

Appendix IV

Summary of the results of studies evaluating different techniques of BCE.			
Author, Year Sample size Study Design	Key Inclusion Criteria	Interventions Comparisons	Results (95% CI, unless otherwise indicated)
RoB			
Abrate, ¹¹⁴ 2019 N= 84 Retrospective Low	M0, distal ureter location Treated with SU	SU with BCE (65) SU with anastomosis (19)	BCE vs. Anastomosis OS 5-year OS: 92.3% vs. 73.7%, p=0.052 aHR 0.314 (0.08-1.18), p=0.09 CSS 5-year CSS: 95.4% vs. 94.7%, p=0.970 aHR 1.16 (0.07-20.0), p=0.91 RFS 5-year RFS: 53.9% vs. 63.2%, p=0.489 aHR 1.41 (0.60-3.33), p=0.4 Recurrence: 46.2% vs. 36.8%, p=0.648 Creatinine change, mean (SD) mg/dL: 0.1 (0.2) vs. 0.0 (0.3), p=0.383 Anastomotic strictures: 4.6% vs. 5.3%
Capitanio, ¹¹⁵ 2009 N= 1,249 Retrospective Moderate	M0, excluded neoadjuvant or adjuvant chemotherapy Treated with NU	Open BCE (477) Endoscopic BCE (61) No BCE (711)	CSM Open BCE vs. no BCE: aHR 1.87, p = 0.07 Endoscopic BCE vs. no BCE: aHR 1.02, p=1.0 Recurrence Open BCE vs. no BCE: aHR 1.61, p=0.1 Endoscopic BCE vs. no BCE: aHR 1.08, p=0.9
Jeldres, ¹¹⁷ 2010 N= 1,475 Retrospective (SEER 1988-2006) Moderate	N0M0, ureteral location Treated with NU	BCE (1,222) No BCE (253)	BCE vs. no BCE CSS 2 years: 89.1% vs. 88.5%, 5 years: 82.2% vs. 80.5% pairwise log-rank p≥0.05 <i>stratified by pT stage</i> pT1-2: 2 years: 94.0% vs. 94.2% 5 years: 88.9% vs. 90.6%, pairwise log-rank p≥0.4 pT3-4 2 years: 78.8% vs. 78.4% 5 years: 67.8% vs. 62.2% pairwise log-rank p≥0.2
Lughezzani, ¹¹⁹ 2010 N= 4,210 Retrospective (SEER 1988-2006) Moderate	T1-4N0-3/NxM0; renal pelvis location Treated with NU	BCE (2,492) No BCE (1,718)	BCE vs. no BCE CSM Overall: aHR 0.76 (0.66-0.88), p<0.01 pT1N0/x: aHR 0.79, p=0.3 pT2N0/x: aHR 1.06, p=0.8 pT3N0/x: aHR 0.80, p=0.04 pT4N0x: aHR 0.69, p=0.02 pT(any)N1-3: aHR 0.72, p=0.04
Kang, ¹¹⁸ 2015 N= 336 Retrospective Moderate	No distant metastases Treated with radical NU	BCE (279) No BCE (57)	BCE vs. no BCE OS, 5-year: 71.5% vs. 57.0%, log-rank p=0.001 CSS. 5-year: 75.8% vs. 63.9%, log-rank p=0.005
Ha, ¹¹⁶ 2017 N= 505 Retrospective Moderate	No distant metastases, no neoadjuvant therapy Treated with radical NU	BCE (445) No BCE (60)	BCE vs. no BCE CSS (log-rank tests) Overall cohort: p=0.061 <i>Subgroup analyses</i> Ureteral tumor: p=0.024 (no BCE worse CSS) Renal pelvis: p=0.493 pTa, CIS, pT1-2: p=0.257 pT3-4: p=0.241 LG: p=0.049 (no BCE worse CSS) HG: p=0.054

			<p>Cancer-related death Ureteral tumor subgroup: aHR 0.232 (0.075-0.717), p=0.011</p> <p>MFS (log-rank tests) <i>Subgroup analyses</i> pTa, CIS, pT1-2: p=0.399 pT3-4 p=0.602 LG: p=0.005 (no BCE worse MFS) HG: p=0.383</p> <p>IVRFS (log-rank tests) <i>Subgroup analyses</i> pTa, CIS, pT1-2: p=0.745 pT3-4: p=0.113 LG: p=0.281 HG: p=0.020 (BCE worse IVRFS)</p>
<p>Nazzani,¹²⁰ 2020 N= 4,266 Retrospective (SEER 2004-2014) Moderate</p>	<p>non-metastatic pT1-3N0, renal pelvic tumors Treated with NU</p>	<p>BCE (2,913) No BCE (1,353)</p>	<p>BCE vs. no BCE</p> <p>CSM 5 years: 19.7% vs. 23.5%, p=0.005 aHR 0.88 (0.75-1.03), p=0.1</p> <p>Subgroups T1: aHR 0.93 (0.65-1.33), p=0.7 T2: aHR 1.00 (0.65-1.56), p=1.0 T3: aHR 0.85 (0.71-1.02), p=0.1 LG: aHR 0.92 (0.58-1.47), p=0.7 HG: aHR 0.86 (0.72-1.02), p=0.1 Tumor size ≤4 cm: aHR 0.88 (0.70-1.11), p=0.3 Tumor size >4 cm: aHR 0.84 (0.66-1.06), p=0.1</p>
<p>Lughezzani,¹¹⁹ 2009^a N= 2,077 Retrospective (SEER 1988-2004)</p>	<p>No distant metastases Treated with NU or SU</p>	<p>NU with BCE (1,400) NU without BCE (677)</p>	<p>CSM NU with BCE vs. NU without BCE: aHR 0.83, p=0.08</p>

Abbreviations: aHR = adjusted hazard ratio; BCE = bladder cuff excision; CI = confidence interval; CIS = carcinoma in situ; CSM = cancer-specific mortality; CSS = cancer-specific survival; HR = hazard ratio; IVRFS = intravesical recurrence-free survival; MFS = metastasis-free survival; NU = nephroureterectomy; OS = overall survival; RFS = recurrence-free survival; SD = standard deviation; SU = segmental ureterectomy

^a This study was excluded due to substantial overlap in patient enrollment dates; data provided for reference.