ACTA ONCOLOGICA, 2016
VOL. 55, NO. S1, 85–90
http://dx.doi.org/10.3109/0284186X.2015.1115122

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RESEARCH ARTICLE

Trends in cancer of the urinary bladder and urinary tract in elderly in Denmark, 2008–2012

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ABSTRACT

Background The aim of this study was to examine the trends in incidence, mortality, survival, and prevalence of cancers of the urinary bladder and urinary tract in Denmark from 1980 to 2012 with particular focus on elderly patients over age 70 years.

Design Cancer of the urinary bladder and urinary tract was defined as ICD-10 codes C67.9, D09.0, D41.4. Data were derived from the NORDCAN database with comparable data on cancer incidence, mortality, prevalence and relative survival in the Nordic countries, where the Danish data were delivered from the Danish Cancer Registry and the Danish Cause of Death Registry.

Results The average annual number of bladder cancers increased from 1478 to 1810 (22%) from 1980 to 2012, with close to 60% occurring in the elderly population. The incidence rates were 7–10 times higher in persons aged 70 years or more compared with younger persons. Mortality rates were decreasing with time in all age groups but 90+-year-old men. The one- and five-year relative survival improved significantly with time for all age groups both in men and women. The prevalence increased two times from 6014 in 1980 to 12 359 in 2012 among men and from 1974 to 4454 among women. There was a relatively higher proportional increase in prevalence among elderly men compared to younger patients.

Conclusion More prospective data are needed, preferably as randomized clinical trials, for determining the influence of age on the decisions of the surgical approach as well as chemo/radiotherapy for the elderly patients with urothelial cancers compared to younger patients.

ARTICLE HISTORY
Received 23 June 2015
Accepted 1 October 2015
Published online
21 December 2015

Bladder cancer (BC) is considered to be a disease of the elderly that occurs most commonly beyond the 70th year of life and is the sixth most common cancer in the US [1]. BC is a highly deadly disease if untreated having a five-year mortality approaching 90% after diagnosis [2,3]. In the US, it is expected that there will be 76 000 new cases and 16 000 deaths in 2015 of BC [4]. Of the roughly 16 000 annual deaths, over 10 000 are in men and fewer than 5000 are in women. Smoking is a well known risk factor accounting for about 50–65% of BC among men and 20–30% among women [5] while occupational exposures have been estimated to be responsible for 5–25% of BC among men and 8–11% among women, yet the exposures responsible for much of occupational BC remain unknown. The reasons for this disparity between the genders are not well understood [6–8].

The population in the US is aging, with the number of elderly in the US expected to double by 2030 (compared to 2000) and exceed 72 million [9]. It is estimated that annual net increase in the US population over 65 years of age between the year 2010 and 2011 is over 900 000 persons and similar aging is expected in the Danish population.

Radical cystectomy for BC is a complex operation known to have the potential for significant morbidity and mortality. This is particularly true for the elderly, and thus treatment decisions for elderly patients with BC constitute an important and difficult clinical challenge. As the population ages the incidence of BC in the elderly will also rise and there for it will become increasingly important to understand who among the elderly with BC are either "fit or frail" with respect to undergoing potentially morbid, but curative, therapy, such as radical cystectomy or bladder preservation therapy with chemo-radiation [10–12].

The purpose of study is to elucidate incidence, mortality, relative survival (RS) and prevalence for elderly patients aged more than 70 years compared with younger patients with BC in Denmark.

Material and methods

Cancer of the urinary bladder and urinary tract was defined as ICD-10 codes C64.9, D09.0, D41.4. A more detailed description of the materials and methods appear elsewhere [13]. In brief,

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Table I. Average annual number of new bladder cancers in Denmark, 1980–2012.

	0–69 years				70–74 years				75–79 years				80–84 years				85–89 years				90 + years				All ages			
	Cases male (incidence)		Cases female (incidence)		Cases male (incidence)		Cases female (incidence)		Cases male (incidence)		Cases female (incidence)		Cases male (incidence)		Cases female (incidence)		Cases male (incidence)		Cases female (incidence)		Cases male (incidence)		Cases female (incidence)		Cases male (incidence)		Cases female (incidence)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
1980	581	53.1	177	46.2	203	18.5	69	18.0	155	14.2	61	15.9	98	8.9	46	11.9	46	4.2	24	6.2	12	1.1	7	1.8	1095	100	383	100
1990	622	48.1	214	44.7	240	18.6	80	16.7	219	16.9	76	15.9	136	10.5	62	13.0	57	4.4	34	7.1	21	1.6	13	2.8	1293	100	479	100
2000	575	43.6	213	43.0	243	18.4	82	16.6	238	18.0	78	15.6	161	12.2	67	13.5	81	6.2	39	7.9	22	1.7	17	3.4	1319	100	496	100
2005	591	43.8	206	42.0	249	18.4	85	17.3	236	17.5	84	17.0	166	12.3	68	13.8	79	5.9	34	7.0	28	2.1	14	2.8	1349	100	491	100
2010	584	43.4	223	43.9	225	16.7	86	16.9	244	18.1	86	16.9	170	12.6	61	12.0	92	6.8	40	7.9	30	2.2	12	2.4	1345	100	508	100
2011	658	45.6	204	39.3	244	16.9	82	15.8	243	16.8	108	20.8	176	12.2	72	13.9	87	6.0	37	7.1	35	2.4	16	3.1	1443	100	519	100
2012	570	42.9	198	41.1	244	18.4	72	14.9	235	17.7	89	18.5	163	12.3	62	12.9	87	6.6	37	7.7	29	2.2	24	5.0	1328	100	482	100

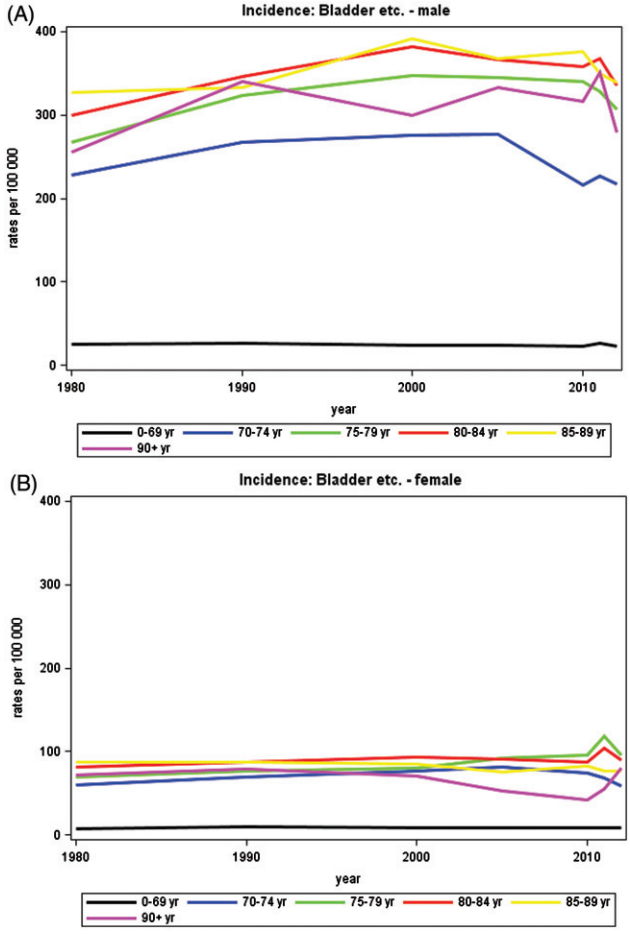

Figure 1. Incidence rates of bladder cancer in Denmark, 1980–2012, by age group. A. Males, B. Females.

data were derived from the NORDCAN database with comparable data on cancer incidence, mortality, prevalence and RS in the Nordic countries, where the Danish data are delivered from the Danish Cancer Registry and the Danish Cause of Death Registry with follow-up for death or emigration until the end of 2013. This study focuses on the elderly population with age categorized as 0–69, 70–79, 80–89 and 90 + years.

For incidence and mortality, age group-specific numbers and rates per 100 000 person years are shown in tables and graphs with calendar periods for time of diagnosis 1978–1982, 1988–1992, 1998–2002, 2003–2007, 2010, 2011 and 2012. Prevalence is defined as the number of cancer patients (including cured patients as well) with that specific diagnosis still alive and is shown in tables by the end of 1980, 1990, 2000, 2005, 2010, 2011 and 2012.

Sex- and age-specific one- and five-year RS proportion ratios were calculated for each of the diagnostic groups for the age groups 0–69, 70–79, 80–89 and 90 + years and for the five-year periods of diagnosis 1968–1972, 1973–1977, . . ., 2003–2007 and 2008–2012.

RS for a group of cancer patients is calculated as the observed survival (where all causes of death are considered events) divided by the expected survival for a group from the Danish population with the same age and year of birth composition. Actuarial method is used for observed survival

Table II. Average annual number of deaths from bladder cancer in Denmark, 1980–2012.

	0–69 years				70–74 years				75–79 years				80–84 years				85–89 years				90 + years				All ages			
	Cases male (mortality)		Cases female (mortality)		Cases male (mortality)		Cases female (mortality)		Cases male (mortality)		Cases female (mortality)		Cases male (mortality)		Cases female (mortality)		Cases male (mortality)		Cases female (mortality)		Cases male (mortality)		Cases female (mortality)		Cases male (mortality)		Cases female (mortality)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
1980	159	38.0	54	32.3	78	18.6	29	17.0	80	19.2	32	18.8	61	14.6	28	16.7	33	7.9	18	10.8	7	1.8	7	4.4	419	100	168	100
1990	142	30.9	53	29.0	87	18.9	27	15.1	93	20.3	35	19.1	81	17.6	35	19.3	41	9.0	20	11.0	15	3.3	12	6.5	460	100	182	100
2000	115	26.6	51	25.4	71	16.3	27	13.3	94	21.7	41	20.6	81	18.7	34	16.8	52	12.0	31	15.4	20	4.6	17	8.6	433	100	200	100
2005	100	25.0	45	23.2	64	16.0	28	14.6	88	21.9	37	19.0	77	19.1	39	19.9	51	12.7	28	14.5	21	5.3	17	8.8	401	100	194	100
2010	120	28.8	50	25.9	64	15.4	38	19.7	79	19.0	38	19.7	69	16.6	33	17.1	61	14.7	21	10.9	23	5.5	13	6.7	416	100	193	100
2011	95	24.0	36	20.1	64	16.2	24	13.4	86	21.7	33	18.4	68	17.2	38	21.2	53	13.4	29	16.2	30	7.6	19	10.6	396	100	179	100
2012	102	26.1	42	21.0	60	15.3	29	14.5	72	18.4	43	21.5	69	17.6	42	21.0	49	12.5	24	12.0	39	10.0	20	10.0	391	100	200	100

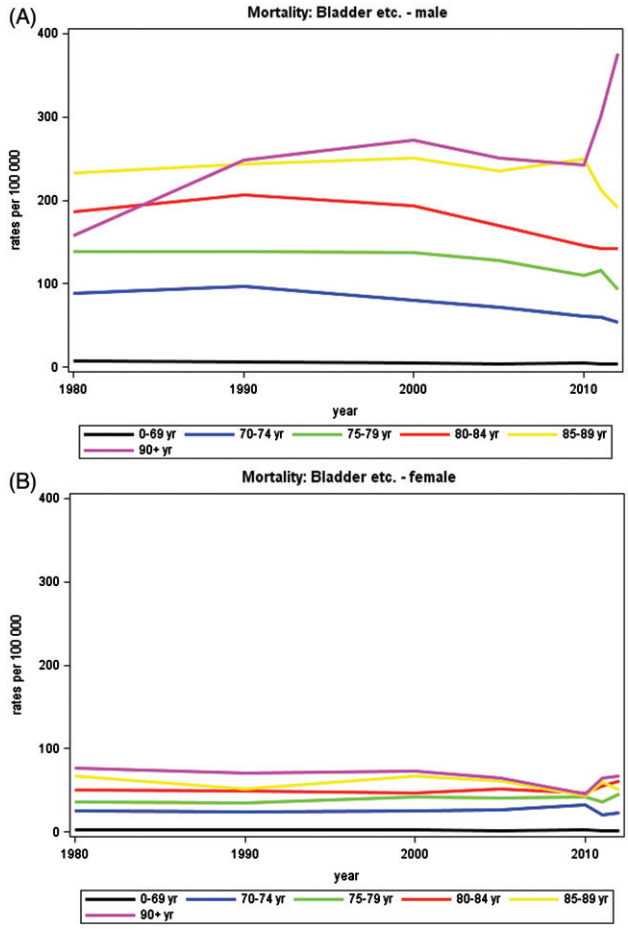

Figure 2. Mortality rates from bladder cancer in Denmark, 1980–2012, by age group. A. Males, B. Females. .

and Ederer II method for expected survival [14]. RS can be interpreted as the survival if the cancer was the only cause of death. For the most recent period, 2008–2012, not all patients can be followed up for death in five years and we used hybrid methods where we supplement with survival experience from cancer patients diagnosed earlier years [15].

Results

The average annual number of newly diagnosed bladder and urinary tract cancers increased in men from 1095 in 1980 to 1328 in 2012 and in women from 383 to 482 (Table I). The proportion of patients diagnosed over the age of 70 years increased from 47% to 57% in men and from 54% to 59% in women. Figure 1 illustrates that the incidence rates were 7–10 times higher in persons aged 70 years or more compared with younger persons. In elderly men, the rates increased up to around 2005 and then decreased while no particular trend was observed in elderly women.

Table II shows that the average annual number of deaths from BC decreased from 419 in 1980 to 391 in 2012 in men but increased in women from 168 to 200, the majority (75–80%) occurring after the age of 70 years. This corresponds to decreasing mortality rates in all age groups 90+-year-old men (Figure 2).

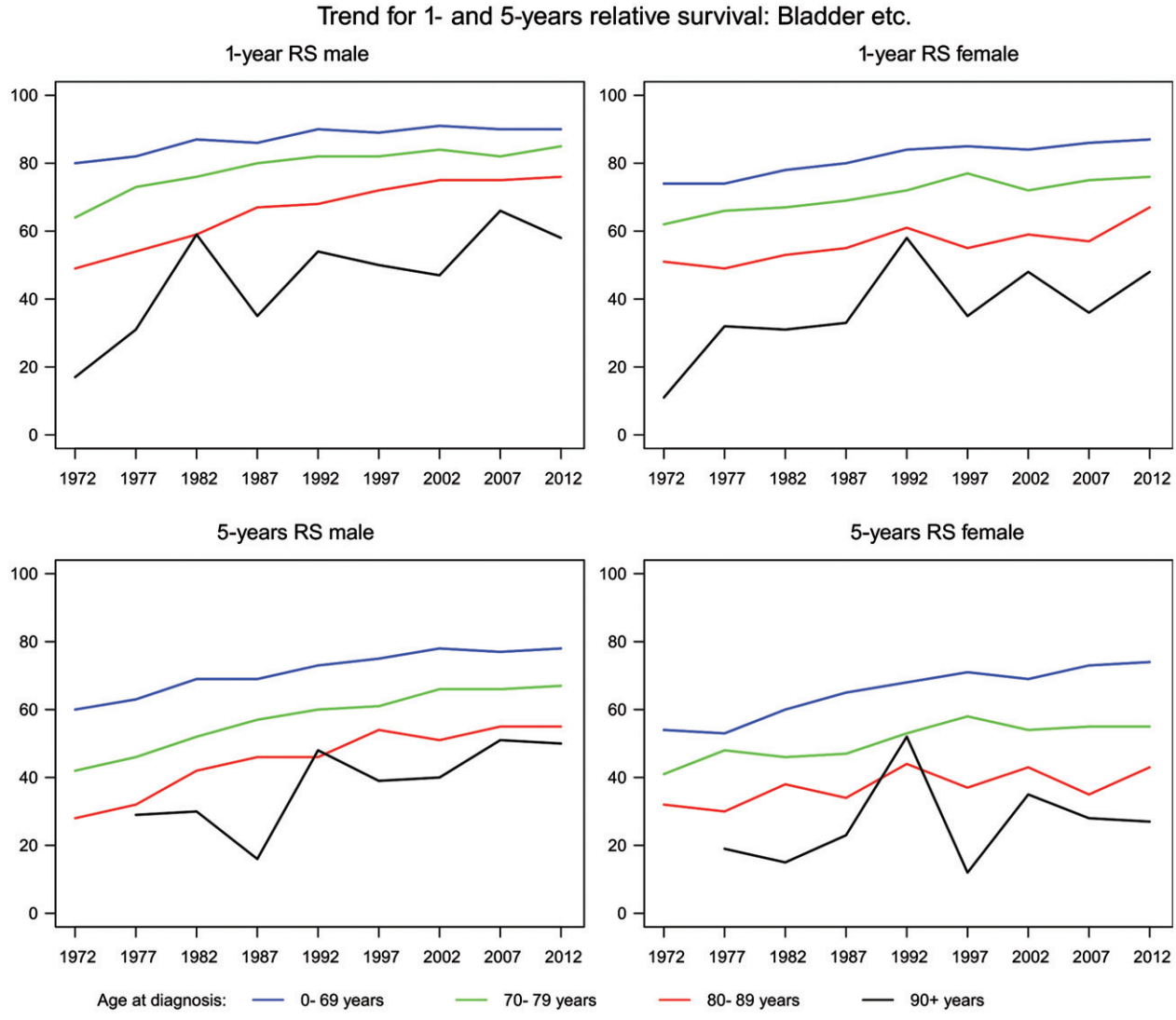

Figure 3. Relative survival after bladder cancer in Denmark.

The one- and five-year RS for BC improved significantly for all age groups in men and women (Figure 3). For men less than 70 years, the one-year RS went up from 80% to 90% and five-year RS from 60% to 78%, while for men more than 70 years the one-year RS increased from 59% to 83% and the five-year RS from 59% to 83%. For women the results were similar with one-year RS increasing from 74% to 87% and five-year RS from 54% to 74% among those aged less than 70 years and corresponding figures of 57–72% and 39–51% among those aged 70 years or more.

The prevalence of cancers of the urinary bladder and tract increased two times for both men and women in the period 1980 to 2012, (N = 6014–12 359, men, N = 1974–4454, women, see Table III). The increase was proportionally higher among elderly over age 70.

Discussion

Incidence rates of cancers of the urinary bladder and urinary tract increased up to around 2005 and then decreased while mortality rates decreased slightly over the period resulting in an increasing survival and prevalence. Incidence and mortality rates were much higher and survival lower in persons aged 70 years or more than in younger persons.

Surgical considerations

The elderly in the present study represented nearly two-thirds of BC patients, and there is no definitive treatment guideline for this group. Radical cystectomy is the best available treatment of BC, which offers a better survival rate than radiotherapy (RT) applied to all age groups [16]. In all, 8034 patients had cystectomy and 2773 RT [16]; Cystectomy was the primary method of treatment in all age groups except for octogenarians. The octogenarians who had a cystectomy with a limited pelvic lymph node dissection or cystectomy alone received little (16 vs. 15 months) or no survival benefit. However, cancer-specific survival was significantly higher in those who had cystectomy including octogenarians if it included a standard lymphadenectomy [16].

Today removal of the bladder is done either by open surgery or robotic-assisted surgery but comparisons between these

Table III. Annual number of persons alive with bladder cancer in Denmark by 31 December, 1980–2012.

	0–69 years				70–74 years				75–79 years				80–84 years				85–89 years				90+ years				All ages			
	Prev cases male		Prev cases female		Prev cases male		Prev cases female		Prev cases male		Prev cases female		Prev cases male		Prev cases female		Prev cases male		Prev cases female		Prev cases male		Prev cases female		Prev cases male		Prev cases female	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
1980	3100	51.5	908	46.0	1170	19.5	351	17.8	940	15.6	321	16.3	507	8.4	231	11.7	248	4.1	122	6.2	49	0.8	41	2.1	6014	100	1974	100
1990	3775	45.0	1273	42.2	1545	18.4	523	17.3	1498	17.9	500	16.6	980	11.7	393	13.0	443	5.3	229	7.6	147	1.8	100	3.3	8388	100	3018	100
2000	4106	40.1	1452	38.6	1849	18.1	619	16.5	1954	19.1	628	16.7	1378	13.5	567	15.1	713	7.0	333	8.9	240	2.3	158	4.2	10240	100	3757	100
2005	4286	38.5	1500	37.3	1936	17.4	682	17.0	2089	18.8	705	17.6	1657	14.9	556	13.8	838	7.5	378	9.4	329	3.0	196	4.9	11135	100	4017	100
2010	4490	37.6	1591	36.6	2069	17.3	732	16.8	2195	18.4	747	17.2	1752	14.7	651	15.0	1037	8.7	388	8.9	397	3.3	241	5.5	11940	100	4350	100
2011	4586	37.5	1610	36.2	2111	17.3	760	17.1	2234	18.3	768	17.3	1813	14.8	661	14.8	1041	8.5	421	9.5	439	3.6	232	5.2	12224	100	4452	100
2012	4555	36.9	1594	35.8	2160	17.5	743	16.7	2262	18.3	771	17.3	1890	15.3	676	15.2	1044	8.4	430	9.7	448	3.6	240	5.4	12359	100	4454	100

two techniques up to this point have been limited by relatively underpowered comparative trials. A recent study compared the postoperative morbidity after robot-assisted or open radical cystectomy and found early in the experience longer operating time associated with robotics but this was also associated with less perioperative blood loss [17]. The authors the analyzed the last 50 robotic-assisted cystectomies and found a significantly lower postoperative complications when compared with open cystectomy group, suggesting fewer complications can be expected with increasing experience of the surgeon [17]. Khan et al. compared complications after robotic-assisted cystectomy versus laparoscopic and open cystectomy [18] and found significantly fewer complications in the robotic group, longer operating time, less bleeding and a shorter hospital stay. The likelihood of having complications was increased four times for open versus robotic-assisted procedure. These studies are limited by the absence of long-term follow-up data and were not analyzed with respect to advantages of the robotic approach in the elderly compared to younger patients.

Oncological considerations

RT is used as a definitive, organ preserving treatment for patients with localized BC and is thus an alternative to cystectomy. This is often considered as the primary therapy for patients with significant co-morbidities as the elderly. Age has been suggested as one of several prognostic factors for success in RT for BC [19] but others have found the opposite results, at least in patients with a good performance status [20]. Comparisons between cystectomy and RT are very limited as there are not randomized trials comparing these approaches and so the available literature is hampered by selection bias. It has been suggested, however, that the proportion of RT BC patients with co-morbidity decreases with age [21]. Other treatment options, including hyperfractionation and concomitant radiosensitizing chemotherapy, have been suggested also for the elderly population, and seem to be feasible, but it is unknown if these treatments result in better tolerability or clinical outcome [22]. RT is a recommended treatment for patients with localized BC who are ineligible for cystectomy, including the elderly [23].

Chemotherapy for metastatic disease is mainly based on cisplatin combinations primarily MVAC (methotrexate, vinblastine, adriamycin and cisplatin) and GC (gemcitabine and cisplatin). In a pivotal randomized trial comparing these two regimens, the median age was 63 years. There was less toxicity for GC but the same efficacy (survival) compared to MVAC. In a univariate analysis there was no significant difference in overall survival or progression-free survival between patients older than 70 years compared to patients 70 or younger [24].

Normally more caution is taken when treating patients older than 70–75 years with cisplatin, and carboplatin is often considered as an alternative, switching from GC to gemcitabine plus carboplatin [25]. It is well known that the kidney function decreases with age and age is included in some definitions of patients being unfit for cisplatin treatment, but apart from kidney function the rationale is questionable, and age is not solely a parameter for worse outcome [26].

Second-line chemotherapy with vinflunine is commonly applied in Europe to patients in good performance status, but is not FDA approved for this indication in the US. In a phase I study including patients even 80 years or older, there was no difference in adverse events compared to the younger population, the side effect profile was the same but pharmacokinetically there was a decreased clearance for the elderly groups, and thus a reduced dose was recommended [27].

Conclusion

The incidence and prevalence of BC has increased over time across most age groups in Denmark. While the RS has also shown improvement, more prospective data are needed, preferably as randomized clinical trials, for determining the influence of age on the decisions of the surgical approach as well as chemo/RT for the elderly patients with urothelial cancers compared to younger patients.

Acknowledgments

We thank Niels Christensen and Anne Mette T. Kejs, Danish Cancer Society, Department of Documentation & Quality, for making the tabulations of incidence, mortality and prevalence, calculation of relative survival and trend graphs. The authors report no conflicts of interest.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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