Comparative effectiveness of en-bloc resection techniques vs. conventional transurethral resection for non-muscle-invasive bladder cancer: A systematic review and meta-analysis

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ABSTRACT

Introduction: Transurethral en-bloc resection of bladder tumor (ERBT) has emerged as an alternate technique to conventional transurethral resection of bladder tumor (cTURBT). While theoretically advantageous, the comparative effectiveness of ERBT across various technical approaches remains unclear. We performed an updated systematic review and meta-analysis to evaluate perioperative, pathologic, and oncologic outcomes of ERBT vs. cTURBT.

KEY MESSAGES

- Transurethral ERBT demonstrated a trend toward improved recurrence-free survival compared to conventional TURBT (cTURBT), particularly with the use of bipolar instruments, highlighting its potential as a superior oncologic approach.
- While ERBT resulted in longer operative times than cTURBT, it was associated with fewer complications, including a reduced risk of obturator nerve reflex and a trend toward lower rates of bladder perforation.
- Differences in the instruments and techniques used for ERBT influenced the outcomes, suggesting that standardization may be necessary to fully realize the potential benefits of this surgical approach.

Methods: We systematically searched PubMed, EMBASE, Scopus, and Google Scholar for randomized controlled trials (RCTs) comparing ERBT and cTURBT. The primary outcome was recurrence-free survival (RFS). Secondary outcomes were operative time, complication rates, detrusor muscle presence, and need for repeated resection. Meta-analyses were performed, with subgroup analyses stratified by ERBT technique.
Results: A total of 10 RCTs with 1973 patients (1012 ERBT, 961 cTURBT) were included. Overall data favored ERBT in RFS (hazard ratio [HR] 0.85, 95% confidence interval [CI] 0.71−1.01, p=0.07, I^2=48%), with bipolar ERBT demonstrating significantly improved RFS (HR 0.51, 95% CI 0.32‒0.81, p=0.004). ERBT had longer operative times compared to cTURBT (MD 3.52 minutes, 95% CI 1.25−5.80, p=0.001, I^2=71%). There were no significant differences in catheter time or hospital stay between groups. ERBT had a non-significant lower incidence of bladder perforation (odds ratio [OR] 0.41, 95% CI 0.16‒1.04, p=0.06, I^2=52%) and obturator nerve reflex (OR 0.27, 95% CI 0.10‒0.74, p=0.01, I^2=79%) compared to cTURBT. ERBT was not significantly associated with higher detrusor muscle presence (OR 2.08, 95% CI 0.94‒4.58, p=0.07, I^2=78%).
Conclusions: ERBT might have oncologic and perioperative benefits, in addition to technical advantages, relative to cTURBT. Variations in resection instruments used impact the consistency of results.

INTRODUCTION

Bladder cancer is the second most common urological malignancy in the U.S. and one of the most common malignancies worldwide.[1] Transurethral resection of the bladder tumor (TURBT), a piece-by-piece resection technique, has been the gold standard for diagnosing and staging bladder cancer.[2] Tumor fragmentation during conventional TURBT (cTURBT) can affect histologic assessment by damaging the tissue with cautery, confusing pathologists due to piecemeal removal, and making it difficult to determine tumor location and depth. The absence of detrusor muscle, present in 30-35% of cases, impairs staging accuracy, prognosis, and often requires re-resection, increasing healthcare costs.[3] This fractional resection method also introduces the risk operative complications such bladder perforation and intraoperative bleeding.[4–6] En-bloc resection of bladder tumor (ERBT) is an alternate technique proposed to improve TURBT outcomes.[7] ERBT offers resection of the entire tumor en-bloc, as opposed to piecemeal extraction allowing for accurate staging and is postulated to reduce disease recurrence. Several studies have reported detrusor muscle presence rates as high as 100% with ERBT as well as a favorable safety profile.[8–10]

Despite promising retrospective data, the superiority of ERBT over cTURBT has not been definitively proven. A recent international consensus highlighted the feasibility of ERBT but called for high-quality randomized controlled trials (RCTs) to confirm its benefits.[11] Many of these RCTs demonstrate the efficacy of ERBT but feature heterogeneity in the methods used and are often single-center studies.[10,12–18] Therefore, synthesizing this body of evidence is crucial to accurately compare conventional TURBT and en-bloc resection techniques.

In 2022, Li et al. published a meta-analysis comparing the two techniques.[19] However, in the past two years, three large RCTs, including two multi-center studies, have been published on the topic.[9,20,21] Thus, an updated meta-analysis is warranted to incorporate these recent findings. This systematic review and meta-analysis aims to provide robust evidence by comparing the surgical, pathological, and oncological outcomes of cTURBT and ERBT, and stratifying results by ERBT technique.

METHODS

In May 2024, following prior registration with PROSPERO(CRD42024563113), we conducted a systematic search adhering to PRISMA guidelines. We searched PubMed, EMBASE, Scopus, and Google Scholar using the following terms: "Bladder cancer","Bladder neoplasm","Bladder carcinoma","Urothelial carcinoma","Non-muscle invasive bladder cancer","NMIBC","Ta/T1 bladder cancer","Transurethral resection of bladder tumor","TURBT","Conventional TURBT","cTURBT","En-bloc resection of bladder tumor","ERBT","En-bloc resection","Monopolar en-bloc resection","Bipolar en-bloc resection","Holmium laser en-bloc resection","Thulium laser en-bloc resection","GreenLight laser en-bloc resection","Hydrodissection en-bloc resection","Hybrid en-bloc resection","Surgical outcomes","Pathological outcomes","Oncological outcomes","Recurrence","Staging accuracy","Obturator nerve reflex","Bladder perforation" and "Intraoperative bleeding." The search was limited to studies published in English and Spanish, with no restrictions on publication date. Two independent reviewers (DEHG, GS) evaluated the results for inclusion, resolving any discrepancies through consensus. Additionally, we reviewed related articles and the bibliographies of the identified studies for further relevant studies. The PRISMA flow diagram in (Figure 1) illustrates the process of study identification, screening, and inclusion.

Study inclusion

Eligible articles were RCTs comparing ERBT and cTURBT. Included studies provided rates or time-dependent analyses reported as hazard ratios (HR) for recurrence free survival (RFS), regardless of follow-up time, which served as our primary endpoint. Additional studies were included if they reported other relevant surgical and pathological outcomes, even without RFS data.

Data extraction and analysis

Two reviewers (TL, GS) independently extracted the data, disagreements were addressed by a third author (DHG). For the primary endpoint, HR and absolute rates were collected. Secondary endpoints included RFS, operative time, resection time, catheter time, hospital length of stay, bladder perforation, obturator nerve reflex, re-TURBT, were extracted as means with standard deviations and absolute rates where appropriate. Subgroup analyses were performed based on the type of surgery: monopolar, bipolar, holmium laser (HolERBT), thulium laser (ThuERBT), GreenLight laser, hydrodissection, and hybrid approaches. Data analysis was conducted using Review Manager (RevMan) version 5.4.2 (Cochrane). Heterogeneity was assessed using Higgins' I^2 statistic. Variables with an I^2 value greater than 50% were considered heterogeneous and were analyzed using a Random-Effects model. Otherwise, a Fixed-Effects model was employed. The generic Inverse-Variance method was used for analysis, with RevMan's built-in calculator estimating the logarithmic function and standard error from provided HR and confidence intervals. For studies that provided only survival curves without HR, Tierney's method was used to estimate HR. The primary outcome was reported as HR with 95% confidence intervals. Dichotomous outcomes were reported as odds ratios (ORs), while continuous outcomes were reported as mean difference (MD). A p-value of less than 0.05 was considered statistically significant. Risk of bias assessment was performed using the Cochrane Risk of Bias Tool 2 (RoB 2). Publication bias assessment was visually supported by funnel plots for the main outcome.

RESULTS

Following our predefined inclusion criteria, we included ten studies with 1,973 patients: 1,012 underwent ERBT, and 961 underwent cTURBT.[9,10,12–18,20,21] All studies were RCTs comparing ERBT with cTURBT. Study characteristics are shown in Supplementary Table 1 (available at *cuaj.ca*). Using the Cochrane Risk of Bias 2 tool, the overall risk of bias for these studies was determined to be low in 4 of them, some concerns in 4, and high in 2. This analysis is presented in Supplementary Figures 1 and 2 (available at *cuaj.ca*).

Recurrence-free survival

Seven studies reported RFS as HR. Overall, no difference was seen with ERBT over cTURBT, with an RFS HR of 0.85 (95% CI [0.71, 1.01], p = 0.07, I^2=48%). When stratifying by type of resection, only bipolar showed a significant reduction in RFS with a HR 0.51 (95% CI [0.32, 0.81], p = 0.004). None of the other resection approaches showed a significant difference on RFS. These findings are summarized in (Figure 2). A subanalysis restricted to studies with low risk of bias (assessed via RoB2 tool) included 4 studies: 2 analyzing ThuERBT, 1 examining HolERBT, and 1 evaluating the combined approach which showed a HR 0.59 (95% CI [0.37, 0.95], p = 0.03, I2 = 0%). Funnel plot for publication bias is presented in Supplemental Material 2.

Obturator nerve reflex

Nine studies reported the incidence of obturator nerve reflex. Overall, ERBT had a significantly lower rate of obturator nerve reflex compared to cTURBT, with an OR of 0.27 (95% CI [0.10, 0.74], p = 0.01, I^2=79%). Bipolar and combined ERBT showed no significant difference in obturator nerve reflex rates compared to cTURBT (p = 0.85). However, greenlight laser, HolERBT and ThuERBT showed a significant reduction with an OR 0.05 (95% CI [0.00, 0.85], p = 0.04), OR 0.03 (95% CI [0.00, 0.53], p = 0.02) and OR 0.04 (95% CI [0.01, 0.19], $p < 0.0001$) respectively. These findings are summarized in (Figure 3).

Bladder perforation

Seven studies reported the rate of bladder perforation. Overall, ERBT appeared to have lower incidence of bladder perforation compared to cTURBT, with an OR of 0.41 (95% CI [0.16, 1.04], p = 0.06, I^2=52%), although not statistically significant. When stratifying by intervention type, only ThuERBT showed a decreased incidence of bladder perforation, relative to cTURBT (OR 0.07 (95% CI [0.01, 0.56], p = 0.01). These results are summarized in (Figure 3).

Operative time

Seven studies reported operative times. Among these, two used combined ERBT techniques, one used Greenlight laser, one used bipolar energy, and three used ThuERBT. Overall, ERBT exhibited a longer operative time, with a MD of 3.52 minutes (95% CI [1.25, 5.80], p = 0.001, I^2=71%). Operative times were significantly longer for bipolar ERBT (MD 8.67, 95% CI [5.06, 12.28], $p < 0.00001$) compared to cTURBT. No significant differences in operative times were observed with the other approaches. These findings are summarized in (Figure 4).

Resection time

Four studies reported resection times for ERBT versus cTURBT groups, using Greenlight laser, HoLERBT, hydrodissection, and ThuERBT techniques. Overall, there was no difference in resection time between ERBT and cTURBT, (MD 1.07, 95% CI [-2.68, 4.82], p = 0.58, I^2=91%). Greenlight laser resections were significantly longer than conventional resections (MD 1.07, 95% CI [0.39, 1.75], p = 0.002), while HoLERBT resections were significantly shorter (MD -7.75, 95% CI [-11.62, -3.88], $p < 0.0001$). Hydrodissection also required more time (MD 14.70, 95% CI [7.70, 21.70], $p < 0.0001$). These findings are summarized in (Figure 4).

Hospital stay

Seven studies reported hospital stay durations. Overall, no significant difference was seen on hospital stay, with a MD of -0.30 days (95% CI [-1.11, 0.51], p = 0.46, I^2=98%). These findings are summarized in (Figure 4).

Catheter time

Six studies reported post operative indwelling catheter times, using combined ERBT approaches, Greenlight laser, HolERBT, hydrodissection, and ThuERBT techniques. Overall, there were no significant differences between ERBT and cTURBT, with a MD of -0.27 days (95% CI [-1.08, 0.54], p = 0.51, I^2=97%). Combined ERBT, represented by one study, showed a significant reduction in catheter placement time compared to cTURBT (p = 0.02). These findings are summarized in (Figure 4).

Detrusor muscle presence

Eight studies reported the presence of detrusor muscle using combined ERBT, Greenlight laser, HolERBT, hydrodissection, ThuERBT, and bipolar techniques. Overall, the data showed higher rates of detrusor muscle presence in ERBT compared to cTURBT, with an OR of 2.08 (95% CI [0.94, 4.58], p = 0.07, I^2=78%), although this difference was not statistically signficant. When stratifying by type of intervention, both Greenlight and HolERBT had a higher rate of detrusor muscle presence with a OR of 3.40 (95% CI [1.66, 7.00], p = 0.0009) and OR of 30.03 (95% CI [3.83, 235.77], p = 0.001), respectively. Weighted average for the rate of presence of detrusor muscle with ERBT stratified by technique was also calculated: HolERBT (98.0%), combined (97.5%), greenlight (89.6%), ThuERBT (87.9%), bipolar (87.2%), TURBT (85.0%) and lastly hydrodissection (73.2%). These findings are summarized in (Figure 5).

Repeated TURBT

Five studies reported the rate of repeated TURBT. Overall, there was no significant difference in the incidence of Re-TURBT between ERBT and cTURBT, with an OR of 1.03 (95% CI [0.73, 1.45], p = 0.87, I^2=10%). These findings are summarized in (Figure 5).

DISCUSSION

This systematic review and meta-analysis compared surgical, pathological, and oncological outcomes between ERBT and cTURBT. The analysis indicated more favorable oncological outcomes with ERBT, particularly in terms of recurrence-free survival (RFS), suggesting the resection method may influence outcomes alongside tumor characteristics and chemotherapy use. The Bipolar laser subgroup showed statistically significant improvements, highlighting the need for further exploration of its advantages over other ERBT techniques.

Prior authors have postulated benefits of ERBT for reducing tumor recurrence stem from the ability to remove the entire lesion en-bloc, potentially minimizing tumor cell scattering and seeding compared to piecemeal conventional resection.[22] Additionally, an intact, high-quality specimen may enable appropriate guidance for adjuvant instillation therapy.[23] Our results indicate that these theoretical advantages might translate into improved RFS across ERBT techniques, as indicated by data favoring RFS within our aggregate analysis. As more RCTs are conducted, we expect larger sample sizes to possibly lead to statistical significance.

In terms of operative metrics, our meta-analysis found that ERBT procedures generally required longer total operative times compared to cTURBT. This trend was consistently observed across studies, with bipolar ERBT showing the largest effect, taking an average of 8.67 minutes longer than conventional resection. However, it's important to note that this result comes from a single study and may be influenced by site-specific factors, surgeon experience, or other variables.

Interestingly, when examining the resection portion of the procedure alone, there was significant heterogeneity across ERBT modalities. Resection times were significantly longer for Greenlight laser and for hydrodissection compared to cTURBT. In contrast, holmium laser was associated with significantly shorter resection times relative to conventional resection. Moreover, the overall longer operative times coupled with comparable or varied resection times suggest that other aspects of the procedure contribute to the time difference. One explanation could be that the larger en-bloc specimens obtained through ERBT may be more challenging to remove through the resectoscope sheath compared to the smaller fragments produced by cTURBT; however, these variations may also be related to surgeon expertise with technique and approach as well as unaccounted for variations in tumor burden. Even if these were statistically significant, the actual clinical relevance of ~10 minute resection time may prove to be lacking impact on actual spending or clinical outcomes.

Catheter times after ERBT were not significantly different from cTURBT overall. Similarly, postoperative hospital lengths of stay were comparable between the two groups. These findings suggest that ERBT does not necessarily increase overall resource utilization from a health economic perspective when taking the full perioperative course into account. It's worth noting that although bladder perforation rates were lower in the ERBT group, this did not translate to significant differences in catheter times. This can be explained by the fact that bladder perforation is a relatively rare event. The majority of patients in both groups required catheters for similar durations, and the few cTURBT patients with perforations and potentially longer catheter times were not numerous enough to significantly increase the overall average catheter time for the group.

Bladder perforation during TURBT is a serious intraoperative complication that can lead to increased morbidity, prolonged hospitalization, and potentially delayed intravesical therapy.[24] In our meta-analysis, we found overall lower bladder perforation rates with ERBT compared to cTURBT. While this difference did not reach statistical significance, it suggests a potential safety advantage of en-bloc resection techniques. Subgroup analysis revealed that thulium laser ERBT was associated with a significantly reduced risk of bladder perforation compared to conventional TURBT. This finding is consistent with previous studies demonstrating the enhanced surgical precision, controlled depth of penetration, and improved visualization afforded by laser energy sources during TURBT.[25] Additionally, enhanced tumor delineation during ERBT may facilitate identification of anatomical planes and may enable a wider margin of resection around the lesion, avoiding narrow fulguration at the tumor periphery that can predispose to perforation. It is important to note that bladder perforation rates were generally low across all study arms, reflecting the overall safety of modern TURBT techniques in experienced centers. However, even a modest reduction in this complication can have significant clinical implications.

A crucial outcome measure evaluated in this meta-analysis was the presence of detrusor muscle in the resected specimen, which serves as a surrogate marker for complete tumor removal and accurate pathological staging.[26] Absence of muscularis propria is associated with an increased risk of upstaging and understaging of disease, impacting clinical risk stratification and potentially leading to inappropriate treatment decisions.[3] We found overall higher detrusor muscle presence rate in ERBT compared to cTURBT, although this did not reach statistical significance. Importantly, subgroup analysis revealed that both Greenlight laser ERBT and holmium laser ERBT were associated with significantly higher rates of detrusor muscle relative to cTURBT. The inherent advantages of these laser modalities, including enhanced visualization, precise cutting, and controlled depth of resection, likely facilitate complete removal of the tumor base and underlying muscularis propria. In contrast, the challenges of achieving full-thickness resection during piecemeal conventional TURBT often lead to inaccurate staging.[27]

There are some limitations to this meta-analysis. Despite restricting to RCTs, the included studies featured heterogeneity in ERBT techniques, patient populations, and outcome reporting, specifically in length of follow-up for RFS. Additionally, long-term oncological data is still lacking.. A notable source of heterogeneity among the included trials was the variable quality of conventional TURBT procedures, particularly evident in the wide range of detrusor muscle sampling rates in the control arms (61-100%). This substantial variation suggests inconsistent surgical technique and quality across studies, which may have influenced the comparative outcomes. The surgeon characteristics and experience levels also varied considerably across trials, ranging from single-operator studies (Liu, 2013) to those involving multiple surgeons (Gallioli, 2022 with multiple surgeons), while some trials did not report surgeon details. Additionally, the trials exhibited marked differences in tumor characteristics, with mean tumor sizes ranging from 1.28 cm to 3.2 cm, and some studies predominantly including smaller tumors (Fan, 2021: 78.9% <2 cm) while others focused on larger lesions (Zhang, 2015: 65.8% >3 cm). Furthermore, the follow-up duration varied substantially (12-48 months), which may have affected the assessment of recurrence rates and other time-dependent outcomes. These factors collectively contribute to the observed heterogeneity and should be considered when interpreting the pooled results. Future studies with extended follow-up are needed to definitively assess the impact of ERBT on disease recurrence and progression.

CONCLUSIONS

ERBT appears to have some oncologic benefit relative to cTURBT. Furthermore, ERBT techniques may have technical advantages and perioperative benefits compared to cTURBT. The choice of resection modality and energy source should be guided by surgeon preference, resource availability, and operative considerations. Further research is warranted to validate long-term oncological outcomes and elucidate optimal surgical strategies.

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FIGURES AND TABLES

Figure 1. PRISMA flowchart.

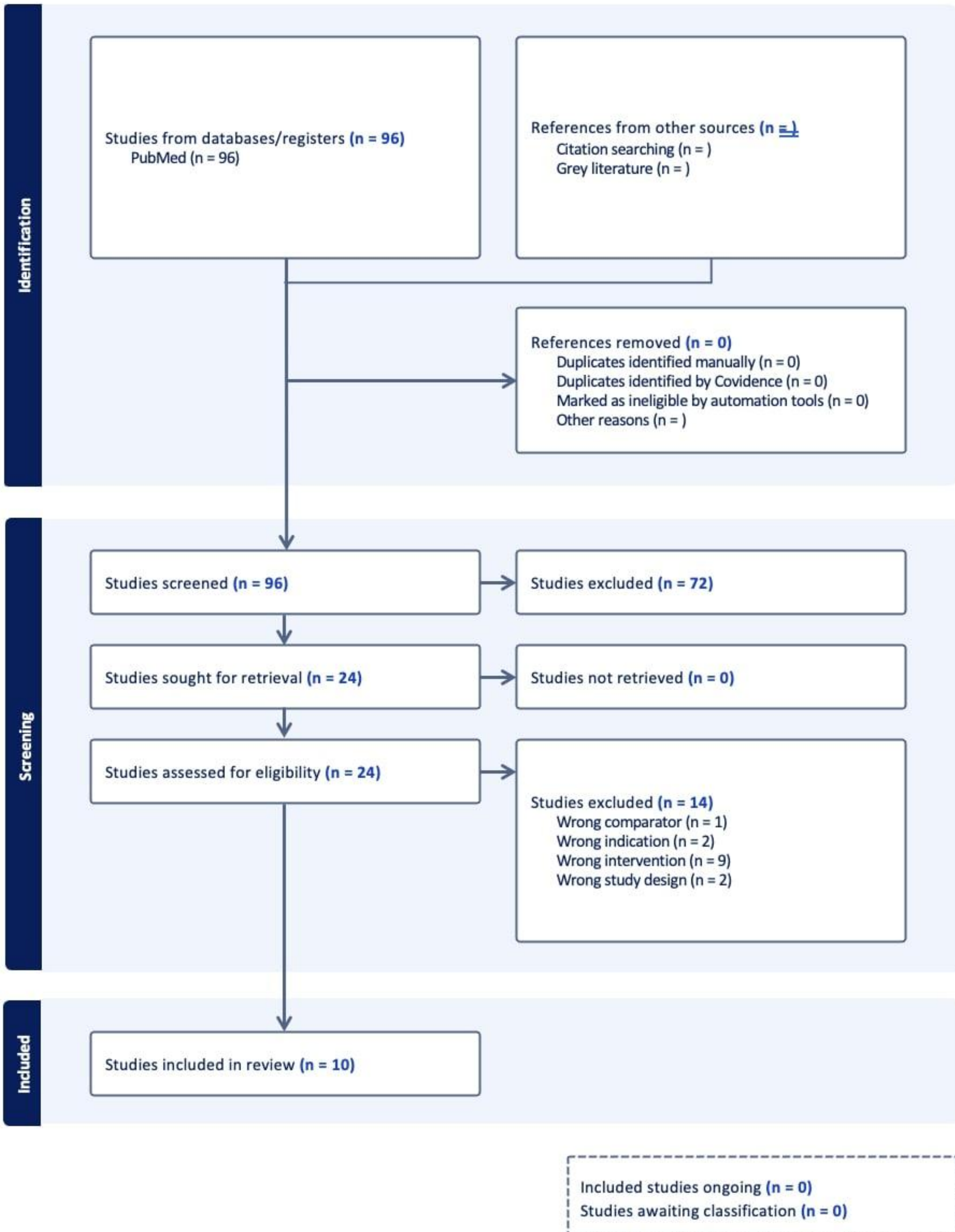

Figure 2. Recurrence free survival in the en-bloc resection group and conventional resection group, stratified by technique.

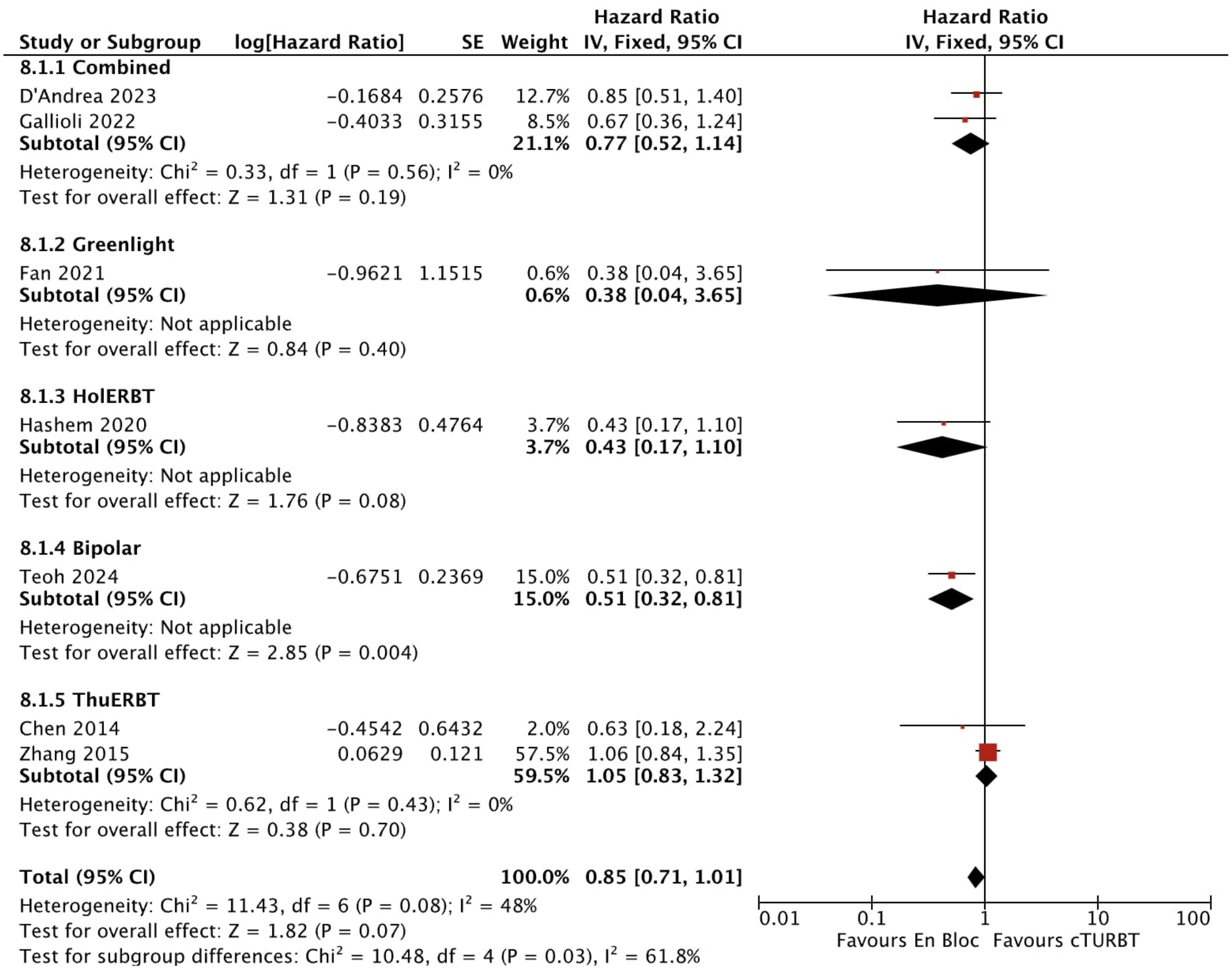

Figure 3. Incidence of complications in the en-bloc resection group and conventional resection group, stratified by ERBT technique. (A) Incidence of obturator nerve reflex. (B) Incidence of bladder perforation.

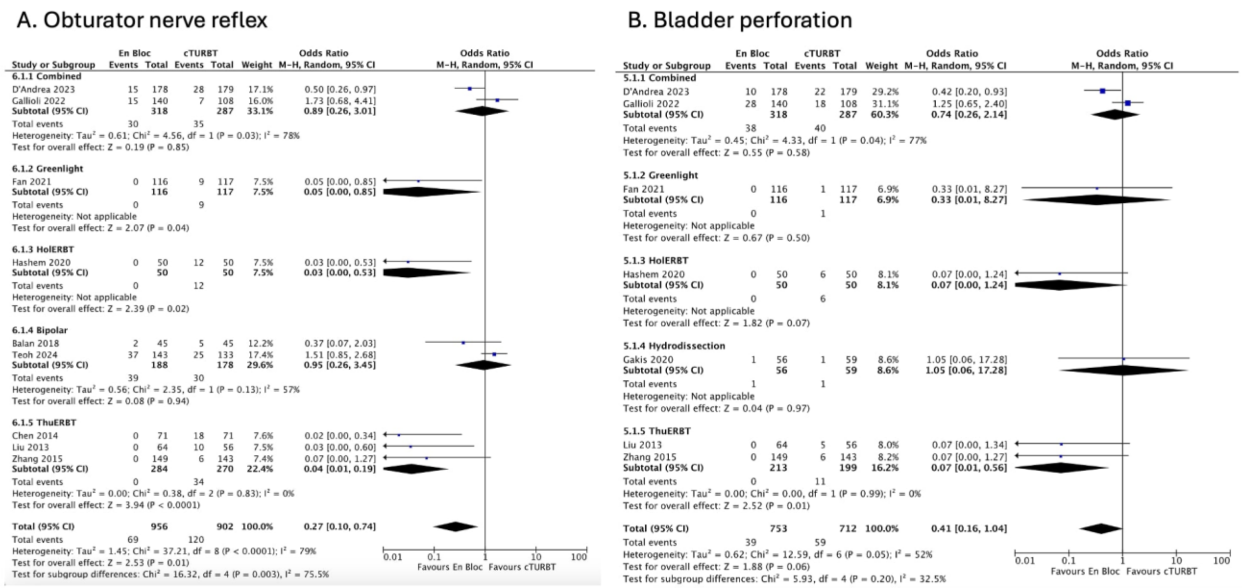

Figure 4. Perioperative outcomes in the en-bloc resection group and conventional resection group, stratified by ERBT technique. (A) Operative time, in minutes. (B) Resection time, in minutes. (C) Hospital stay, in days. (D) Catheter time in days.

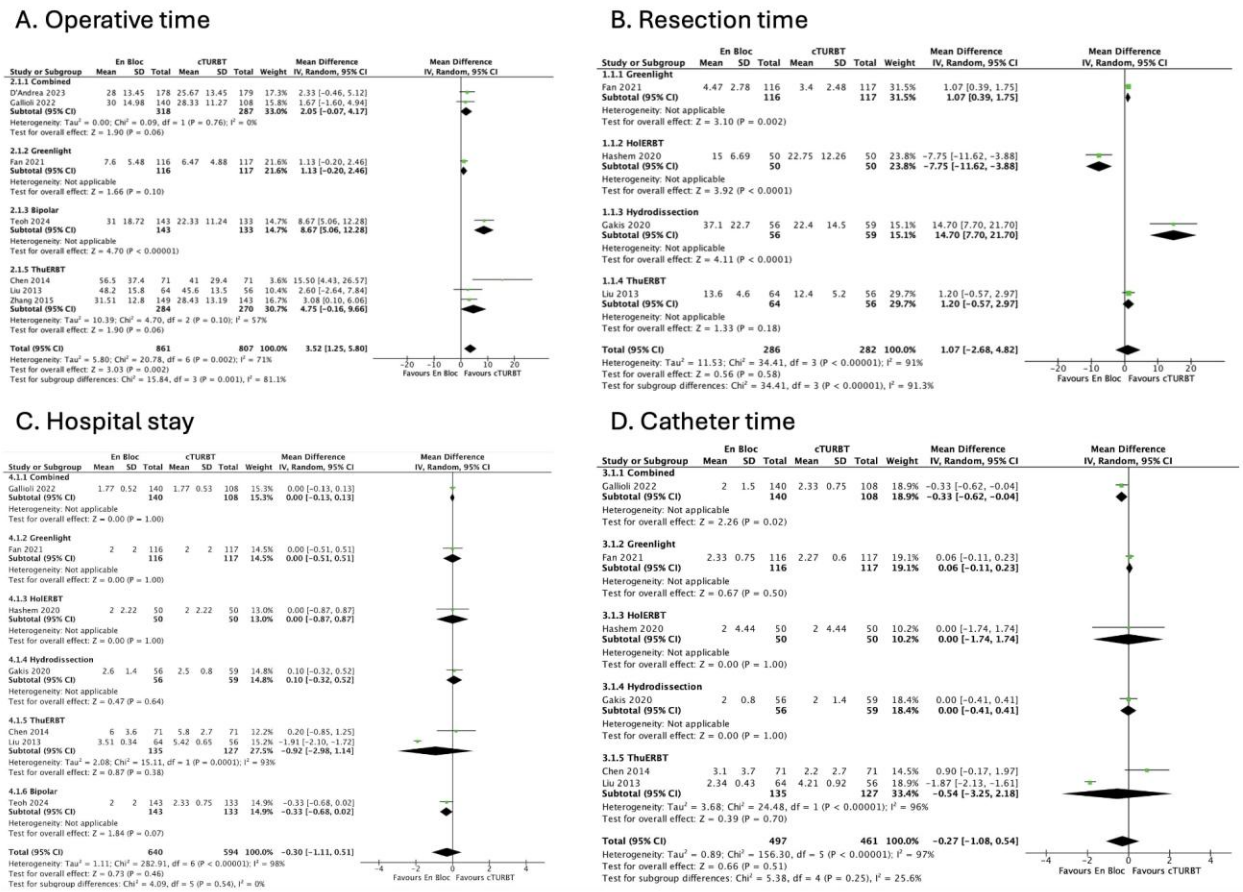

Figure 5. Technical outcomes in the en-bloc resection group and conventional resection group, stratified by ERBT technique. (A) Incidence of patients requiring re-TURBT. (B) Incidence of present detrusor muscle upon resection.