Survival of patients with urinary bladder cancer in Jordan, 2005–2014

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Abstract

Background: Urinary bladder cancer is the fourth most common cancer in Jordan. No research on survival from bladder cancer at the national level has been conducted before.

Aims: This study aimed to estimate the probability of survival in patients with bladder cancer in Jordan and identify factors associated with survival.

Methods: Data were obtained from the database of the Jordan cancer registry. All cases of urinary bladder cancer in Jordanians registered during 2005–2014 were included in the study (n = 2139). Data collected for each case included: age, sex, date of diagnosis, and stage and grade at diagnosis. Actuarial life table survival analysis was used to determine the overall survival probabilities. Cox proportional hazard regression was used to identify independent factors associated with survival.

Results: The overall 1-, 3-, 5- and 10-year survival probabilities for urinary bladder cancer were 85%, 73%, 69% and 59%, respectively (standard error = 0.01 for each). No significant difference in survival probabilities was found between males and females (P = 0.642). The overall survival probabilities decreased significantly as age at diagnosis increased (P < 0.005). Better survival was observed in patients with early stage and well differentiated tumours at diagnosis.

Conclusions: The survival of patients with bladder cancer in Jordan is comparable to that reported from developed countries. A high percentage of data was missing and the reporting of some variables was inconsistent. To improve the quality of cancer data, regular training is needed for hospital focal points on recording complete data.

Key words: urinary bladder cancer, survival analysis, life tables, Jordan

Introduction

Urinary bladder cancer is a form of cancer primarily arising in the tissues of the urinary bladder. It is the most common malignancy of the urinary system. There are three main types of bladder cancer: transitional cell carcinoma, squamous cell carcinoma and adenocarcinoma (1). Urothelial (transitional cell) carcinoma is the most common histological type of bladder cancer, accounting for almost 90% of all cases. Squamous cell carcinoma accounts for about 4% of cases of bladder cancer, adenocarcinoma for about 2% and all other types for about 4% of cases (2).

According to the global cancer statistics, bladder cancer is the 10th most common cancer in the world, with an estimated 549 393 new cases and 7.2/100 100 population crude death rate in 2018 (3,4). About 60% of all bladder cancer cases and 50% of bladder cancer deaths occur in the less developed regions of the world (5). Greece is reported to have the highest rates of bladder cancer among men with an age standardized rate of 40.4 cases per 100 000, while Lebanon has the highest rate among women with 9.4 cases per 100 000 in 2018 (6). According to the National Cancer Institute in the United States of America (USA), urinary bladder cancer is the

sixth most common cancer in the country, accounting for 4.7% of new cases of cancer and 2.8% of all cancer deaths in 2017 (7). The 5-year, 10-year and 15-year survival rates were 77.3%, 70.0% and 65.0%, respectively (8). Survival rates varies significantly among age groups. The overall 5-year survival decreased significantly from 90.8% in patients younger than 50 years to 81.3% in patients older than 50 years (9). In Sweden, the 5-year relative survival rate for 31 266 patients (74% men, 26% women) with urinary bladder cancer diagnosed from 1997 to 2011 was 72% (10). In the Islamic Republic of Iran, the 1-, 3-, 5- and 10-year relative survival rates for 514 patients from 2001 to 2009 were 89.9%, 71.3%, 57.5%, and 24.6%, respectively. Significant differences in survival rates among age groups and treatment types were also found. Older patients had lower survival rates. Patients who received chemotherapy or radiotherapy alone had lower survival rates than those who received combination therapy (radiotherapy and chemotherapy) (11).

In Jordan, urinary bladder cancer is the fourth most common cancer with 537 new cases reported in 2018, accounting for 4.9% of all cancer cases diagnosed (3). In 2013, the annual report of the Jordan cancer registry shows that 4.1% of cancer deaths were due to bladder

cancer (4). However, no research on survival from urinary bladder cancer at the national level has been conducted before. Our study is the first to assess the survival of patients with urinary bladder cancer in Jordan. The main objectives of this study were to estimate the probability of survival in patients with bladder cancer in Jordan and identify factors associated with survival.

Methods

Study design and population

This was a survival analysis of patients with bladder cancer. All Jordanians with urinary bladder cancer registered in the Jordan cancer registry between 2005 and 2014 were included in this study. The Jordan Cancer Registry has a CanReg format. The registry has focal points in each hospital assigned to obtain all needed data for any case of cancer and report it to the cancer registry. All diagnosed urinary bladder cancer cases are notified and registered in the Jordan cancer registry.

Data collection

The data collected included: personal information (age, sex and national identification number), demographic information (telephone number, address and nationality) and tumour information (stage, grade, date of diagnosis, primary site and histology). All data from this study were obtained from the national cancer registry.

The date of the last contact for all cases was 30 October 2017 which is when our data were obtained from the Jordan cancer registry database. The vital status (whether the case had died or survived) and the date of death were obtained from the civil registration department, which is updated yearly using the national identification number for all cases.

The follow-up period was calculated by subtracting the date of diagnosis from the date of death for the cases that died, and subtracting the date of diagnosis from the 30 October 2017 (the last updated date for vital status in Jordan cancer registry) for those who had survived until the last date of check-up. The end point of the follow-up was death. We assumed that bladder cancer was the cause of death for the cases that died in the study population. However, there might be other underlying causes of death apart from cancer because the cancer registry does not have full access to data on specific cause of death.

Data analysis

We used *SPSS*, version 20 to analyse the data. We used actuarial life table survival analysis to determine overall survival probabilities over time. We also computed separate life tables according to relevant variables such as stage and grade of cancer at diagnosis, and age and sex of the case. We used Cox proportional hazard regression analysis to identify independent factors related to survival. A *P*-value ≤ 0.05 was considered statistically significant. We used RGui, 2.15.1 to plot the overall survival with confidence intervals in Figure 1. We used GraphPad

Prism 5 to plot survival by sex, age, and cancer grade and stage in Figures 2 and 3.

Ethical considerations

Ethical approval was obtained from the Institutional Review Board in Jordan University of Science and Technology (IRB # 6/111/2017), the Jordanian Ministry of Health and the deanship of research committee (research no. 20170382).

This research was based on a secondary analysis of national data from the cancer registry. We neither obtained nor used individual names and identifiers in our analysis. The need for informed consent was therefore waived by the review bodies mentioned above.

Results

Characteristics of the cases

A total of 2139 patients diagnosed with urinary bladder cancer were registered in the Jordan cancer registry during the period 2005–2014. Men accounted for 87.8% of the cases. More than 60% of the patients were older than 60 years at diagnosis in both sexes. For all patients (males and females combined), the median age at diagnosis was 63 years, inter-quartile range (IQR): 52–74. The demographic and clinical characteristics according to sex are shown in Table 1. Most patients (57.7%) had localized tumours. The greatest proportion for both men and women were poorly differentiated tumours, 38.4% and 30.7%, respectively. Of all patients diagnosed between 2005 and 2014, 35.4% had died by the end of 2017.

Overall survival

We included 2083 patients in the survival analysis: 56 patients were excluded because of missing data on follow-up time. The patients were followed to the last date of observation: 30 October 2017 if the patient was alive and the date of death if the patient had died. Follow-up time ranged from a few months to 12.8 years with a median of 5 (IQR: 2.3–8.2) years. The overall 1-, 3-, 5- and 10-year survival probabilities for urinary bladder cancer were 85%, 73%, 69% and 59%, respectively with standard error of 0.01 for each (Table 2 and Figure 1). Just over half (55%) of the patients were alive at the end of the follow-up period.

Survival by sex and age group

The difference in survival probability between males and females was insignificant (*P* = 0.642) (Figure 2A). The overall survival probabilities decreased significantly as the age increased (Figure 2B). Patients younger than 50 years had significantly higher overall survival probabilities compared with the older age groups: the 1-, 3-, 5- and 10-year survival probabilities decreased significantly from 93%, 87%, 85% and 80% for those aged < 50 years to 77%, 61%, 53% and 43%, respectively, for those aged ≥ 70 years (*P* < 0.001).

Survival probability decreased in females with increasing age, but the difference was not statistically

Table 1 **Characteristics of patients diagnosed with urinary bladder cancer between 2005 and 2014, according to sex, Jordan**

Characteristic	Females (*n* = 261)	Males (*n* = 1878)	Total (*n* = 2139)
	No. (%)	No. (%)	No. (%)
Age (years)			
19–49	43 (16.8)	316 (17.0)	359 (16.9)
50–59	39 (15.2)	373 (20.0)	412 (19.5)
60–69	70 (27.3)	558 (30.0)	628 (29.7)
≥ 70	104 (40.6)	615 (33.0)	719 (33.9)
Mean (SD)	64 (24-94)	63 (19-94)	63 (13.2)
Median (IQR)	66 (55-72)	64 (54-72)	65 (54.72)
Marital status			
Single	9 (3.6)	31 (1.7)	40 (2.0)
Married	215 (86.0)	1745 (97.5)	1960 (96.1)
Other	26 (10.4)	14 (0.8)	40 (2.0)
Year of diagnosis			
2005	31 (11.9)	148 (7.9)	179 (8.4)
2006	18 (6.9)	177 (9.4)	195 (9.1)
2007	26 (10.0)	157 (8.4)	183 (8.6)
2008	27 (10.3)	171 (9.1)	198 (9.3)
2009	22 (8.4)	185 (9.9)	207 (9.7)
2010	25 (9.6)	196 (10.4)	221 (10.3)
2011	29 (11.1)	171 (9.1)	200 (9.4)
2012	30 (11.5)	216 (11.5)	246 (11.5)
2013	17 (6.5)	213 (11.3)	230 (10.8)
2014	36 (13.8)	244 (13.0)	280 (13.1)
Status			
Alive	172 (65.9)	1162 (61.9)	1334 (62.4)
Dead	83 (31.8)	675 (35.9)	758 (35.4)
Unknown	6 (2.3)	41 (2.2)	47 (2.2)
Summary stage			
In situ	19 (7.3)	136 (7.2)	155 (7.2)
Localized	148 (56.7)	1086 (57.8)	1234 (57.7)
Regional	21 (8.0)	144 (7.7)	165 (7.7)
Distant metastasis	25 (9.6)	134 (7.1)	159 (7.4)
Unknown	48 (18.4)	378 (20.1)	426 (19.9)
Grade			
Well differentiated	56 (21.5)	418 (22.3)	474 (22.2)
Moderately differentiated	37 (14.2)	209 (11.1)	246 (11.5)
Poorly differentiated	80 (30.7)	722 (38.4)	802 (37.5)
Undifferentiated	3 (1.1)	30 (1.6)	33 (1.5)
Unknown	85 (32.6)	499 (26.6)	584 (27.3)

SD= standard deviation; IQR= interqiuartile range.

significant (Figure 2C). Among males, however, the decrease in survival probability with age was statistically significant (Figure 2D).

Survival by grade and stage of tumour

Figure 3A shows the differences in survival probability between the different tumour grades. Patients with well-differentiated tumours had the highest survival probability compared with patients with other grades. Patients with poorly differentiated tumours had the lowest survival probability even when compared with undifferentiated tumours. The *P*-values shown in figure are derived from the Cox proportional hazard regression for differences in survival probability among different grades.

Table 2 Actuarial life table of cases of urinary bladder cancer diagnosed, Jordan 2005–2014

Interval (year)	No. at beginning of interval	No. withdrawn during interval	Adjusted no. at risk	No. of deaths	Proportion surviving the interval (%)	Cumulative survival proportion (%)	Standard error of cumulative survival
0	2083	8	2079.0	314	85	85	0.01
1	1761	3	1759.5	139	92	78	0.01
2	1619	41	1598.5	98	94	73	0.01
3	1480	171	1394.5	54	96	71	0.01
4	1255	157	1176.5	31	97	69	0.01
5	1067	154	990.0	31	97	67	0.01
6	882	141	811.5	25	97	64	0.01
7	716	131	650.5	22	97	62	0.01
8	563	113	506.5	17	97	60	0.01
9	433	110	378.0	9	98	59	0.01
10	314	115	256.5	4	98	58	0.01
11	195	97	146.5	5	97	56	0.02
12	93	92	47.0	1	98	55	0.02

Figure 3B shows the survival probability for the different stages of cancer at diagnosis. The earlier the stage of cancer at diagnosis, the higher the survival probability. While 97% of patients with in-situ tumours survived the first year after diagnosis, only 56% of patients with distant metastatic tumours survived the first year. The *P*-values shown in figure are derived from Cox proportional hazard regression for differences in survival probability among different stages.

Discussion

The present study is the first in Jordan that aimed to assess the survival probability of bladder cancer in the Jordanian population at the national level. The findings

Figure 1 Overall survival curve with confidence intervals for bladder cancer, Jordan 2018
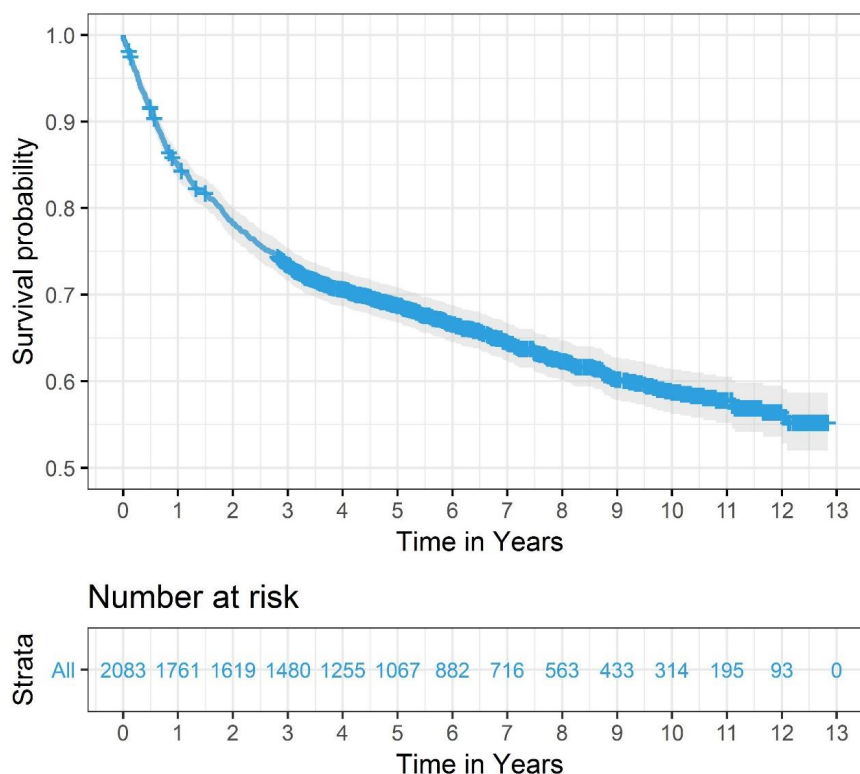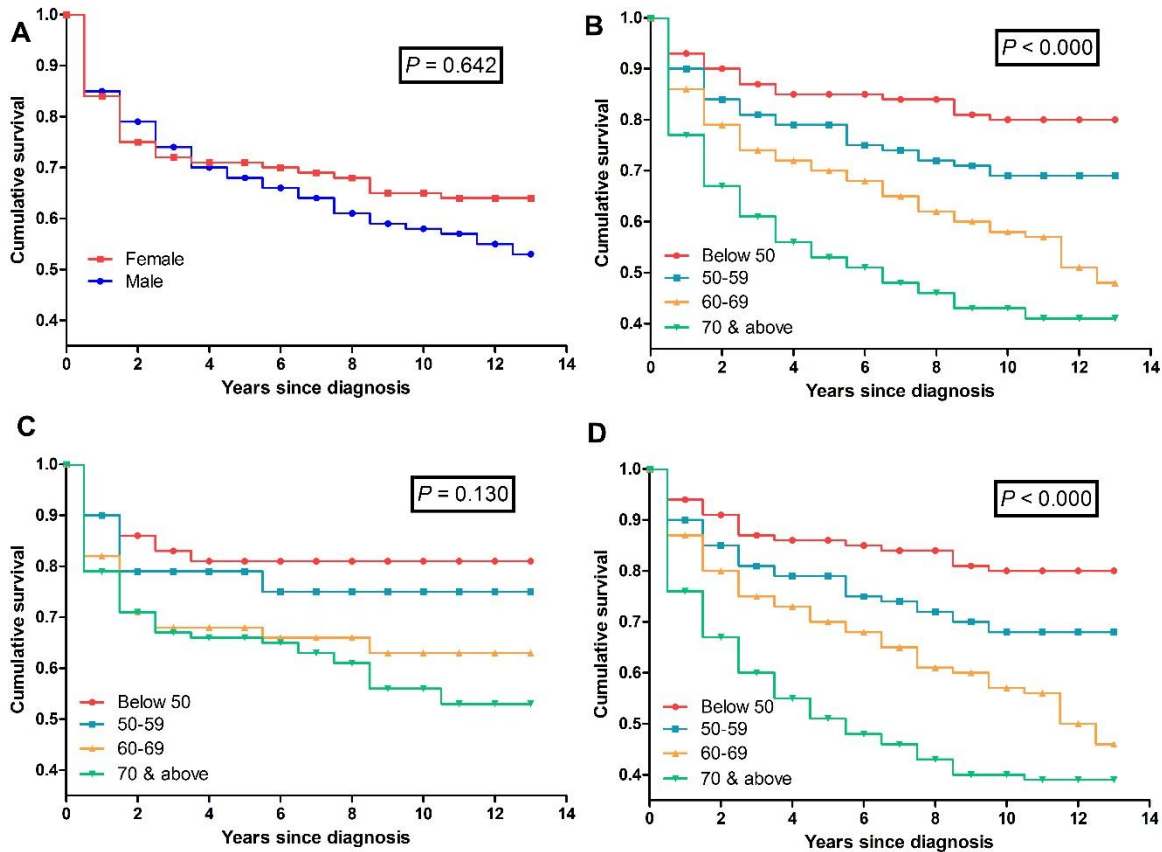
Figure 2 Survival probabilities for patients with urinary bladder cancer diagnosed during 2005-2014, Jordan, 2018, by sex (A), age (B), age in females (C), age in males (D)


can be considered a national record because they are based on a large population and an almost consistent reporting method. All urinary bladder cancer cases in Jordanians registered in the Jordan cancer registry during 2005–2010 were included in the study. We also aimed to identify groups of the population at higher risk of lower survival.

In the USA, the 5-year survival for urinary bladder cancer was 76.8% for patients diagnosed in the period 2008–2014 (7). According to the International Agency for Research on Cancer, the 5-year survival for urinary

bladder cancer exceeded 70% in China, Singapore and the Republic of Korea compared with less than 50% survival in other countries in Asia (12). In a survival analysis study in the Islamic Republic of Iran, the 5-year survival rate was 57.5% in 514 patients who were diagnosed with urinary bladder cancer between 2001 and 2009 (11). Our study showed that the overall 5-year survival rate for patients with urinary bladder cancer in Jordan was 69%. This comparison shows that patients with urinary bladder cancer in Jordan have relatively high survival compared with other countries in Asia and comparable

Figure 3 Survival probabilities for patients with urinary bladder cancer diagnosed during 2005-2014, Jordan, 2018, by summary grade (A) and stage (B)
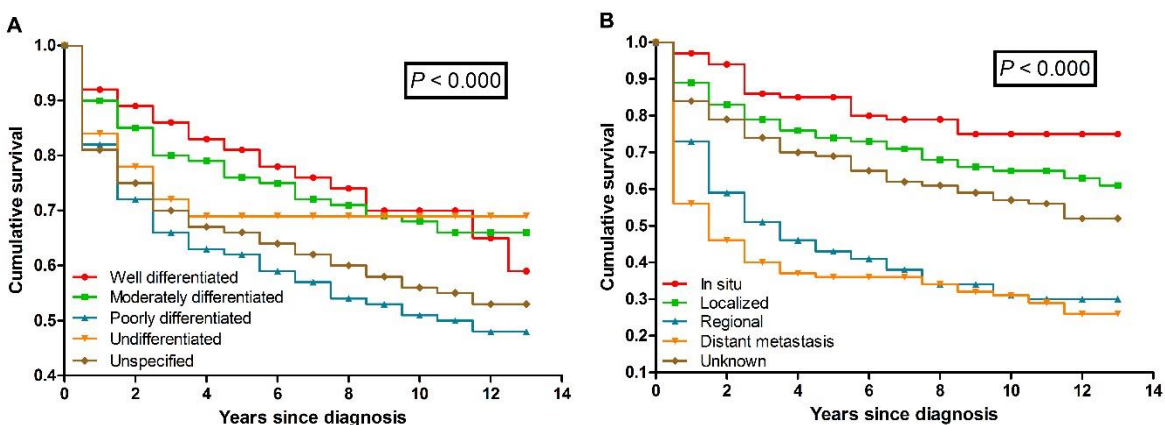
survival to that reported in the developed countries. The better survival in Jordan might be explained by the more advanced cancer care in Jordan compared with some neighbouring countries (13). However, the cancer grade of 27.3% of the patients in our study was unknown. If the unknown cases were better classified, it might result in a higher percentage with favourable grade and stage and hence better survival rates among our patients. Better pathological classification might shed a light on the unknown grades.

Bladder cancer was more common in males than females. According to the American Society of Clinical Oncology, men were four times more likely than women to be diagnosed with bladder cancer (14). This cancer is the fourth most common cancer in men in the USA and the eighth in the United Kingdom of Great Britain and Northern Ireland (15,16). In 2014, bladder cancer in Jordan ranked third of the top 10 cancers in men (4). Our study supports this ranking as most (87.8%) bladder cancer patients were men. Several studies have investigated differences in survival of bladder cancer by sex (17,18). In Norway, a study that included 15 129 patients diagnosed with bladder cancer between 1997 and 2011 found that men had a better prognosis than women. The 2-, 5- and 10-year relative survival rates were, respectively, 84.0%, 75.1%, and 66.3% for men and 79.6%, 71.7%, and 64.5% for women (17). A population-based cohort study that included 36 344 patients with urinary bladder cancer diagnosed between 1997 and 2014 found that women had slightly higher mortality than men. This higher mortality in women was limited to those diagnosed with muscle-invasive tumours (18). In another population-based study in Canada, the 5-year cancer-specific survival and overall survival of the full cohort of 5259 patients did not differ between women and men (19). However, our study did not find any significant difference in survival between males and females. The 5-year survival rates were 68% and 71% in males and females, respectively. This lack of difference in survival might be due to the similarity in tumour properties such as stage and grade between males and females.

Survival rates for bladder cancer are generally higher in younger patients and decrease with increasing age. Therefore, age is widely accepted as a strong and independent risk factor for developing bladder cancer. In the USA, the overall 5-year survival decreased significantly from 90.8% in patients younger than 50 years to 81.3% in patients older 50 years (9). In England, the 5-year net survival for men with bladder cancer ranged from 73% in patients younger than 50 years to 43% in patients older than 80 years during 2009–2013 (16). As expected, our study showed the same pattern as the overall survival decreased significantly as the age of the patients increased. The overall 5-year survival dropped from 85% in patients younger than 50 years to 53% in patients older than 70 years. Even after categorizing our study population into only two age groups (younger and older than 50 years), survival differed significantly between the two groups.

Different clinical and pathological prognostic factors have been proposed for survival of bladder cancer, including tumour stage, differentiation of tumour, and surgical and distant metastasis. A high proportion (80%) of bladder cancer cases in Jordan have a known stage recorded at diagnosis. Most patients (57.7%) in our study were diagnosed at stage I (localized tumour) and only 7% were diagnosed with distant metastatic tumours. In the USA about half of bladder cancer patients are diagnosed at stage I (15). Poorly differentiated tumours were the most common grade among our patients representing 37.5% of the cases. Our analysis showed that grade and stage were significant predictors of survival of bladder cancer. The probability of dying was significantly higher for those with poorly differentiated tumours compared with those with well differentiated tumours. Survival probability was much higher for patients diagnosed at early cancer stages, such as in-situ and localized tumours compared with those with regional and metastatic tumours. The 5-year survival probability dropped from 85% for the in-situ tumours to 36% for metastatic tumours. Previous studies have shown that bladder cancer survival is highly dependent on stage at diagnosis. The 5-year survival probability varied from 92.4% for localized stage cancers to 25.4% for distant metastatic cancer (9). Highly and moderately differentiated tumours had a survival probability of 93.5%, while poorly differentiated tumours had a survival probability of 65.8% (9).

Our study has some limitations. We only analysed data available at the Jordan cancer registry. This database lacks information about some risk factors (e.g. dietary factors and occupational exposure to carcinogens). Therefore, we were unable to investigate the effect of these factors. In addition, a high percentage of data was missing, and the reporting of some variables was inconsistent, such as bladder cancer type, smoking status and treatment, so it was not possible to examine the effect of those variables on the survival probability of our patients. In performing our analysis, we assumed that bladder cancer was the cause of death. However, there might be another underlying cause of death since the cancer registry does not have access to data on the specific cause of death. Therefore, our survival probability might be under-estimated as deaths from other causes were included in the analysis.

Regular training for focal points at the hospitals about complete documentation and reporting is needed to improve the quality of cancer data. More attention should be paid to cancer survival, since cancer is the second most common cause of death in Jordan. For instance, a new systematic method is needed to improve patient follow-up. An annually updated database on the incidence, prevalence, mortality and survival of all cancers in Jordan needs to be developed. This database can be a trusted source of information to assess cancer treatment programmes and monitor progress of our national cancer control programme.

Survie des patients atteints de cancer de la vessie, Jordanie, 2005-2014

Résumé

Contexte : Le cancer de la vessie est le quatrième cancer le plus fréquent en Jordanie. Aucune recherche sur la survie au cancer de la vessie au niveau national n'a été menée auparavant.

Objectifs : La présente étude visait à estimer la probabilité de survie des patients atteints de cancer de la vessie en Jordanie et à identifier les facteurs associés à la survie.

Méthodes : Les données ont été obtenues à partir de la base de données du registre jordanien du cancer. Tous les cas de cancer de la vessie enregistrés en Jordanie entre 2005 et 2014 ont été inclus dans l'étude (*n* = 2139). Les données collectées pour chaque cas incluaient l'âge, le sexe, la date du diagnostic, le stade et le degré du diagnostic. On a recouru à une analyse actuarielle de la survie avec des tables de survie pour déterminer les probabilités de survie globale. La régression de Cox à risques proportionnels a été utilisée pour identifier des facteurs indépendants associés à la survie.

Résultats : Les probabilités globales de survie à 1, 3, 5 et 10 ans pour le cancer de la vessie étaient respectivement de 85 %, 73 %, 69 % et 59 % (erreur type = 0,01 respectivement). Aucune différence significative dans les probabilités de survie n'a été observée entre les hommes et les femmes (*p* = 0,642). Les probabilités de survie globale diminuaient significativement avec l'augmentation de l'âge au moment du diagnostic (*p* < 0,005). Une meilleure survie a été observée chez les patients présentant un stade précoce et des tumeurs bien différenciées au moment du diagnostic.

Conclusions : La survie des patients atteints de cancer de la vessie en Jordanie est comparable à celle rapportée dans les pays à revenu élevé. Il manquait un pourcentage élevé de données et la notification de certaines variables était incohérente. Pour améliorer la qualité des données sur le cancer, les points focaux hospitaliers doivent recevoir une formation régulière sur l'enregistrement des données complètes.

نجاة المرضى المصابين بسرطان المثانة البولية، الأردن، 2005–2014

نور عبده، مجد السخني، أنور بطيحة، كمال عرقوب

الخلاصة

الخلفية: يأتي سرطان المثانة البولية في المرتبة الرابعة بين أكثر أنواع السرطان شيوعًا في الأردن. ولم تُجرَ أي بحوث من قبل حول النجاة من سرطان المثانة على المستوى الوطني.

الأهداف: هدفت هذه الدراسة إلى تقدير احتمالية النجاة لدى المرضى المصابين بسرطان المثانة في الأردن، وتحديد العوامل المرتبطة بالنجاة.

طرق البحث: تم الحصول على البيانات من قاعدة بيانات السجل السرطاني الأردني. وأُدرجت جميع حالات سرطان المثانة البولية لدى الأردنيين المسجلين خلال الفترة 2005–2014 في الدراسة (العدد = 2139). وتضمنت البيانات المُجمَّعة لكل حالة: العمر والجنس وتاريخ التشخيص والمرحلة والتصنيف عند التشخيص. واستُخدم التحليل الإكتواري لجدول مجريات الحياة في تحديد احتمالات النجاة بوجه عام. واستُخدم انحدار كوكس للمخاطر التناسبية في تحديد العوامل المُستقلة المرتبطة بالنجاة.

النتائج: بلغت احتمالات النجاة الإجمالية من سرطان المثانة البولية بعد سنة واحدة و3 سنوات و5 سنوات و10 سنوات 85٪ و73٪ و69٪ و59٪ على التوالي (الخطأ المعياري = 0.01 لكل احتمالية). ولم يُوجد أي فرق جوهري في احتمالات النجاة بين الذكور والإناث (p=0.642). وانخفضت احتمالات النجاة الإجمالية انخفاضًا كبيرًا مع زيادة العمر عند التشخيص (0.005> p). ولُوحِظَ تحسنٌ في احتمالات النجاة بين المرضى في المرحلة المبكرة من المرض والمصابين بأورام متمايزة تمايزًا جيدًا عند التشخيص.

الاستنتاجات: تضاهي احتمالات نجاة المرضى المصابين بسرطان المثانة في الأردن تلك المُبلَّغ عنها في البلدان المتقدمة. وكانت نسبة كبيرة من البيانات مفقودة، وكان الإبلاغ عن بعض المتغيرات غير متسق. ولتحسين جودة بيانات السرطان، يلزم تدريب مسؤولي التنسيق في المستشفيات بانتظام على تسجيل البيانات كاملة.

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