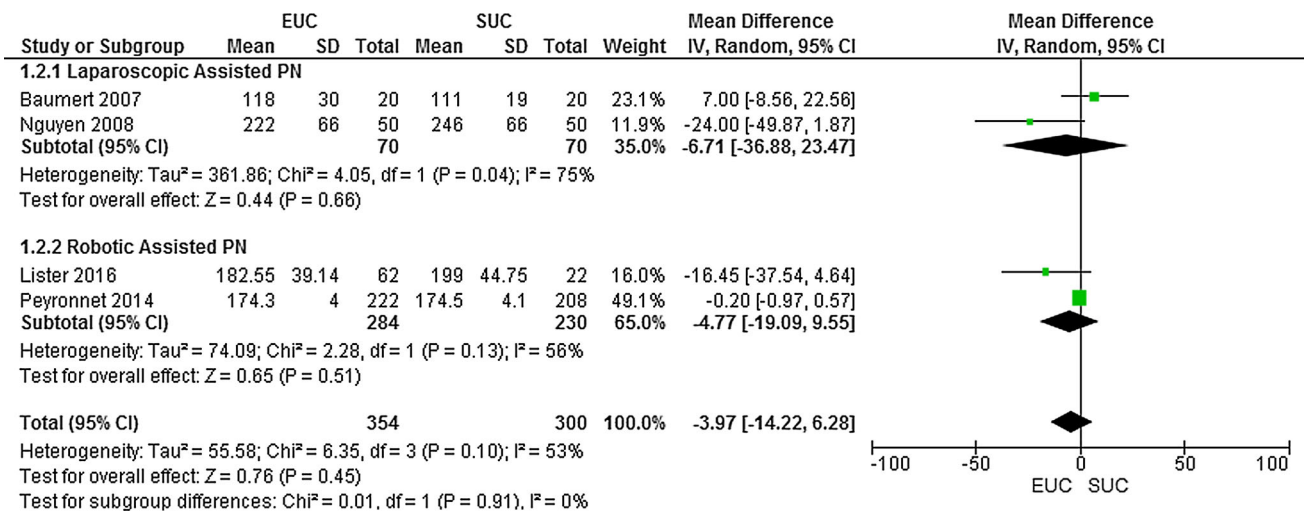


Fig. 3 Meta-analysis of observational studies reporting on operative time (OT)

(mean difference (IV, Random, 95% CI) 78.01 [15.14, 140.87]). In the robotic subgroup, there was no statistical difference between the two techniques (mean difference (IV, Random, 95% CI) 39.38 [-157.32, 236.08]).

Transfusion rate (Fig. 5)

Three studies from the literature and the LC were considered suitable for meta-analysis [4, 5, 10]. Kondo et al. was excluded from the meta-analysis as the standard deviation was not reported [9]. Two studies used a laparoscopic approach [5, 10] and two used a robotic approach [9]. A fixed model was used for analysis as there was low to medium level of heterogeneity across all categories. There was no statistically significant difference in transfusion rates across all subgroups between the two techniques:

Overall: odds ratio (M-H, Random, 95% CI) 1.22 [0.66, 2.24]).

Laparoscopic: odds ratio (M-H, Random, 95% CI) 0.18 [0.01, 4.01]).

Robotic: odds ratio (M-H, Random, 95% CI) 1.37 [0.73, 2.58]).

Overall complications rates (Fig. 6)

Four studies from the literature and LC were deemed suitable for a meta-analysis [4, 5, 9, 10]. Two studies used a laparoscopic approach [4, 5] and 3 studies used a robotic approach [9, 10]. A random effect model was used for analysis as there was a high degree of heterogeneity. There was no statistically significant difference in overall complication rates across all subgroups between the two techniques:

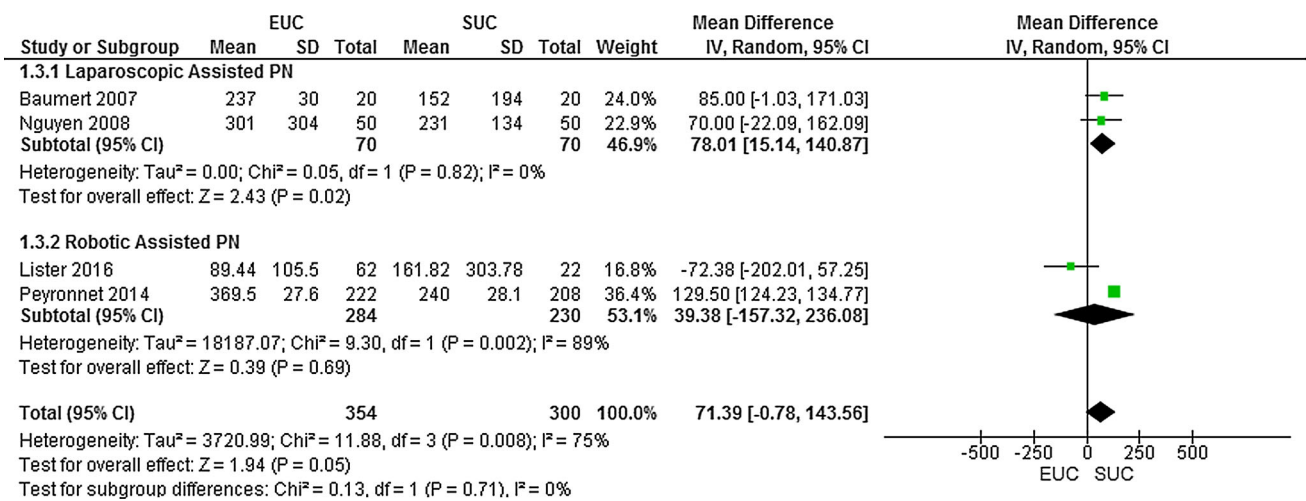


Fig. 4 Meta-analysis of observational studies reporting on estimated blood loss (EBL)

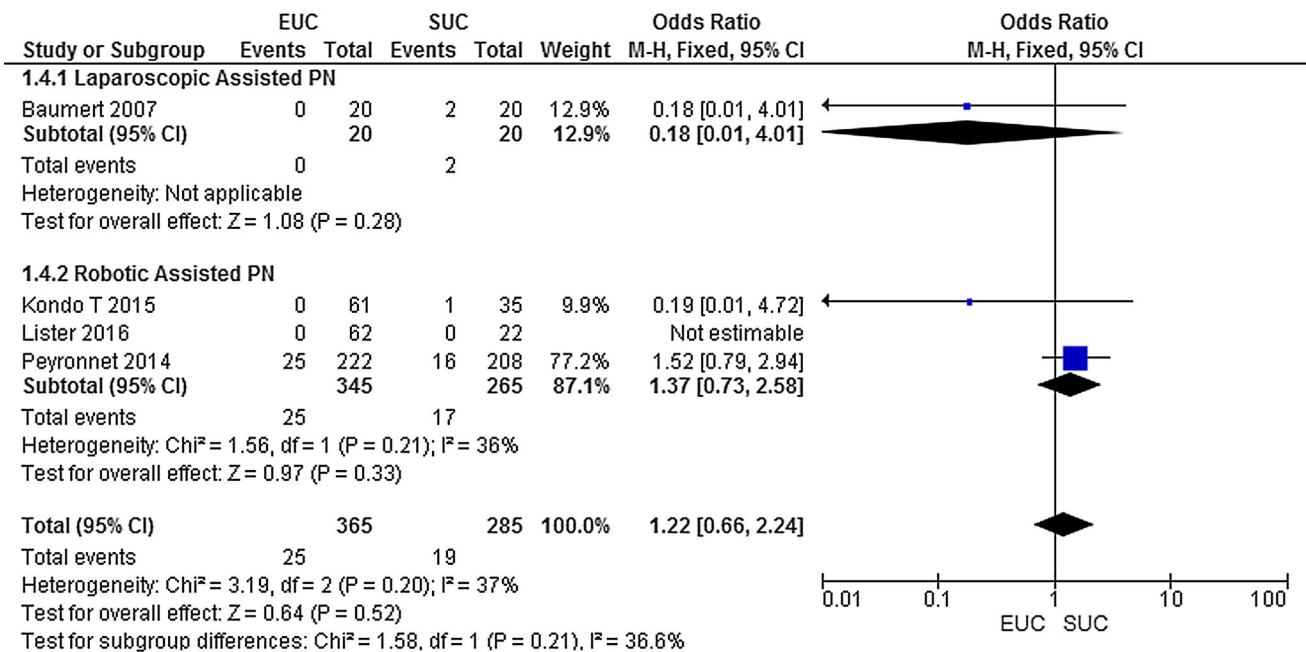


Fig. 5 Meta-analysis of observational studies reporting on transfusion rates

Overall: odds ratio (M-H, Random, 95% CI), 0.59 [0.27, 1.29]).

Laparoscopic: odds ratio (M-H, Random, 95% CI), 0.71 [0.31, 1.61]).

Robotic: odds ratio (M-H, Random, 95% CI) 0.51 [0.14, 1.79]).

≥Clavien 3a complication rates (Fig. 7)

Four studies from the literature and LC was deemed suitable for a meta-analysis [4, 5, 9, 10]. Two studies used a laparoscopic approach [4, 5] and 3 studies used a robotic approach [9, 10]. A fixed model was used for analysis as there was a low degree of heterogeneity across all

subgroups. There was no statistically significant difference in Clavien 3 or higher complications across all subgroups between the two techniques:

Overall: odds ratio (M-H, Random, 95% CI), 0.68 [0.42, 1.11]).

Laparoscopic: odds ratio (M-H, Random, 95% CI), 0.36 [0.11, 1.22]).

Robotic: odds ratio (M-H, Random, 95% CI), 0.78 [0.46, 1.35]).

Quality assessment of studies (Table 3)

All four studies from the systematic review [4, 5, 9, 10] and the Lister cohort were level 2b evidence. This included

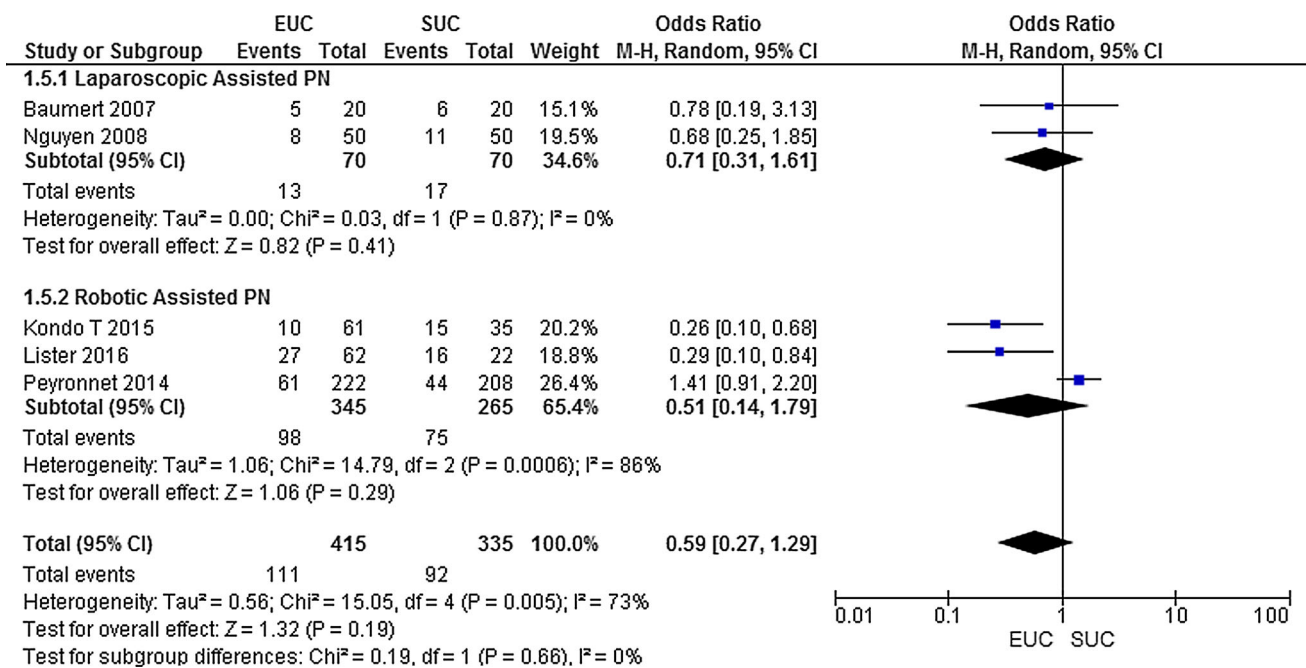


Fig. 6 Meta-analysis of observational studies reporting on overall complication rates

three prospective cohort studies, including the Lister cohort [4, 5], and two retrospective studies [9, 10]. There were no randomised controlled trials.

Discussion

This analysis highlights that the EUC technique significantly reduces WIT regardless of the approach employed. There was a trend towards increased blood loss with the EUC technique, which appeared to be more pronounced in the LAPN sub-group. Within the robotic sub-group increased blood loss was not consistently observed across all studies. Interestingly, in the LC the EBL was significantly lower in the EUC cohort. Kondo et al. which was not included in the meta-analysis, reported no difference in EBL between the EUC and SUC cohorts. Peyronnet et al. which was a large multi-institutional study with surgeons of varying expertise did suggest significantly higher EBL in the EUC cohort. However, it must be noted that in this study the RENAL nephrometry score in the EUC cohort was significantly higher than the SUC cohort in this study. This would suggest more complex tumours in the EUC cohort and thus likely more difficult surgery. It is plausible that in experienced hands the EBL is unlikely to be higher with EUC approach. Despite the perceived risk of increased EBL with the EUC technique, the transfusion rates between the two groups were not dissimilar. Both the techniques had equivalent complication rates.

The impact of ischemia time on long-term renal dysfunction is an area of much contention and debate. Thompson et al. reported in a cohort of 362 patients with a solitary kidney who underwent either an open or LAPN using warm ischemia with hilar clamping an increase in renal dysfunction after 25 min of WIT [17]. They went on to show that each additional minute of WIT was associated with a 5% increase in risk of developing AKI and 6% increased risk of new onset stage IV CKD. However, in another prospective study, Parekh et al. evaluated the tolerance of the human kidney to isolated controlled clamp ischemia, specifically observing the nature of the structural injury to the kidney that develops during and immediately after hilar clamping, and the behaviour of biomarkers. They concluded that human kidneys can safely tolerate 30–60 min of controlled clamp ischemia with only mild structural changes and no acute functional loss [18].

Whilst uncertainly exists regards the long-term renal consequence of the duration of ischemic time, a pragmatic approach would be to employ a limited period of ischemic time. The authors believe EUC technique offers a balance between offering adequate ischemic time without compromising perioperative outcomes and morbidity. Furthermore, apart from reducing WIT, the EUC technique allows the surgeon to identify significant bleeding points from the resected renal bed [4, 5, 19], permitting accurate hemostasis. Interestingly Kondo et al., in a series of 96 patients who underwent a RAPN, reported that early unclamping reduces the risk of asymptomatic renal artery pseudoaneurysm by 78% [9]. They too cite the fact that in

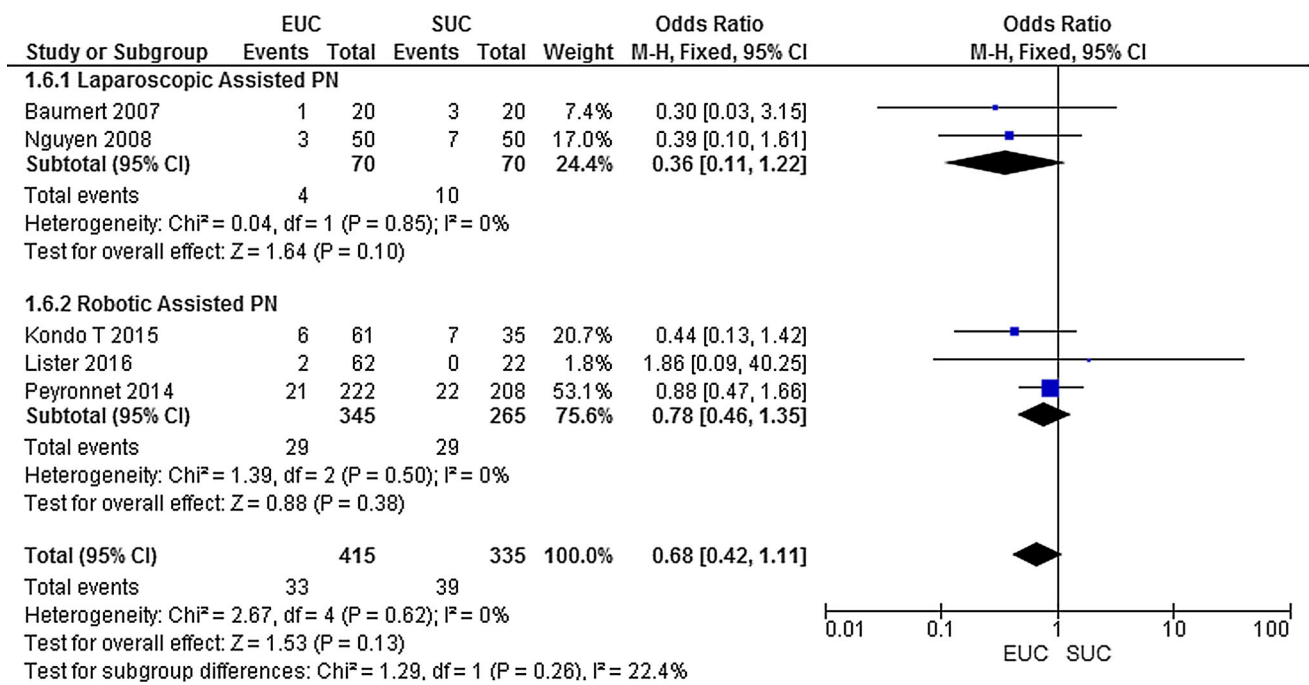


Fig. 7 Meta-analysis of observational studies reporting on \geq Clavien 3 complication rates

Table 3 The quality of the studies included according to criteria from the centre of evidence-based medicine [7]

Author	Year	Country	Study design	Level of evidence
Lister cohort	2016	United Kingdom	Prospective cohort	2b
Baumert [2]	2007	France	Prospective cohort	2b
Nguyen [6]	2008	USA	Prospective cohort	2b
Peyronnet [5]	2014	France	Retrospective cohort	2b
Kondo [9]	2015	Japan	Retrospective cohort	2b

open procedures it is standard to momentarily unclamp the renal pedicle to ensure there are no arterial bleeding points, and that with early unclamping this again becomes possible. Furthermore, it must be emphasised that reconstructive steps in RAPN are likely to be less technically challenging in comparison with LAPN and more widely adoptable [20]. Hence the issue with potential increased intraoperative blood loss in RAPN as observed in this review is less likely to be a concern. Additionally the need for a second outer parenchymal layer closure, particularly with the availability of sophisticated haemostatic agents, is in itself is contentious. The secondary closure does involve loss of vital nephrons and in select cases may not be necessary.

Two key limitations of this meta-analysis should be noted. The evidence quality was low, with no Level 1 prospective randomised control trials included. The follow-up period was short and so the long-term effect on renal function cannot be determined. Further research should look to address the limitations described. A large, randomised trial is warranted to provide robust evidence in favour of EUC by removing the confounding inherent in

the current selection of cohort studies. In particular long-term renal dysfunction in this patient population should be studied to determine the effect of reducing WIT, especially in the RAPN group. Furthermore, studies comparing EUC to other selective and off-clamp techniques will be of interest.

Conclusion

The EUC technique for minimally invasive PN appears to offer a safe limited period of WIT without compromising perioperative outcomes and morbidity. The robotic approach appears to further mitigate issues of such blood loss potentially associated with EUC technique due to the easier reconstructive ability. The EUC technique appears to offer balance between offering adequate ischemic time without compromising perioperative outcomes and morbidity. How EUC compares to other off-clamp and selective clamping approaches continues to be a matter of debate and future research interest.

Compliance with ethical standards

Conflict of interest Authors Stonier, Rai, Trimboli, Abroaf, Patel, Gowrie-Mohan, Prasad, Vasdev and Adshead declare that they have no conflict of interest.

Ethical standards All procedures performed in the studies involving human participants were in accordance with the ethical standards of our institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Formal consent from the patients was not required for this study.

References

- Huang WC, Levey AS, Serio AM, Snyder M, Vickers AJ, Raj GV et al (2006) Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. *Lancet Oncol* 7(9):735–740
- Lane BR, Gill IS, Fergany AF, Larson BT, Campbell SC (2011) Limited warm ischemia during elective partial nephrectomy has only a marginal impact on renal functional outcomes. *J Urol* 185(5):1598–1603
- Gill IS, Matin SF, Desai MM, Kaouk JH, Steinberg A, Mascha E et al (2003) Comparative analysis of laparoscopic versus open partial nephrectomy for renal tumors in 200 patients. *J Urol* 170(1):64–68
- Baumert H, Ballaro A, Shah N, Mansouri D, Zafar N, Molinie V et al (2007) Reducing warm ischaemia time during laparoscopic partial nephrectomy: a prospective comparison of two renal closure techniques. *Eur Urol* 52(4):1164–1169
- Nguyen MM, Gill IS (2008) Halving ischemia time during laparoscopic partial nephrectomy. *J Urol* 179(2):627–632 (**discussion 32**)
- Cawley O, Roman A, Brown M, Challacombe B (2015) Exploring the evidence for early unclamping during robot-assisted partial nephrectomy: is it worth the time and effort? *BJU Int* 115(4):506–507
- Phillips BSD, Badenoch D, Straus S, Haynes B (2016) Levels of evidence and grades of recommendation. <http://www.cebm.net/index.aspx?o=1025.%5D>. Accessed 20 Oct 2016
- Higgins JPT, Green S (2011) *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0: The Cochrane Collaboration
- Kondo T, Takagi T, Morita S, Omae K, Hashimoto Y, Kobayashi H et al (2015) Early unclamping might reduce the risk of renal artery pseudoaneurysm after robot-assisted laparoscopic partial nephrectomy. *Int J Urol Off J Jpn Urol Assoc* 22(12):1096–1102
- Peyronnet B, Baumert H, Mathieu R, Masson-Lecomte A, Grassano Y, Roumiguie M et al (2014) Early unclamping technique during robot-assisted laparoscopic partial nephrectomy can minimise warm ischaemia without increasing morbidity. *BJU Int* 114(5):741–747
- Aron M, Koenig P, Kaouk JH, Nguyen MM, Desai MM, Gill IS (2008) Robotic and laparoscopic partial nephrectomy: a matched-pair comparison from a high-volume centre. *BJU Int* 102(1):86–92
- Williams SB, Kacker R, Alemozaffar M, Francisco IS, Mechaber J, Wagner AA (2013) Robotic partial nephrectomy versus laparoscopic partial nephrectomy: a single laparoscopic trained surgeon's experience in the development of a robotic partial nephrectomy program. *World J Urol* 31(4):793–798
- Gill IS, Kamoi K, Aron M, Desai MM (2010) 800 Laparoscopic partial nephrectomies: a single surgeon series. *J Urol* 183(1):34–41
- Carlos AS, Tobias-Machado M, Starling ES, Correa de Araujo FB, Faria EF, Nogueira L et al (2013) Alternative techniques to reduce warm ischemia time in laparoscopic partial nephrectomy. *Int Braz J Urol Off J Braz Soc Urol* 39(1):145 (**discussion 6**)
- San Francisco IF, Sweeney MC, Wagner AA (2011) Robot-assisted partial nephrectomy: early unclamping technique. *J Endourol Endourol Soc* 25(2):305–308
- Lah K, Desai D, Chabert C, Gericke C, Gianduzzo T (2015) Early vascular unclamping reduces warm ischaemia time in robot-assisted laparoscopic partial nephrectomy. *F1000 Res* 4:108
- Thompson RH, Blute ML (2007) At what point does warm ischemia cause permanent renal damage during partial nephrectomy? *Eur Urol* 52(4):961–963
- Parekh DJ, Weinberg JM, Ercole B, Torkko KC, Hilton W, Bennett M et al (2013) Tolerance of the human kidney to isolated controlled ischemia. *J Am Soc Nephrol JASN* 24(3):506–517
- Hung AJ, Cai J, Simmons MN, Gill IS (2013) “Trifecta” in partial nephrectomy. *J Urol* 189(1):36–42
- Vasdev N, Giessing M, Zengini H, Adshead JM, Rabenalt R (2014) Robotic versus traditional laparoscopic partial nephrectomy: comparison of outcomes with a transition of techniques. *J Robot Surg* 8(2):157–161