Bladder | **2017** | Vol. 4(2) | e29
DOI: 10.14440/bladder. 2017.552

ARTICLE

Cystectomy survival outcomes: A single center experience in Australia

Richard Hoffmann[1]*, Callum Logan[1], Michael E. O'Callaghan[1,2,3], Darren Foreman[1]

[1]Department of Urology, Repatriation General Hospital, Adelaide, Australia
[2]Flinders Centre for Innovation in Cancer, Adelaide, Australia
[3]Discipline of Medicine, University of Adelaide, Adelaide, Australia

*Corresponding author: Richard Hoffmann, Email: richard.hoffmann@sa.gov.au

Competing interests: The authors have declared that no competing interests exist.

Abbreviations used: BCG, Bacillus Calmette-Guérin; CIS, carcinoma *in situ*; CSS, cancer specific survival; IQR, interquartile range; LVI, lymphovascular invasion; MDT, multi-disciplinary team; MIBC, muscle invasive bladder cancer; NMIBC, non-muscle invasive bladder cancer; TUR, transurethral resection

Received February 22, 2017; Revision received June 3, 2017; Accepted June 13, 2017; Published August 22, 2017

ABSTRACT

OBJECTIVE: Survival following cystectomy is influenced by gender, age and initial pathology. We report on variation in biopsy versus final surgical pathology and its impact on survival, five-year survival of those undergoing cystectomy for bladder urothelial carcinoma, and evaluate any difference between gender and age.

METHODS: Patients were selected from our hospital cancer database who underwent a cystectomy for bladder urothelial carcinoma between 1987 and 2015. Patients were considered as having bladder cancer if they had muscle invasive cancer, non-muscle invasive cancer or carcinoma *in situ* on their final biopsy pathology. Pathology was recorded at last cystoscopy before surgery and based on surgical specimen.

RESULTS: One hundred and twenty-six patients were included, 71% male, and 29% female, with a median age at cystectomy of 69.2 years. Fifty-seven point nine percent of patients had no change in variation between their biopsy and cystectomy histopathology and 18.3% of patients were downgraded, 16.6% of patients were upgraded, and 7.1% had incomplete pathology data. Median survival was 4.6 years and five-year overall survival 58.2%. There was no significant difference in survival between genders and no difference when comparing between gender and age > 70 and < 70 years. There was no statistical difference in survival between patients who had their final pathology upgraded, downgraded, or confirmed.

CONCLUSIONS: We found lower rates of variation in biopsy versus surgical pathology than reported elsewhere and did not observe a significant association with survival. Our survival outcomes are similar to those within the literature. Gender did not impact on survival, even when comparing between age > 70 and < 70 years.

Keywords: bladder cancer pathology, gender, survival

INTRODUCTION

Bladder urothelial carcinoma is the tenth most common cancer in Australia, accounting for 2.0% of all cancer [1]. Within Australia, bladder urothelial carcinoma mortality is 4.09 deaths per 100000 [1]. Unlike many other cancers, males have a greater five-year survival compared with women, (72% *vs*. 67%) [2], with females showing an 11% increased likelihood of death [3,4]. Cystectomy is recommended for those with muscle invasive disease, failure to respond to Bacillus Calmette-Guérin (BCG) therapy, or recurrence after BCG therapy [5].

Pathological staging of bladder urothelial carcinoma determines both management of disease (European Association of Urology (EAU) guidelines) and disease survival [5]. Several studies have looked at the differences between biopsy staging and surgical staging with the largest study finding concordance in only 35.6% of cases and that variation in pathological staging impacted survival [6-9]. When considering the completeness of resection for trans-urethral resection (TUR) of tumors, Herr *et al*. reported 76% of patients having residual tumors on

How to cite this article: Hoffmann R, Logan C, O'Callaghan ME, Foreman D. Cystectomy survival outcomes: A single center experience in Australia. *Bladder* 2017;4(2):e29. DOI: 10.14440/bladder.2017.552

a second TUR, and between 4%–29% of second TUR being upstaged [10]. Furthermore, inter-observer diagnosis of carcinoma *in situ* (CIS) has a reported concordance rate of 70%–78% [11,12].

Cystectomy is associated with high morbidity, with 56% experiencing any complication and a mortality rate of 3.2% [13,14]. A combination of the increasing incidence of bladder urothelial carcinoma along with older patients undergoing cystectomy has led to an increase in the total number of cystectomies [14]. Factors affecting survival at time of radical cystectomy are known to include tumor stage and type, lymphovascular invasion (LVI), lymph node involvement, surgical margin clearance, and delay to surgery > 3 months [15-17]. There is still relatively scarce data in Australia examining cystectomy outcomes for the treatment of bladder urothelial carcinoma. Patel *et al*. reported that those within New South Wales undergoing radical cystectomy had disease-specific survival and overall survival outcomes comparable to international data [18]. In a separate publication, the same group found that within New South Wales female survival is worse only in those over 70 (five-year bladder urothelial carcinoma disease specific survival 56% *vs*. 66%) [19]. When examining pathological staging and quality of surgical specimens of 201 people undergoing cystectomy within New South Wales, Ahmadi *et al*. found comparable results to those of a large international cohort with five-year cancer specific survival (CSS) 65% and 10-year CSS 61% [15,16]. Interestingly, Ahmadi *et al*. did not find a survival difference between the genders.

We aim to report the five and ten-year survival following cystectomy, the effect of gender on survival, and the effect on survival of pathology upgrading between TUR and surgery.

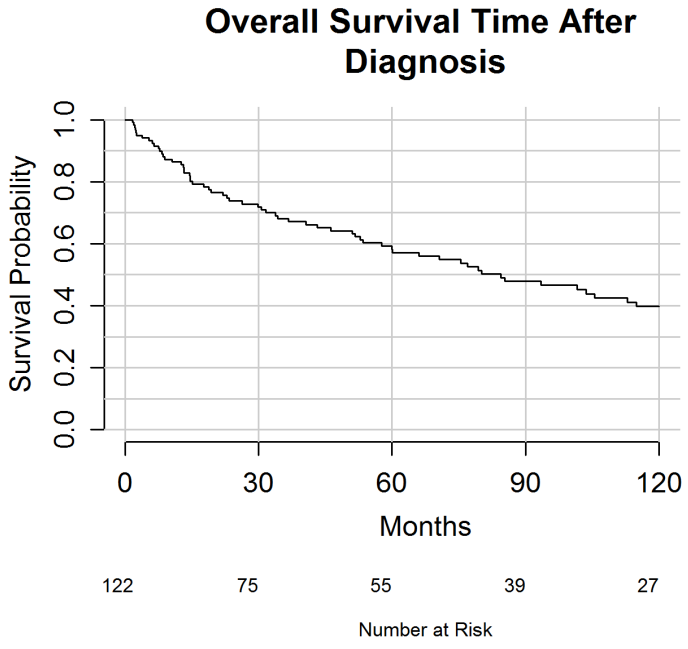

Figure 1. Overall survival time after diagnosis.

PATIENTS AND METHODS

For this retrospective study, ethics approval was sought and granted from the relevant hospital ethics committee. All research was conducted in accordance with appropriate standards.

Patients were selected from a single center hospital bladder urothelial carcinoma database who underwent a cystectomy for bladder urothelial carcinoma between January 1987 and September 2015. Patients were considered as having bladder urothelial carcinoma if they had muscle invasive bladder urothelial carcinoma, non-muscle invasive bladder urothelial carcinoma (NMIBC) or CIS on their final biopsy pathology. Pathology was recorded at last cystoscopy before surgery and based on surgical specimen. Death data was retrieved from the state death registry. Ethics approval was granted from the hospital ethics committee.

We performed open radical cystectomy with formation of an ileal conduit. Lymph node dissection is performed to the level of the iliac bifurcation as standard. Data relating to lymph node involvement and surgical margin clearance was not routinely recorded in the database and was not available for statistical analysis. All patients who were scheduled for cystectomy underwent discussion at a multi-disciplinary team (MDT) meeting, and were considered for neoadjuvant chemotherapy by the medical oncologist. MDT members consisted of urologists, radiologists, pathologist, medical oncologists, radiation oncologists, and nursing staff. This has been routine practice at our institution for the past 10 years, since 2005.

STATISTICAL ANALYSIS

Survival curves for cystectomy patients were plotted using the Kaplan Meir technique. Survival measurement commenced at the date of surgery with events being death recorded in the state births, deaths and marriages registry. Patients who had not died at September 2015 were censored. Strata by gender and pathology upstaging were compared using log-rank tests and multivariable Cox proportional hazards modeling. For Cox modeling, the proportional hazards assumption was tested using as described previously [20]. All analysis was conducted using R 3.3.1. (Vienna, Austria) [21].

RESULTS

One hundred and forty-three patients were available from the database and eligible for inclusion in this study. From this, 126 had pre-cystectomy pathology available. Seventy-one percent (90 patients) were male, 29% (36 patients) were female. The median age at first diagnosis was 67.1 years (interquartile range (IQR) 60.29–75.15). The median age at cystectomy was 69.2 (IQR 62.1–76.6) Twenty-eight point six percent of patients had undergone prior BCG treatment (**Table 1**). On final surgical pathology 16 (12.7%) patients had no cancer (pT0), 26 (20.6%) patients had NMIBC, 75 (59.5%) patients had muscle invasive cancer, and 9 (7.1%) patients had no information on final surgical pathology. Three patients had squamous cell carcinoma (2.4%), three patients had adenocarcinoma (2.4%), and the remainder had urothelial carcinoma (95.2%) as their final pathology. There was insufficient data to assess for completeness of resection.

Median survival was 4.6 years (95% confidence interval (CI) 1.21–9.2). Five year overall survival was 58.2% (95% CI 49.6–68.3) and 10 year overall survival is 39.8% (30.9–51.2)(**Fig. 1**). At five years, cancer specific mortality was 33.3% and other cause mortality was 8.5%. LVI was present in 39 patients (31.0%). Survival in those with no cancer was better than those with non-muscle invasive cancer (Ta, Tis, T1), which

in turn was better than those with muscle invasive cancer (T2, T3, T4) (P = 0.0015) (**Fig. 2**). Survival over time was found to be unchanged (hazard ratio (HR) 1.01 95% CI 0.91–1.09, P = 0.61). When modeling was performed for the inclusion of neoadjuvant chemotherapy after the introduction of a MDT meeting, 15 (20%) patients of an eligible 75 had undergone neoadjuvant chemotherapy. Survival of those patients was not seen to be improved compared to those who did not receive neoadjuvant treatment (HR 0.91 95% CI 0.38–2.19, P = 0.83).

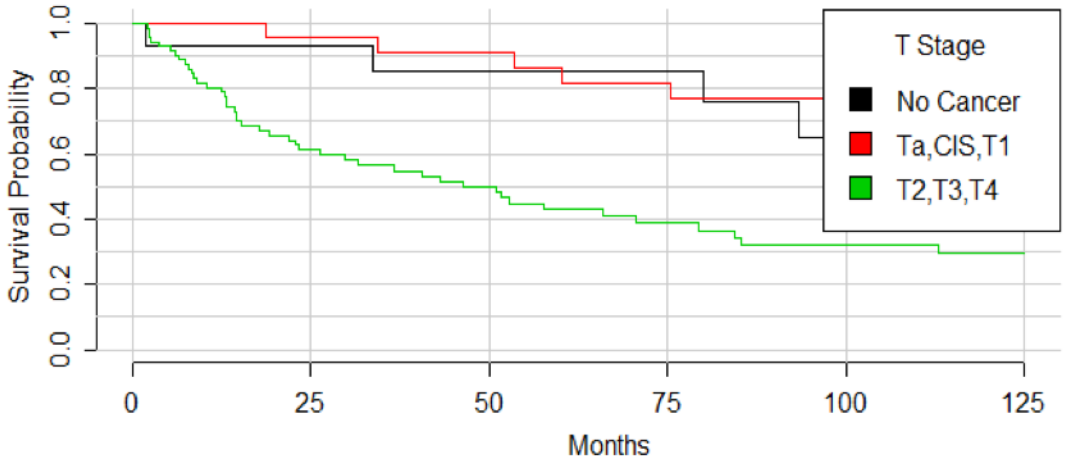

Figure 2. Overall survival time after diagnosis based on pT category.

Table 1. Demographic data.

	Median (IQR)	*n* (%)
Age at diagnosis	67.1 (60.29, 75.15)	
Age at operation	69.2 (62.1, 76.6)	
Male		90 (71.4)
Female		36 (28.6)
BCG - Yes		36 (28.6)
BCG - No		90 (71.4)
Death events		67 (53.6)
Bladder urothelial carcinoma death events		45 (36)
Median survival (years)	4.6 (1.21, 9.2)	
Neoadjuvant chemotherapy following MDT		15 (20)
Pathology pre-cystectomy		
CIS		21 (17)
pT1		15 (12)
pT2		41 (33)
pT3		28 (22)
pT4		12 (10)
Final surgical pathology		
No cancer		16 (12.7)
NMIBC		26 (20.6)
Muscle invasive		75 (59.5)
No information		9 (7.1)
Lymph node status		
Patients with positive lymph nodes		21 (16.6)
Patients with negative lymph nodes		66 (52.4)
Missing data		39 (31.4)

Table 2. Effect of variation in pathology on survival.

	HR (95%CI)	*P* value
Model 1*		
Upgrade	1.63 (0.90–2.96)	0.11
Downgrade	0.80 (0.90–1.63)	0.54
Model 2**		
Upgrade	1.09 (0.58–2.05)	0.79
Downgrade	0.84 (0.41–1.73)	0.64

*Model 1 includes gender, age, treatment year, and variation in pathology.
**Model 2 includes Model 1 and LVI status.

In a log rank test between patients divided by gender, there was no significant difference in survival post cystectomy (P = 0.49). When comparing survival differences between the gender and age, there was no significant difference between those over 70 or under 70 years (Over 70 years: HR 1.27, 95% CI 0.59–2.76; Under 70 years: HR 0.55 95% CI 0.24–1.27). The proportional hazards assumption was checked in each model and was met in all cases.

The 30, 60, and 90-day survival rates were examined: 30 d 100%, 60 d 98.3% (95% CI 96.1–100), and 90 d 95% (95% CI 91.9–99). These were then plotted on a graph to compare survival trends over time. Despite the overall low mortality rate, there was an observable trend for improving mortality (**Fig. 3**).

Of the patients with sufficient data to compare biopsy staging and surgical staging, 57.9% of patients had no change, 18.3% of patients were downgraded, and 16.6% of patients were upgraded. There was no statistically significant difference in survival comparing cystectomy patients who had pathology at surgery upgraded, downgraded or confirmed (P = 0.14), although their effect measures were in the directions expected (downgrade HR 0.80 95%CI 0.90–1.63, upgrade 1.63 (0.90–2.96). Furthermore, when including the presence of LVI in the model of those who had a change in pathology, there was no statistically significant effect on survival (downgrade: HR 0.84 95%CI 0.41–1.73, upgrade 1.09 95%CI 0.58–2.05). This was also true when

patients were stratified by final surgical pathology (Ta, CIS, T1 P = 0.16; T2, T3, T4 P = 0.59) (**Table 2**). Within the non-muscle invasive group (n = 25), 5 patients were downgraded, 20 patients were unchanged and no patients were upgraded. Within the muscle invasive group (n = 74), 21 patients were upgraded, 51 patients had no change, and only 2 patients were downgraded to NMIBC (**Table 3**). No statistical difference in survival was noted within the non-muscle invasive cancer (P = 0.16) and muscle invasive cancer (P = 0.59) groups. As expected the presence of LVI negatively affected survival (univariable HR 2.5, 95% CI 1.46–4.2, P = 0.0007).

Table 3. Variation in pathology according to pre-cystectomy pathology.

Pre-cystectomy pathology	Downgraded	Unchanged	Upgraded
Ta, CIS, T1	5 (20%)	20 (80%)	0
T2, T3, T4	2 (2.7%)	51 (68.9%)	21 (28.4%)

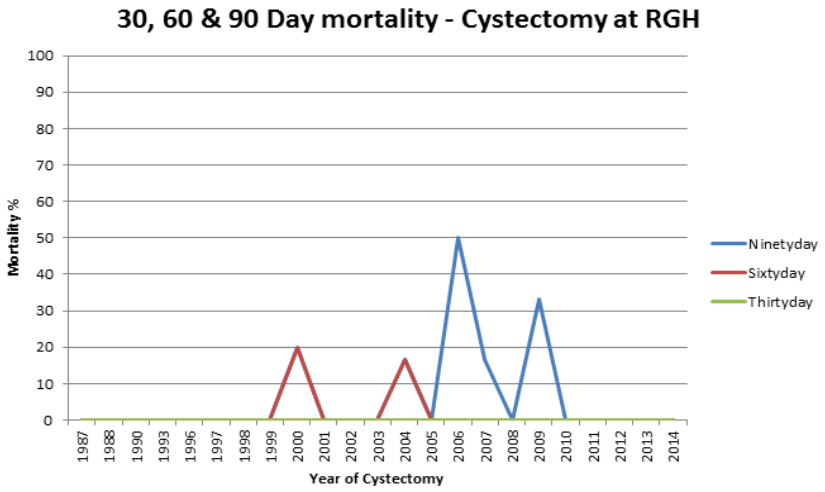

Figure 3. 30-, 60- and 90-day mortality.

DISCUSSION

Survival rates in this series are comparable to those seen within Australia and internationally [18,19,22]. Our median survival was 4.6 years and five-year overall survival 58.2%, compared to 59.6% reported by Patel *et al*. in Australia and 67.6% seen across 15 international centers reported by Ploussard *et al*. [18,22].

We found that our biopsy pathology was more consistent with the final surgical pathology than reported in studies elsewhere [6-9,23,24]. Within the literature, upstaging occurs in 40%–45% of surgical specimens compared to 18.3% at our center. Furthermore, Shariet *et al*. reported that 40% of patients who had NMIBC were found to have muscle invasive cancer on final pathology, compared to zero patients in our study [6]. The reported range of downstaging in the literature ranges from 5%–22% with most series around 20%, which is consistent with our findings [6,23,24]. Furthermore, we found that when there was a variation in pathology, this did not affect survival, an observation in contrast to that reported elsewhere [16,23,24]. This could in part be explained by the sample size, or that no patient was upgraded from non-muscle invasive cancer to muscle invasive cancer, and thus remained in a stage with known better survival outcomes. Only two muscle invasive patients were downgraded to NMIBC. We did not look at individual pathological staging survival outcomes for two reasons: our data would not support further divisions, and secondly as the management is divided between non-muscle invasive and muscle invasive groups, our model provides a more pragmatic representation of the data.

Within the non-muscle invasive group, we accepted the treating clinician's decision that cystectomy was the gold standard treatment. We do know that 28.6% of patients had previous BCG treatment, indicating that non-operative treatment measures had failed.

We found no significant difference in survival between gender, contrasting with the established view that females have worsened mortality. Contemporary bladder urothelial carcinoma survival data from New South Wales found that females have worse survival, but with one study finding this to be true only in those over 70 years [3,19]. Although we only examined those that had undergone cystectomy, we did not find a difference in survival between the genders, even when comparing those under or over 70 years. This is in contrast with cystectomy-only survival studies by both Patel *et al*. and Mitra *et al*. [18,19,25]. Patel *et al*. found that there was no difference in presentation stage between genders and this was not to account for the gender survival differences [19]. Alternatively, Mitra *et al*. found females presented with more advanced disease, 64.7% of females presented with pT2 or greater disease compared to only 55.5% of males, and that this was the reason given for

poorer female survival [25]. We found that 69.7% of females and 61.9% of males presented with pT2 or greater disease, a difference not large enough to support Mitra *et al*.'s argument for poorer female outcomes but consistent with Patel *et al*.

We found no difference in survival when accounting for the addition of neoadjuvant chemotherapy. This is likely a result of the small number of people considered suitable for chemotherapy and the reduced cohort size, examining only those since the introduction of the MDT meeting.

It is accepted that large volume centers have better outcomes for certain oncological surgical procedures [26-29]. Birkmeyer *et al*. noted that there was only a small survival difference comparing low volume to high volume centers (35.4% *vs*. 39.0%) [30] whereas Finks *et al*. attributed a decline of 37% in cystectomy mortality over a nine year period due to higher hospital volumes [31]. Based on Birkmeyer *et al*., hospital volume defined as the number of operations performed each year is categorized as low (≤ 3), moderate (4–5), and high (≥ 6) [30]. On average, in the years 2010–2014, our unit performed 6.4 cystectomies each year, classifying our hospital as a high-volume center. This is reflected in our acceptable mortality outcomes with no recorded deaths within 90 days of operation over the past five years. Our data did not assess morbidity, which may be another marker of improvement if monitored over time.

This is a retrospective analysis. Whilst there is selection bias in those undergoing cystectomy, the purpose of the study was to compare the final biopsy pathology with the surgical biopsy along with overall survival outcomes.

Additionally, progression in pathology prior to cystectomy is a real possibility. However, this falls outside the scope of this study and was thus not included.

Collecting a deep enough biopsy to ensure that detrusor muscle is present is often a difficult task. From our own data we know that only approximately 40% of first TUR include detrusor muscle, comparable to the broad range reported within the literature (10%–80%) [32-34]. One possible explanation for why we did not have any NMIBC patients upgraded was that all potential cystectomy patients required detrusor muscle present in their biopsy sample. Further limitations include the absence of lymph node involvement and surgical margin clearance rates.

In conclusion, in our center we found lower rates of variation in biopsy pathology versus surgical pathology than reported elsewhere in the literature. Furthermore, in contrast to previously published reports we did not find that alterations in final pathology affected survival. Our overall survival outcomes are similar to that seen within Australia and also internationally. We also found that gender did not impact on survival in those undergoing radical cystectomy for bladder urothelial carcinoma.

Acknowledgments

We gratefully acknowledge Sheryl Edwards who has managed the bladder cancer database at the Repatriation General Hospital.

References

1. Australian Institute of Health and Welfare (2013) Cancer survival and prevalence in Australia: period estimates from 1982 to 2010. Asia Pac J Clin Oncol 9:29-39. doi: 10.1111/ajco.12062. PMID: 23418847
2. Scelo G, Brennan P (2007) The epidemiology of bladder and kidney cancer. Nat Rev Urol 4: 205-217. doi: 10.1038/ncpuro0760. PMID: 17415353
3. Tracey E, Roder D, Luke C, Bishop J (2009) Bladder cancer survivals in New South Wales, Australia: why do women have poorer survival than men?. BJU Int 104: 498-504. doi: 10.1111/j.1464-410X.2009.08527.x. PMID: 19338538
4. Marks P, Soave A, Shariat SF, Fajkovic H, Fisch M, et al. (2016) Female with bladder cancer: what and why is there a difference?. Transl Androl Urol 5: 668-682. doi: 10.21037/tau.2016.03.22. PMID: 27785424
5. Babjuk M, Böhle A, Burger M, Compérat E, Kaasinen E, et al. European Association of Urology (2015) Guidelines of non-muscle invasive bladder cancer (Ta, T1, and CIS).
6. Shariat SF, Palapattu GS, Karakiewicz PI, Rogers CG, Vazina A, et al. (2006) Discrepancy between clinical and pathologic stage: impact on prognosis after radical cystectomy. Eur Urol 51: 137-149. doi: 10.1016/j.eururo.2006.05.021. PMID: 16793197
7. May M, Brookman-Amissah S, Roigas J, Hartmann A, Störkel S, et al. (2009) Prognostic accuracy of individual uropathologists in noninvasive urinary bladder carcinoma: a multicentre study comparing the 1973 and 2004 World Health Organisation classifications. Eur Urol 57: 850-858. doi: 10.1016/j.eururo.2009.03.052. PMID: 19346063
8. Van Der Meijden A, Sylvester R, Collette L, Bono A, Ten Kate F (2000) The role and impact of pathology review on stage and grade assessment of stages Ta and T1 bladder tumors: a combined analysis of 5 European Organization for Research and Treatment of Cancer Trials. J Urol 164: 1533-1537. PMID: 11025698
9. Miladi M, Peyromaure M, Zerbib M, Saighi D, Debre B (2003) The value of a second transurethral resection in evaluating patients with bladder tumours. Eur Urol 43: 241-245. PMID: 12600426
10. Herr HW, Donat SM (2008) Quality control in transurethral resection of bladder tumours. BJU Int. 2008;102(9 Pt 102: 1242-6.
11. Murphy WM, Takezawa K, Maruniak NA (2002) Interobserver discrepancy using the 1998 World Health Organization/International Society of Urologic Pathology classification of urothelial neoplasms: practical choices for patient care. J Urol 168: 968-972. doi: 10.1097/01.ju.0000024393.13257.3b. PMID: 12187201
12. Witjes JA, Moonen PMJ, van der Heijden AG (2006) Review pathology in a diagnostic bladder cancer trial: effect of patient risk category. Urology 67: 751-755. doi: 10.1016/j.urology.2005.10.028. PMID: 16566990
13. Patel HD, Ball MW, Cohen JE, Kates M, Pierorazio PM, et al. (2015) Morbidity of urologic surgical procedures: an analysis of rates, risk factors, and outcomes. Urology 85: 552-559. doi: 10.1016/j.urology.2014.11.034. PMID: 25733265
14. Hounsome LS, Verne J, McGrath JS, Gillatt DA (2014) Trends in operative caseload and mortality rates after radical cystectomy for bladder cancer in England for 1998-2010. Eur Urol 67: 1056-1062. doi: 10.1016/j.eururo.2014.12.002. PMID: 25530608
15. Ahmadi N, Delprado WJ, Brooks AJ, Brenner PC, Coombes GM, et al. (2014) Pathological evaluation and quality of surgery in radical cystectomy in New South Wales, Australia. ANZ J Surg 85: 145-149. doi: 10.1111/ans.12383. PMID: 25410154
16. Shariat SF, Svatek RS, Tilki D, Skinner E, Karakiewicz PI, et al. (2010) International validation of the prognostic value of lymphovascular invasion in patients treated with radical cystectomy. BJU Int 105: 1402-1412. doi: 10.1111/j.1464-410X.2010.09217.x. PMID: 20132195
17. Margulis V, Lotan Y, Montorsi F, Shariat SF (2008) Predicting survival after radical cystectomy for bladder cancer. BJU Int 102: 15-22. doi: 10.1111/j.1464-410X.2008.07594.x. PMID: 18325050
18. Patel MI, Bang A, Gillatt D, Smith DP (2015) Contemporary radical cystectomy outcomes in patients with invasive bladder cancer: a population-based study. BJU Int 116 Suppl 3: 18-25. doi: 10.1111/bju.13152. PMID: 26334934
19. Patel MI, Bang A, Gillett D, Cheluvappa R, Smith DP (2015) Poor survival of females with bladder cancer is limited to those aged 70 years or over: a population-wide linkage study, New South Wales, Australia. Cancer Med 4: 1145-1152. doi: 10.1002/cam4.452. PMID: 25914165
20. Grambsch PM, Therneau TM (1994) Proportional hazards tests and diagnostics based on weighted residuals. Biometrika 81: 515-526.
21. R Development Core Team (2013) R: A language and environment for statistical computing. Vienna, Austria: the R Foundation for Statistical Computing. ISBN: 3-900051-07-0. Available online at http://www.R-project.org/.
22. Ploussard G, Shariat SF, Dragomir A, Kluth LA, Xylinas E, et al. (2013) Conditional survival after radical cystectomy for bladder cancer: evidence for a patient changing risk profile over time. Eur Urol 66: 361-370. doi: 10.1016/j.eururo.2013.09.050. PMID: 24139235
23. Gray PJ, Lin CC, Jemal A, Shipley WU, Fedewa SA, et al. (2014) Clinical-pathologic stage discrepancy in bladder cancer patients treated with radical cystectomy: results from the national cancer data base. Int J Radiat Oncol Biol Phys 88: 1048-56. doi: 10.1016/j.ijrobp.2014.01.001. PMID: 24661658
24. Svatek RS, Shariat SF, Novara G, Skinner EC, Fradet Y, et al. (2011) Discrepancy between clinical and pathological stage: external validation of the impact on prognosis in an international radical cystectomy cohort. BJU Int 107: 898-904.

doi: 10.1111/j.1464-410X.2010.09628.x. PMID: 21244604
25. Mitra AP, Skinner EC, Schuckman AK, Quinn DI, Dorff TB, et al. (2014) Effect of gender on outcomes following radical cystectomy for urothelial carcinoma of the bladder: a critical analysis of 1,994 patients. Urol Oncol 32: 51-52. doi: 10.1016/j.urolonc.2013.08.007. PMID: 24239476
26. Birkmeyer JD, Siewers AE, Finlayson EV, Stukel TA, Lucas FL, et al. (2002) Hospital volume and surgical mortality in the United States. N Engl J Med 346: 1128-1137. doi: 10.1056/NEJMsa012337. PMID: 11948273
27. Begg CB, Cramer LD, Hoskins WJ, Brennan MF (1998) Impact of hospital volume on operative mortality for major cancer surgery. JAMA 280: 1747-1751. PMID: 9842949
28. Dudley RA, Johansen KL, Brand R, Rennie DJ, Milstein A (2000) Selective referral to high-volume hospitals: estimating potentially avoidable deaths. JAMA 283: 1159-1166. PMID: 10703778
29. Halm EA, Lee C, Chassin MR (2002) Is volume related to outcome in health care? A systematic review and methodologic critique of the literature. Ann Intern Med 137: 511-520. doi: 10.7326/0003-4819-137-6-200209170-00012. PMID: 12230353
30. Birkmeyer JD, Sun Y, Wong SL, Stukel TA (2007) Hospital volume and late survival after cancer surgery. Ann Surg 245: 777-783. doi: 10.1097/01.sla.0000252402.33814.dd. PMID: 17457171
31. Finks JF, Osborne NH, Birkmeyer JD (2011) Trends in hospital volume and operative mortality for high-risk surgery. N Engl J Med 364: 2128-2237. doi: 10.1056/NEJMsa1010705. PMID: 21631325
32. Roupret M, Yates DR, Varinot J, Phe V, Chartier-Kastler E, et al. (2012) The presence of detrusor muscle in the pathological specimen after transurethral resection of primary pT1 bladder tumors and its relationship to operator experience. Can J Urol 19: 6459-6464. PMID: 23040628
33. Capogrosso P, Capitanio U, Ventimiglia E, Boeri L, Briganti A, et al. (2015) Detrusor muscle in TUR-derived bladder tumor specimens: Can we actually improve the surgical quality?. J Endourol 30: 400-405. doi: 10.1089/end.2015.0591. PMID: 26597334
34. Shoshany O, Mano R, Margel D, Baniel J, Yossepowitch O (2014) Presence of detrusor muscle in bladder tumor specimens--predictors and effect on outcome as a measure of resection quality. Urol Oncol 32: 40. doi: 10.1016/j.urolonc.2013.04.009. PMID: 23911682