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One, 5 and 10 Year Net Survival Rates for Male and Female Bladder Cancer Patients; Why are they so Different?

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Abstract

The most common symptom of bladder cancer is blood in the urine (haematuria), which is usually painless. Haematuria can be frank (macroscopic), visible to the patient, or invisible (microscopic), which is normally detected during a routine urine dipstick test. Haematuria in its visible and invisible forms can represent a disease process within the urinary tract. These diseases can range from benign causes to malignant causes such as bladder cancer. Indeed, it is common for no obvious cause to be identified after detailed investigations. These investigations include cystoscopy, cytology and radiological imaging of the upper urinary tract. In many cases, there are significant delays in diagnosing bladder cancer in women as many women ignore the most basic symptom, haematuria which they often associate with menstruation or menopause. Furthermore, even after the problem has been reported to their GP, haematuria can still be misdiagnosed as cystitis or a urinary tract infection. Women are less likely than men to undergo a complete and timely evaluation for haematuria. As such, there can be a significant delay in a bladder cancer diagnosis. Late diagnosis and developing rare forms of the disease are among the possible factors which may explain the disparity between male and female bladder cancer survival rates.

Keywords: Bladder cancer; Cystoscopy; Cytology; Occupational exposure; Haematuria; Gender; Smoking; Survival rate

Abbreviations: NMI: Non-muscle invasive; MI: Muscle invasive; OE: Occupational exposure; TUR: Transurethral resection

Introduction

In 2012, 5242 people in the UK lost their lives to bladder cancer [1]. That's more than the number of deaths caused by road accidents (1754 deaths) [2], kidney cancer (4300 deaths) [3], ovarian cancer (4271 deaths) [4], liver cancer (4514 deaths) [5] or brain cancers (5187 deaths) [6] in the same year. So it is somewhat surprising that bladder cancer receives less than 1.0% of the total budget that is allocated for cancer research in the UK. The story is no different in the US where research funding for bladder cancer has been in decline at a rate disproportionate to the increased cost of bladder cancer care [7]. In 2013, NCI funding for bladder cancer was $20.3 million out of a $4.79 billion budget (0.4%) [8]. As a consequence, bladder cancer management has not significantly advanced over the last 20 years and patient outcomes remain unchanged with 5-year survival rates lower than 15% in patients presenting with late-stage disease [9]. Surprisingly, even though bladder cancer disease remains one of the most expensive urothelial cancers for our health service to treat due to the frequent recurrence rates and intensive surveillance strategies (cystoscopy, cytology, and radiologic imaging), management of bladder cancer and novel therapies to treat this disease remain stagnant.

Bladder cancers are more common in older adults, with the median age at diagnosis being 68 years. Rates of bladder cancer are three times higher in men than in women [10]. However, this gender gap is decreasing year on year [11]. One of the possible reasons for an increase in female bladder cancers are that women are now employed in occupations that historically would have been male dominated e.g., bus drivers, taxi drivers, airline pilots, construction workers, painters and decorators, electricians, plumbers, and mechanical engineers.

Bladder cancers are classified as non-muscle invasive (NMI), muscle invasive (MI), or metastatic, with NMI accounting for the majority of cancers on presentation. Non-muscle invasive bladder cancer (NMIBC) is potentially curable with tumour resection (TURB; transurethral resection of the bladder). However, the rate of recurrence for NMIBC is high and 10 to 25% of these patients will go on to develop life threatening MIBC.

A strong relationship exists between smoking habits (past and present) and bladder cancer, with current smokers at least three times more likely to develop the disease [10]. Furthermore, it is estimated that half of all cases of bladder cancer are caused by smoking and the risk increases with the number of pack-years of cigarette smoking [12].

Occupational exposure (OE) to hazardous chemicals previously used in manufacturing are also a known cause of bladder cancer [13]. This is attributable to both the latency periods that can often exceed 20 years, and the significant range of chemical agents associated with an increased risk of bladder cancer [14,15].

Women are at greatest risk of dying from bladder cancer as it is easy to dismiss the signs and symptoms of the disease as a simple urinary tract infection and treat with antibiotics. This process can normally be repeated over several visits until more serious symptoms develop. As such, women are more likely to be diagnosed with advanced disease. Furthermore, one in four of these women are also more than likely to have developed a rare type of bladder cancer making treatment options limited. Frontline physicians should be aware that haematuria is a significant problem in our aging population and a detailed investigation should be carried out, regardless of patient sex.

The highest incidence and mortality rates for bladder cancer are found in the north of England [11]. However, mortality from bladder cancer is below average in the south and midlands of England [11]. The rates of bladder cancer are higher in males (approximately 3:1 male:

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female ratio; Cancer Research UK, 2011). However, the 1, 5 and 10 year net survival rates (Cancer Research UK, 2011) are considerably better for males than females.

Patients and Methods

Incidence and mortality data was supplied by Cancer Research UK. Age standardised bladder cancer incidence rates per 100,000 populations, by sex for Great Britain; 1-, 5- and 10-year net survival data, adults aged 15-99, England and Wales and bladder cancer average number of deaths per year and age-specific mortality rates per 100,000 population was also supplied by Cancer Research UK. Cancer survival estimates were provided by the Cancer Research UK Cancer Survival Group at the London School of Hygiene and Tropical Medicine http://www.ishtm.ac.uk/eph/ncde/cancersurvival/

Results

Bladder cancer, European age-standardised incidence rates per 100,000 population, United Kingdom 1993 to 2011 (Figure 1).

The age-standardised bladder cancer incidence rates for both males and females have fallen significantly since 1993. Bladder cancer incidence rates are down 43% (31.2 to 17.7) in males and 39% (8.9 to 5.5) in females. However, the decrease in bladder cancer incidence rates for both males and females has been modest since 2002. Bladder cancer incidence rates in both males and females have decreased 16.1% (21.1 to 17.7) and 10% (6.0 to 5.4), respectively from 2002 to 2011. The most significant change in bladder cancer incidence rates are observed from 1993 to 2002; were a rate change of 32.4% (31.2 to 21.1) for males and 32.6% (8.9 to 6.0) for females was observed.

Bladder cancer average number of deaths per year and age-specific mortality rates per 100,000 populations, United Kingdom (2010 to 2012) (Table 1).

The average number of yearly deaths from bladder cancer (2010 to 2012) for both males and females were 5077; males 3405 (67.1%) and females 1672 (32.9%) (For all ages, specific mortality rates were 11.0 (males), and 5.2 (females) per 100,000 population. Bladder cancer death rates were 2-fold higher in females < 44 years of age. However, for females > 45 years of age, death rates from bladder cancer reduced significantly, with respect to male bladder cancer death rates.

One-, Five- and ten-year net survival rates for England and Wales (patients diagnosed 2010 to 2011) (Figure 2).

Female and male net survival rates for England and Wales (patients diagnosed in 2010 to 2011) are shown in Figure 2. Female net survival rates were lower than males by 19.6% (61.6% v's 76.6%), 19.9% (45.6% v's 56.9%) and 27.3% (39.5% v's 54.3%) at 1, 5 and 10 years, respectively.

Five- and ten-year survival was predicted for patients diagnosed in 2010 to 2011 (using an excess hazard statistical model) 95% LCL and 95% UCL are the 95% lower and upper confidence limits.

Discussion

The number of patients now presenting with haematuria is progressively increasing in our aging population. Unfortunately, the diagnoses of serious diseases like bladder cancer in some of these patients are still delayed when triage is ineffective.

Over 10,000 cases of bladder cancer were diagnosed in 2011 making bladder cancer the seventh (3.1%) most common malignancy reported in the UK. The most common causes of bladder cancer are carcinogenic substances in urine and an important source of these chemicals is cigarette smoke [10]. However, 20% of all bladder cancers are caused by exposure to chemicals in the workplace [16]. Occupations that are associated with an increased risk of bladder cancer include foundry workers [17], working with textiles and dyestuffs [18], chemical and plastic industries [19], tyre and rubber manufacture [20], metalwork [21], hairdressing [22], painters [23], auto and truck mechanics [24].

The rates of bladder cancer are decreasing in our general population. Most notable is that this trend is greater in males were smoking habits have been falling faster than that observed in women [25].

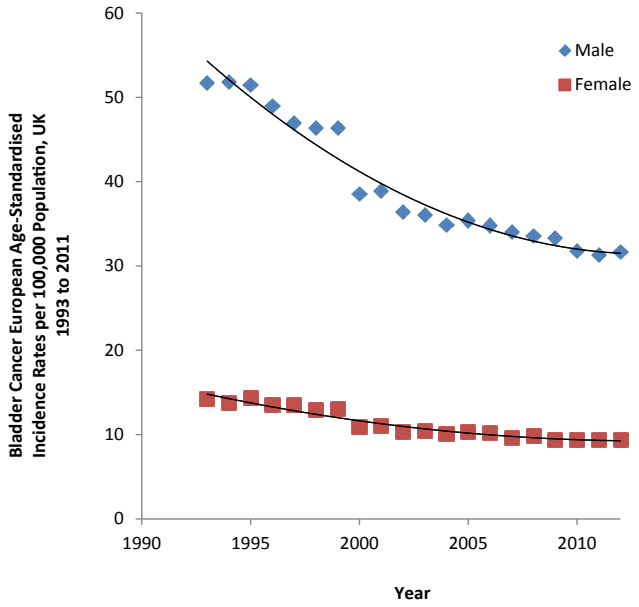

Figure 1: Bladder cancer, European age-standardised incidence rates per 100,000 population, United Kingdom 1993 to 2011 (Cancer Research UK).

Age Range	Male Deaths	Female Deaths	Male Rates	Female Rates
00 to 04	0	0	0.0	0.0
05 to 09	0	0	0.0	0.0
10 to 14	0	0	0.0	0.0
15 to 19	0	0	0.0	0.0
20 to 24	0	0	0.0	0.0
25 to 29	0	1	0.0	0.0
30 to 34	2	2	0.1	0.1
35 to 39	2	5	0.1	0.2
40 to 44	7	13	0.3	0.5
45 to 49	24	17	1.0	0.7
50 to 54	45	25	2.2	1.2
55 to 59	98	44	5.5	2.4
60 to 64	196	71	10.7	3.8
65 to 69	323	120	21.3	7.5
70 to 74	430	177	36.9	13.6
75 to 79	602	232	66.0	20.9
80 to 84	710	335	114.5	37.8
85+	965	629	210.8	66.3
All Ages	3405	1672	11.0	5.2

Table 1: Bladder cancer average number of deaths per year and age-specific mortality rates per 100,000 population, United Kingdom (Bladder Cancer (C67): 2010 to 2012) (Cancer Research UK).

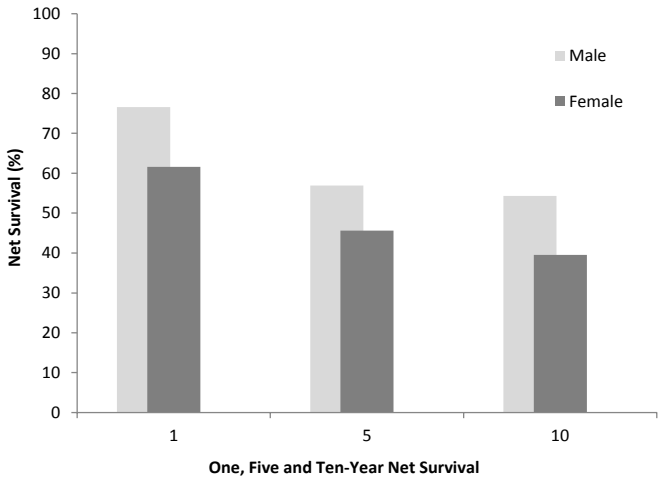

Figure 2: One-, five- and ten-year net survival (%), adults aged 15-99, England and Wales (for patients diagnosed with bladder cancer in 2010 to 2011) (Cancer Research UK).

Bladder cancer death rates reported by Cancer Research UK for 2010 to 2012 were higher in females < 44 years of age with respect to male bladder cancer patients of the same age. This is a very worrying trend. Unfortunately there is no single reason why this should be the case. However, it would suggest that female patients with haematuria who are younger than <44 years of age are not getting the proper screening for bladder cancer that men do [26,27]. This observation is also borne out by the 1, 5 and 10 year survival rates. Female bladder cancer patients in England and Wales had almost 20% lower survival rates at 1 and 5 years, and almost 30% lower survival rates at 10 years, with respect to males. As such, this would suggest that female patients are presenting with more advanced bladder cancer disease than males. Furthermore, 1 in 4 women present with a rare form of the disease making them more likely to have a cystectomy or radical radiotherapy treatments. As such, females that present with haematuria in the 35 to 44 age groups should be considered 'high risk' if they also smoke and have a history of occupational exposure to chemicals.

Currently, there is no reliable evidence to show that population screening reduces mortality rates from any form of urological cancer [28]. Furthermore, the data that is available is somewhat limited. However, the clinical and economic impact of delayed detection of life threatening bladder cancer in women needs to be addressed. Women who present with haematuria (microscopic or macroscopic) need to be given the same diagnostic consideration that is currently being offered to men. A multivariate analyses controlling for sex and race found that 39% of men with haematuria were referred to an urologist by their GP, compared with 17% of women with haematuria. Furthermore, men were more likely than women to have a complete evaluation (22% vs 12%) and less likely to have an incomplete evaluation (55% vs 69%) for haematuria [29].

It is unsafe to assume that microscopic haematuria in women may be of lesser relevance than in men [30]. Furthermore, the costs and considerations of caring for this disease [31], present and future burden [32], will require new and innovative approaches [33], and potentially, a reworking of the haematuria clinic [34].

Limitations

The study is limited to the information that was supplied by Cancer Research UK.

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