Cause-specific survival by stage of bladder and urinary tract cancers and factors collected by Mallorca Cancer Registry associated to survival

Maria Ramos (mramos@dgsanita.caib.es)
Balearic Island Public Health Deparment https://orcid.org/0000-0002-0903-5264
Joana Ripoll
Mallorca Primary Health Care Department
Juanjo Montaño
University of the Balearic Islands
Jaume Pons
Balearic Islands Public Health Deparment
Alberto Ameijide
Tarragona Cancer Registry
Paula Franch
Balearic Islands Public Health Department

Research article

Keywords: bladder neoplasms, survival, stage, multiple imputation

Posted Date: February 4th, 2020

DOI: https://doi.org/10.21203/rs.2.22589/v1

Abstract

Background: 1) to find out the distribution of bladder and urinary tract cancers by stage; 2) to determine cause-specific survival by stage of bladder and urinary tract cancers; 3) to identify factors that explain and predict the likelihood of survival and the risk of dying from these cancers.

Methods: Incident bladder and urinary tract cancer cases diagnosed between 2006 and 2011 were identified through the Mallorca Cancer Registry. Inclusion criteria: cases with codes C65–C68 according to the ICD-O 3rd edition with any behaviour. Cases identified exclusively through the death certificate were excluded. We collected the following data: sex; age; date and method of diagnosis; histology according to the ICD-O 3rd edition; T, N, M and stage at the time of diagnosis; and date of follow-up or death. End point of follow-up was 31 December 2015. Multiple imputation (MI) was performed to estimate cases with unknown stage. Cases with benign or indeterminate behaviour were excluded for the survival analysis. Actuarial and Kaplan-Meier methods and Cox regression models were used for survival analysis.

Results: 2060 cases were identified. 15% were women and 65.2% were 65 years or older. 93.6% consisted of bladder and other urinary tracts. 55.7% were papillary transitional neoplasia, 37.7% solid transitional, 0.6% microcytic, and the rest of other histology. 3.7% had no stage (benign or undetermined behaviour) and 12.5% had unknown stage. After MI, 35.7% were in stage 0a (non-invasive papillary carcinoma), 3.1% in stage 0is (carcinoma in situ), 33.3% in stage I, 11.9 % in Stage II, 4.7% in stage III, and 11.1% in stage IV. Survival was 73% at 5 years. Survival by stage: 98% at stage 0a, 88% at stage 0is, 84% at stage I, 44% at stage II, 33% at stage III, and 7% at stage IV. The Cox model showed that age, histology, and stage were associated with survival.

Conclusion: Bladder and urinary tract cancers survival vary greatly with stage, among both non-invasive and invasive cases.

Background

Bladder cancer is the second most frequent genitourinary cancer after prostate cancer. Europe has one of the highest bladder cancer incidences, especially in Italy and Spain [1]. According to the Spanish Network of Cancer Registries (REDECAN), bladder cancer is the third most frequent cancer in men and the seventh in women, considering colon and rectal cancer separately. Estimated world adjusted incidence rates for 2019 were 37.7 (CI at 95%: 33.6–42.3) by 100,000 habitants in men and 7.4 (5.6–9.6) in women [2]. In 2015, adjusted mortality rates were 10.46 by 100,000 habitants in men and 1.71 in women [3].

The EUROCARE-5 study estimated, for the period 2000–2007, a relative survival at 5 years for bladder cancer of 70.4% (69.3–71.4) for Spain; slightly higher than the European average, which was 68.6% (68.3–68.9). A huge variability in bladder cancer survival was observed due to the inclusion or not of non-invasive cases [4].

Stage at diagnosis is the most important prognostic factor for invasive bladder cancer, while grade is the most important prognostic factor for non-invasive bladder cancer [5]. Regarding stage, most studies use the simplified classification based on: localized, regional, and distant categories [6–8]. Information about survival by stage in bladder cancer according to the TNM system is scarce [9], as well as about survival of non-invasive bladder cancer [8]. Clinicians use the classification based on: non-muscle invasive bladder cancer (NMIBC), including in situ carcinomas and T1, and muscle-invasive bladder cancer (MIBC), including T2–T4 tumours. Even with optimal treatment, bladder cancer recurs in more than 50% of cases of NMIBC and can progress to MIBC in up to 20% of patients [10].

Having information about survival by stage is useful for the monitoring of survival trends and for health services planning purposes. One of the problems that face population based cancer registries collecting stage is missing values; the handling of which becomes a challenge in epidemiological research because it introduces bias. Multiple imputation (MI) solves bias and underestimation of population variability by offering similar estimates to the ones obtained with complete data [11], and it is an appropriate method to handle with missing values of stage in survival cancer studies [12].

The aims of this study were: 1) to find out the distribution of bladder and urinary tract cancers by stage; 2) to determine cause-specific survival by stage of bladder and urinary tract cancers; 3) to identify factors that explain and predict the likelihood of survival and the risk of dying from these cancers.

Methods

Retrospective follow-up study of patients living in Mallorca diagnosed with bladder and urinary tract cancers between 2006 and 2011, identified through the Mallorca Cancer Registry.

Study population: cases with codes C65–C68 according to the ICD-O 3rd edition with any behaviour and histology except lymphomas (from 9590 to 9720 both included) were included, while cases identified exclusively through the death certificate (DCO cases) were excluded.

IACR/IARC rules for multiple cancers were used [13]. Thus, only the first cancer was registered, whether it was uncertain behaviour, in situ, or invasive. If, subsequently, there was a progression from non-invasive to invasive, the first registered cancer was not modified.

The following data were collected: sex, age, diagnostic method, site and sub-site; histology and behaviour according to the ICD-O 3rd edition [13]; date of diagnosis; pathological or clinical tumour size (T), pathological or clinical regional lymph nodes (N), metastasis (M) and stage; date of last follow-up or date of death, and cause of death (bladder and urinary tract cancer or other causes).

Age was grouped as: 15–44 years old, 45–54, 55–64, 65–74, and 75 and over. Diagnostic method was recorded as clinical, pathological, or unknown. Site and sub-site were grouped as: urinary bladder, renal pelvis, overlapping and unspecified urinary organs, ureter, and urethra. Histology was recorded as: papillary transitional cell neoplasia (8130), solid transitional cell neoplasia (8120), microcytic carcinoma (8041, 8045), and other histology and unspecified (8000, 8001, 8010, 8020, 8033, 8070, 8071, 8082, 8140, 8310, 8480, 8490, 8255, 8900). Behaviour was registered as uncertain, in situ, and invasive.

Stage was calculated according to the UICC 7th edition [14], but regrouped in the following categories: 0a, 0is, I, II, III, IV, no stage (uncertain behaviour). Pathological T or N status was prioritised over clinical. An integrated approach [14] was used by combining pathological and clinical components to obtain the stage. The clinical records of cases with missing stage were reviewed in depth to minimise the number of lost values. We did the following assumptions: if T was 1 and N and M were missing, we assigned stage 1; if T was 2 and N and M were missing, we assigned stage 2, as some authors recommend for prostate cancer [15].

Time was calculated from date of diagnosis to date of death or date of the last follow-up. Vital status referred to the state (alive or dead from bladder or urinary tract cancer or from other causes) at the time of the last follow-up. The clinical records of deceased cases were reviewed in depth to establish precisely the cause of death. Cases that emigrated from Mallorca and lost cases were censored, as well as deaths from other causes for cause-specific survival. The starting point of follow-up was the date of diagnosis, and the end point was 31 December 2015.

Statistical analysis: MI was used to obtain stage when this was unknown, following three main steps [16]. First, we ran the imputation model and replaced each missing value with a set of five imputations by applying the multiple imputation chained equation (MICE) procedure. We made the imputation using the variables sex, age, site and sub-site, histology, vital status and survival time. Secondly, we analysed the resulting five imputed and complete data sets independently by applying the Cox regression model. Finally, we obtained a single Cox model using Rubin's rules [17] to combine the five estimates resulting from the previous Cox regression model. A more detailed description about the MICE procedure can be found in Ramos et al. [18].

We applied the cause-specific survival analysis developed by actuarial and Kaplan-Meier methods to estimate likelihood of survival and risk of death; relative survival using the Ederer II method [19]; the log-rank test to evaluate the statistical differences of the observed survival curves by each categorical variable; the log-rank test for trend to analyze the type of trend of the two variables that can be considered as ordinal, age groups and stage; and the Cox regression models to identify prognostic factors of the risk of death. Cases with uncertain behaviour were excluded for the survival analysis, since they have no stage, our main study variable. We considered age as a continuous variable because our interest was to know the effect of each unit increase on the risk of dying from bladder or urinary tract cancer. The proportional hazard assumption for each covariate was tested by introducing time dependent variables. Since age and histology did not meet this assumption, we applied the extended Cox regression, which not only analyses the effect of covariates on the risk of dying, but also allows for the modelling of the time dependent effect of age and histology covariates. The procedure for selecting the variables in the final Cox model was based on the maximum likelihood criterion. Thus, initially, sex, age, site, histology and stage were introduced into the model, as well as time-dependent variables of age and histology. To compare the effect of the imputation procedure on the hazard ratio estimation of covariates, the extended Cox regression was performed before and after MI.

MI was carried out with STATA 13, cause-specific survival analysis with SPSS 23 and relative survival with the "relsurv" library of R.

Results

A total of 2093 cases of bladder and urinary tract cancers were identified between 2006 and 2011. We worked with 2060 cases because 10 DCO, 1 lymphoma, and 22 cases without follow up data were excluded. Of the 2060 cases, only 15% were women and 65.2% were 65 years or older. 96.3% were diagnosed by pathological methods and 93.6% were bladder cancer. There were 12.5% of cases with unknown stage. After MI, 35.7% were in stage 0a (non invasive papillary carcinoma), 3.1% in stage 0is (carcinoma in situ), 33.3% in stage I, 11.9% in stage II, 4.7% in stage III, and 11.1% in stage IV. Almost three of four cases (72.1%) were NMIBC. Full description of the sample is presented in Table 1.

Survival analysis was performed with 1983 cases, since cases with uncertain behaviour were excluded. Mean time of survival was 6.2 years. Cause-specific survival was 87% one year after diagnosis, 78% at 3 years, 73% at 5 years, and seemed to stabilise 6 years after diagnosis (Table 2). Relative survival was 86% one year after diagnosis, 75% at 3 years and 67% at 5 years. Cause-specific survival rates at 5 years after diagnosis were: 99% for stage 0a, 88% for stage 0is, 86% for stage I, 48% for stage II, 36% for stage III, and 9% for stage IV. Without MI, survival would have been a little overestimated in each stage (Supplemental material). Relative survival rates 5 years after diagnosis were: 90% for stage 0a, 80% for stage 0is, 75% for stage I, 42% for stage II, 24% for stage III and 7% for stage IV.

Survival curves showed differences in bladder cancer survival by sex (p<0.001), age (p<0.001), method of diagnosis (p<0.001), site (p<0.001), histology (p<0.001) (Fig. 1), and stage (p<0.001) (Fig. 2). Comparing each variable by pair of categories, the group of 75 and older had worse survival, while urinary bladder and papillary transitional cell carcinoma presented better survival. Stage 0a had better survival; and no differences were observed between stage 0is and stage I, and between stage II and stage III. Trend analysis shows that age and stage have a significant linear trend (p<0.001).

The maximum likelihood criterion included age, histology and stage in the final Cox model. Therefore, sex, site and time-dependent variables of age and histology were excluded. Table 3 shows the Cox model before and after MI. Both models (original vs. MI model) determined that younger cases, patients with papillary transitional cell carcinoma, and patients diagnosed in stage 0is and stage I, have a better prognosis. The hazard ratio, except for stage IV, was lower for the different categories after MI.

Discussion

Cause-specific bladder and urinary tract survival at 5 years in Mallorca was 73%, and relative survival was 66.7%, similar to the unadjusted European average (66.28%) [20], even though our percentage of non invasive cancers (0a and 0is) was high (38.8%).

Survival by stage in bladder and urinary tract cancer varied greatly according to stage, among both non-invasive and invasive cancers. In non-invasive carcinomas, it is probably related with the grade. As far as we know, this is the first study that shows survival by stage in bladder and urinary tract cancers using the UICC 7th edition instead of the simplified classification (localized, regional and distant), which masks important differences in survival under the category of localized. We have observed a different survival between 0a and 0is, as well as a similar survival between 0is and T1. Between stage I and stage II, survival at 5 years halved. Survival for stage IV was very poor, lower than 10%, as found in other studies [7, 8]. The use of multiple imputation for unstaged cases was important in order to not overestimate the survival by stage, as probably happened in other studies [7]. Relative survival was lower than cause-specific survival, globally and in each stage, as expected according other studies [21, 22].

Apart from stage, age and histology were associated with survival in bladder and urinary tract cancers, but not sex. These cancers are closely related with age. In our study, two of three cases were 65 or more years old, but age was also associated to survival, especially in people older than 74. It is concordant with some studies [4, 7], but not with all of them [8]. Papillary transitional cell carcinoma cases had better survival than solid transitional ones, as expected, but no significant differences were found between solid transitional cell carcinoma cases and microcytic cell cases. The other histology and unspecified category was heterogeneous and showed that the survival of these cases was better than the solid transitional cell cases. All together could add information to the results of a systematic review, which did not find worse prognosis for histological variants [23].

Regarding sex, most studies have found worse survival of bladder cancer in women respect to men, contrary to what happens with other cancers. Differences in stage at the diagnosis, anatomical differences, diagnostic delay, or more accurate diagnosis and treatment in men have been argued to explain such difference in survival [4, 9, 24–26]. Nevertheless, a study has recently observed that women have a less favourable prognosis in bladder cancer only the first two years after diagnosis, particularly in a muscle invasive disease [9]. We found worse survival in women in bivariant analysis, but no differences in survival by sex adjusting by age, histology, and stage. Differences in mortality were found after adjusting also by stage, but by simplified classification. So, we add evidence to the no differences of survival by sex in bladder and urinary tract cancers.

We opted for cause-specific survival instead of relative survival, because the Mallorca Cancer Registry has complete access to the cause of death from the Balearic Islands Mortality Registry, and because since 2008, both registries have improved the quality of the data thanks to the access to electronic clinical records from public hospitals and health centres. We are aware that the cause-specific survival, but also the relative survival, are useful for epidemiologic purposes, but not for the risk communication between clinicians and patients, where the crude mortality, considering competitive risks, is more adequate [27, 28].

Nonetheless, our study is subject to some limitations related to the procedures of the Mallorca Cancer Registry. First, it did not register the grade for non-invasive bladder and urinary tract cancers. Even though there is agreement in that grade is the most important prognostic factor in non invasive bladder cancers [5], there are some discrepancies about which is the optimal classification along with inter observer variability in the pathologist's grade qualification [29]. In any case, without collecting the grade, the Mallorca Cancer Registry identify part of the high-grade non-invasive bladder and urinary tract cancers, all the solid transitional cases, but we miss the papillary transitional high-grade cases.

Secondly, until 2018, the Mallorca Cancer Registry only registered the first bladder and urinary tract cancer even if the first was non invasive and the second was invasive. This has changed and, nowadays, it collects all recurrences.

Finally, 0is may be underreported because some pathologist reports show the diagnosis is transitional papillary carcinoma, but their corresponding complete texts indicate that areas of carcinoma in situ are also viewed. We are aware that, sometimes, we missed this detail.

Conclusion

Bladder and urinary tract cancers survival vary greatly with stage, among both non-invasive and invasive cases. Stage is the main factor associated to survival. Age and histology are also associated to survival, but sex has no association.

Abbreviations

DCO
Cases identified only through death certificate.
EUROCARE-5
Survival of cancer patients in Europe, 5th edition.
HR
Hazar ratio.
ICD-O
International Classification of Diseases for Oncology.
M
The absence or presence of distant metastasis. It's a component of TNM.
MI
Multiple imputation.
MIBC
Muscle-invasive bladder cancer.
NMIBC
Non-muscle invasive bladder cancer.
N
The absence or presence of regional lymph node metastatis. It's a component of TNM.
N_PT
Pathological or clinical N.
REDECAN
Spanish Network of Cancer Registries.
T
The extent of the primary tumour.
TNM
Classification of malignant tumours. International Union Against Cancer.
T_PT
Pathological or clinical T.

Declarations

Ethics approval and consent to participate: This study was approved by the ethics committee of Balearic Islands on the 23rd July 2014. (IB 2363/14).

Consent for Publication: All authors have approved the submitted manuscript.

Availability of data and material: All data of the study are available to other authors.

Competing interests: We declare that we have no competing interests.

Funding: This study was funded by a public grant from the Ministry of Health, Carlos III Institute and the European Union (FEDER) (PI14/01199).

Authors' contributions: Maria Ramos (MR) and Juanjo Montaño (JM) designed the study. Paula Franch (PF) collected the data. Joana Ripoll (JR), JM and Alberto Ameijide (AA) did the analysis. MR, JM, JP and JM discussed the results. MR, JR and JP wrote the first version of the manuscript. MR, JM, JR, JP, AA and PF reviewed the manuscript.

Acknowledgements: We are deeply grateful to Juan Gervasio Rebollo Roca for his English review of the manuscript.

References

1. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015; 136:E359-86.
2. Galceran J, Carulla M, Almela F, Chico M, Marcos AI, Marcos-Gragera R, Sánchez MJ, Perucha J, Franch P, Chirlaque MD, Ardanaz E, Ameijide A; Mateos A, Quirós JR, López de Munain A and Alemán A, on behalf of the Spanish Network of Cancer Registries (REDECAN). Estimates of Cancer Incidence in Spain, 2019. Oral communication presented at: XLIV Annual Meeting of the Groupe pour l'Epidémiologie et l'Enregistrement du Cancer dans les Pays de Langue Latine; 2019, 29-31 May; Lisbon, Portugal.
3. Mortalidad de cáncer en España. Instituto de Salud Carlos III. Available at: http://ariadna.cne.isciii.es/MapaP/ [checked the 08/09/19].
4. Marcos-Gragera R, Mallone S, Kiemeney LA, Vilardell L, Malats N, Allory Y, Sant M, and the EUROCARE-5 Working Group. Urinary tract cancer survival in Europe 1999-2007: Results of the population-based study EUROCARE-5. Eur J Cancer. 2015;51:2217–30.
5. Kamat AM, Hahn NM, Efstathiou JA, Lerner SSP, Malmström PU, Choi W, Guo CC, Lotan Y, Kassouf W. Bladder cancer. Lancet. 2016; 388: 2796-810.
6. Al-Husseini MJ, Kunbaz A, Saad AM, Santos JV, Salahia S, Iqbal M and Alahdab F. Trends in the Incidence and Mortality of Transitional Cell Carcinoma of the Bladder for the Last Four Decades in the USA: A SEER-Based Analysis. BMC Cancer. 2019;19:46.
7. Abdollah F, Gandaglia G, Thuret R, Schmitges J, Tian Z, Jeldres C, Passoni NM, Briganti A, Shariat SF, Perrotte P, Montorsi F, Karakiewicz PI, Sun M. Incidence, survival and mortality rates of stage-specific bladder cancer in United States: A trend analysis. Cancer Epidemiol. 2013; 37: 219–25.
8. Andreassen BK, Aagnes B, Gislefoss R, Andreassen M and Wahlqvist R. Incidence and Survival of urothelial carcinoma of the urinary bladder in Norway 1981-2014. BMC Cancer. 2016; 16:799.
9. Andreassen BK, Grimsrud TK, Haug ES. Bladder cancer survival: Women better off in the long run. Eur J Cancer. 2018; 95: 52-58.
10. Wallerand H, Bernhard J-C, Culine S, Ballanger P, Robert G, Reiter RE, et al. Targeted therapies in non-muscle-invasive bladder cancer according to the signaling pathways. Urol Oncol. 2011; 29:4–11.
11. Pedersen AB, Mikkelsen EM, Cronin-Fenton D, et al. Missing data and mul-tiple imputation in clinical epidemiological research. Clin Epidemiol. 2017; 9:157–66.
12. Eisemann N, Waldmann A, Katalinic A. Imputation of missing values oftumour stage in population-based cancer registration. BMC Med Res Methodol.2011;11:129.26.
13. Fritz A, Percy C, Jack A, et al. International classification of diseases for oncology (ICD-O), 1st rev., 3rd ed. Geneva: World Health Organization; 2013. Available at: https://apps.who.int/iris/bitstream/handle/10665/96612/9789241548496%20eng.pdf;jsessionid=7B2E052FBC84832B13B32AC8B483E069?sequence=1 [checked the 05/07/19].
14. Sobin LH, Gospodarowicz MK, Wittekind C. TNM Classification of malignant tumours. 7 th ed. Oxford: Wiley-Blackwell; 2011.
15. Parrya MG, Sujenthiranb A, Cowlinga TE, Charmanb S, Nossitera J, Aggarwala A, Clarkee NW, Payneg H, Van der Meulena J. Imputation of missing prostate cancer stage in English cancer registry data based on clinical assumptions. Cancer Epidemiol. 2019; 58:44-51.
16. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. Stat Med. 2011; 30:377–99.
17. Rubin DB. Multiple imputation for nonresponse in surveys. New York: John Wiley & Sons; 1987.
18. Ramos M, Montano J, Esteva M, et al. Colorectal cancer survival by stage of cases diagnosed in Mallorca, Spain, between 2006 and 2011 and factors associated with survival. Cancer Epidemiol. 2016; 41:63–70.
19. Ederer F, Heise H. The effect of eliminating de-aths from cancer on general population survival rates, methodological note 11. end results evaluation section. Nacional Cancer Institute; 1959.
20. EUROCARE web. Available at: https://w3.iss.it/site/EU5Results/forms/SA0007.aspx [checked the 23/12/19].
21. Damgaard K, Bray F, Moller B. A comparison of relative and cause-specific survival by cancer site, age and time since diagnosis. Int J Cancer. 2013; 135: 196-203.
22. Makkar N, Ostrom QT, Kruchko C, Barnholtz-Sloan JS. A comparison of relative survival and cause-specific survival methods to measure net survival in cancer populations. Cancer Med. 2018; 7:4773-80.
23. Chen Q, Li L, Wang G, Hu J, Sun T, Fu B. Do histological variants in urothelial carcinoma of the bladder portend poor prognosis? A systematic review and meta-analysis. Oncotarget. 2017; 8: 48263-71.
24. Bilski, K., Zapała, Ł., Skrzypczyk, M. A., Oszczudłowski, M., & Dobruch, J. Review on gender differences in non-muscle invasive bladder cancer. Transl Androl Urol. 2018; 8: 12–20.
25. Dobruch J, Daneshmand S, Fisch M, Lotan Y, Noon AP, Resnick MJ, Shariat SF, Zlotta AR, Boorjian SA. Gender and bladder cancer: A collaborative review of etiology, biology and outcomes. Eur Urol. 2016; 69: 300-10.
26. Wolff I, Brookman-May S, May M. Sex difference in presentation and outcomes of bladder cancer: biological reality of statistical fluke? Curr Opin Urol. 2015; 25: 418-26.

27. Eloranta S, Adolfsson J, Lambert PC, Stattin P, Akre O, Andersson TML, Dickman PW. How can we make cancer survival statistics more useful for patients and clinicians: An illustration using localized prostate cancer in Sweden. Cancer Causes Control. 2013; 24:505-15.
28. Andreassen BK, Myklebust TA, Haug ES. Crude mortality and loss of life expectancy of patients diagnosed with urothelial carcinoma of the urinary bladder in Norway. Scand J Urol. 51(1):38-43.
29. Poletajew S, Biernacki R, Buraczynski P, Chojnacki J, Czarniecki S, Gajewska D, Pohaba T, Sondka J, Skrzypczyk M, Suchojad T, Wojtkowiak D, Zaforemski B, Zapala L, Zemla A, Radziszewski P. Stage of bladder cancer in Central Europe – Polish perspective. Neoplasma. 2016; 63: 642-7.

Tables

Table 1. Sociodemographic and clinical description of bladder and urinary tract cancer cases diagnosed in Mallorca between 2006–2011 (N=2060).

Variable	Categories	N	%	% Valid	After MI
Sex	Women	310	15.0	15.0	
	Men	1750	85.0	85.0	
Age	15–44	47	2.3	2.3	
	45–54	190	9.2	9.2	
	55–64	476	23.1	23.1	
	65–74	616	29.9	29.9	
	75 or +	731	35.3	35.3	
Diagnostic method	Pathological	1983	96.3	96.3	
	Clinical	71	3.4	3.4	
	Unknown	6	0.3	0.3	
Site	Urinary bladder	1926	93.5	93.6	
	Renal pelvis	73	3.5	3.5	
	Overlapping and unspecified urinary organs	26	1.3	1.2	
	Ureter	25	1.2	1.2	
	Urethra	10	0.5	0.5	
Histology	Papillary transitional neoplasia	1148	55.7	55.7	
	Solid transitional neoplasia	777	37.7	37.7	
	Mitrocytic carcinoma	12	0.6	0.6	
	Other histology and unspecified	123	6.0	6.0	
Behaviour	Invasive	1288	62.5	62.5	
	In situ	695	33.7	33.7	
	Uncertain	77	3.7	3.7	
Clinical or pathological tumour size (T_PT)	1	588	28.5	42.4	
	2	226	11.0	16.3	
	3	105	5.1	7.6	
	4a	72	3.5	5.2	
	4b	1	0.0	0.1	
	a (histology 8130 and behaviour in situ)	304	14.8	21.9	
	is (histology 8120 and behaviour in situ)	13	0.6	0.9	
	uncertain behaviour	77	3.7	5.6	
	Missing	674	32.7		
Clinical or pathological regional lymph nodes (N_PN)	0	215	10.4	67.0	
	1	41	2.0	12.8	
	2	59	2.9	18.4	
	3	6	0.3	1.9	
	Missing	1739	84.6		
Metastasis (M)	0	274	13.3	77.0	
	1	82	4.0	23.0	
	Missing	1704	17.3		
Stage	0a	638	31.0	37.0	35.7
	0is	55	2.7	3.2	3.1
	I	584	28.3	33.8	33.3
	II	197	9.6	11.4	11.9
	III	78	3.8	4.5	4.7
	IV	174	8.4	10.1	11.1
	No stage	77	3.7		

	Missing	257	12.5			

Table 2. Cause-specific survival rates of bladder and urinary tract cancer cases diagnosed in Mallorca between 2006–2011 by actuarial method by follow-up year in percentages.

	Original data set n = 1726							Imputed data set n = 1983						
r	Stage 0a	Stage 0is	Stage I	Stage II	Stage III	Stage IV	Total	Stage 0a	Stage 0is	Stage I	Stage II	Stage III	Stage IV	Total
	100	98	96	74	70	41	87	100	98	96	72	67	41	87
	99	98	94	59	50	24	81	99	97	93	57	47	24	81
	99	94	91	55	44	17	78	99	93	89	52	40	16	78
	99	88	88	50	44	11	75	99	88	87	47	40	10	75
	99	88	86	48	36	9	73	98	88	84	44	33	7	73
	98	83	84	46	36	7	72	98	83	83	43	33	6	72
	97	83	84	46	36	7	72	97	83	83	43	33	6	72
	97	83	84	46	36	7	72	97	83	83	43	33	6	72

Table 3. Cox regression model of bladder and urinary tract cancer cases diagnosed in Mallorca between 2006–2011.

	Model 1 Original data set n = 1726				Model 2 Imputed data set n = 1983			
	HR	Std. Err.	p	95% CI	HR	Std. Err.	p	95% CI
ge	1.06	0.00	0.000	1.05; 1.07	1.06	0.00	0.000	1.04; 1.06
stology (ref. solid)								
pillary transitional	0.4	0.08	0.004	0.3; 0.6	0.5	0.1	0.000	0.4; 0.7
icrocytic	0.9	0.33	0.829	0.4; 1.8	0.9	0.3	0.994	0.5; 2.03
her and unspecified	2.06	0.3	0.000	1.4; 2.8	1.9	0.3	0.000	1.4; 2.6
age (ref. stage 0a)								
age 0is	3.1	1.7	0.037	1.1; 9.1	3.3	1.7	0.030	1.1; 9.5
age I	4.8	1.7	0.000	2.4; 9.7	5.5	1.9	0.000	2.7; 10.8
age II	17.9	6.7	0.000	8.6; 37.3	20.4	7.3	0.000	10.1; 41.5
age III	32.2	12.6	0.000	14.9; 69.3	34.3	12.5	0.000	16.6; 70.6
age IV	78.03	28.5	0.000	38.1; 159.9	70.2	23.9	0.000	35.8; 137.5

Note: HR=Hazard ratio

Figures

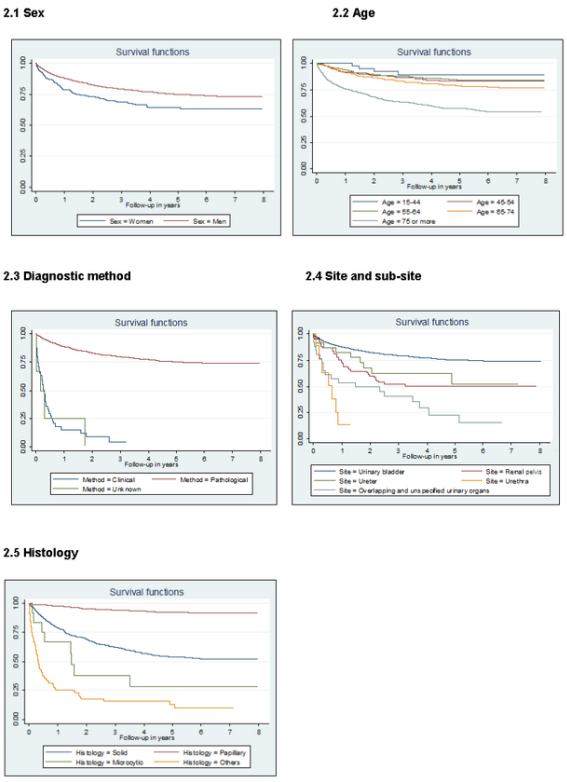

Figure 1

Survival of bladder and urinary tract cancer cases diagnosed in Mallorca between 2006–2011 by sex, age, method of diagnosis, site and histology.

Figure 2. Survival by stage of bladder and urinary tract cancer cases diagnosed in Mallorca between 2006–2011 after multiple imputation.

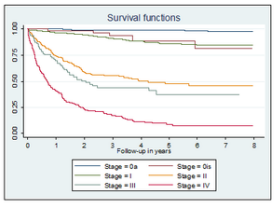

Figure 2

Survival by stage of bladder and urinary tract cancer cases diagnosed in Mallorca between 2006–2011 after multiple imputation.