Published in final edited form as:
Cancer. 2009 March 1; 115(5): 988–996. doi:10.1002/cncr.24052.

MORTALITY INCREASES WHEN RADICAL CYSTECTOMY IS DELAYED MORE THAN 12 WEEKS: RESULTS FROM A SEER-MEDICARE ANALYSIS

John L. Gore, MD[1,3], **Julie Lai, MS**[4], **Claude M. Setodji, PhD**[4], **Mark S. Litwin, MD MPH**[3,4], **Christopher S. Saigal, MD MPH**[3,4], and **the Urologic Diseases in America Project**

1*VA Greater Los Angeles Healthcare System, Los Angeles, CA*

2*Robert Wood Johnson Clinical Scholars Program, University of California-Los Angeles, Los Angeles, CA*

3*Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA*

4*RAND Corporation, Santa Monica, CA*

Abstract

Background: Single-institution series have documented the adverse impact of a 12-week delay between resection of muscle-invasive bladder cancer and radical cystectomy. These data are derived from tertiary centers, in which referral populations may confound outcomes. We sought to examine the survival impact of a delay in radical cystectomy using nationally representative data.

Methods: From the linked SEER-Medicare dataset, we identified subjects with stage 2 transitional cell carcinoma (TCC) of the bladder who underwent radical cystectomy between 1992 and 2001. We examined delays of 8, 12, and 24 weeks and incorporated these delay cutoffs into multivariate Cox proportional hazards survival models. Covariates included age, race/ethnicity, marital status, Charlson comorbidity index, and cancer grade.

Results: We identified 441 subjects with stage 2 TCC who underwent cystectomy during the study period. Compared with immediate surgery (i.e., within 4–8 weeks of transurethral resection), longer time to cystectomy increased the risk of both disease-specific and overall mortality (HR 2.0, $p<0.01$ and HR 1.6, $p<0.01$, respectively, for those delayed 12-24 weeks; HR 2.0, $p<0.01$ for disease-specific and overall death among those delayed beyond 24 weeks 1 year following diagnosis). Covariates associated with overall mortality included older age (HR 1.04, $p<0.01$) and comorbidity (HR 2.0 for Charlson ≥ 3 vs Charlson 0-1, $p<0.01$).

Conclusions: Delay in definitive surgical treatment beyond 12 weeks conferred an increased risk of disease-specific and all-cause mortality among subjects with stage 2 bladder cancer.

Keywords

bladder cancer; radical cystectomy; survival; access to care

INTRODUCTION

Patients with stage II, muscle-invasive bladder cancer have 5-year disease-specific survival ranging from 62-80% following radical cystectomy.[1, 2] The aggressiveness of muscle-invasive

Corresponding author: John L. Gore, MD 911 Broxton Ave., 3rd Floor Los Angeles, CA 90024 Fax: 310 794-3288 Phone: 310 794-3508 Email: jgore@mednet.ucla.edu.

transitional cell carcinoma of the bladder mandates prompt evaluation and management. Yet the medical comorbidities that are common among bladder cancer patients confound aggressive surgical management. Because tobacco is the predominant risk factor for bladder cancer, many patients suffer from affiliated conditions, including chronic pulmonary and cardiovascular diseases. Prior to radical cystectomy and urinary diversion, a major undertaking, these patients often require extensive medical evaluation and clearance, significant preoperative counseling, and, potentially, the transfer of care to experienced high-volume cystectomy providers. Beyond resolution of clinical barriers, patients must achieve mental acceptance of the drastic change in voiding and potential affect on their body image conferred by a radical cystectomy and urinary diversion.

This delay between diagnosis of muscle invasion and cystectomy may have serious consequences. Retarding the definitive surgical management of muscle-invasive bladder cancer may confer increased risks of pathologic upstaging at cystectomy and worsened disease-specific and overall survival.[3-6] These results have been questioned and the literature suggesting an inverse relationship between time to cystectomy and outcome reflects the experience of tertiary referral centers.[7, 8] The reasons for treatment delays at these high-volume institutions may not generalize to the typical patient newly-diagnosed with muscle-invasive bladder cancer.[1] Hence, we sought to utilize a nationally-representative dataset to evaluate the relationship between the timing of radical cystectomy following a diagnosis of muscle-invasive bladder cancer and patient clinical outcome.

MATERIALS AND METHODS

Patient population

From a linked database integrating data from the Surveillance, Epidemiology, and End Results (SEER) national cancer registry and the Medicare claims database, we identified subjects with AJCC/UICC stage II (T2 N0 M0: tumor extension into but not beyond the muscularis propria of the bladder wall [T2], no regional lymph node metastases [N0], no distant metastases [M0]) transitional cell carcinoma (TCC) of the urinary bladder who underwent radical cystectomy in the contiguous years 1992–2001.[2] Stage explicitly included in the SEER registry and represents the stage at initial diagnosis of transitional cell carcinoma (TCC) of the urinary bladder. For the years studied, the SEER registry contains detailed cancer-related information from 11 US regions generalizable to the US population.[3] Medicare claims include the Patient Entitlement and Diagnosis Summary File (PEDSF), which contains demographic information and links to the SEER registry, the Medicare Provider Analysis and Review (MEDPAR) file, with diagnosis and procedure codes for each hospital admission, National Claims History (NCH) records that contain provider billing information, and a hospital file comprising variables from the Healthcare Cost Report (HCRIS) and Provider of Service (POS) survey. The combined SEER-Medicare dataset merges detailed cancer-specific information from SEER with Medicare claims that permit analysis of procedures performed, dates of any treatments received, and determination of subjects' comorbid conditions.

We identified study subjects from primary malignancy, diagnosis, and procedure codes. Included subject claims contained either International Classification of Diseases (9th revision [ICD-9]) code 57.71 or Current Procedural Terminology Coding System (4th edition [CPT]) code 51570 or 51575 indicative of a radical cystectomy. Those with stage 2 bladder cancer, based on AJCC/UICC TNM Classification and Stage groupings, were identified from the SEER registry.[2] Determination of stage from SEER is considered highly valid and conforms to standards set forth by the North American Association of Central Cancer Registries, achieving complete case ascertainment in 98% of subjects.[4]

Time from diagnosis to radical cystectomy was determined from procedure dates in the MEDPAR and NCH records. The time from the most recent transurethral resection of a bladder tumor (TURBT), identified from either ICD-9 (57.33, 57.4, 57.49) or CPT-4 codes (52234, 52235, or 52240), to radical cystectomy constituted the time lapse to definitive treatment. Only 6% of study subjects had multiple TURBT's prior to cystectomy. We excluded those with non-TCC histology and those who underwent radical cystectomy within 4 weeks of diagnosis, as those procedures likely represented emergent indications. We also excluded those who underwent cystectomy more than 52 weeks after diagnosis to minimize bias toward adverse outcomes in the delayed cohort.

Covariates in our multivariate models examining survival after radical cystectomy included subject age, gender, marital status, comorbidity, cancer grade, and geographic region. Due to the small proportion of non-whites in the study sample, we dichotomized race/ethnicity as white and non-white. The Charlson index, a weighted score based on diagnosis claims, was used to quantify subject comorbidity, with a higher score representing a greater burden of comorbid conditions.[5, 6] The SEER registry classifies TCC grade from one through four, with a higher grade indicating poorer histologic differentiation. We consolidated the SEER registry regions into corresponding US Census regions.

Statistical analysis

Descriptive statistics are presented for demographic and clinical data. We created Cox proportional Hazards models to evaluate the independent association on survival of time between TURBT and radical cystectomy . We modeled survival time since diagnosis rather than time since cystectomy to minimize lead-time bias in the analysis. We evaluated various cutoffs in time to cystectomy with a 4–8 week time lapse as the referent. To account for violation of the proportional hazards assumption of the Cox model, we created an interaction term combining the dichotomous variable of whether there was a delay beyond 24 weeks and the log of the follow-up time in days since diagnosis. The mortality hazard for patients with a time to cystectomy beyond 24 weeks can be calculated from the addition of the coefficient for the variable reflecting a delay in treatment greater than 24 weeks with the coefficient for the interaction term multiplied by the natural log of the number of days of follow-up since diagnosis, as expressed in the equation below:

$$Hazard = \beta_{>24\ weeks} + [(\beta_{\text{int}\ eraction})\ \ln(\text{time since diagnosis})]$$

Exponentiating this calculated coefficient yields a hazard ratio that reflects the increase in mortality at that time point compared with a 4–8 week time lapse between TURBT and cystectomy, adjusting for all other covariates in the model.

To display the survival outcomes graphically we created Cox models stratified by time lapse between diagnosis and cystectomy. The violation of the proportional hazards assumptions necessitated utilization of the stratified model. The estimates for all adjusted covariates were similar for this stratified model when compared with the time interaction model, thus permitting use of the graphical results from the stratified model as a representation of the survival curves for each time-lapse group. Because this is a survival curve based on the model predictions, all the covariates were held at discrete values chosen based on the predominant category for each covariate. Thus, the survival curves represent the effect of the various cutoffs in time lapse to cystectomy for a 65 year-old white married male with a Charlson score of 2 and a cancer grade of 4 residing in the West US Census Region. We used an alpha of 0.05 for all statistical tests. All statistical analyses were performed with SAS 9.1 (SAS Institute, Cary, NC).

RESULTS

Characteristics of the study sample stratified by time to cystectomy are displayed in Table 1. We identified 441 subjects with stage 2 TCC of the bladder who underwent radical cystectomy between 1992 and 2001. Most subjects were male, white, and married. Charlson indices ranged from 0 to 5, with 93% of subjects having comorbidity indices of 0 or 1. Time from diagnosis to radical cystectomy ranged from 4 to 52 weeks. Eighty-nine percent of subjects underwent definitive surgical extirpation within 24 weeks of diagnosis, of whom 73% underwent cystectomy within 12 weeks. The demographic characteristics of the sample did not vary by time to cystectomy. However, although not statistically significant, non-whites and unmarried individuals trended toward longer time to cystectomy. Over the study period, 279 subjects (63.3%) died, most often from bladder cancer (136 subjects [30.8%] a median 16.0 months following diagnosis) or cardiovascular disease.

Table 2 shows results of the multivariate Cox proportional hazards model evaluating disease-specific mortality following diagnosis of invasive bladder cancer. Subjects delayed 8–12 weeks were not impacted in terms of mortality risk compared with those who underwent cystectomy within 4–8 weeks of diagnosis. However, those delayed 12–24 weeks suffered significantly worse mortality, with 2.0 times the hazard of death of those delayed 4–8 weeks. Beyond 24 weeks, subjects suffered worsening disease-specific mortality proportional to the follow-up interval: 1 year after diagnosis, those delayed over 24 weeks had 2.0 times the hazard of disease-specific mortality of those without a delay. Two years after diagnosis the hazard ratio increases to 7.7. Thus, beyond a 12-week delay between diagnosis and definitive surgical treatment, we identified a time-dependent adverse impact on survival following radical cystectomy. No other covariates were found to impact disease-specific survival.

Table 3 displays the multivariate Cox proportional hazards model of all-cause mortality following diagnosis of invasive bladder cancer. Similar to the disease-specific survival model, subjects delayed 8–12 weeks had a mortality risk similar to those who underwent surgery 4–8 weeks after diagnosis. Beyond a 12-week time lapse, all-cause mortality was significantly higher compared with those delayed 4–8 weeks. Among those delayed more than 24 weeks, 1-year and 2-year mortality risk was 1.6 and 2.5-fold higher, respectively, than those who underwent cystectomy within 4–8 weeks. Covariates associated with overall survival included age and comorbidity. Older age was associated with higher risk of death after cystectomy. Compared with subjects whose Charlson index was 0-1, those with a Charlson index of at least 3, consistent with substantial comorbid disease, had a significantly increased 2.3-fold higher risk of mortality over time.

Figures 1 and 2 display survival curves following radical cystectomy stratified by time from diagnosis to definitive surgery. These curves reflect the impact of a delay in cystectomy for a subject with characteristics representative of the commonest category of each covariate. Subjects delayed 4–8 and 8–12 weeks demonstrated similar survival curves. Beyond a 12-week lapse between diagnosis and radical cystectomy, a dose-response relationship was identified: increasing the delay in cystectomy beyond 12 weeks conferred a progressive adverse impact on subject disease-specific and overall survival. Those delayed beyond 24 weeks demonstrated rapid degradation of survival over time compared with those delayed 12–24 weeks.

CONCLUSIONS

A delay of more than 12 weeks between diagnosis and radical cystectomy for TCC of the urinary bladder significantly compromises patient survival. This adverse impact affects both disease-specific and overall survival and is exacerbated by increasing time from diagnosis to

cystectomy. Our findings corroborate prior single-institution series that identified a 12-week cutoff as conferring an increased risk of pathologic upstaging and mortality.[7-10]

Common reasons for delays in definitive treatment of muscle-invasive bladder cancer patients include extra time for medical clearance, given the preponderance of comorbid disease in this population, the need for transfer to centers equipped to manage the burden of care for cystectomy patients, and time required to overcome patient reluctance to undergo surgery that radically affects their voiding function and, potentially, their body image. Radical cystectomy with urinary diversion is a uniquely morbid operation. Complication rates after radical cystectomy range from 28 –to 37% in studies derived from analysis of nationally representative datasets.[11, 12] Many of these complications are medical and relate to the high prevalence of smoking history, vascular disease, coronary artery disease, and chronic pulmonary disease in bladder cancer patients. These conditions are likely more prevalent among elderly bladder cancer patients, explaining their underuse of aggressive therapy.[13] These circumstances necessitate preoperative optimization of patients' medical condition to reduce these risks.

Given the operative time, length of inpatient stay, extensive care required during the convalescent period, and poor reimbursement for the procedure and postoperative care, many providers refer patients with indications for a cystectomy to higher volume centers. The 1990s witnessed a marked urbanization of radical cystectomy as these patients were regionalized in an *ad hoc* manner to urban, high-volume, academic facilities.[14] High-volume cystectomy centers have better perioperative mortality outcomes; incorporation of processes of care such as rates of continent urinary diversion enhances differences in clinical outcomes between high and low-volume centers.[15, 16] Although regionalization of radical cystectomy for bladder cancer to high-volume centers may be associated with improved perioperative outcomes, the incumbent delay required for such a transfer of care may worsen patients' long-term survival.

Our analysis is strengthened by the study sample and data source utilized. Differential referral patterns may bias the association between a delay in cystectomy and pathologic and survival outcomes at tertiary referral centers. Patient populations at these centers may not generalize to the average patient with muscle-invasive bladder cancer. In contrast, our study utilizes nationally representative data that includes patients treated at academic and community institutions, by providers with varying degrees of surgical volume. Similarly, referrals in our sample should reflect community patterns that may differ from those seen exclusively at tertiary referral centers. We restricted our sample to those with stage 2 TCC in order to eliminate equivocal treatment algorithms as a source of delays in cystectomy. Those with more advanced locoregional disease may suffer postponements related to the consideration of alternative treatments such as chemotherapy that could potentially bias our results. Similarly, the study period, with patients treated in an era that preceded more earnest consideration of neoadjuvant chemotherapy before cystectomy, favors the results of our study.

Our study is limited by the use of claims data to study procedural specifics and survival outcomes. We attempted to create an algorithm to measure time from diagnosis to cystectomy; however, we could not precisely determine, in the context of multiple TURBTs prior to cystectomy, the biopsy that confirmed muscle invasion. Among the small proportion of subjects who underwent multiple resections prior to cystectomy, many may have had reoperations for symptoms such as refractory hematuria. Re-resection is uncommon and likely not indicated for patients with pathologically confirmed muscle invasion, thus our algorithm for determining time to cystectomy is intuitively valid. Also, our staging algorithm involved identification of the initial diagnosis of bladder cancer. In the majority of cases, this stage classification is derived from the initial TURBT, with no account for upstaging at the time of cystectomy. Furthermore, we could not identify upstaging as an outcome in our sample, which may have further validated the adverse impact of a delay in cystectomy.

Determination of cause-specific survival from claims or registry data is often confounded by submission or coding errors, limiting analysis of disease-specific survival in this population. A selection bias may have further confounded the analysis. This may explain the crossing of the survival curves in Figure 1. To sustain a delay in cystectomy beyond 24 weeks, subjects had to survive those 6 months; that the survival curve for these subjects eventually dropped below all other time lapse categories may represent deaths from bladder cancer exclusively. We cannot account for subjects delayed beyond 24 weeks who eventually received no cancer-directed care. Contemporary management of invasive bladder cancer mandates consideration of neoadjuvant chemotherapy based upon randomized controlled trials demonstrating some survival benefit.[17] We specifically excluded subjects who received chemotherapy prior to cystectomy and our results do not apply to patients appropriately selected for neoadjuvant chemotherapy. The impact of chemotherapy on optimal pathways of care that include radical cystectomy has yet to be clearly delineated. Importantly, these results should not be interpreted as an indictment of neoadjuvant chemotherapy due to the resultant impact on time to cystectomy. Finally, our analysis focused on Medicare beneficiaries, which may limit generalizability of our results. However, most patients with newly diagnosed bladder cancer are between the ages of 60–79 years and, thus, are of Medicare age.[18]

We sought to determine the impact of delays between the diagnosis of muscle-invasive bladder cancer and definitive extirpative treatment with radical cystectomy. We could not adjust for delays in care between symptomatic presentation and eventual diagnosis, which may be a more critical determinant of cancer-specific outcome than delays between diagnosis and cystectomy. Patients with hematuria may receive treatment with antibiotics prior to referral for further evaluation. For muscle-invasive cancers, the prolongation of time to evaluation engendered by this inappropriate management may be more condemning than their management once diagnosed.

Despite these limitations, these results demonstrate the detrimental impact of a delay beyond 12 weeks between diagnosis of muscle-invasive bladder cancer and definitive treatment with radical cystectomy. Delaying cystectomy for patients with muscle-invasive TCC of the bladder beyond 12 weeks confers worse disease-specific and overall survival. Prompt treatment remains fundamental to the management of stage 2 bladder cancer; those processes that expedite care in this population should be disseminated in order to minimize the magnitude of the cohort delayed beyond 12 weeks.

ACKNOWLEDGEMENT

This study used the linked SEER-Medicare database. The design of the study, interpretation and reporting of these data, and preparation of the manuscript were the sole responsibility of the authors. The authors acknowledge the efforts of the Applied Research Program, NCI; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

Source of funding: National Institute of Diabetes and Digestive and Kidney Diseases N01-DK-7-0003

References

1. Liu JH, Zingmond DS, McGory ML, et al. Disparities in the utilization of high-volume hospitals for complex surgery. JAMA Oct 25;2006 296(16):1973–1980. [PubMed: 17062860]
2. Greene, FL.; Page, DL.; Fleming, ID., et al. AJCC Cancer Staging Manual. Vol. 6th ed. Springer-Verlag; New York: 2002.
3. Potosky AL, Riley GF, Lubitz JD, Mentnech RM, Kessler LG. Potential for cancer related health services research using a linked Medicare-tumor registry database. Med Care Aug;1993 31(8):732–748. [PubMed: 8336512]

4. Hofferkamp, JE. Standards for Cancer Registries Volume III: Standards for Completeness, Quality, Analysis, Management, Security, and Confidentiality of Data. North American Association of Central Cancer Registries; Springfield, IL: 2008.
5. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40(5):373–383. [PubMed: 3558716]
6. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol Jun;1992 45(6):613–619. [PubMed: 1607900]
7. Chang SS, Hassan JM, Cookson MS, Wells N, Smith JA Jr. Delaying radical cystectomy for muscle invasive bladder cancer results in worse pathological stage. J Urol Oct;2003 170(4 Pt 1):1085–1087. [PubMed: 14501697]
8. Lee CT, Madii R, Daignault S, et al. Cystectomy delay more than 3 months from initial bladder cancer diagnosis results in decreased disease specific and overall survival. J Urol Apr;2006 175(4):1262–1267. [PubMed: 16515975]discussion 1267
9. May M, Nitzke T, Helke C, Vogler H, Hoschke B. Significance of the time period between diagnosis of muscle invasion and radical cystectomy with regard to the prognosis of transitional cell carcinoma of the urothelium in the bladder. Scand J Urol Nephrol 2004;38(3):231–235. [PubMed: 15204377]
10. Sanchez-Ortiz RF, Huang WC, Mick R, Van Arsdalen KN, Wein AJ, Malkowicz SB. An interval longer than 12 weeks between the diagnosis of muscle invasion and cystectomy is associated with worse outcome in bladder carcinoma. J Urol Jan;2003 169(1):110–115. [PubMed: 12478115] discussion 115
11. Barbieri CE, Lee B, Cookson MS, et al. Association of procedure volume with radical cystectomy outcomes in a nationwide database. J Urol Oct;2007 178(4 Pt 1):1418–1421. [PubMed: 17706712] discussion 1421-1412
12. Konety BR, Allareddy V, Herr H. Complications after radical cystectomy: analysis of population-based data. Urology Jul;2006 68(1):58–64. [PubMed: 16806414]
13. Konety BR, Joslyn SA. Factors influencing aggressive therapy for bladder cancer: an analysis of data from the SEER program. J Urol Nov;2003 170(5):1765–1771. [PubMed: 14532772]
14. Hollenbeck BK, Taub DA, Miller DC, Dunn RL, Montie JE, Wei JT. Regionalization of radical cystectomy. J Urol April;2004 171(4 suppl):36.abstract 137
15. Gore JL, Saigal CS, Hanley JM, Schonlau M, Litwin MS. Variations in reconstruction after radical cystectomy. Cancer Aug 15;2006 107(4):729–737. [PubMed: 16826589]
16. Hollenbeck BK, Dunn RL, Miller DC, Daignault S, Taub DA, Wei JT. Volume-based referral for cancer surgery: informing the debate. J Clin Oncol Jan 1;2007 25(1):91–96. [PubMed: 17194909]
17. Grossman HB, Natale RB, Tangen CM, et al. Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. N Engl J Med Aug 28;2003 349(9):859–866. [PubMed: 12944571]
18. Jemal A, Murray T, Ward E, et al. Cancer statistics, 2005. CA Cancer J Clin Jan-Feb;2005 55(1):10–30. [PubMed: 15661684]

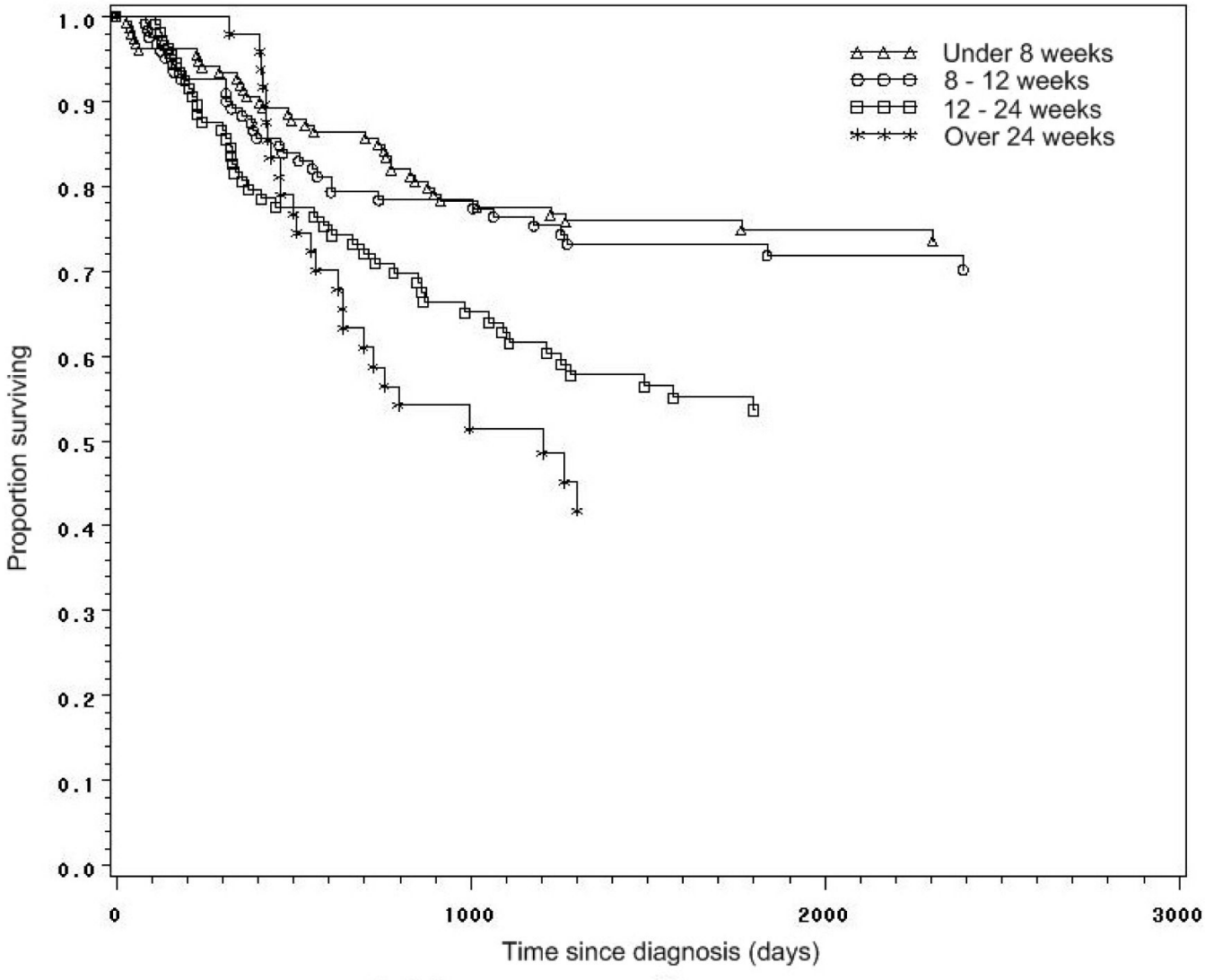

Figure 1.
Disease-specific survival following diagnosis of muscle-invasive bladder cancer stratified by time between diagnosis and radical cystectomy.

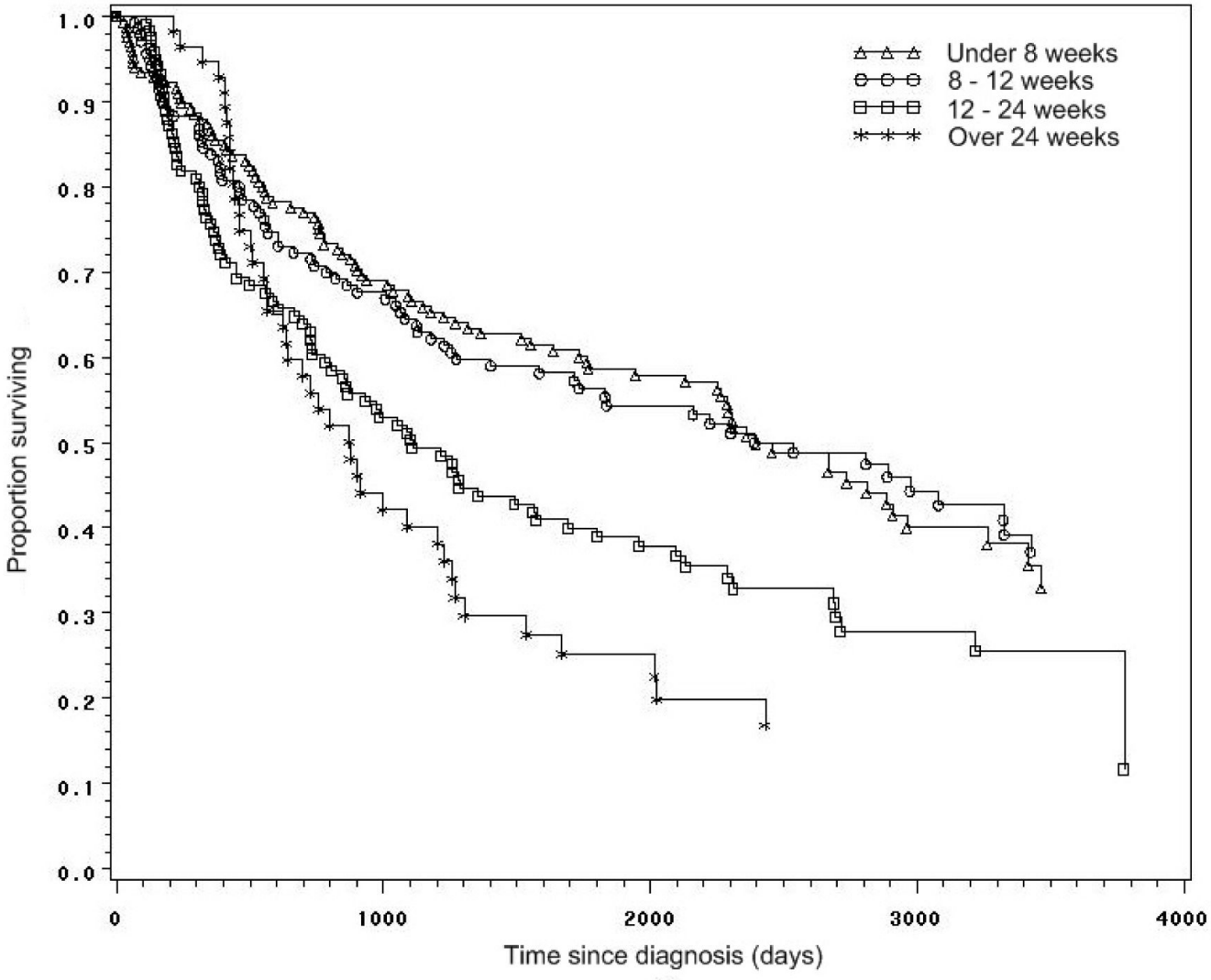

Figure 2.
Overall survival following diagnosis of muscle-invasive bladder cancer stratified by time between diagnosis and radical cystectomy.

Table 1

Characteristics of the study sample.

	Time to cystectomy		
	≤ 12 weeks	**> 12 weeks**	**p-value**
Age (years), mean ± SD	73.8 ± 5.6	73.6 ± 6.6	0.77
Gender			
Male	193 (67.5)	108 (69.7)	0.64
Female	93 (32.5)	47 (30.3)	
Race/ethnicity			
White	256 (89.5)	130 (83.9)	0.10
African American	12 (4.2)	11 (7.1)	
Hispanic	6 (2.1)	9 (5.8)	
Other	12 (4.2)	5 (3.2)	
Married	267 (93.4)	137 (88.4)	0.07
Charlson comorbidity index			
0	239 (83.6)	117 (75.5)	0.15
1	30 (10.5)	26 (16.8)	
2	10 (3.5)	5 (3.2)	
≥ 3	7 (2.4)	7 (4.5)	
Cancer grade			
1	2 (0.7)	0	0.68
2	33 (11.7)	18 (11.7)	
3	172 (60.8)	101 (65.6)	
4	76 (26.8)	35 (22.7)	
US Census Region			
Northeast	51 (17.8)	36 (23.2)	0.06
South	9 (3.2)	9 (5.8)	
Midwest	75 (26.2)	48 (31.0)	
West	151 (52.8)	62 (40.0)	

Table 2

Multivariate Cox Proportional Hazards model of disease-specific survival following diagnosis of muscle-invasive bladder cancer and subsequent radical cystectomy.

	Parameter estimate	Hazard ratio	p-value
Age	0.019	1.02	0.23
Female gender	0.11	1.12	0.55
Nonwhite race (vs. white)	−0.25	0.78	0.39
Married marital status (vs. unmarried)	−0.35	0.71	0.23
Charlson comorbidity index (vs. 0-1)			
2	0.38	1.46	0.07
≥ 3	0.23	1.26	0.62
Cancer grade (vs. 4)			
2	0.053	1.05	0.87
3	0.053	1.05	0.81
US Census region (vs. West)			
Northeast	0.16	1.17	0.49
South	−0.34	0.72	0.52
Midwest	0.13	1.14	0.54
Time to cystectomy (vs. 4-8 weeks)			
8-12 weeks	0.16	1.17	0.53
12-24 weeks	0.70	2.01	0.003
24 weeks	−4.4	*	
≥ 24 weeks * log(delay time)	0.86	*	0.008

*Hazard ratio for those delayed greater than 24 weeks is a function of time since diagnosis

Table 3

Multivariate Cox Proportional Hazards model of overall survival following diagnosis of muscle-invasive bladder cancer and subsequent radical cystectomy.

	Parameter estimate	Hazard ratio	p-value
Age	0.037	1.04	0.001
Female gender	−0.090	0.91	0.50
Nonwhite race (vs. white)	−0.18	0.84	0.40
Married marital status (vs. unmarried)	0.008	1.01	0.98
Charlson comorbidity index (vs. 0-1)			
2	0.30	1.35	0.06
≥ 3	0.71	2.03	0.017
Cancer grade (vs. 4)			
2	−0.23	0.80	0.33
3	−0.022	0.98	0.89
US Census region (vs. West)			
Northeast	0.073	1.08	0.66
South	0.35	1.42	0.23
Midwest	0.058	1.06	0.71
Time to cystectomy (vs. 4-8 weeks)			
8-12 weeks	0.013	1.01	0.94
12-24 weeks	0.46	1.59	0.004
24 weeks	−3.6	*	
≥ 24 weeks * log(delay time)	0.68	*	0.001

*Hazard ratio for those delayed greater than 24 weeks is a function of time since diagnosis