Impact of bladder cuff management on oncologic outcomes following radical nephroureterectomy for upper tract urothelial carcinoma: A systematic review and meta-analysis

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ABSTRACT

Introduction: Bladder cuff excision (BCE) is an integral component of radical nephroureterectomy (RNU) for upper tract urothelial carcinoma (UTUC). While many approaches have been described, the optimal technique for BCE to provide maximal oncologic control remains unanswered. We aimed to perform a systematic review and meta-analysis to compare oncologic outcomes of different BCE techniques.

Methods: The Ovid MEDLINE, Embase, CENTRAL, and Web of Science databases were searched for studies comparing oncologic outcomes of RNU for UTUC based on different BCE approaches. Techniques for BCE were categorized as intravesical, extravesical, or endoscopic. Our primary outcomes were intravesical recurrence rate (IVR) and intravesical recurrence-free survival (IVRFS). Secondary outcomes included recurrence-free survival (RFS) and cancer-specific survival (CSS). Meta-analysis was

KEY MESSAGES

- A systematic review and meta-analysis of comparative studies assessing oncologic outcomes of nephroureterectomy and bladder cuff excision (BCE) for upper tract urothelial carcinoma (UTUC) was performed.
- Open intravesical BCE is associated with superior oncologic outcomes when compared to non-intravesical BCE.
- Endoscopic and non-endoscopic BCE demonstrate equivalent oncologic outcomes.

performed to compare the recurrence rates and survival outcomes associated with different BCE techniques.
Results: Forty studies assessing a total of 17 168 patients were identified for inclusion. Open intravesical BCE was associated with superior univariate IVRFS (hazard ratio [HR] 1.27, 95% confidence interval [CI] 1.13–1.42, p=0.04, I^2=43%), multivariate IVRFS (HR 1.44, 95% CI 1.16–1.80, p<0.0001, I^2=75%), univariate RFS (HR 2.30, 95% CI 1.04–5.10, p=0.0002, I^2=71%), and multivariate CSS (HR 1.62, 95% CI 1.22–2.15, p=0.33, I^2=14%) when compared to non-intravesical techniques. Subgroup analysis revealed that this difference was primarily driven by the inferiority of the open extravesical approach. Endoscopic and non-endoscopic BCE demonstrated equivalent univariate and multivariate IVRFS, RFS, and CSS.
Conclusions: Open intravesical BCE is associated with superior oncologic outcomes when compared to non-intravesical techniques. This difference is primarily driven by the open intravesical approach's superiority to the open extravesical approach. Endoscopic BCE showed equivalent outcomes when compared to non-endoscopic approaches. Prospective randomized trials can shed further light on the optimal approach to BCE.

INTRODUCTION

Radical nephroureterectomy (RNU) with bladder cuff excision (BCE) is the gold standard for treatment of localized high-risk upper tract urothelial carcinoma (UTUC). UTUC is associated with high rates of postoperative intravesical recurrence (IVR), likely due to tumour seeding prior to or during RNU[1–3]. Resection of the ipsilateral bladder cuff has been shown to lead to improved IVR compared to RNU without bladder cuff excision [4,5]. Both the European Association of Urology (EAU) and the American Urological Association (AUA) guidelines for management of localized UTUC recommend BCE for all cases of non-metastatic high-risk UTUC to minimize the risk of IVR [6–8].

Multiple different techniques have been described for performing BCE during RNU. Intravesical BCE involves creating an anterior cystotomy, allowing the ureteric orifice and surrounding bladder mucosa to be to be directly visualized and excised from within the bladder lumen, after which the bladder defect is formally closed in a watertight fashion to prevent extravasation of urine, facilitate early urethral catheter removal, and allow for intravesical instillation of chemotherapeutic agents. Extravesical BCE omits a formal cystotomy and instead involves the en bloc resection of the distal ureter and surrounding bladder mucosa. Laparoscopic and endoscopic approaches allow for omission of a second large abdominal incision for BCE, facilitating an entirely intracorporeal excision. The advent of robotic-assisted RNU has allowed for the minimally invasive implementation of both intravesical and extravesical BCE [9].

Endoscopic BCE techniques have been proposed to minimize the surgical complexity associated with open and laparoscopic BCE. This approach may be more suitable for patients with a prior history of pelvic surgery and radiation, for whom non-endoscopic approaches may be technically challenging. The pluck technique involves transurethral circumferential excision of the ureteric orifice and surrounding bladder mucosa with a Collin's knife, after which traction is applied to the ureter to separate, or "pluck", the bladder cuff from the rest of the bladder. Variations of the pluck technique utilizing laser excision of the intramural ureter have also been described [10,11]. In the intussusception technique, also known as the stripping technique, the ureteric orifice is intubated with a ureteric catheter, ureteric stone basket, or vein stripper in a retrograde fashion. The ureter is then ligated, thereby securing it to the inserted device, and divided proximally. The distal ureter is then intussuscepted into the bladder using gentle traction, after which the intramural ureter is excised in a transurethral fashion. As the intussusception technique involves intubation of the distal ureter, it is contraindicated for distal ureteric tumours.

The optimal BCE technique for maximizing oncologic outcomes remains unclear and to date there has been no randomized controlled trial (RCT) comparing outcomes when different approaches are utilized. As a result, the technique used often depends on surgeon preference. In this study, we aimed to perform a systematic review and meta-analysis of studies comparing oncologic outcomes between different methods of BCE.

METHODS

Search strategy

The research protocol was created a priori and was prospectively registered on PROSPERO (CRD42023476291). This review was conducted in accordance with the Cochrane Handbook for Systematic Reviews of Intervention and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. A comprehensive literature search was conducted on June 19, 2024 to identify articles comparing outcomes of different BCE techniques during RNU for UTUC. Databases searched included Ovid MEDLINE, Embase, CENTRAL, and Web of Science, with all duplicates being removed. We also searched grey literature, Google Scholar, and PubMed, as well as the references of included articles, in order to identify any published or unpublished studies that may have been missed in the initial literature search and were eligible for inclusion. Two reviewers performed title and abstract screening, full text review, and data collection (J.K. and A.A.). Our strategy is outlined in Supplemental Figure 1.

Data extraction

The inclusion and exclusion criteria were developed a priori. Inclusion criteria included studies that (1) compared outcomes between two or more methods of BCE during RNU for UTUC; (2) included adult patients (age ≥ 18 years) with UTUC; (3) reported on oncologic outcomes of RNU for UTUC. Exclusion criteria included: (1) case reports, expert and narrative reviews, conference abstracts, and editorials; (2) animal or basic science studies; (3) non-comparative studies; (4) studies that included RNU for treatment of conditions other than UTUC; (5) studies that did not report on oncologic outcomes; (6) studies that did not describe the BCE technique used; (7) studies that only compared RNU with and without BCE; (8) studies that different approaches to RNU without specifying differences in the BCE technique used; and (9) non-English studies for which an English translation was not available.

BCE techniques were classified into three groups, as previously described [12,13]. Technique that involved making a cystotomy and excising the ureteric orifice from within the bladder were classified as intravesical BCE. Excision of the bladder cuff and surrounding bladder without creating a cystotomy or entering the bladder, in either an open or laparoscopic manner, was classified as extravesical BCE. Transurethral resection or manipulation of the ureteric orifice were classified as endoscopic BCE. Transvesical BCE, which involves the percutaneous insertion of small laparoscopic ports directly into the bladder, were classified as endoscopic BCE in our study as these approaches require cystoscopy in order to guide trocar placement [14,15]. These techniques were further divided into subgroups based on the specific approach.

Primary outcomes included intravesical recurrence (IVR), described as a proportion, and intravesical recurrence-free survival (IVRS), presented as a hazard ratio (HR) with 95% confidence intervals (CI). Secondary outcomes included recurrence-free survival (RFS) and cancer-specific survival (CSS), presented as an HR with 95% CI. We also extracted data on other surgical and oncologic variables, including the rates of neoadjuvant chemotherapy, adjuvant chemotherapy, intravesical therapy, surgical approach), time to IVR, rates of lymph node dissection (LND), and rates of positive margins on final pathology. We included both univariate and multivariate calculations of HR.

In cases where we identified multiple studies which were published by the same authors, research group, or institution and there was a high likelihood that study data from these studies were drawn from significantly overlapping patient population, data analysis was conducted using only data from the study with the largest number of included patients.

For studies in which Kaplan-Meier curves were published without their associated HR, the curves was digitized using the online tool WebPlotDigitizer v4.6 (Rohatgi, Pacifica, California), which has previously demonstrated reliability in extracting data from published graphs [16,17]. The univariate HR was then extracted from the digitized curve data using the method outlined by Tierney et al. (2007) [18].

Assessment of study quality

The quality of non-randomized studies was assessed using the Newcastle-Ottawa scale [19]. Study quality was determined based on the score according to this scale. A score <4 was considered as having high risk of bias, a score of 4-6 was considered as having moderate risk of bias, and a score ≥7 was considered as having low risk of bias.

Statistical analysis

Extracted study data were summarized using descriptive statistics and analyzed using Review Manager v5.4 (The Cochrane Collaboration, London, United Kingdom). Meta-analysis of proportional data was performed using a random effects model and inverse variance method;

resulting odds ratios (OR) were presented with 95% CI. Meta-analysis of HR was performed using a random effects model and converted to log(HR) using generic inverse variance method; resulting HR was presented with 95% CI. Heterogeneity was assessed using a χ^2 test with N-1 degrees of freedom, with $\alpha = 0.05$ for statistical significance. The I^2 test was used to evaluate variability across studies, with an I^2 value ≥50% indicating high heterogeneity. Missing data were excluded from analysis. A p-value of <0.05 was considered statistically significant.

Sensitivity analysis was performed to assess the effect of follow up duration and history of bladder cancer on the meta-analysis by excluding studies with insufficient follow up, deemed to be <24 months, or studies that included patients with a prior or concomitant history of bladder cancer. Studies in which follow up or history of bladder cancer was not recorded were also excluded during sensitivity analysis.

RESULTS

Study identification

The initial database search retrieved 8 639 articles. After removal of duplicates, abstract review, full text review, and application of inclusion and exclusion criteria, a total of 36 studies were identified for inclusion; our manual search identified an additional four studies in our manual search and subsequently included in our study for a total of 40 studies included in our systemc review [10,20–31,31–57]. Figure 1 summarizes the search in a PRISMA flow diagram.

Study and population characteristics

Of the 40 included studies, all were observational studies, with 35 being retrospective and five being prospective. Publication dates ranged from 2005 to 2023. Included studies were most often published in Asia (13), North America (11), and Europe (11). In regards to surgical approach, 29 studies included open RNU, 29 included laparoscopic RNU, two included robot-assisted RNU, two included hand-assisted laparoscopic RNU, and one included hand-assisted retroperitoneoscopic RNU.

The pooled population consisted of 17 168 patients, with an average age of 68.7 years and 63.8% of patients being male. Of the 14 studies that reported on patient smoking status, 43.3% of included patients had a history of tobacco use. 14 studies excluded patients with a history of urothelial carcinoma of the bladder while 15 included patients with a prior bladder cancer; of these 15 studies, 27.8% of patients had history of bladder cancer. In the 11 remaining studies, bladder cancer history was not recorded. Across all studies, 19.2% of included patients had a previous history of bladder cancer. 11 studies reported on patients receiving LND, with 36.9% of patients undergoing lymphadenectomy.

23 studies reported on patients receiving chemotherapy. 17 studies reported on adjuvant chemotherapy status, with 13.5% of patients receiving postoperative chemotherapy. 13 studies reported on neoadjuvant chemotherapy status, the overall rate of neoadjuvant chemotherapy was 1.0% across these studies and 10 studies reported that no patients received preoperative chemotherapy. Postoperative instillation of intravesical chemotherapy was reported in 9 studies,

with 20.8% of patients receiving intravesical chemotherapy; only two of these studies reported on the type of intravesical chemotherapy used, with one study using mitomycin C and the other administering hydroxycamptothecin.

The median follow up period across studies was 40.9 months. 36 (90%) of 40 studies were considered to have low risk of bias based on their Newcastle-Ottawa scale score. Study characteristics and patient demographics are summarized in Table 1.

Intravesical recurrence

20 studies reported rates of IVR after RNU based on BCE technique (Fig 2). Meta-analysis of these studies demonstrated no significant differences in IVR rate between non-endoscopic (intravesical or extravesical) and endoscopic BCE (OR 0.91, 95% CI 0.72-1.14; p = 0.002, I^2 = 52%), extravesical (open or laparoscopic) and open intravesical BCE (OR 1.14, 95% CI 0.92-1.40; p = 0.02, I^2 = 54%), and stripping and non-stripping techniques (OR 1.23, 95% CI 0.62-2.42; p = 0.41, I^2 = 0%). However, sensitivity analysis revealed that, when only considering studies that excluded patients with a history of bladder cancer, intravesical BCE demonstrated a superior IVR rate compared to extravesical approaches (OR 1.31, 95% CI 1.07-1.61; p = 0.46, I^2 = 0%).

14 studies reported intravesical recurrence-free survival (IVRFS) after RNU based on BCE approach (Fig 3). Meta-analysis revealed that, when compared to open extravesical BCE, the open intravesical approach demonstrated superior univariate (HR 1.38, 95% CI 1.26-1.51; p = 0.60, I^2 = 0%) and multivariate (HR 1.52, 95% CI 1.21-1.92; p = 0.005, I^2 = 70%) IVRFS (Fig 3A, 3C). In contrast, there was no difference in univariate or multivariate IVRFS when comparing open intravesical BCE to the endoscopic approach. Similarly, endoscopic and extravesical (open or laparoscopic) BCE did not demonstrate any differences in univariate or multivariate IVRFS (3B, 3D).

Sensitivity analysis found that these results were preserved when excluding studies with follow up <24 months and studies including patients with a history of bladder cancer. While endoscopic BCE did demonstrate superior multivariate IVRFS compared to open extravesical BCE when only analyzing studies that excluded patients with a history of bladder cancer, this resulted in only a single study being included for meta-analysis; thus, this result was omitted from our sensitivity analysis.

Recurrence-free survival and cancer-specific survival

Ten studies reported RFS following RNU based on the BCE technique used (Fig 4). Our meta-analysis demonstrated that univariate RFS was superior with open intravesical BCE when compared to non-intravesical BCE modalities (HR 1.25, 95% CI 1.02-1.53; p = 0.0002, I^2 = 71%) (Fig 4A). There were no differences in univariate RFS when comparing endoscopic and non-endoscopic techniques (Fig 4B). We also did not identify any differences in multivariate RFS when comparing different BCE approaches (Fig 4C-D)

Nine studies described CSS after RNU according to BCE technique (Fig 5). Our meta-analysis identified no difference in univariate CSS when comparing non-intravesical to open intravesical BCE or when comparing non-endoscopic to endoscopic BCE (Fig 5A, 5B). However, we did find that open intravesical BCE was associated with superior multivariate CSS when compared to non-intravesical approaches (HR 1.62, 95% CI 1.22-2.15; $p = 0.33$, $I^2 = 14\%$). Additionally, open intravesical BCE demonstrated superior multivariate CSS when compared to the open extravesical approach (HR 1.41, 95% CI 1.09-1.84; $p = 0.92$, $I^2 = 0\%$) (Fig 5C). When comparing endoscopic to non-endoscopic BCE techniques, while there was no overall difference in CSS between groups, we found that endoscopic BCE was associated with superior multivariate CSS when compared to open extravesical BCE (HR 1.26, 95% CI 1.08-1.47; $p = 0.78$, $I^2 = 0\%$) (Fig 5D).

Sensitivity analysis demonstrated that, when excluding papers with follow up <24 months, univariate RFS became equivalent between non-intravesical and intravesical techniques. However, there was no impact on multivariate RFS, univariate CSS, or multivariate CSS. As the majority of papers included for analysis of RFS and CSS included patients with a history of bladder cancer, sensitivity analysis could not be performed on these results.

DISCUSSION

In the present meta-analysis, we found that the open intravesical approach to BCE was associated with superior univariate and multivariate IVRFS as well as multivariate CSS when compared to other techniques. Subgroup analysis found that this was primarily driven by the inferiority of the open extravesical approach to open intravesical BCE. The open intravesical approach was also associated with superior univariate RFS but this finding was not preserved in our sensitivity analysis, which found that, when excluding studies with follow up of <24 months, open intravesical BCE did not demonstrate superior univariate RFS when compared to non-intravesical approaches.

One potential explanation for the inferior oncologic outcomes associated with extravesical BCE when compared to the intravesical approach may be the increased risk of incomplete removal of the bladder cuff. While extravesical techniques allow for potential total intracorporeal excision of the intramural ureter during laparoscopic surgery, thus avoiding the need for a large incision, it prohibits visualization of the ureteric orifice, thereby increasing the risk of incomplete excision of the intramural ureter and injury to the contralateral ureteric orifice or trigone.

Previous meta-analyses examining oncologic outcomes based on BCE technique have suggested that endoscopic BCE is oncologically inferior to the intravesical approach [58–60]. In contrast, a systematic review by Yuan et al. (2014) found no difference in oncologic outcomes between endoscopic and transvesical BCE but focused on a multitude of risk factors for IVR rather than specifically focusing on different BCE techniques [61]. Compared to these previous meta-analyses, our study assessed a much larger number of studies and included only comparative studies. In addition, rather than analyzing the rate of recurrence alone, we incorporated data from survival analyses in the form of univariate and multivariate hazard ratios, as calculated with Kaplan-Meier curves and Cox proportional hazard regression, respectively. The inclusion of multivariate data allowed for mitigation of the impacts of potential confounders, such as tumour stage, patient age, adjuvant therapies, on our results. Therefore, our finding that endoscopic BCE is not inferior to the standard intravesical approach is likely to be supported by more robust data.

Previous reports have raised theoretical concerns regarding the increased risk of recurrence associated with endoscopic BCE techniques. Similar to extravesical BCE, endoscopic resection has been thought to increase the risk of incomplete excision of the intramural ureter. Prior studies have highlighted the potential increased risk of tumour seeding associated with endoscopic BCE due to the use of irrigation, which can promote extravasation of urine. The intussusception technique has been particularly scrutinized, as this technique involves eversion of the distal ureter into the bladder, which may promote IVR; indeed, the EAU guidelines specifically recommend against ureteric stripping for BCE [7]. Results of previous studies are inconclusive, with some studies reporting higher rates of BCE failure and worse oncologic outcomes with the stripping technique and others describing no equivalent outcomes when compared to other BCE techniques [62,63].

Our study found that endoscopic BCE demonstrated equivalent oncologic outcomes when compared to non-endoscopic techniques. This is in contrast to the aforementioned previous meta-analyses, which both found that endoscopic bladder cuff management was associated with worse oncologic outcomes [59,60]. This discrepancy may be due to the risk of tumour seeding during endoscopic BCE being overstated. The use of techniques that result in occlusion of the distal ureter prior to endoscopic resection may contribute to minimizing this risk. Multiple such techniques have been described in the literature, including coagulation of the orifice prior to resection or the use of a clip, balloon catheter, Endoloop® device, or fibrin sealant [14,64–66]. Furthermore, we also found that the intussusception technique did not demonstrate worse IVR compared to other techniques. However, this analysis is limited by the relative paucity of studies comparing the stripping technique to other approaches, as the majority of included studies that utilized an endoscopic approach used the pluck technique.

Our study is not without its limitations. To our knowledge, no RCT has been conducted to prospectively compare different BCE techniques during RNU. As a result, our results are derived from data extracted from non-randomized, retrospective, and observational studies. Additionally, we categorized both pluck and intussusception approaches as endoscopic BCE. However, when we analyzed the few studies comparing stripping to other BCE techniques, we found that stripping was not associated with an increased rate of IVR. Our sensitivity analysis was also unable to assess the impact of bladder cancer history on RFS and CSS as the majority of papers included patients with a history of bladder cancer; however, the impact of this confounder was accounted for by the multivariate results in our analysis.

Another limitation is the small sample size of patients that received chemotherapy or underwent LND in the included studies. In the few studies that did report this data, the majority of patients did not receive any form of chemotherapy or LND. Multiple meta-analyses including data from RCTs have supported the addition of neoadjuvant and adjuvant systemic chemotherapy as well as perioperative intravesical chemotherapy, to RNU for management of UTUC [67–72]. Similarly, LND at the time of RNU is recommended for prognostication and therapeutic purposes, particularly in high grade UTUC [73–76]. These data are reflected in the most recent guidelines from the AUA and EAU recommend that chemotherapy, in the form of adjuvant chemotherapy, neoadjuvant chemotherapy, and intravesical chemotherapy, and LND should both be considered in patients undergoing RNU for UTUC [4,5]. The small proportion of patients receiving chemotherapy or LND can be partially explained by the fact that many of the studies included in our meta-analysis were published prior to the implementation of these recommendations.

CONCLUSIONS

Open intravesical BCE during RNU is associated with superior oncologic outcomes when compared to non-intravesical techniques. This difference is primarily driven by the open intravesical approach's superiority to the open extravesical approach. Endoscopic BCE techniques showed equivalent outcomes when compared to non-endoscopic approaches. Further prospective randomized trials are needed to shed further light on the optimal approach to BCE.

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FIGURES AND TABLES

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

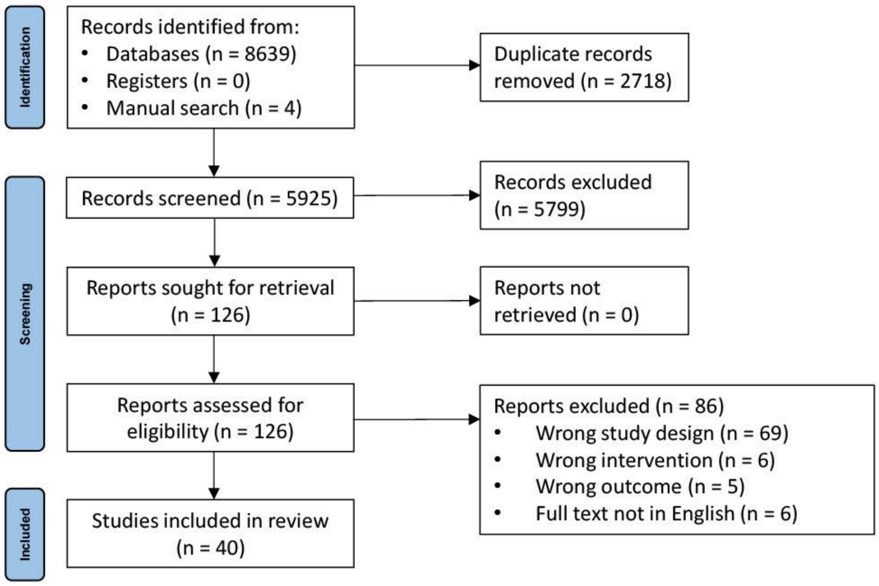
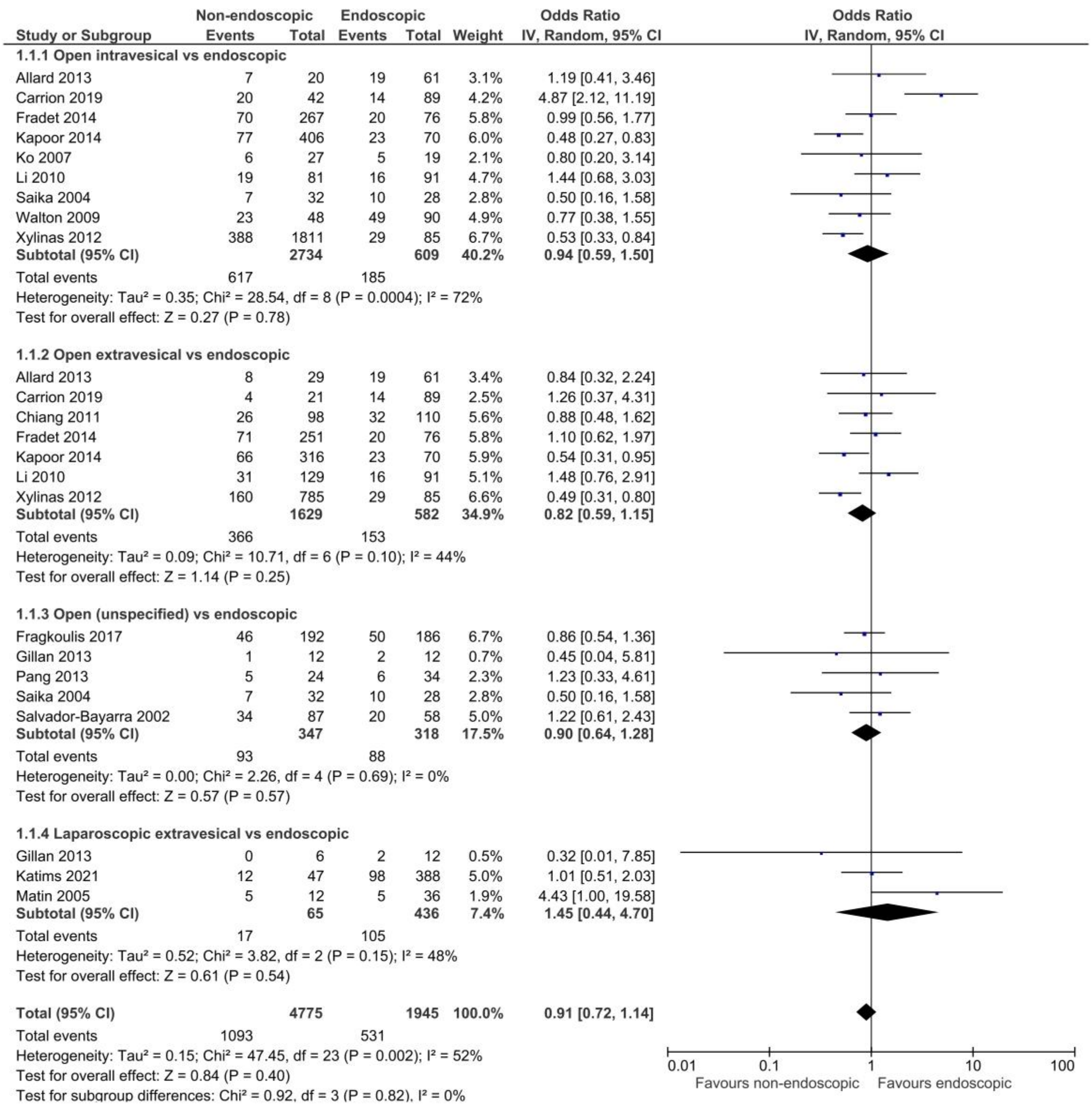
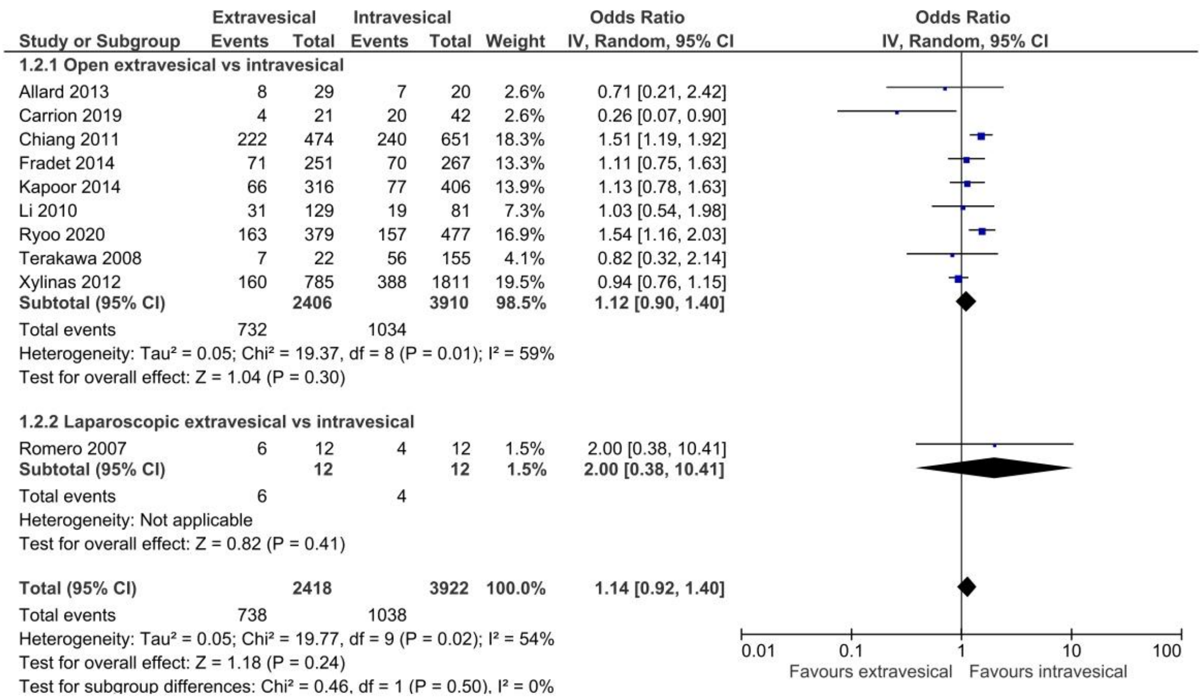


Figure 2. Forest plots comparing intravesical recurrence (IVR) rate in (A) non-endoscopic vs. endoscopic bladder cuff excision (BCE); (B) extravesical vs. intravesical BCE; and (C) non-stripping vs. stripping endoscopic BCE. CI: confidence interval.

A)



B)


Extravesical
Intravesical
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.2.1 Open extravesical vs intravesical
Allard 2013 8 29 7 20 2.6% 0.71 [0.21, 2.42]
Carrion 2019 4 21 20 42 2.6% 0.26 [0.07, 0.90]
Chiang 2011 222 474 240 651 18.3% 1.51 [1.19, 1.92]
Fradet 2014 71 251 70 267 13.3% 1.11 [0.75, 1.63]
Kapoor 2014 66 316 77 406 13.9% 1.13 [0.78, 1.63]
Li 2010 31 129 19 81 7.3% 1.03 [0.54, 1.98]
Ryoo 2020 163 379 157 477 16.9% 1.54 [1.16, 2.03]
Terakawa 2008 7 22 56 155 4.1% 0.82 [0.32, 2.14]
Xylinas 2012 160 785 388 1811 19.5% 0.94 [0.76, 1.15]
Subtotal (95% CI) 2406 3910 98.5% 1.12 [0.90, 1.40]
Total events 732 1034
Heterogeneity: Tau² = 0.05; Chi² = 19.37, df = 8 (P = 0.01); I² = 59%
Test for overall effect: Z = 1.04 (P = 0.30)
1.2.2 Laparoscopic extravesical vs intravesical
Romero 2007 6 12 4 12 1.5% 2.00 [0.38, 10.41]
Subtotal (95% CI) 12 12 1.5% 2.00 [0.38, 10.41]
Total events 6 4
Heterogeneity: Not applicable
Test for overall effect: Z = 0.82 (P = 0.41)
Total (95% CI) 2418 3922 100.0% 1.14 [0.92, 1.40]
Total events 738 1038
Heterogeneity: Tau² = 0.05; Chi² = 19.77, df = 9 (P = 0.02); I² = 54%
Test for overall effect: Z = 1.18 (P = 0.24)
Test for subgroup differences: Chi² = 0.46, df = 1 (P = 0.50), I² = 0%
0.01 0.1 1 10 100
Favours extravesical Favours intravesical

C)

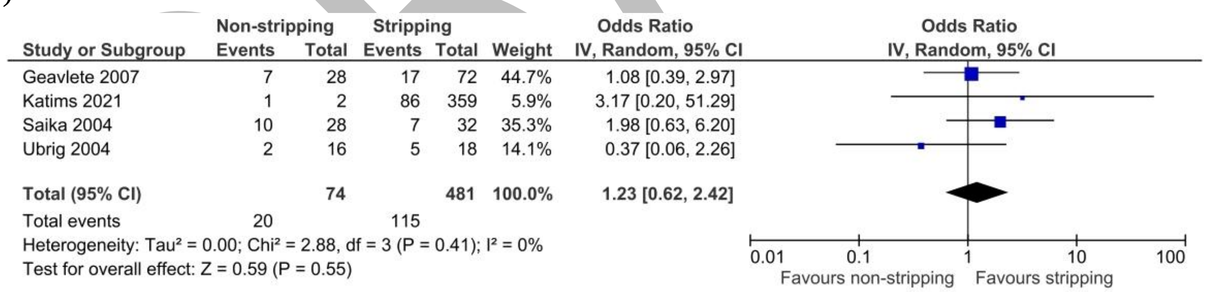
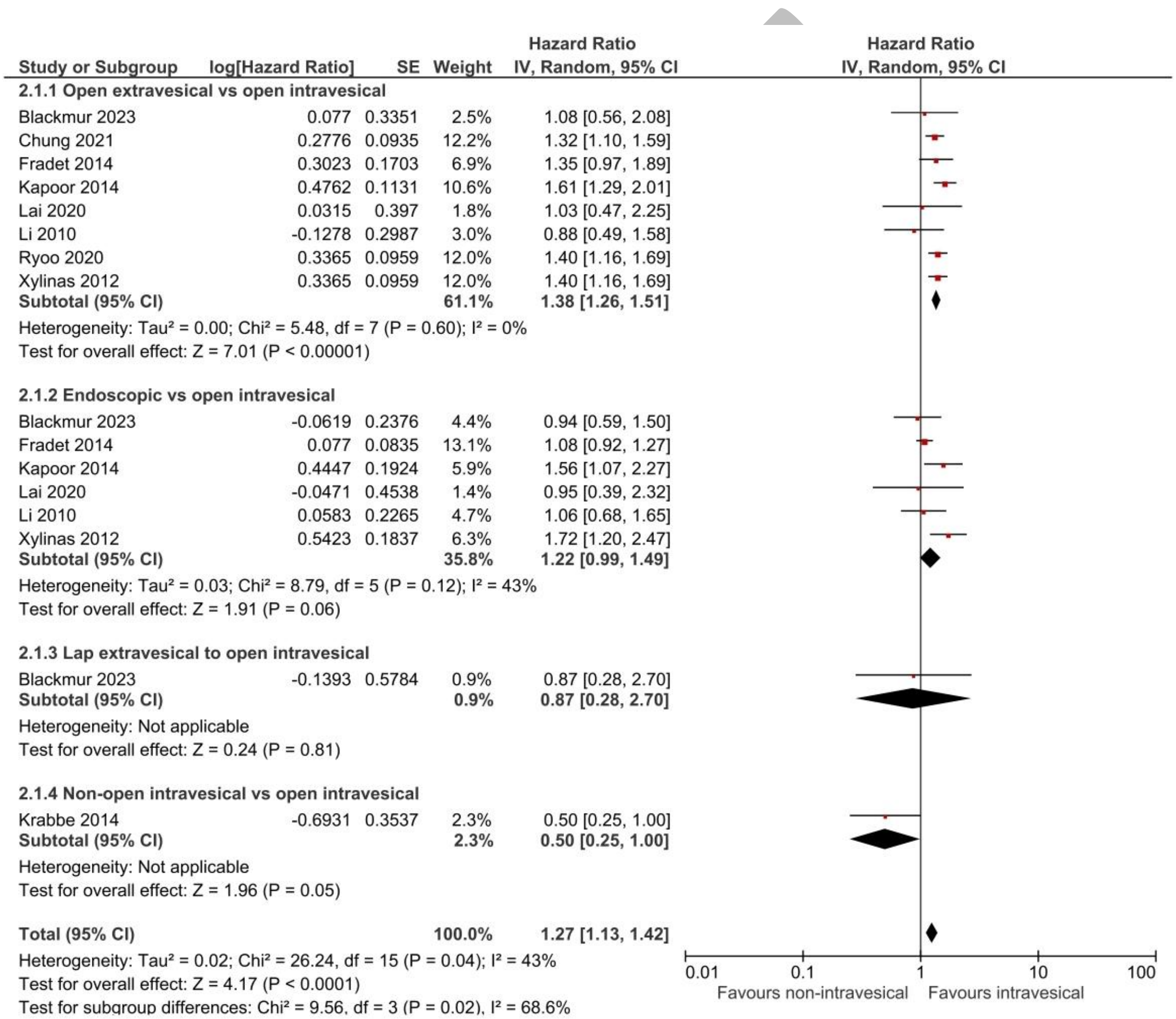

Non-stripping
Stripping
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Geavlete 2007 7 28 17 72 44.7% 1.08 [0.39, 2.97]
Katims 2021 1 2 86 359 5.9% 3.17 [0.20, 51.29]
Saika 2004 10 28 7 32 35.3% 1.98 [0.63, 6.20]
Ubrig 2004 2 16 5 18 14.1% 0.37 [0.06, 2.26]
Total (95% CI) 74 481 100.0% 1.23 [0.62, 2.42]
Total events 20 115
Heterogeneity: Tau² = 0.00; Chi² = 2.88, df = 3 (P = 0.41); I² = 0%
Test for overall effect: Z = 0.59 (P = 0.55)
0.01 0.1 1 10 100
Favours non-stripping Favours stripping

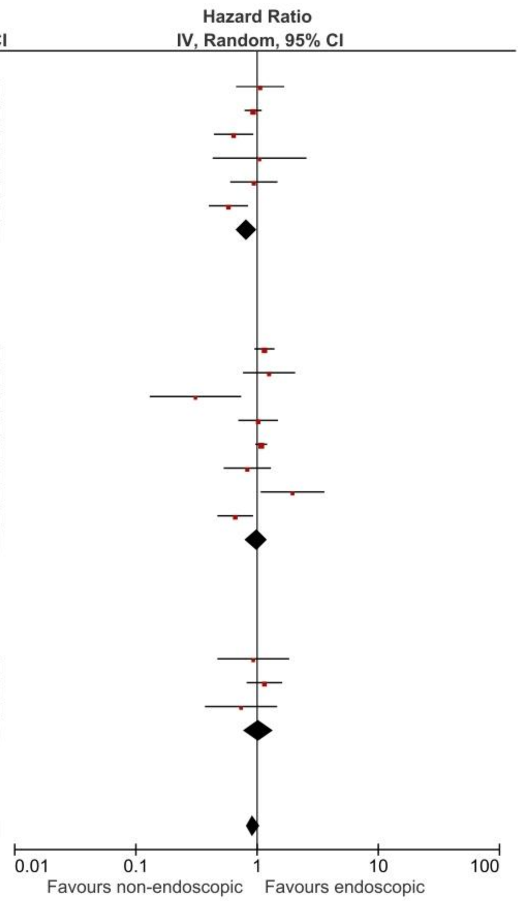
Figure 3. Forest plots comparing (A) univariate intravesical recurrence-free survival (IVRFS) in non-open intravesical vs. open intravesical bladder cuff excision (BCE); (B) univariate IVRFS in non-endoscopic vs. endoscopic BCE; (C) multivariate IVRFS in non-open intravesical vs. open intravesical bladder cuff excision (BCE); and (D) multivariate IVRFS in non-endoscopic vs. endoscopic BCE. CI: confidence interval.

A)

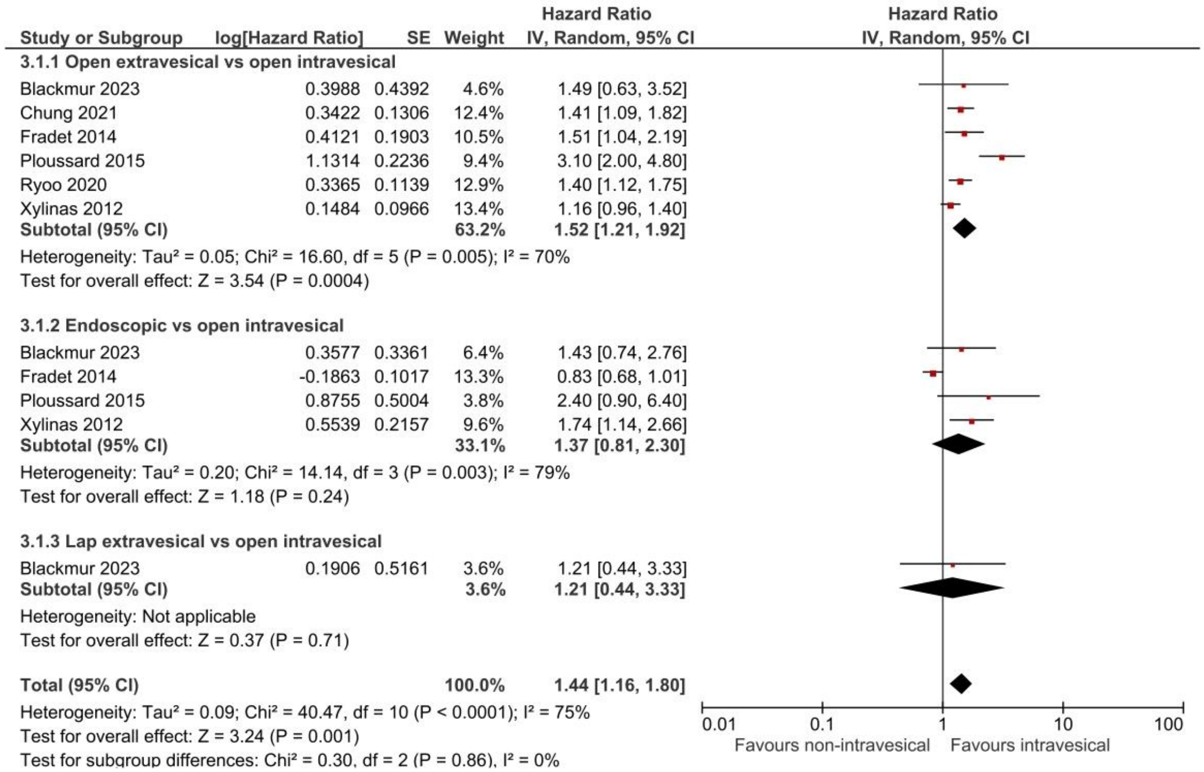


B)

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
2.2.1 Open intravesical vs endoscopic				
Blackmur 2023	0.0583	0.2341	5.1%	1.06 [0.67, 1.68]
Fradet 2014	-0.0758	0.0829	10.9%	0.93 [0.79, 1.09]
Kapoor 2014	-0.4463	0.1912	6.4%	0.64 [0.44, 0.93]
Lai 2020	0.0469	0.4545	1.9%	1.05 [0.43, 2.55]
Li 2010	-0.0619	0.2291	5.2%	0.94 [0.60, 1.47]
Xylinas 2012	-0.5447	0.1896	6.5%	0.58 [0.40, 0.84]
Subtotal (95% CI)			**36.0%**	**0.82 [0.67, 1.01]**
Heterogeneity: Tau² = 0.02; Chi² = 8.65, df = 5 (P = 0.12); I² = 42%				
Test for overall effect: Z = 1.90 (P = 0.06)				
2.2.2 Open extravesical vs endoscopic				
Blackmur 2023	0.1398	0.0975	10.3%	1.15 [0.95, 1.39]
Fradet 2014	0.2271	0.2532	4.6%	1.25 [0.76, 2.06]
Hara 2011	-1.1712	0.4434	2.0%	0.31 [0.13, 0.74]
Kapoor 2014	0.0198	0.1921	6.4%	1.02 [0.70, 1.49]
Lai 2020	0.0788	0.0573	12.0%	1.08 [0.97, 1.21]
Li 2010	-0.1863	0.2289	5.2%	0.83 [0.53, 1.30]
Luo 2014	0.6729	0.3088	3.5%	1.96 [1.07, 3.59]
Xylinas 2012	-0.4155	0.1732	7.0%	0.66 [0.47, 0.93]
Subtotal (95% CI)			**51.0%**	**0.99 [0.81, 1.21]**
Heterogeneity: Tau² = 0.05; Chi² = 21.56, df = 7 (P = 0.003); I² = 68%				
Test for overall effect: Z = 0.10 (P = 0.92)				
2.2.3 Lap extravesical vs endoscopic				
Blackmur 2023	-0.0726	0.3482	2.9%	0.93 [0.47, 1.84]
Gillan 2013	0.1395	0.1724	7.1%	1.15 [0.82, 1.61]
Katims 2021	-0.3052	0.3502	2.9%	0.74 [0.37, 1.46]
Subtotal (95% CI)			**12.9%**	**1.03 [0.78, 1.36]**
Heterogeneity: Tau² = 0.00; Chi² = 1.41, df = 2 (P = 0.50); I² = 0%				
Test for overall effect: Z = 0.23 (P = 0.82)				
Total (95% CI)			**100.0%**	**0.93 [0.81, 1.06]**
Heterogeneity: Tau² = 0.04; Chi² = 38.92, df = 16 (P = 0.001); I² = 59%				
Test for overall effect: Z = 1.12 (P = 0.26)				
Test for subgroup differences: Chi² = 2.35, df = 2 (P = 0.31), I² = 14.8%				



C)


Hazard Ratio
Hazard Ratio
Study or Subgroup log[Hazard Ratio] SE Weight IV, Random, 95% CI
IV, Random, 95% CI
3.1.1 Open extravesical vs open intravesical
Blackmur 2023 0.3988 0.4392 4.6% 1.49 [0.63, 3.52]
Chung 2021 0.3422 0.1306 12.4% 1.41 [1.09, 1.82]
Fradet 2014 0.4121 0.1903 10.5% 1.51 [1.04, 2.19]
Ploussard 2015 1.1314 0.2236 9.4% 3.10 [2.00, 4.80]
Ryoo 2020 0.3365 0.1139 12.9% 1.40 [1.12, 1.75]
Xylinas 2012 0.1484 0.0966 13.4% 1.16 [0.96, 1.40]
Subtotal (95% CI) 63.2% 1.52 [1.21, 1.92]
Heterogeneity: Tau² = 0.05; Chi² = 16.60, df = 5 (P = 0.005); I² = 70%
Test for overall effect: Z = 3.54 (P = 0.0004)
3.1.2 Endoscopic vs open intravesical
Blackmur 2023 0.3577 0.3361 6.4% 1.43 [0.74, 2.76]
Fradet 2014 -0.1863 0.1017 13.3% 0.83 [0.68, 1.01]
Ploussard 2015 0.8755 0.5004 3.8% 2.40 [0.90, 6.40]
Xylinas 2012 0.5539 0.2157 9.6% 1.74 [1.14, 2.66]
Subtotal (95% CI) 33.1% 1.37 [0.81, 2.30]
Heterogeneity: Tau² = 0.20; Chi² = 14.14, df = 3 (P = 0.003); I² = 79%
Test for overall effect: Z = 1.18 (P = 0.24)
3.1.3 Lap extravesical vs open intravesical
Blackmur 2023 0.1906 0.5161 3.6% 1.21 [0.44, 3.33]
Subtotal (95% CI) 3.6% 1.21 [0.44, 3.33]
Heterogeneity: Not applicable
Test for overall effect: Z = 0.37 (P = 0.71)
Total (95% CI) 100.0% 1.44 [1.16, 1.80]
Heterogeneity: Tau² = 0.09; Chi² = 40.47, df = 10 (P < 0.0001); I² = 75%
Test for overall effect: Z = 3.24 (P = 0.001)
Test for subgroup differences: Chi² = 0.30, df = 2 (P = 0.86), I² = 0%
0.01 0.1 1 10 100
Favours non-intravesical Favours intravesical

D)

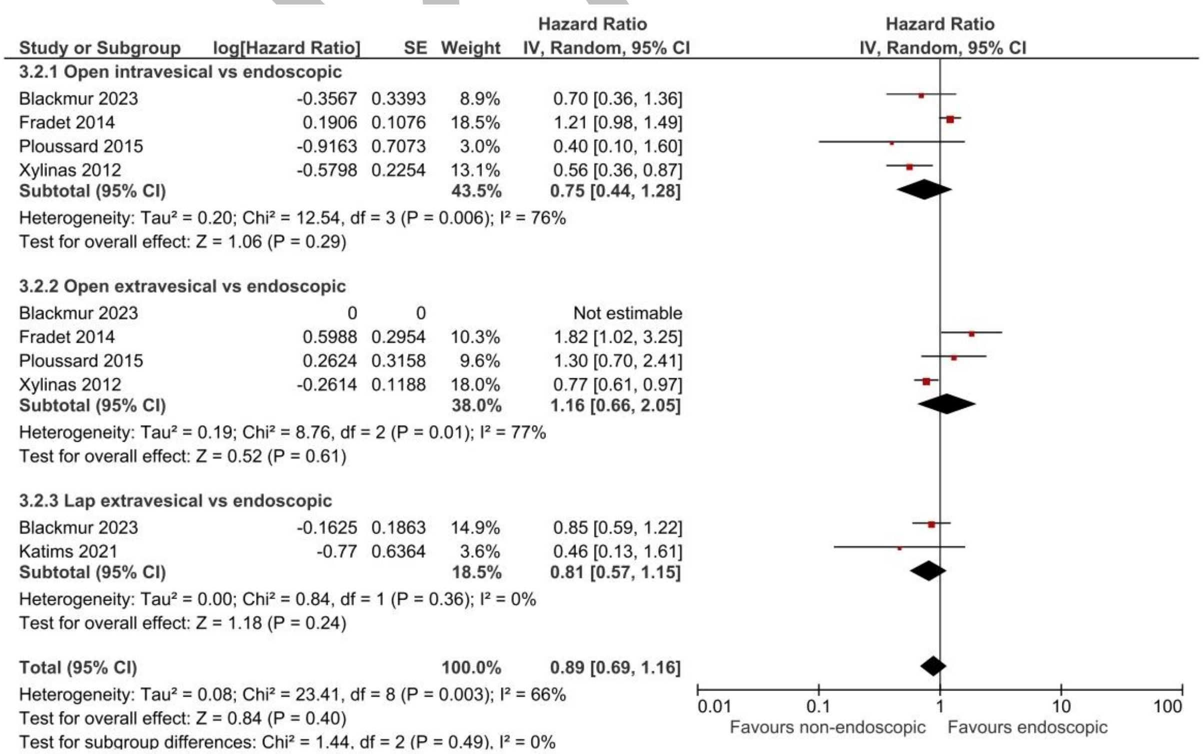
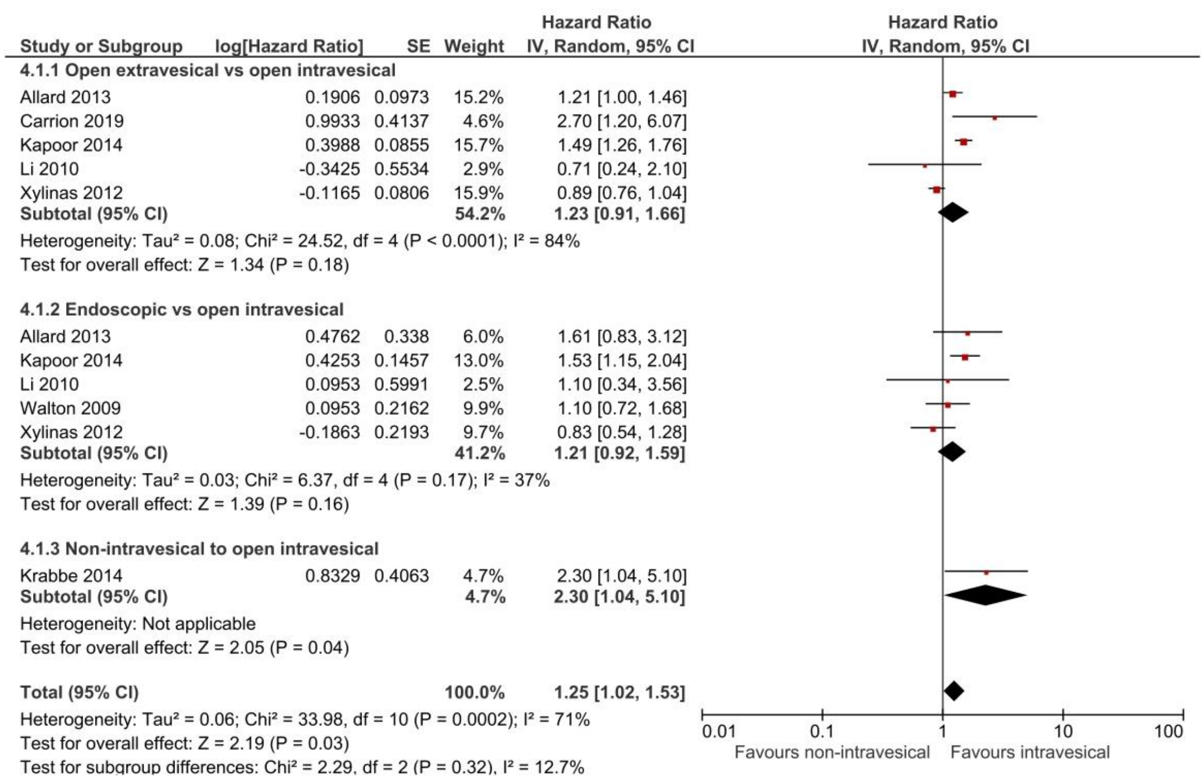
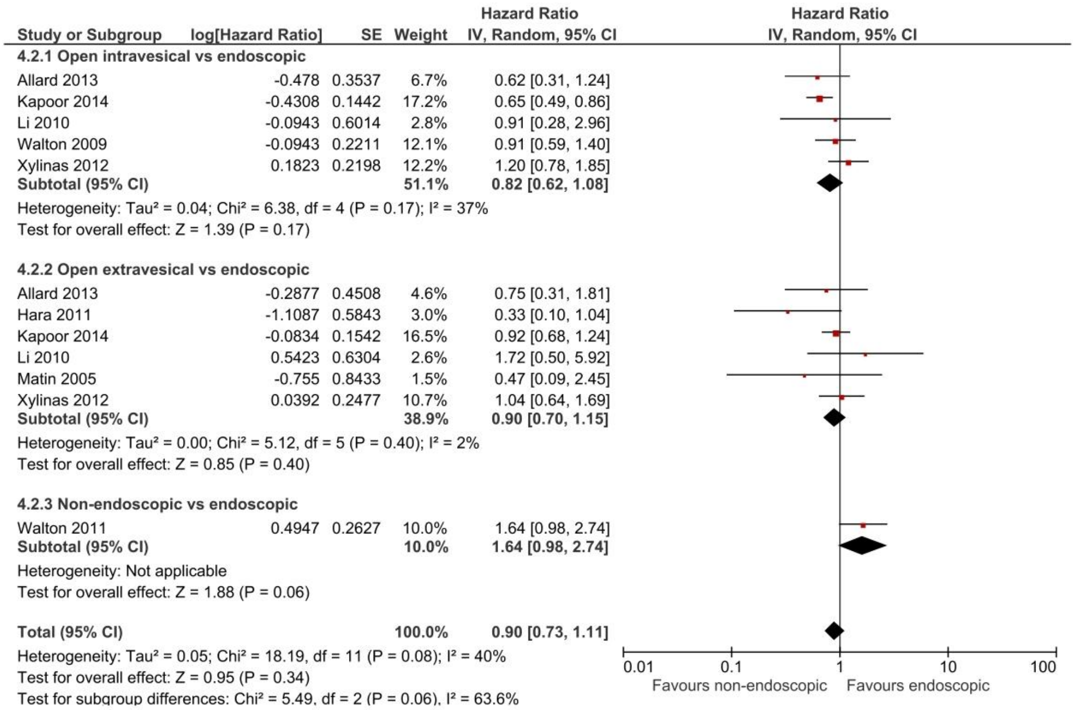

Hazard Ratio
Hazard Ratio
Study or Subgroup log[Hazard Ratio] SE Weight IV, Random, 95% CI
IV, Random, 95% CI
3.2.1 Open intravesical vs endoscopic
Blackmur 2023 -0.3567 0.3393 8.9% 0.70 [0.36, 1.36]
Fradet 2014 0.1906 0.1076 18.5% 1.21 [0.98, 1.49]
Ploussard 2015 -0.9163 0.7073 3.0% 0.40 [0.10, 1.60]
Xylinas 2012 -0.5798 0.2254 13.1% 0.56 [0.36, 0.87]
Subtotal (95% CI) 43.5% 0.75 [0.44, 1.28]
Heterogeneity: Tau² = 0.20; Chi² = 12.54, df = 3 (P = 0.006); I² = 76%
Test for overall effect: Z = 1.06 (P = 0.29)
3.2.2 Open extravesical vs endoscopic
Blackmur 2023 0 0 Not estimable
Fradet 2014 0.5988 0.2954 10.3% 1.82 [1.02, 3.25]
Ploussard 2015 0.2624 0.3158 9.6% 1.30 [0.70, 2.41]
Xylinas 2012 -0.2614 0.1188 18.0% 0.77 [0.61, 0.97]
Subtotal (95% CI) 38.0% 1.16 [0.66, 2.05]
Heterogeneity: Tau² = 0.19; Chi² = 8.76, df = 2 (P = 0.01); I² = 77%
Test for overall effect: Z = 0.52 (P = 0.61)
3.2.3 Lap extravesical vs endoscopic
Blackmur 2023 -0.1625 0.1863 14.9% 0.85 [0.59, 1.22]
Katims 2021 -0.77 0.6364 3.6% 0.46 [0.13, 1.61]
Subtotal (95% CI) 18.5% 0.81 [0.57, 1.15]
Heterogeneity: Tau² = 0.00; Chi² = 0.84, df = 1 (P = 0.36); I² = 0%
Test for overall effect: Z = 1.18 (P = 0.24)
Total (95% CI) 100.0% 0.89 [0.69, 1.16]
Heterogeneity: Tau² = 0.08; Chi² = 23.41, df = 8 (P = 0.003); I² = 66%
Test for overall effect: Z = 0.84 (P = 0.40)
Test for subgroup differences: Chi² = 1.44, df = 2 (P = 0.49), I² = 0%
0.01 0.1 1 10 100
Favours non-endoscopic Favours endoscopic

Figure 4. Forest plots comparing (A) univariate recurrence-free survival (RFS) in non-open intravesical vs. open intravesical bladder cuff excision (BCE); (B) univariate RFS in non-endoscopic vs. endoscopic BCE; (C) multivariate RFS in non-open intravesical vs. open intravesical bladder cuff excision (BCE); and (D) multivariate RFS in non-endoscopic vs. endoscopic BCE. CI: confidence interval.

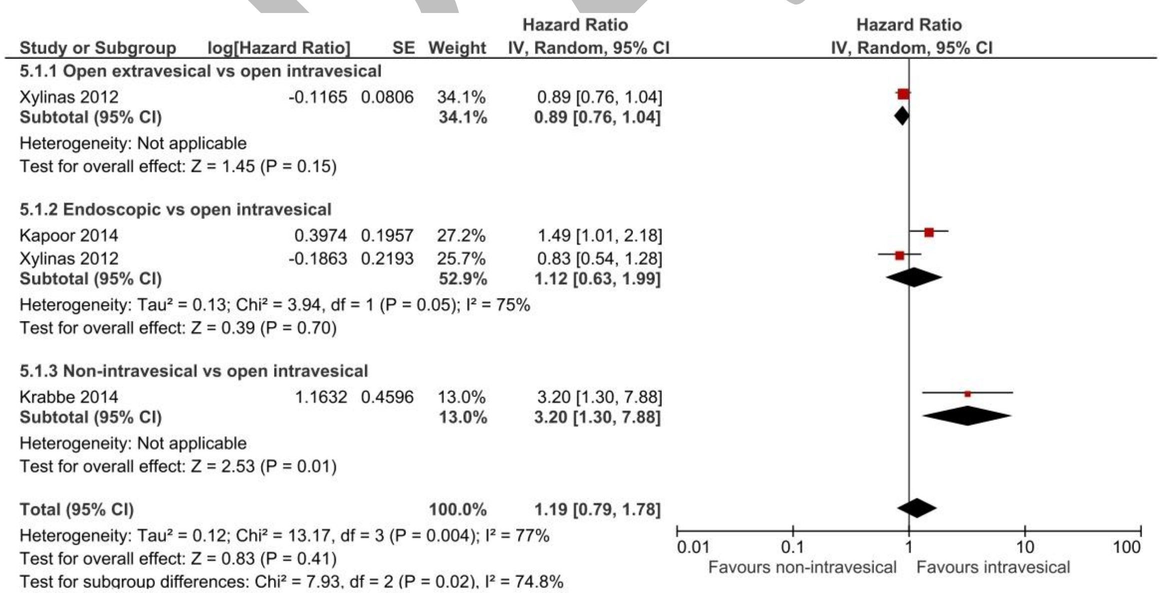
A)



B)


Study or Subgroup
log[Hazard Ratio]
SE
Weight
Hazard Ratio IV, Random, 95% CI
Hazard Ratio IV, Random, 95% CI
4.2.1 Open intravesical vs endoscopic
Allard 2013 -0.478 0.3537 6.7% 0.62 [0.31, 1.24]
Kapoor 2014 -0.4308 0.1442 17.2% 0.65 [0.49, 0.86]
Li 2010 -0.0943 0.6014 2.8% 0.91 [0.28, 2.96]
Walton 2009 -0.0943 0.2211 12.1% 0.91 [0.59, 1.40]
Xylinas 2012 0.1823 0.2198 12.2% 1.20 [0.78, 1.85]
Subtotal (95% CI) 51.1% 0.82 [0.62, 1.08]
Heterogeneity: Tau² = 0.04; Chi² = 6.38, df = 4 (P = 0.17); I² = 37%
Test for overall effect: Z = 1.39 (P = 0.17)
4.2.2 Open extravesical vs endoscopic
Allard 2013 -0.2877 0.4508 4.6% 0.75 [0.31, 1.81]
Hara 2011 -1.1087 0.5843 3.0% 0.33 [0.10, 1.04]
Kapoor 2014 -0.0834 0.1542 16.5% 0.92 [0.68, 1.24]
Li 2010 0.5423 0.6304 2.6% 1.72 [0.50, 5.92]
Matin 2005 -0.755 0.8433 1.5% 0.47 [0.09, 2.45]
Xylinas 2012 0.0392 0.2477 10.7% 1.04 [0.64, 1.69]
Subtotal (95% CI) 38.9% 0.90 [0.70, 1.15]
Heterogeneity: Tau² = 0.00; Chi² = 5.12, df = 5 (P = 0.40); I² = 2%
Test for overall effect: Z = 0.85 (P = 0.40)
4.2.3 Non-endoscopic vs endoscopic
Walton 2011 0.4947 0.2627 10.0% 1.64 [0.98, 2.74]
Subtotal (95% CI) 10.0% 1.64 [0.98, 2.74]
Heterogeneity: Not applicable
Test for overall effect: Z = 1.88 (P = 0.06)
Total (95% CI) 100.0% 0.90 [0.73, 1.11]
Heterogeneity: Tau² = 0.05; Chi² = 18.19, df = 11 (P = 0.08); I² = 40%
Test for overall effect: Z = 0.95 (P = 0.34)
Test for subgroup differences: Chi² = 5.49, df = 2 (P = 0.06), I² = 63.6%
0.01
0.1
1
10
100
Favours non-endoscopic
Favours endoscopic

C)


Study or Subgroup
log[Hazard Ratio]
SE
Weight
Hazard Ratio IV, Random, 95% CI
Hazard Ratio IV, Random, 95% CI
5.1.1 Open extravesical vs open intravesical
Xylinas 2012 -0.1165 0.0806 34.1% 0.89 [0.76, 1.04]
Subtotal (95% CI) 34.1% 0.89 [0.76, 1.04]
Heterogeneity: Not applicable
Test for overall effect: Z = 1.45 (P = 0.15)
5.1.2 Endoscopic vs open intravesical
Kapoor 2014 0.3974 0.1957 27.2% 1.49 [1.01, 2.18]
Xylinas 2012 -0.1863 0.2193 25.7% 0.83 [0.54, 1.28]
Subtotal (95% CI) 52.9% 1.12 [0.63, 1.99]
Heterogeneity: Tau² = 0.13; Chi² = 3.94, df = 1 (P = 0.05); I² = 75%
Test for overall effect: Z = 0.39 (P = 0.70)
5.1.3 Non-intravesical vs open intravesical
Krabbe 2014 1.1632 0.4596 13.0% 3.20 [1.30, 7.88]
Subtotal (95% CI) 13.0% 3.20 [1.30, 7.88]
Heterogeneity: Not applicable
Test for overall effect: Z = 2.53 (P = 0.01)
Total (95% CI) 100.0% 1.19 [0.79, 1.78]
Heterogeneity: Tau² = 0.12; Chi² = 13.17, df = 3 (P = 0.004); I² = 77%
Test for overall effect: Z = 0.83 (P = 0.41)
Test for subgroup differences: Chi² = 7.93, df = 2 (P = 0.02), I² = 74.8%
0.01
0.1
1
10
100
Favours non-intravesical
Favours intravesical

D)

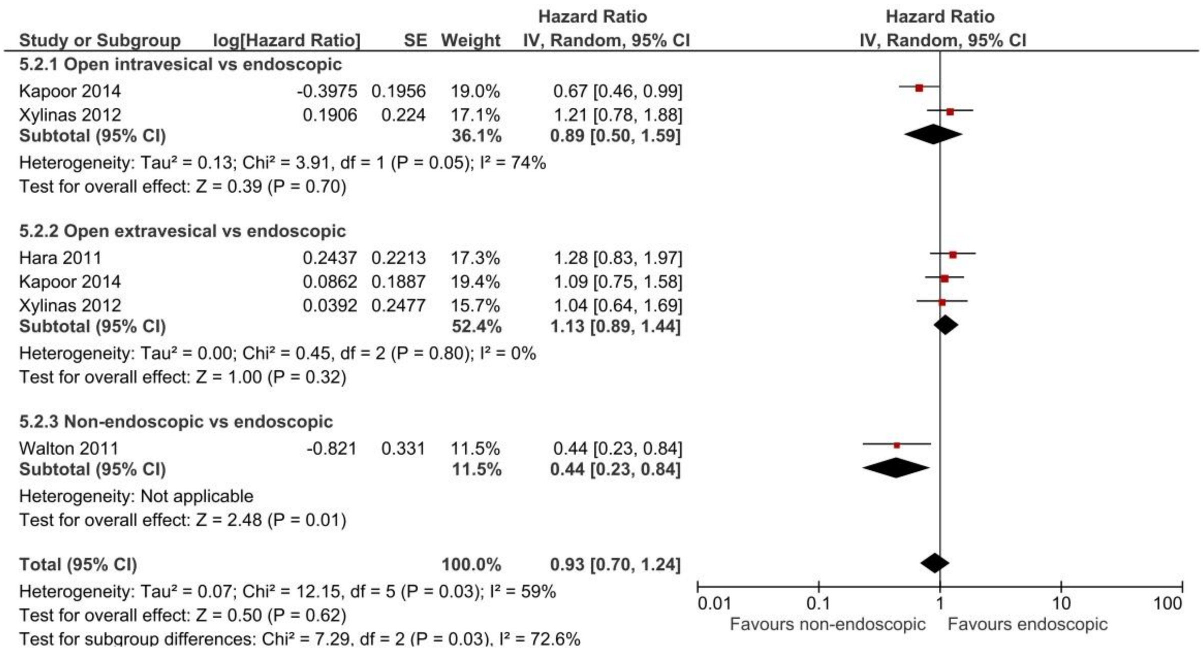
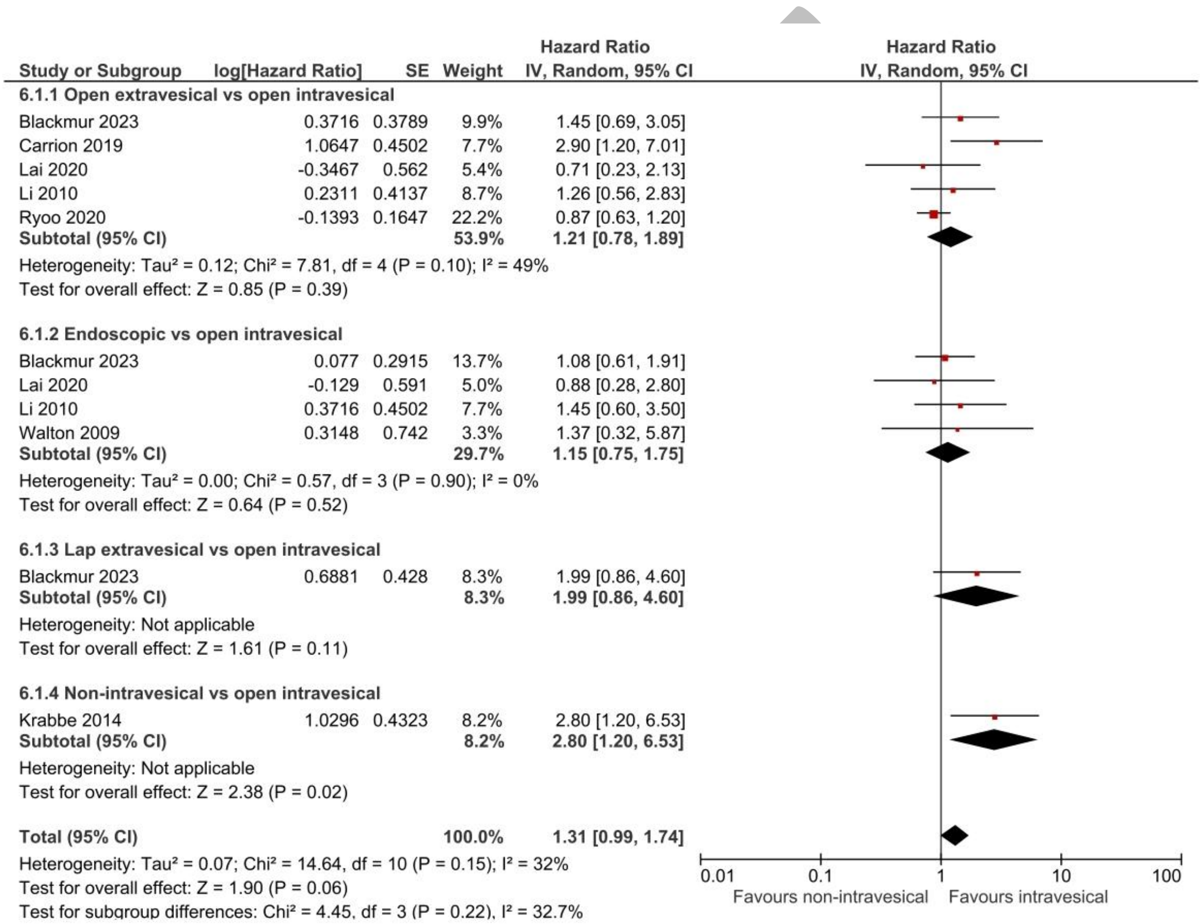
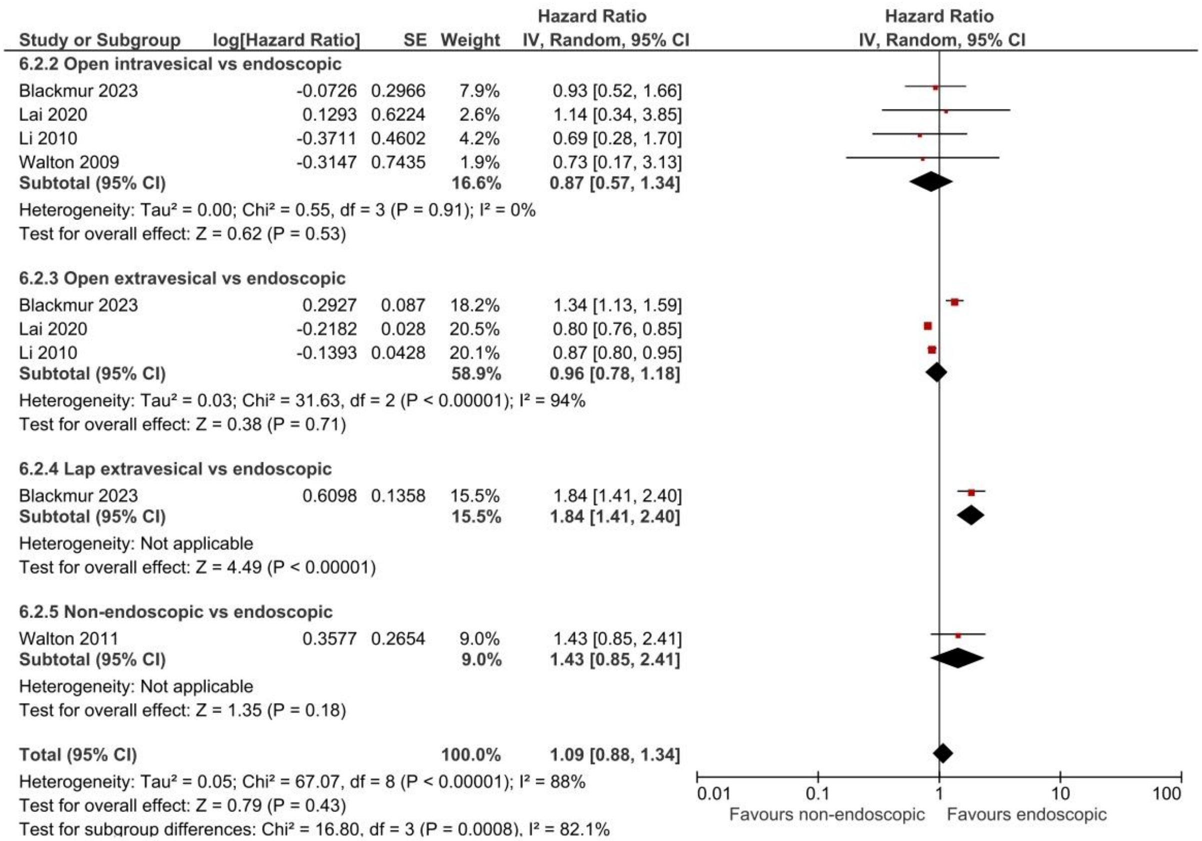

Study or Subgroup
log[Hazard Ratio]
SE
Weight
Hazard Ratio IV, Random, 95% CI
Hazard Ratio IV, Random, 95% CI
5.2.1 Open intravesical vs endoscopic
Kapoor 2014 -0.3975 0.1956 19.0% 0.67 [0.46, 0.99]
Xylinas 2012 0.1906 0.224 17.1% 1.21 [0.78, 1.88]
Subtotal (95% CI) 36.1% 0.89 [0.50, 1.59]
Heterogeneity: Tau² = 0.13; Chi² = 3.91, df = 1 (P = 0.05); I² = 74%
Test for overall effect: Z = 0.39 (P = 0.70)
5.2.2 Open extravesical vs endoscopic
Hara 2011 0.2437 0.2213 17.3% 1.28 [0.83, 1.97]
Kapoor 2014 0.0862 0.1887 19.4% 1.09 [0.75, 1.58]
Xylinas 2012 0.0392 0.2477 15.7% 1.04 [0.64, 1.69]
Subtotal (95% CI) 52.4% 1.13 [0.89, 1.44]
Heterogeneity: Tau² = 0.00; Chi² = 0.45, df = 2 (P = 0.80); I² = 0%
Test for overall effect: Z = 1.00 (P = 0.32)
5.2.3 Non-endoscopic vs endoscopic
Walton 2011 -0.821 0.331 11.5% 0.44 [0.23, 0.84]
Subtotal (95% CI) 11.5% 0.44 [0.23, 0.84]
Heterogeneity: Not applicable
Test for overall effect: Z = 2.48 (P = 0.01)
Total (95% CI) 100.0% 0.93 [0.70, 1.24]
Heterogeneity: Tau² = 0.07; Chi² = 12.15, df = 5 (P = 0.03); I² = 59%
Test for overall effect: Z = 0.50 (P = 0.62)
Test for subgroup differences: Chi² = 7.29, df = 2 (P = 0.03), I² = 72.6%
0.01
0.1
1
10
100
Favours non-endoscopic
Favours endoscopic

Figure 5. Forest plots comparing (A) univariate cancer-specific survival (CSS) in non-open intravesical vs. open intravesical bladder cuff excision (BCE); (B) univariate CSS in non-endoscopic vs. endoscopic BCE; (C) multivariate CSS in non-open intravesical vs. open intravesical bladder cuff excision (BCE); and (D) multivariate CSS in non-endoscopic vs. endoscopic BCE. CI: confidence interval.

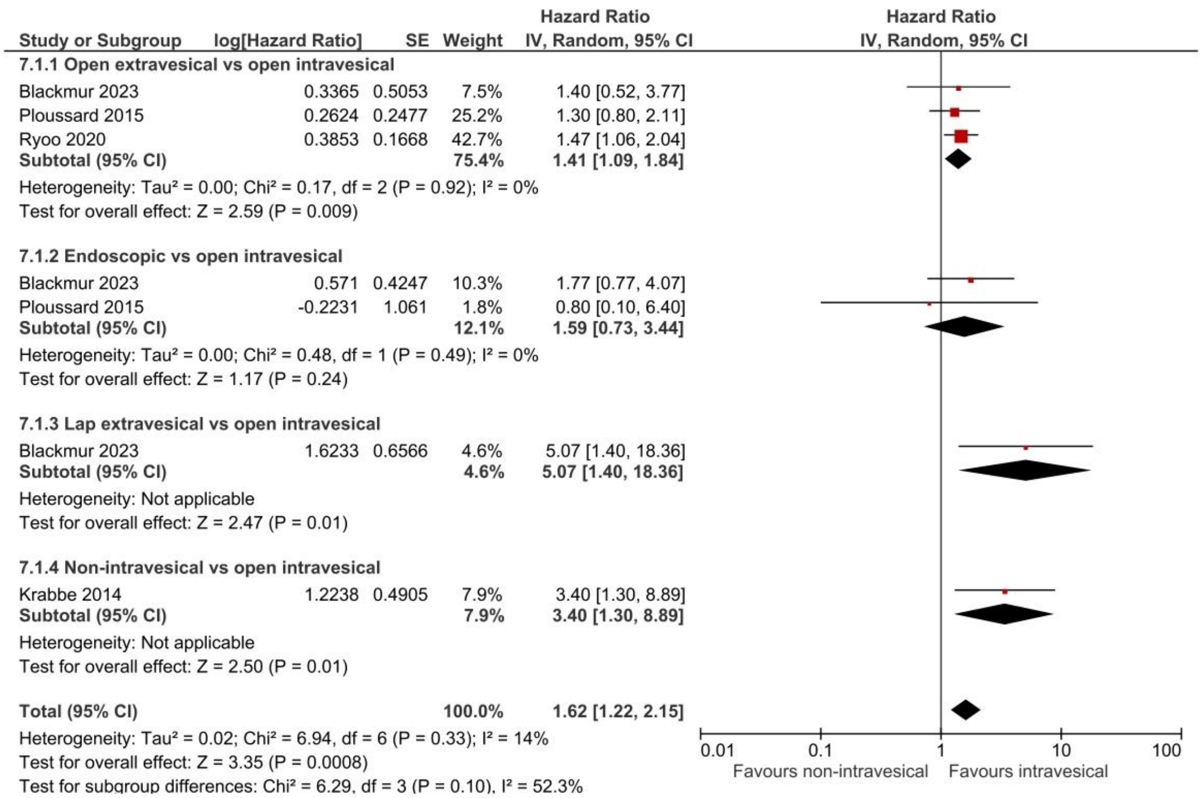
A)



B)


Study or Subgroup | log[Hazard Ratio] | SE | Weight | Hazard Ratio IV, Random, 95% CI | Hazard Ratio IV, Random, 95% CI
6.2.2 Open intravesical vs endoscopic
Blackmur 2023 -0.0726 0.2966 7.9% 0.93 [0.52, 1.66]
Lai 2020 0.1293 0.6224 2.6% 1.14 [0.34, 3.85]
Li 2010 -0.3711 0.4602 4.2% 0.69 [0.28, 1.70]
Walton 2009 -0.3147 0.7435 1.9% 0.73 [0.17, 3.13]
Subtotal (95% CI) 16.6% 0.87 [0.57, 1.34]
Heterogeneity: Tau² = 0.00; Chi² = 0.55, df = 3 (P = 0.91); I² = 0%
Test for overall effect: Z = 0.62 (P = 0.53)
6.2.3 Open extravesical vs endoscopic
Blackmur 2023 0.2927 0.087 18.2% 1.34 [1.13, 1.59]
Lai 2020 -0.2182 0.028 20.5% 0.80 [0.76, 0.85]
Li 2010 -0.1393 0.0428 20.1% 0.87 [0.80, 0.95]
Subtotal (95% CI) 58.9% 0.96 [0.78, 1.18]
Heterogeneity: Tau² = 0.03; Chi² = 31.63, df = 2 (P < 0.00001); I² = 94%
Test for overall effect: Z = 0.38 (P = 0.71)
6.2.4 Lap extravesical vs endoscopic
Blackmur 2023 0.6098 0.1358 15.5% 1.84 [1.41, 2.40]
Subtotal (95% CI) 15.5% 1.84 [1.41, 2.40]
Heterogeneity: Not applicable
Test for overall effect: Z = 4.49 (P < 0.00001)
6.2.5 Non-endoscopic vs endoscopic
Walton 2011 0.3577 0.2654 9.0% 1.43 [0.85, 2.41]
Subtotal (95% CI) 9.0% 1.43 [0.85, 2.41]
Heterogeneity: Not applicable
Test for overall effect: Z = 1.35 (P = 0.18)
Total (95% CI) 100.0% 1.09 [0.88, 1.34]
Heterogeneity: Tau² = 0.05; Chi² = 67.07, df = 8 (P < 0.00001); I² = 88%
Test for overall effect: Z = 0.79 (P = 0.43)
Test for subgroup differences: Chi² = 16.80, df = 3 (P = 0.0008), I² = 82.1%
0.01 0.1 1 10 100
Favours non-endoscopic Favours endoscopic

C)


Study or Subgroup
log[Hazard Ratio]
SE
Weight
Hazard Ratio IV, Random, 95% CI
Hazard Ratio IV, Random, 95% CI
7.1.1 Open extravesical vs open intravesical
Blackmur 2023 0.3365 0.5053 7.5% 1.40 [0.52, 3.77]
Ploussard 2015 0.2624 0.2477 25.2% 1.30 [0.80, 2.11]
Ryoo 2020 0.3853 0.1668 42.7% 1.47 [1.06, 2.04]
Subtotal (95% CI) 75.4% 1.41 [1.09, 1.84]
Heterogeneity: Tau² = 0.00; Chi² = 0.17, df = 2 (P = 0.92); I² = 0%
Test for overall effect: Z = 2.59 (P = 0.009)
7.1.2 Endoscopic vs open intravesical
Blackmur 2023 0.571 0.4247 10.3% 1.77 [0.77, 4.07]
Ploussard 2015 -0.2231 1.061 1.8% 0.80 [0.10, 6.40]
Subtotal (95% CI) 12.1% 1.59 [0.73, 3.44]
Heterogeneity: Tau² = 0.00; Chi² = 0.48, df = 1 (P = 0.49); I² = 0%
Test for overall effect: Z = 1.17 (P = 0.24)
7.1.3 Lap extravesical vs open intravesical
Blackmur 2023 1.6233 0.6566 4.6% 5.07 [1.40, 18.36]
Subtotal (95% CI) 4.6% 5.07 [1.40, 18.36]
Heterogeneity: Not applicable
Test for overall effect: Z = 2.47 (P = 0.01)
7.1.4 Non-intravesical vs open intravesical
Krabbe 2014 1.2238 0.4905 7.9% 3.40 [1.30, 8.89]
Subtotal (95% CI) 7.9% 3.40 [1.30, 8.89]
Heterogeneity: Not applicable
Test for overall effect: Z = 2.50 (P = 0.01)
Total (95% CI) 100.0% 1.62 [1.22, 2.15]
Heterogeneity: Tau² = 0.02; Chi² = 6.94, df = 6 (P = 0.33); I² = 14%
Test for overall effect: Z = 3.35 (P = 0.0008)
Test for subgroup differences: Chi² = 6.29, df = 3 (P = 0.10), I² = 52.3%
0.01
0.1
1
10
100
Favours non-intravesical
Favours intravesical

D)

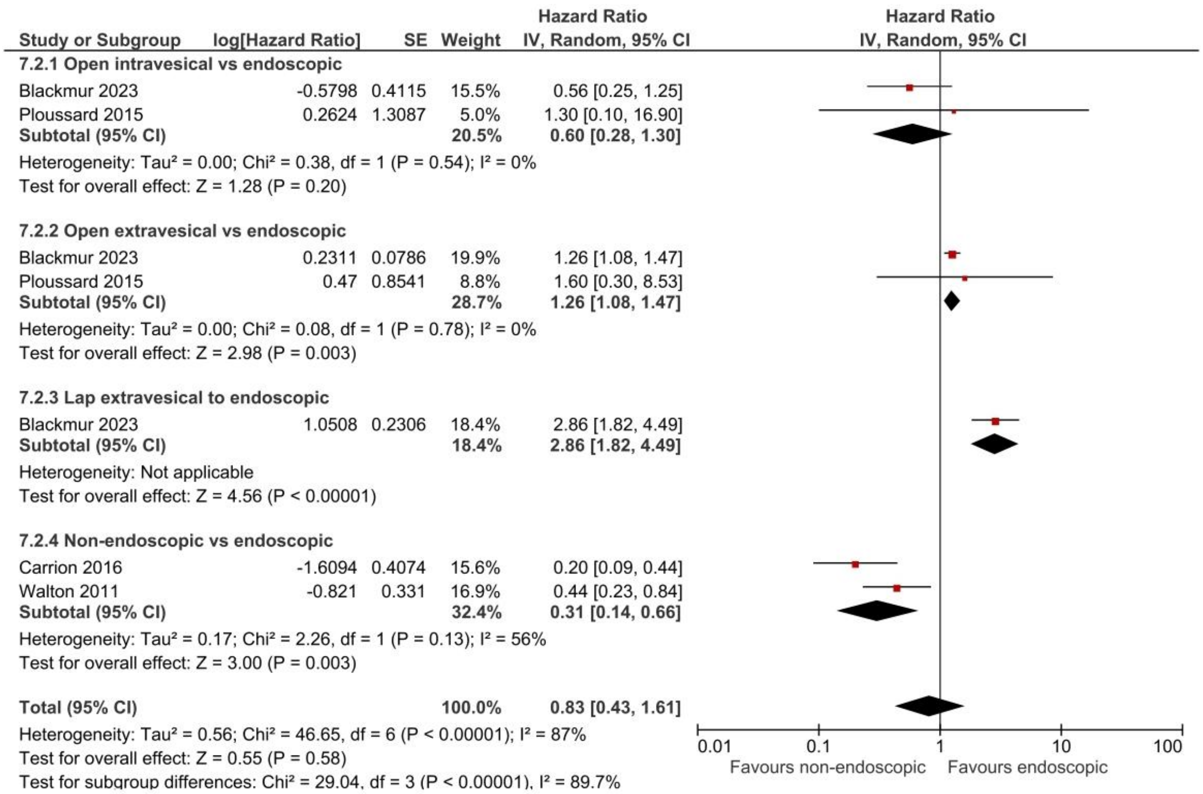

Study or Subgroup
log[Hazard Ratio]
SE
Weight
Hazard Ratio IV, Random, 95% CI
Hazard Ratio IV, Random, 95% CI
7.2.1 Open intravesical vs endoscopic
Blackmur 2023 -0.5798 0.4115 15.5% 0.56 [0.25, 1.25]
Ploussard 2015 0.2624 1.3087 5.0% 1.30 [0.10, 16.90]
Subtotal (95% CI) 20.5% 0.60 [0.28, 1.30]
Heterogeneity: Tau² = 0.00; Chi² = 0.38, df = 1 (P = 0.54); I² = 0%
Test for overall effect: Z = 1.28 (P = 0.20)
7.2.2 Open extravesical vs endoscopic
Blackmur 2023 0.2311 0.0786 19.9% 1.26 [1.08, 1.47]
Ploussard 2015 0.47 0.8541 8.8% 1.60 [0.30, 8.53]
Subtotal (95% CI) 28.7% 1.26 [1.08, 1.47]
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%
Test for overall effect: Z = 2.98 (P = 0.003)
7.2.3 Lap extravesical to endoscopic
Blackmur 2023 1.0508 0.2306 18.4% 2.86 [1.82, 4.49]
Subtotal (95% CI) 18.4% 2.86 [1.82, 4.49]
Heterogeneity: Not applicable
Test for overall effect: Z = 4.56 (P < 0.00001)
7.2.4 Non-endoscopic vs endoscopic
Carrion 2016 -1.6094 0.4074 15.6% 0.20 [0.09, 0.44]
Walton 2011 -0.821 0.331 16.9% 0.44 [0.23, 0.84]
Subtotal (95% CI) 32.4% 0.31 [0.14, 0.66]
Heterogeneity: Tau² = 0.17; Chi² = 2.26, df = 1 (P = 0.13); I² = 56%
Test for overall effect: Z = 3.00 (P = 0.003)
Total (95% CI) 100.0% 0.83 [0.43, 1.61]
Heterogeneity: Tau² = 0.56; Chi² = 46.65, df = 6 (P < 0.00001); I² = 87%
Test for overall effect: Z = 0.55 (P = 0.58)
Test for subgroup differences: Chi² = 29.04, df = 3 (P < 0.00001), I² = 89.7%
0.01
0.1
1
10
100
Favours non-endoscopic
Favours endoscopic

Table 1. Study characteristics, patient demographics, and clinical parameters of included studies

Author	Publication year	Study design	Surgical approach	Patients	Age (years)	Male (%)	Smoking (%)	History of bladder cancer (%)	Concomitant bladder cancer (%)	Average followup (months)	Neoadjuvant chemotherapy (%)	Adjuvant chemotherapy (%)	Intravesical therapy (%)	Lymph node dissection (%)
Allard et al	2013	Retrospective cohort	Laparoscopic	110	71	58.2	56.4	16	NR	22	NR	4.5	NR	26
Blackmur et al	2023	Retrospective cohort	Open and laparoscopic	402	71	61.9	51	23.1	NR	29	NR	NR	19.7	NR
Brown et al	2005	Retrospective cohort	Hand-assisted laparoscopic	55	73	58	NR	NR	NR	24	NR	NR	NR	NR
Carrion et al	2019	Retrospective cohort	Laparoscopic	151	69.9	76.3	NR	27	36	32	0	NR	0	17.2
Carrion et al	2016	Retrospective cohort	Laparoscopic	117	70	72.6	57.8	31.6	19.7	20	0	58	NR	NR
Chiang et al	2011	Retrospective cohort	Hand-assisted retroperitoneo-scopic	208	66.3	49.04	11	21.6	NR	26.7	NR	NR	NR	NR
Chung et al	2021	Retrospective cohort	Open and laparoscopic	1125	NR	NR	52.5	21.8	NR	51	NR	22	NR	NR
Fradet et al	2014	Retrospective cohort	Open and laparoscopic	594	69.7	59	68.4	0	0	40.4	0	9.9	NR	NR
Fragkoulis et al	2017	Retrospective cohort	Open	378	NR	66	NR	0	0	80.4	NR	NR	NR	NR
Geavlete et al	2007	Retrospective cohort	Open and laparoscopic	100	57.5	71.4	NR	11	0	44	NR	NR	NR	0
Gillan et al	2013	Retrospective cohort	Laparoscopic	30	73.4	77	NR	0	0	12	NR	NR	0	NR
Greco et al	2009	Prospective cohort	Open and laparoscopic	140	66.8	54	NR	NR	NR	60	NR	NR	NR	NR
Hara et al	2011	Retrospective cohort	Open	142	66	85	NR	NR	2.2	NR	6	3	NR	NR

Huang et al	2023	Retrospective cohort	Open and laparoscopic	452	71.9	46	17.9	0	0	29.5	NR	25	0	NR
Kapoor et al	2014	Retrospective cohort	Open and laparoscopic	792	69.6	63.4	NR	NR	NR	24.6	NR	11.1	NR	72.9
Katims et al	2021	Retrospective cohort	Laparoscopic or robot-assisted	435	69.3	63.1	55.7	0	0	20.5	NR	12.4	26.3	NR
Ko et al	2007	Retrospective cohort	Open and laparoscopic	46	NR	52	NR	NR	6.5	23.2	NR	NR	NR	89.1
Krabbe et al	2014	Retrospective cohort	Open and laparoscopic	122	69	63.1	NR	33.6	NR	32	7	9	NR	30
Lai et al	2020	Retrospective cohort	Open and laparoscopic	248	69	49.2	17.7	0	0	44.2	0	30	31	NR
Li et al	2010	Retrospective cohort	Open and laparoscopic	301	65.4	44	NR	0	0	33	0	NR	NR	NR
Liu et al	2017	Retrospective cohort	Open and lapaparo-scopic	265	62	74.7	40.4	15.1	16.6	60	NR	21.5	NR	NR
Luo et al	2014	Retrospective cohort	NR	396	66.41	48	12.6	23.7	NR	40.65	NR	NR	NR	NR
Matin et al	2005	Prospective cohort	Open and laparoscopic	51	73	70	NR	43.3	66.7	23	NR	NR	NR	NR
Pang et al	2013	Retrospective cohort	Open	58	NR	56.9	19	0	0	NR	0	NR	NR	NR
Pizzighella et al	2022	Retrospective cohort	Open and robot-assisted	117	68	63	28.2	0	0	40.4	0	15	4	22
Ploussard et al	2015	Retrospective cohort	Open and laparoscopic	3344	70	66.2	NR	NR	NR	32.7	NR	10.6	NR	NR
Ritch et al	2011	Retrospective cohort	Laparoscopic	36	70	69.6	NR	NR	NR	15	NR	NR	100	NR
Romero et al	2007	Retrospective cohort	Open and laparoscopic	24	NR	NR	NR	0	0	46.8	NR	NR	NR	NR
Ryoo et al	2020	Retrospective	Open and	856	64.8	NR	NR	0	0	37.7	NR	22.8	NR	NR

		cohort	laparoscopic											
Saika et al	2004	Prospective cohort	Open	60	67	67	NR	0	0	NR	NR	NR	NR	0
Salvador-Bayarri et al	2002	Retrospective cohort	Open	145	64	84.1	NR	NR	0	44	NR	NR	NR	NR
Simone et al	2009	Prospective cohort	Open and laparoscopic	80	NR	50	NR	0	0	41	NR	NR	NR	0
Terakawa et al	2008	Retrospective cohort	Open and laparoscopic	177	NR	NR	NR	0	0	31	NR	NR	NR	NR
Ubrig et al	2004	Retrospective cohort	Open and laparoscopic	29	63.4	71	NR	NR	NR	44	NR	NR	NR	NR
Walton et al	2011	Retrospective cohort	Open and laparoscopic	773	68	69	NR	27.7	NR	34	0	10.4	NR	23.9
Walton et al	2009	Retrospective cohort	Open	138	NR	63	70.3	21	NR	43	NR	NR	NR	0
Wolf et al	2005	Prospective cohort	Hand-assisted laparoscopic	53	69.7	67	NR	20.8	NR	29	100	NR	NR	NR
Xiao et al	2021	Retrospective cohort	Laparoscopic	98	NR	44	NR	NR	NR	NR	NR	NR	100	NR
Xylinas et al	2014	Retrospective cohort	Open and laparoscopic	1839	70	66.9	NR	28.7	NR	45	0	10.7	NR	NR
Xylinas et al	2012	Retrospective cohort	Open and laparoscopic	2681	68.4	67.4	NR	33.6	NR	57.5	0	9.8	NR	NR

NR: not reported.