ORIGINAL PAPER

Renal cell carcinoma trends in Latvia: incidence, mortality, and survival rates. Population-based study

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Introduction Baltic States including Latvia are reported as having one of the highest renal cell carcinoma (RCC) incidence and mortality rates in the world. However, data are often presented without stage-specific stratification, making assessment of the overall RCC diagnosis and survival trends challenging.
Material and methods We collected data on all newly diagnosed RCC patients from the national population-based cancer registry between 1997 and 2016. We analyzed RCC incidence, mortality and survival trends using Joinpoint analysis. Kaplan-Meier analysis was performed for 5- and 10-year cancer specific survival rate calculations.
Results There were a total of 7893 patients with newly diagnosed RCC. The age standardized (AS) incidence rate (per 100,000) increased slightly from 8.9 in 1997 to 9.8 in 2016. There were no specific changes in the incidence rate trend. Detection of early stage RCC increased by 5.4% annually. The AS mortality rates (per 100,000) decreased from 4.9 in 1997 to 3.9 in 2016, however, it did not reach a statistically significant change. The mortality rates decreased significantly in females and in the age group of 60-69 years. The 5-year cancer specific survival (CSS) rate increased from 55.1% in 1997-2001 to 66.6% in years 2007–2011. The 10-year CSS rate increased from 49.1% in 1997–2001 to 56.5% in years 2002–2006.
Conclusions During the study period, RCC incidence rates increased and overall mortality rates did not change. Similar to the rest of the world, the incidence of RCC diagnosed at an earlier stage increased and 5- and 10-year survival rates improved.

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INTRODUCTION

In 2018, kidney cancer led to more than 155,000 deaths [1] and renal cell carcinoma (RCC) accounted for 90% of all primary renal neoplasms [2]. Most commonly, RCC is found in people 60 to 80 years of age [3]. RCC is more common in males. It was the 9th leading malignancy for men and 14th most common malignancy for women in 2012. Also, in 2012 RCC was the 16th most common cause of cancer mortality [4].

The international Agency of Research on Cancer (GLOBOCAN) data base receives information from country specific Population-based cancer registries (PBCRs). It is commonly used to report worldwide and European specific renal neoplasm statistics. Studies using GLOBOCAN data report the Czech Republic and Baltic States as having the highest RCC incidence and mortality in the world [4–8]. However, survival rates are frequently presented without stage-specific stratification, making representation

of early detection and treatment trends challenging. To the best of our knowledge, we conducted our own population based RCC analysis for the first time in Latvia. We evaluated RCC incidence, mortality, and survival trends between 1997 and 2016.

MATERIAL AND METHODS

This was a retrospective cohort study. We used data obtained from The Latvian Center for Disease Prevention and Control (LCDPC). The LCDPC gathers cancer specific incidence, treatment, and survival data in Latvia. Additionally, the LCPDC Population-based disease registry collects patient demographic data, information on primary tumor site, tumor morphology, stage at diagnosis, the first course of treatment, and follow up data including survival. The registry captures close to 100% of all diagnosed cancer cases [9].

The initial data received from the LCDPC included information on all patients older than 18 years who carried a diagnosis of renal cancer, including RCC and upper urinary tract urothelial cancer between January 1st, 1997 and December 31st, 2016. Only patients with a new RCC diagnosis were selected. For the final analysis we included only patients with an International Classification of Diseases for Oncology (ICD-O) topographical code of C64.9. and morphological codes of 8260/3, 8310/0, 8310/3, 8311/1, 8312/3, 8317/3, 8318/3, 8319/3, 8320/3 [10]. All tumor stages were included in the analysis.

For cancer specific incidence and mortality calculations, we obtained study period population data from the Central Statistical Bureau of Latvia.

The annual RCC incidence (new RCC diagnoses/population that year) and mortality (number of cancer specific mortality/population at risk) rates were age-standardized to the world standard population [11]. The study population was divided into selected age groups: <60 years old, 60–69 years old, 70–79 years old and >80 years old, similar to that reported by Cancer Research UK [12]. To detect changes in RCC incidence and mortality trends, we performed Joinpoint analysis based on the patient's age group and cancer stage at diagnosis (I–II, III–IV and unknown stage). The Joinpoint analysis uses years as an independent variable and, in the log linear slope of the trend, identifies time segments that are separated by points of significant change in the trend, so called Joinpoints. The Joinpoint Regression Program (version 4.3.1.0, Apr 2016, USA) from the Surveillance Research Program of the US National Cancer Institute was used for this purpose. We also calculated the annual percentage of change (APC) for each separate linear segment. For the survival analysis, a cohort of RCC patients with at least a 5-year follow-up were selected. We calculated 5, 10 and overall cancer-specific survival rates using Kaplan-Meier analysis. Additionally, to represent the quality of data, we calculated a proportion of cases diagnosed by death certificate only (DCO) and a proportion of morphologically verified cases [16].

RESULTS

Study population

A total of 8489 patients with renal or upper urinary tract urothelial cancer were identified. From those, 7893 patients had a first time diagnosis of RCC. Patient population characteristics are represented in Table 1. RCC was more commonly seen in males, accounting for 54.9% (N = 4336) of cases. The majority of patients were in the age group between 60 and 69 years (total of 2462 patients or 31.2%), followed by <60 year age group (2392 patients or 30.3%). There were a total of 2266 (28.7%) patients in the age group of 70–79 years, and only 773 (9.8%) patients older than 80 years. Based on the cancer stage at diagnosis, patient distribution was as follows: stage I – 1884 (23.9%) cases, stage II – 1422 (18%) cases, stage III – 1416 (17.9%) cases, stage IV – 1630 (20.7%) cases, and unknown stage – 1541 (19.5%) cases. The number of RCC patients differed based on geographical area of residence. There were 2624 (33.2%) cases in the capital city of Riga, 1663 (21.1%) cases in all other major cities, excluding Riga, and 3606 (45.7%) cases in small towns or rural areas.

Incidence and mortality trends

Overall and sex specific RCC incidence trends are represented in Figure 1 and Table 2. Overall, there was a slight increase in the age standardized (ASR) RCC incidence rate between 1997 and 2016 (8.9 vs. 9.8 respectively). ASR rates were as follows: 8.9 (males 12.9, females 6.3) in 1997, 9.3 (males 13.4, females 6.5) in 2008, 10.7 (males 14.6, females 7.8) in 2012 and 9.8 (males 13.8, females 7.1) in 2016. The overall average annual percentage of change (APC) was 1.0% (95% CI 0.4–1.7). There were no Joinpoints indicating changes in the incidence trend during this time period. A similar incidence trend was observed in males and females with an APC of 0.8 % (95% CI 0.5–1.5) and 1.0% (95% CI 0.4–1.7) respectively.

Table 2 represents age and RCC stage specific incidence trends. Significantly increased RCC incidence was observed in age groups <60 years (APC 2.3%, 95% CI 1.5 to 3.2), and >80 years (APC 3.1%, 95% CI 1.3 to 5.0). There was no RCC incidence change in the age group 60–69 years (APC 0.7, 95% CI -0.1 to

1.4) and only minimal RCC incidence increase in the age group 70–79 years (APC 1.1%, 95% CI 0.1 to 2.0). There were no Joinpoints indicating incidence trend changes over the study period in all age groups.

The incidence rate of RCC diagnosed at an early stage (stage I–II) increased by 5.4% annually (95% CI 4.3 to 6.4), while the incidence rate of RCC diagnosed at an advanced stage (stage III–IV)

Table 1. *Main characteristics of renal cell carcinoma patient population by time periods*

	Total		1997–2001		2002–2006		2007–2011		2012–2016	
	N	100	N	100	N	100	N	100	N	100
Total	7893	100	1808	100	1871	100	2128	100	2018	100
Gender										
Male	4336	54.9	1002	55.4	1043	55.7	1178	55.4	1113	53.4
Female	3557	45.1	806	44.6	828	44.3	950	44.5	973	46.6
Age										
<60	2392	30.3	565	31.3	567	30.3	637	29.9	623	29.9
60–69	2462	31.2	649	35.9	611	32.7	610	28.7	592	28.4
70–79	2266	28.7	481	26.6	537	28.7	652	30.6	596	28.6
80+	773	9.8	113	6.3	156	8.3	229	10.8	275	13.2
Stage										
I	1884	23.9	51	2.8	266	14.2	631	29.7	936	44.9
II	1422	18.0	473	26.2	494	26.4	252	11.8	203	9.7
III	1416	17.9	591	32.7	381	20.4	292	13.7	152	7.3
IV	1630	20.7	434	24.0	398	21.3	412	19.4	386	18.5
Unknown	1541	19.5	259	14.3	332	17.7	541	25.4	409	19.6
Residence										
Riga	2624	33.2	635	35.1	661	35.3	688	32.3	640	30.7
Other cities, except Riga	1663	21.1	377	20.9	407	21.8	427	20.1	452	21.7
Small town or rural area	3606	45.7	796	44.0	803	42.9	1013	47.6	994	47.7
Data quality indicators										
%DCO/%Autopsy	594	7.5	103	5.7	163	8.7	235	11.0	93	4.5
%MV	4938	62.6	1046	57.9	1187	63.4	1281	60.2	1424	68.3

% – autopsy, percentage of all cases diagnosed at autopsy; %DCO – percentage of cases based on death certificate only; %MV – percentage of all microscopically verified cases; N – number
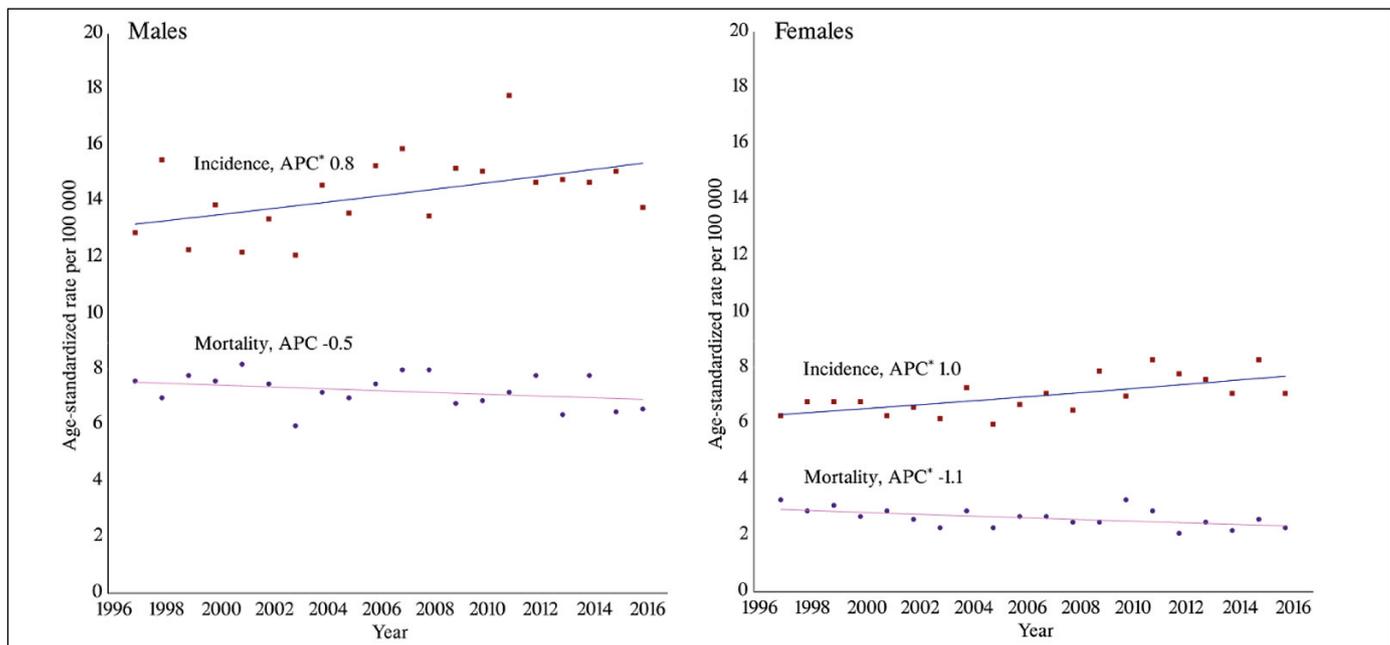

Figure 1. *Sex specific renal cell carcinoma incidence and mortality trends using Joinpoint analysis.*
APC – annual percentage of change; * represents statistically significant change

Table 2. *Age standardized renal cell carcinoma incidence and mortality trends using Joinpoint analysis*

	Incidence		Mortality	
	N of joinpoints, year (95% CI)	APC (95% CI)	N of joinpoints	APC (95% CI)
Overall	0	1.0 (0.4–1.7)	0	-0.7 (-1.3–0.2)
Sex				
Males	0	0.8 (0.1–1.5)	0	-0.5 (-1.2–0.2)
Females	0	1.0 (0.4–1.7)	0	-1.1 (-2.0–-0.2)
Age group				
<60	0	2.3 (1.5–3.2)	0	-1.5 (-3.0–0.1)
60–69	0	0.7 (-0.1–1.4)	0	-1.2 (-1.9– -0.5)
70–79	0	1.1 (0.1–2.0)	0	0.5 (-0.5–1.5)
80+	0	3.1 (1.3–5.0)	0	4.7 (3.0–6.5)
Stage				
I–II	0	5.4 (4.3–6.4)		
III–IV	0	-4.3 (-5.1–-3.5)		
unknown	1, 2009 (2006–2013)	8.2 (4.2–12.4)		
		-8.5 (-16.0–0.3)		

APC – annual percentage of change; CI – confidence interval; N – number

decreased by 4.3% annually (95% CI -5.1 to -3.5). In the year 2009, there was one Joinpoint for standardized incidence rate for unknown RCC stage. The incidence increased until 2009 (APC 8.2%, 95% CI 4.2 to 12.4) and decreased afterwards (APC -8.5%, 95% CI -16.0 to -0.3).

Age standardized overall and sex specific RCC mortality rate trends are represented in Figure 1 and Table 2. The AS mortality rates did not significantly change during the study period (AAP -0.7% annually, 95% CI -1.3 to 0.2). They were as follows: 4.9 (males 7.6, females 3.3) in 1997, 4.6 (males 8.0, females 2.5) in 2008, 4.2 (males 7.8, females 2.0) in 2012, and 3.9 (males 6.5, females 2.3) in 2016. In females, the mortality rate decreased from 3.3 in 1997 to 2.3 in 2016 (APC -1.1%, 95% CI -2.0 to -0.2). In males, there was no statistically significant change (APC -0.5, 95% CI -1.2 to 0.2).

A slight decrease in the RCC mortality rate was observed in the age group 60-69 years (APC -1.2%, 95% CI -1.9 to -0.5). However, RCC mortality rates significantly increased in the age group >80 years (APC 4.7%, 95% CI 3.0 to 6.5).

Survival analysis

A total of 7893 cases were identified with a minimum of 5-year follow-up data. From those, 642 patients were excluded from survival analysis as 594 cases were detected by DCO and postmortem examination, 39 cases had renal cancer as a secondary location and 9 cases were lost at follow-up. During the study period, the overall survival (OS) increased significantly. In 1997–2001, 5-year OS was 46.0% (95% CI, 43.6–48.4); in 2002-2006 it was 52.7% (95% CI, 50.3–55.1) and in 2007–2011 it was 56.4% (95% CI 54.2–58.7) (Figure 2A and Table 3). The 5-year OS rate increased by 10.4 percentage points from 46.0% in years 1997-2001 to 56.4% in years 2007–2011. Observed 5-year cancer specific survival (CSS) increased by 11.5 percentage points from 55.1% in years 1997–2001 to 66.6% in years 2007–2011 (Figure 2B and Table 3).

Observed 10-year OS rate increased by 4.9 percentage points from 34.3% in years 1997–2001 to 39.2% in years 2002–2006 (Figure 2A and Table 3). Observed 10-year CSS rates increased by 6.4 percentage points from 49.1 % in years 1997–2001 to 56.5% in years 2002–2006 (Figure 2B and Table 3).

DISCUSSION

RCC is the most common form of kidney neoplasm and one of the most common forms of male cancer. There are a lot of publications devoted to the epidemiology of RCC. However, during the last 28 years, there are no comprehensive and detailed studies done in Latvia. This is the first study describing the recent RCC epidemiological situation in the country. Furthermore, this is the largest project devoted to the epidemiology of RCC ever to be conducted in Latvia. Over past few last decades, RCC is becoming more frequently diagnosed worldwide in both men and women due to the more widespread use of abdominal ultrasound and computer tomography (CT) [13, 14]. Our study showed that in Latvia, the standardized RCC incidence rate has increased from 8.9 in 1997 to 9.8 in 2016, with an annual percentage of change of 0.8%. There was no change in the incidence trend during this time period and the RCC incidence in-
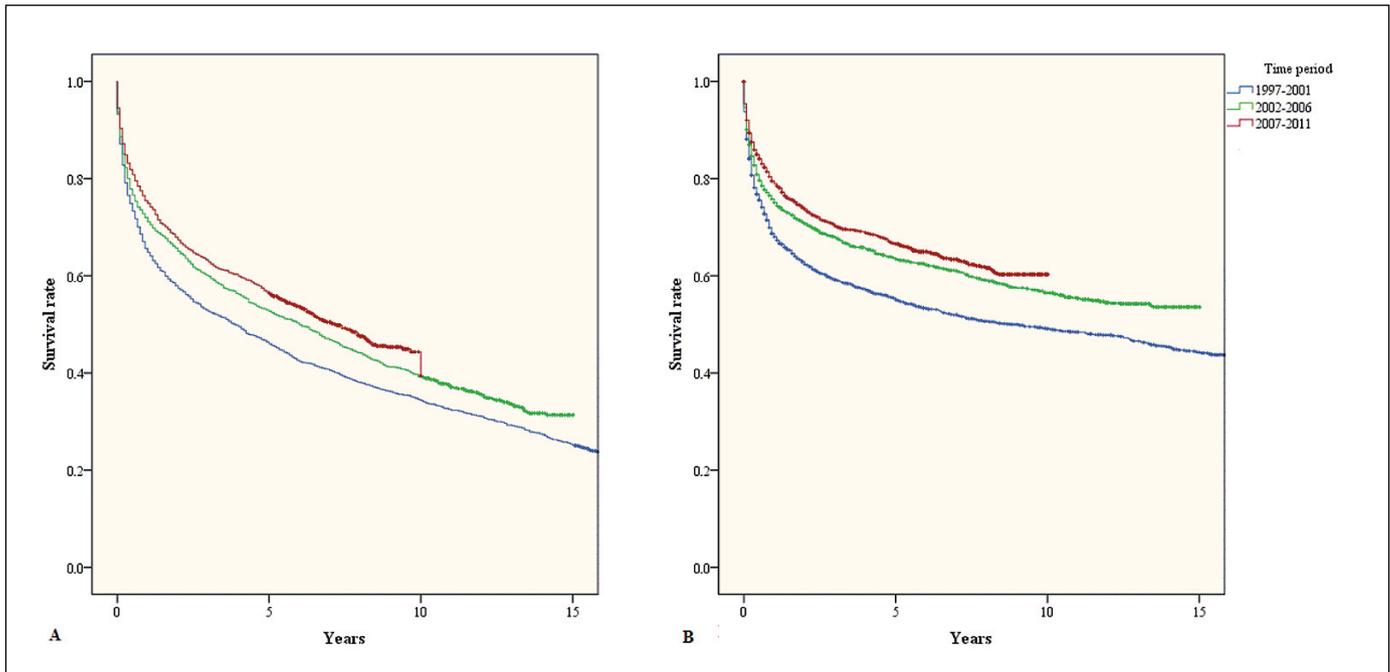
Figure 2. *Overall **(A)** and cancer specific **(B)** renal cell carcinoma survival by three time periods.*

Table 3. *Five and 10-year survival rates in the three time periods*

Survival rates		1997–2001	2002–2006	2007–2011
5-year (95% CI)	OS	46.0 (43.6–48.4)	52.7 (50.3–55.1)	56.4 (54.2–58.7)
	CSS	55.1 (52.6–57.5)	63.5 (61.1–65.8)	66.6 (64.4–68.8)
10-year (95% CI)	OS	34.3 (32.0–36.5)	39.2 (36.9–41.5)	
	CSS	49.1 (46.6–51.6)	56.5 (54.0–59.0)	

CI – confidence interval; CSS – cancer specific survival; OS – overall survival

creased similarly in men and women. Our reported incidence is similar to that described in prior studies using the GLOBOCAN database. Based on their data, the RCC incidence rate in Latvia in 2012 was 10.9 [8, 15]. Moreover, our analysis revealed that the age standardized RCC incidence rate in 2012 was 14.6 for men and 7.8 for women. This is very similar to the data represented using the GLOBOCAN database, which describes an RCC age standardized incidence of 15.0 for men and 7.3 for women [4].

Compared to the rest of the world, RCC incidence rates in Latvia are relatively high. According to GLOBOCAN data from 2003 to 2007, age standardized RCC incidence ranged from approximately 1 in African countries to more than 15 the in Check Republic, where the age standardized incidence rate in men is 22.1 and 9.9 in women [8, 15]. The heterogeneity in disease classification and cancer detection practices might explain some variations in reported RCC incidence rates across countries. For example, increased detection rates are seen in countries where abdominal ultrasound imaging is commonly per-

formed for nonspecific symptoms [16]. However, increased detection rates cannot entirely explain the high RCC incidence rate differences. Unfortunately, publicly reported data frequently contain RCC and upper tract transitional cell carcinomas. Although most kidney cancers coded C64 are renal cell carcinoma, the percentage of unspecified histologic types, for example DCO cases, could vary between registries. If these cases are included under the RCC diagnosis, this could potentially alter RCC incidence rates. This should be taken in account when reporting the data. The European Network of Cancer Registries has defined common standards for data collection and coding. Their implementation is an important step towards obtaining comparable data on cancer type and stage at diagnosis. However, as the data exclusion methods from GLOBOCAN vary, there is a need for more high-quality population-based regional and national cancer registries to further describe cancer specific patterns and trends [17].

Besides the frequent use of cross-sectional imagining, a combination of environmental risk factors,

like tobacco use, obesity, hypertension, diet, and specific occupations are linked to increased risk of RCC [18–23]. Therefore, it is not surprising that in our study the gender specific age standardized RCC incidence in Latvia is similar to that seen in our neighboring country Lithuania, where the RCC age standardized incidence rate in 2003 to 2007 was 17.6 in men and 8.1 in women [4]. Similar age standardized incidence rates are also observed in Slovakia, with 15.0 for men and 7.5 for women [4]. Additional international collaborative studies are needed to further evaluate geographical patterns across countries in Europe to uncover new lifestyle and environmental risk factors that are similar in different countries and lead to an increased risk of RCC.

Over the study period, detection of RCC at earlier tumor stages (stage I–II) increased by 5.5% yearly, while the incidence rate of RCC diagnosed at advanced tumor stages (stage III–IV) decreased by 4.2% annually. Similar trends are seen worldwide [24], owing to the widespread use of cross-sectional imaging and improved diagnostic modalities.

In this study, we demonstrate increased overall and cancer specific survival rates. CSS 5-year survival has increased from 55.1% in the late 90's to 66.6% in more recent years. However, this is lower than reported survival rates in other countries. For example, in Estonia, the relative survival rate (RSR) was: 72% in 2000–2004, 76% in 2005–2009 and reached 78% in 2010–2014 [24]. Similarly, in Canada, RSR was 68% in 1998–2004 and 71% in 2004–2008 [25]. Interestingly, in the Netherlands, RSR was 54% in 2000–2004 and 58% in 2005–2009 [26], which is close to our reported CSS rates in Latvia. Despite the fact that both CSS and RSR are net survival estimates, CSS measures depend on death certificate information and may differ from relative survival estimates [27]. It should be noted that RCC data in Latvia contain a rather high percentage of DCO cases, which are excluded from survival analysis. This may lead to increased survival rate estimates.

Our reported ASR mortality rate is similar to the mortality rate for Latvia as reported by Znaor et al. using GLOBOCAN data, with an ASR mortality rate of 7.2 for men and 2.6 for women 2.6 [4]. Similar to other countries, mortality rates have stabilized in Latvia over recent years and are similar to our neighboring countries. In 2012, the ASR mortality rate in Lithuania was 4.9, 4.6 in Estonia, and 4.8 in the Czech Republic [15, 28].

This study is not without limitations. While LCDPC captures the majority of cancer cases, the accuracy of data depends on the physician reporting it and the availability of clinical data. Furthermore, we were unable to evaluate factors affecting survival, as the LCDPC has incomplete information on treatment received, histological evaluation data or data reflecting socioeconomic factors. Despite these limitations, our study is the largest study done in Latvia evaluating recent RCC trends. Information gathered in this study reflects the most accurate RCC incidence, mortality and survival rates in the country.

CONCLUSIONS

Latvia has one of the highest incidence rates of RCC and, similar to the rest of the world, it continues to rise over the past two decades. It is most likely due to the increased use of abdominal cross-sectional imaging, leading to incidental detection. This has also resulted in an increased predominance of early stage RCC in recent years. Although 5-year and 10 year survival rates are improving in Latvia, they remain relatively low as compared to the rest of the world. Further increased efforts to improve earlier RCC detection and treatment strategies are needed.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018; 68: 394-424.

2. Eble JN, Sauter G, I. Epstein J, Sesterhenn IA. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs. World Heal Organ Classif Tumours. 2004; p. 354.

3. Thompson RH, Ordonez MA, Iasonos A, et al. Renal cell carcinoma in young and old patients--is there a difference? J Urol. 2008; 180: 1262-1266.

4. Znaor A, Lortet-Tieulent J, Laversanne M, Jemal A, Bray F. International variations and trends in renal cell carcinoma incidence and mortality. Eur Urol. 2015; 67: 519-530.

5. Bosetti C, Bertuccio P, Chatenoud L, Negri E, La Vecchia C, Levi F. Trends in mortality from urologic cancers in Europe, 1970-2008. Eur Urol. 2011; 60: 1-15.

6. Znaor LP, Holcatova A. Words of Wisdom Re: Regional Geographic Variations in Kidney Cancer Incidence Rates in European Countries. Eur Urol. 2015; 68: 335-336.

7. Li P, Znaor A, Holcatova I, et al. Regional Geographic Variations in Kidney Cancer Incidence Rates in European Countries. Eur Urol. 2015; 67: 1134-1141.

8. Wong MCS, Goggins WB, Yip BHK, et al. Incidence and mortality of kidney cancer: Temporal patterns and global trends in 39 countries. Sci Rep. 2017; 7: 15698.

9. Ferlay J, Colombet M, Soerjomataram I, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. Eur J Cancer. 2018; 103: 356-387.

10. Trott PA. International Classification of Diseases for Oncology. J Clin Pathol. 1977; 30: 782.

11. Dos Santos Silva I. Interpretation of epidemiological studies; in: Cancer Epidemiology Principles and Methods. International Agency for Research on Cancer WHO. 1999: 277-302.

12. Kidney cancer survival statistics | Cancer Research UK. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/kidney-cancer/survival#heading-One. Accessed February 24, 2019.

13. De P, Otterstatter MC, Semenciw R, Ellison LF, Marrett LD, Dryer D. Trends in incidence, mortality, and survival for kidney cancer in Canada, 1986-2007. Cancer Causes Control. 2014; 25: 1271-1281.

14. Van De Schans SAM, Aben KKH, Mulders PFA, et al. Modest improvement in 20 years of kidney cancer care in the Netherlands. Eur J Cancer. 2012; 48: 1822-1830.

15. Capitanio U, Bensalah K, Bex A, et al. Epidemiology of Renal Cell Carcinoma. Eur Urol. 2019; 75: 74-84.

16. Rossi SH, Klatte T, Usher-Smith J, Stewart GD. Epidemiology and screening for renal cancer. World J Urol. 2018; 36: 1341-1353.

17. Antoni S, Soerjomataram I, Møller B, Bray F, Ferlay J. An assessment of GLOBOCAN methods for deriving national estimates of cancer incidence. Bull World Health Organ. 2016; 94: 174-184.

18. Benichou J, Chow WH, McLaughlin JK, Mandel JS, Fraumeni Jr JF. Population attributable risk of renal cell cancer in Minnesota [see comments]. Am J Epidemiol. 1998; 148: 424-430.

19. Sosnowski R, Bjurlin MA, Verze P, et al. Role of cigarette smoking in urological malignancies and clinical interventions for smoking cessation. Cent Eur J Urol. 2016; 69: 366-369.

20. Chow W-H, Dong LM, Devesa SS, et al. Epidemiology and risk factors for kidney cancer. Nat Rev Urol. 2010; 7: 245-257.

21. White MC, Holman DM, Boehm JE, Peipins LA, Grossman M, Henley SJ. Age and cancer risk: a potentially modifiable relationship. Am J Prev Med. 2014; 46 (3 Suppl 1): S7-15.

22. Markevičius M, Jankevičius F. Epidemiology and risk factors of renal cell carcinoma : literature review and correlation according to Lithuanian people epidemiological risk factors. Lithuanian Surgery. 2015; 14: 141-148.

23. Innos K, Sepp T, Baburin A, et al. Increasing kidney cancer incidence and survival in Estonia: role of age and stage. Acta Oncol (Madr). 2019; 58: 1-8.

24. Patel HD, Gupta M, Joice GA, et al. Clinical Stage Migration and Survival for Renal Cell Carcinoma in the United States. Eur Urol Oncol. 2019; 2: 343-348.

25. De P, Otterstatter MC, Semenciw R, Ellison LF, Marrett LD, Dryer D. Trends in incidence, mortality, and survival for kidney cancer in Canada, 1986-2007. Cancer Causes Control. 2014; 25: 1271-1281.

26. Van De Schans SAM, Aben KKH, Mulders PFA, et al. Modest improvement in 20 years of kidney cancer care in the Netherlands. Eur J Cancer. 2012; 48: 1822-1830.

27. 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: 4773-4780.

28. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. Eur J Cancer. 2013; 49: 1374-1403. ■