Established in 1871

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Original article | Published 16 June 2022 | doi:10.4414/SMW.2022.w30175
Cite this as: Swiss Med Wkly. 2022;152:w30175

Incidence and outcome of patients with renal cell carcinoma treated with partial or radical nephrectomy in the Cantons St Gallen and Appenzell 2009–2018

Stefanie Aeppli[a], Daniel S. Engeler[b], Stefanie Fischer[a], Aurelius Omlin[a], Manolis Pratsinis[b], Christian Hermann[c*], Christian Rothermundt[a*]

[a] Division of Oncology and Haematology, Kantonsspital St. Gallen, Switzerland
[b] Department of Urology, Kantonsspital St. Gallen, Switzerland
[c] Cancer Registry St. Gallen-Appenzell, St. Gallen, Switzerland
[*] Christian Herrmann and Christian Rothermundt contributed equally to this work.

Summary

BACKGROUND: Over recent years, the incidence of renal cell carcinoma (RCC) has remained unchanged in Switzerland and is low compared with other European countries. Partial or radical nephrectomy is the mainstay of treatment in patients with localised disease.

METHODS: We conducted an analysis of data from the cancer registry of Eastern Switzerland on patients with surgery for RCC from 2009 to 2018, focusing on a comparison of surgical technique and outcome in tertiary and non-tertiary hospitals.

RESULTS: 492 nephrectomies were performed. Out of 441 curative procedures, 226 were radical and 195 partial nephrectomies (20 unknown). At the tertiary hospital, statistically significantly more partial nephrectomies were performed in non-metastatic patients than at non-tertiary hospitals. We demonstrate a trend towards better disease-free survival after partial compared with radical nephrectomy. The 5-year overall survival for patients diagnosed between 2009 and 2013 was 85%, 83%, and 70% in stage I, II, and III, respectively, compared with 96%, 78%, and 72% for patients diagnosed between 2014 and 2018.

CONCLUSION: RCC incidence in Switzerland has been stable during the past decade in contrast to other European countries, and no stage migration occurred. We demonstrated that patients with localised renal cancer at our tertiary centre were more likely to be treated with renal preserving surgery compared with non-tertiary hospitals. This analysis underlines the importance of local cancer registries in the comparison of treatment and outcome over time.

Correspondence:
Stefanie Aeppli, MD
Division of Oncology and Haematology
Kantonsspital St. Gallen
Rorschacherstrasse 95
CH-9007 St. Gallen
stefanie.aeppli[at]kssg.ch

Introduction

Renal cell carcinoma (RCC) is the 9th most common cancer in men and the 13th most common cancer in women in Switzerland. Between 2013 and 2017, an average of 690 newly diagnosed cases in males and about 310 cases in females were documented per year, and almost 200 male patients and around 110 female patients died of this disease each year. The median age at diagnosis was 67 years for males and 72 years for females [1]. Over the past 30 years, the incidence in Switzerland has remained unchanged and is low compared with other European countries. This is noteworthy because in other countries, such as the United Kingdom, the incidence has increased substantially. Several regions had both high incidence rates and increasing rates over time, including the southern part of the Czech Republic, Estonia, Latvia and Belarus [2–4]. Around 15% of patients present with distant metastases on initial diagnosis [5].

For patients with localised disease, partial or radical nephrectomy is the mainstay of treatment [6]. A systematic review showed improved survival in patients with partial nephrectomy for tumours ≤4 cm, with equivalent outcomes seen for laparoscopic and open surgery [7]. In the event of complete tumour resection, patients enter follow-up. About 40% of patients may suffer from a recurrence in the course of surveillance [8, 9]. Three trials investigated the effect of adjuvant systemic therapy with the tyrosine kinase inhibitors (TKIs) sunitinib, sorafenib or pazopanib [10–12]. Only one of those studies, the S-TRAC trial, was able to demonstrate an increased disease-free survival with adjuvant treatment, though it did not translate into an overall survival benefit. Adjuvant systemic therapy is currently not part of standard treatment after partial or complete nephrectomy. However, adjuvant trials with checkpoint inhibitors are ongoing and promising [13].

For patients with metastatic disease and good performance status cytoreductive nephrectomy has been the standard of care for many years. Studies have shown a survival benefit of around 6 months for patients undergoing cytoreductive nephrectomy followed by interferon-alpha therapy compared with interferon-alpha therapy alone [14, 15].

The French CARMENA trial investigated immediate cytoreductive nephrectomy versus immediate treatment with sunitinib and deferred cytoreductive nephrectomy [16]. For patients with intermediate-risk and poor-risk disease (Memorial Sloan-Kettering Cancer Center [MSKCC] risk score) sunitinib alone was non-inferior to cytoreductive nephrectomy followed by sunitinib in regard to overall survival, and patients with a MSKCC favourable-risk disease had an improved overall survival with cytoreductive nephrectomy followed by sunitinib compared with sunitinib alone.

The role of cytoreductive nephrectomy in patients with synchronous metastatic RCC is still a subject of debate, and the optimal sequence of therapy is being investigated. In any case, careful patient selection is necessary. Current guidelines strongly recommend omitting cytoreductive nephrectomy in the MSKCC poor-risk population [17, 18].

In this analysis, we sought to depict the surgical care provided for patients with kidney cancer in Eastern Switzerland over the past decade, reflecting the paradigm shifts attributed to recent therapeutic insights. We also investigated the impact of the respective therapies on patient outcomes.

Methods

For this analysis, we retrospectively collected data from patients with RCC, treated between 2009 and 2018 in the cantons of St Gallen and Appenzell. The total population at risk in these cantons was 547,612 in 2010 and 579,076 in 2018. Patient characteristics (age, gender), type of surgery (partial vs radical nephrectomy), histological subgroups as well as overall survival were assessed. This was performed by using the Eastern Switzerland cancer registry, which encompasses patient data collected from all hospitals of the catchment area. The cantons St Gallen and Appenzell have a number of hospitals, which we divided in two distinct groups. Tertiary hospitals, which are defined through highly specialised staff and technical equipment, have teaching activities and clinical services that are highly differentiated by function. Size ranges from 300–1500 beds. Only the cantonal hospital of St Gallen meets this definition. All other hospitals were grouped together as non-tertiary hospitals, which include secondary- and primary level hospitals.

Data sources and inclusion criteria

The cancer registry of Eastern Switzerland [19] provided data on patients with RCC. The cancer registry covers the cantons of St Gallen, Appenzell Ausserrhoden, Appenzell Innerrhoden and Thurgau. Inclusion criteria were cases with (1) invasive RCC according to the International Classification of Diseases for Oncology (ICDO-3) [20] morphology codes 8050/3, 8260/3, 8290/3, 8310/3, 8312/3, 8317/3, 8318/3 together with the topography code C64·9; (2) diagnosis in 2009–2018; (3) place of residence at diagnosis within the catchment area of the registry; and (4) having undergone any type of nephrectomy.

The data included information on type (partial or radical nephrectomy) and place of treatment, time of diagnosis and possible relapse / metastatic disease, time and state of follow up (alive, died, lost-to-follow-up), ICDO-3 morphology and tumour staging information according to the UICC TNM Classification of Malignant Tumours (TNM staging) [21].

Statistical analysis

We grouped the data according to place of treatment into patients treated in the tertiary hospital vs non-tertiary hospitals. The type of surgery was classified by the cancer registry as partial, total/radical and unknown type of nephrectomy.

The type of nephrectomy was unknown in 5% (n = 26) of cases. These cases were excluded in the survival analysis and all analyses comparing types of nephrectomies.

TNM information was grouped into the four UICC stages I, II, III and IV, with stage I being tumours ≤7 cm limited to the kidney, stage II tumours >7 cm limited to the kidney, stage III tumours not limited to the kidney but without distant metastases and not beyond Gerota fascia, and stage IV primary metastatic tumours or tumours invading beyond Gerota fascia.

In multivariable analysis, a possible time trend was assessed by dividing the data set into two equal time periods, 2009–2013 and 2014–2018.

We used Stata 15 [22] for data analysis. Between-group and within-group variation was assessed using χ^2-tests and one-way ANOVA (analysis of variance). Equal variances were verified with Bartlett's test.

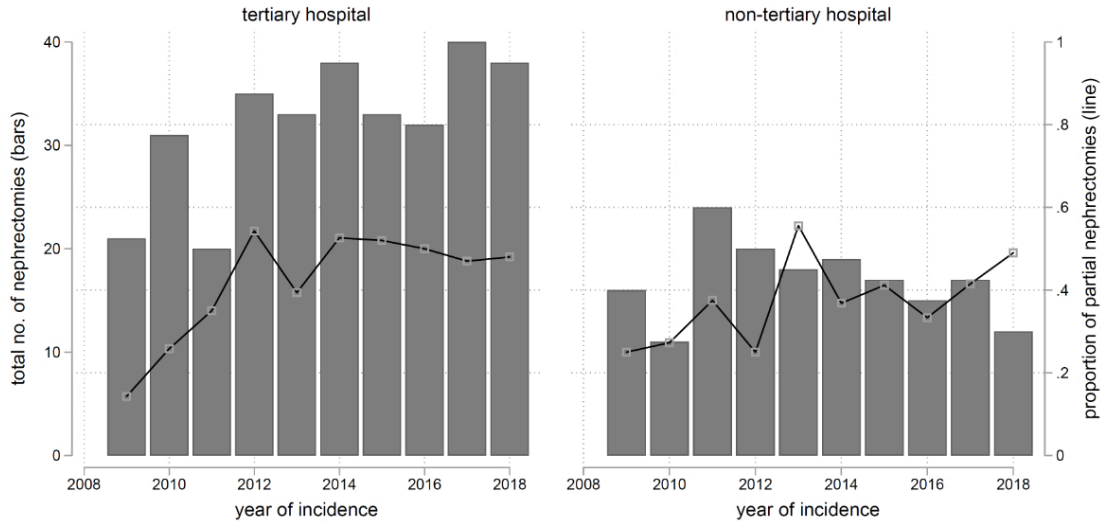
We calculated the number of nephrectomies per year and treatment place and the proportion of partial nephrectomies thereof.

The development of stage distribution by year was calculated by using the age-standardised incidence rate (ASR) according to the Europa standard[23].

Overall survival was evaluated using Kaplan-Meier survival estimates and pointwise 95% confidence interval (CI) bands, and log-rank tests were used for testing the equality of survivor functions. Relative survival was calculated using the Ederer II method using the Stata command, strs [24]. The influence of the period, type of nephrectomy and TNM stage on relapse-free survival was analysed using the Cox proportional hazards regression model. The proportional hazards assumption was tested and confirmed. The variables were selected with forward and backward selection, based on the model with lowest Bayesian information criterion.

Disease-free survival was defined as the time from primary diagnosis to last known date without a relapse, whether local or distant. The relapse rate by period was calculated by dividing the number of patients with local or distant relapse by the total person years at risk. The calculations according to relapse were restricted to patients with known relapse status.

Figure 1: Number of nephrectomies and proportion of partial nephrectomies over time.



Results

Between 2009 and 2018 (10 years) a total of 492 nephrectomies were performed in the cantons St Gallen and Appenzell. The two most common histological subtypes seen were clear cell carcinoma in 59%, and papillary carcinoma in 21% (table 1). Tumours with multiple histological subtypes (i.e., clear cell with sarcomatoid component) were classified by the leading subtype or as renal cell carcinoma not otherwise specified if no predominant subtype was present.

A total of 441 patients underwent surgery in curative intent, consisting of 226 radical nephrectomies and 195 partial nephrectomies; in 26 cases the extent of surgery is unknown. The tertiary hospital performed proportionally more partial nephrectomies (48%) in patients without metastases than the non-tertiary hospitals (37%). This difference was statistically significant (p = 0.029) (table 2).

When the cases were limited to to stage I and II tumours, the tertiary centre performed partial nephrectomy in 63% of cases, compared with 49% of cases in non-tertiary hospitals (p = 0.038).

In total, the number of surgical procedures as well as the percentage of partial nephrectomies increased over time at the tertiary centre of care. In 2009, a total of 39 surgical procedures for renal cancer were performed, of which 18% were partial nephrectomies. In 2018, a total number of 49 procedures were performed, 47% of which constituted partial nephrectomies (fig. 1).

Patients with metastatic disease were more commonly treated at the tertiary hospital: a total of 13% of all patients surgically treated for renal cancer at the tertiary hospital had primary metastatic disease, compared with 5% of all patients treated at non-tertiary hospitals (p = 0.006) (table 3).

There were some changes in stage distribution observed over time, though they did not appear to be statistically significant (p = 0.099) (fig. 2).

In the majority of kidney cancer patients no lymphadenectomy is performed, hence lymph node TNM staging is done by clinical assessment. Out of 492 patients, 441 were classified as N0 and this was confirmed by pathology in 53 patients, 2 were up-staged to pN+.

The 5-year overall survival for patients diagnosed between 2009 and 2013 was 85%, 83%, and 70% in stages I, II and III, respectively. For patients diagnosed between 2014 and 2018 the 5-year overall survival was 96%, 78%, and

Table 1:
Distribution of morphology types.

Morphology type	n	%
Clear cell	290	59%
Papillary	101	21%
Renal cell carcinoma NOS / unclassified	40	8%
Chromophobe	51	10%
Pure sarcomatoid	10	2%
Total	492	100%

Table 2:
Distribution of patients without metastases by type of nephrectomy and place of treatment, p = 0.029.

Type of nephrectomy	Treatment hospital, n (%)		Total
	Tertiary	Non-tertiary	
Radical	132 (47)	94 (58)	226 (51)
Partial	134 (48)	61 (37)	195 (44)
Total	266	155	421

72% in stages I, II and III, respectively. Five-year overall survival for patients diagnosed in stage IV was 6% in 2009–2013 and 36% in 2014–2018; however, due to small numbers this difference was not statistically significant (p = 0.07) (table 4).

The best Cox proportional hazards model with the lowest Bayesian information criteria included only individual stages and age as continuous variable. Survival of patients with stage I and II was similar, stages III and IV had significantly lower survival (hazard ratios [HRs] 2.0, p = 0.009 and 10.5, p <0.001). Higher age at diagnosis was associated with a lower survival (table 5).

After nephrectomy, median disease-free survival was 10.0 years with no significant differences seen with regards to the period of diagnosis (p = 0.39). Survival after partial nephrectomy was better than after radical nephrectomy adjusted for age and stage at diagnosis. However, the difference was not statistically significant either (log-rank test, p = 0.11) (fig. 3).

Discussion

With this study, we provide an insight into the treatment patterns and outcomes of patients with RCC treated by partial or radical nephrectomy in Eastern Switzerland.

Clear cell RCC was the most common histological subtype, accounting for almost 60% of cases. With 101 cases (21%), papillary RCC was the second most common subtype in this population. Interestingly, this appeared to be double what is usually described in epidemiological datasets [25]. Further classification into type 1 and 2 was not possible. Recent advances in molecular pathology suggest, however, that papillary RCC is a very heterogeneous group that will have to be divided in additional subtypes [26].

The incidence of RCC and especially early stages has been rising since the 1980s in most European countries. Within our observation period, this was the case neither in our cohort in Eastern Switzerland nor in the whole of Switzerland, with a stable incidence. There is no information on

Figure 2: Age-standardised incidence rates (ASR) of renal cell carcinoma in St Gallen-Appenzell by year of diagnosis and stage.

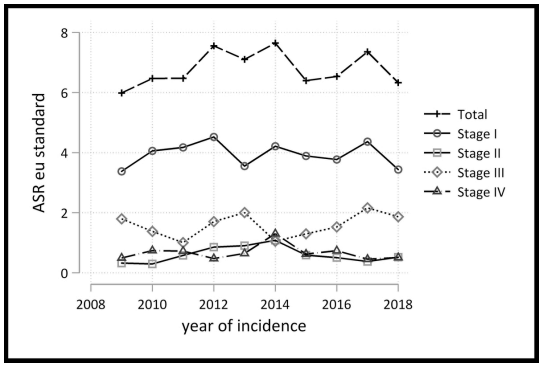


Figure 3: Disease-free survival, adjusted for age (reference 64 years of age) and stage (reference stage II).

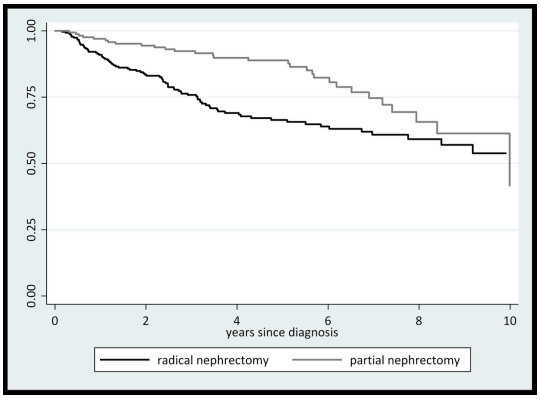


Table 3:
Distribution of patients with (M-status 1) vs without (M-status 0) primary metastatic disease in tertiary and non-tertiary hospitals (p = 0.006).

M-status	Tertiary hospital	Non-tertiary hospitals	Total
0	278 (87%)	163 (95%)	441 (90%)
1	42 (13%)	9 (5%)	51 (10%)
Total	320	172	492

Table 4:
Five-year overall survival by stage and period.

Stage	2009-2013		2014-2018		
	5-year OS (%)	95% CI	5-year OS	95% CI	
I	85.2	77.5–90.4	96.1	90.8–98.4	p = 0.003
II	83.3	56.8–94.3	78.0*	51.2–91.2	p = 0.68
III	69.8	55.5–80.3	71.8*	35.4–90.0	p = 0.89
IV	5.9**	0.4–23.5	36.0**	9.4–64.3	p = 0.07

CI: confidence interval; OS overall survival; p-values are for differences between periods in 5-year OS by stage.

Table 5:
Cox regression results, best model. Overall survival.

		Hazard ratio	p-value	95% Confidence interval	
Stage	I	(reference)			
	II	1.2	0.636	0.54	2.75
	III	2.0	0.009	1.19	3.23
	IV	10.5	<0.001	6.02	18.25
Age at diagnosis (per each 10 years of increased age)		1.5	<0.001	1.25	1.88

any genetic, lifestyle or environmental factors that could explain the notable regional differences. Geographic variations could be caused by environmental factors that have yet to be discovered. Further studies integrating more regional and up-to-date records are needed to investigate geographic variations in kidney cancer incidence rates to improve cancer prevention and identification of risk factors [2]. Some changes in stage distribution could be seen in this analysis between 2009 and 2018. This effect is called stage migration, which can be partly attributed to the increase in abdominal imaging in routine clinical practice. According to US data, stage migration has ended [27], and this is also supported by our data, as differences in stage distribution did not change statistically significantly over time.

There may be a bias because only resected tumours were included in our study. Today, it is common practice to survey small tumours (up to 3 cm) especially in elderly patients, as they are unlikely to metastasise. These patients often do not undergo biopsy because of a lack of consequences. Furthermore, alternative treatment options such as ablative techniques or super-selective embolisation can be used to treat smaller tumours [6], and therefore not necessarily be listed in the cancer registry.

Partial nephrectomy, also called nephron-sparing surgery, has been compared with radical nephrectomy in several retrospective cohorts [7]. In 2011, the first randomised, prospective trial compared the oncological outcome of radical with partial nephrectomy for small renal tumours (<5 cm), showing comparable cause-specific survival. Furthermore, nephron-sparing surgery demonstrated a better preservation of kidney function, thereby potentially lowering the risk of cardiovascular disease [28, 29]. Our analysis showed a significantly higher percentage of partial nephrectomies in the tertiary hospital compared to non-tertiary hospitals, especially in early stages. We observed an increase in partial nephrectomies at the tertiary hospital between 2008 and 2012, in line with the publication of van Poppel et al. This rise was not as evident in non-tertiary hospitals, though a similar trend is apparent as of 2012. Furthermore, the advent of laparoscopic and robot-assisted laparoscopic surgery has further advanced renal preserving surgery. Such technological advances are often implemented in tertiary centres of care first, before they find widespread use in smaller hospitals, which may partially explain the differences perceived in our study. A trend towards better disease-free survival after partial compared to radical nephrectomy could be seen. However, this was not statistically significant, perhaps owing to the small cohort. This trend cannot be explained by the better prognosis of smaller tumours, which are more likely to be treated by partial nephrectomy, as the analysis was adjusted for age and stage.

In addition, our data did not show a change in disease-free survival over time. We hypothesise this was due to the lack of treatments in the adjuvant setting and no stage migration.

In the time period from 2014 to 2018, 5-year overall survival was statistically significantly superior for stage I disease when compared with the earlier period. In the multivariable Cox regression model, neither period nor surgical technique were significant factors. Hence, this may be attributed to age differences and improvement in life expectancy.

This analysis included 51 patients with primary metastatic disease, who underwent partial or radical nephrectomy. The CARMENA trial, published in 2018, demonstrated that patients with MSKCC intermediate- and poor-risk disease may be treated with systemic therapy alone and cytoreductive nephrectomy can be omitted or at least deferred [16]. Only a small proportion of the population in this analysis was treated after publication of this seminal paper.

The calculation of relapse rate and relapse-free survival was restricted to patients with known relapse status. A limitation of this approach is a possible overestimation of relapse as information on relapse might be more likely to reach the cancer registry than the information of a disease free status.

Conclusion

In this analysis, we show that RCC incidence in Switzerland has been stable during the past decade in contrast to other European countries, and no stage migration occurred. Therefore, overall survival has not changed. We expected an improvement in overall survival for stage IV disease due to novel systemic treatments. However, this could not be observed due to the small stage IV cohort.

We demonstrated that patients with localised renal cancer at our tertiary centre were more likely to be treated with renal preserving surgery than those at non-tertiary hospitals. This is relevant with respect to organ function preservation. Outcome for patients with partial nephrectomy was not inferior to radical nephrectomy, and this supports partial nephrectomy as the treatment of choice in well-selected patients and experienced centres.

Local cancer registries can be of assistance when comparing the treatment and outcome of patients over time, and should be widely implemented in accordance with the local authorities.

Conflicts of Interest

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest.

SA reports grants from Kantonsspital St. Gallen, Medizinisches Forschungszentrum, St. Gallen, Switzerland, during the conduct of the study; others from MSD Oncology, Sanofi-Genzyme, Pfizer, and Merck outside the submitted work.

AO reports other support from AstraZeneca, Astellas, Bayer, Janssen, Molecular Partners, MSD, Pfizer, Roche, Sanofi Aventis, outside the submitted work; research support (institutional) from TEVA, Janssen; travel support from Astellas, Bayer, Janssen, Sanofi Aventis, Speakers Bureau (compensated, institutional), Bayer, Astellas, Janssen.

CR reports other from Pfizer, other from Bristol-Myers Squibb, other from MSD Oncology, other from Roche Pharma AG, personal fees and other from Merck (Schweiz) AG, from Bayer (Schweiz) AG, outside the submitted work.

No other potential conflict of interest was disclosed.

Financial disclosure

The data analysis was supported by the Forschungskommission Kantonsspital St. Gallen (Project Nr. 18/04) and the East Switzerland Cancer Registry.

References

1. Bundesamt für Statistik NK. Krebs, Neuerkrankungen und Sterbefälle: Anzahl, Raten, Medianalter und Risiko pro Krebslokalisation. 12 November 2020.
2. Li P, Znaor A, Holcatova I, Fabianova E, Mates D, Wozniak MB, et al. Regional geographic variations in kidney cancer incidence rates in European countries. Eur Urol. 2015 Jun;67(6):1134–41. http://dx.doi.org/10.1016/j.eururo.2014.11.001. PubMed. 1873-7560
3. Scelo G, Larose TL. Epidemiology and Risk Factors for Kidney Cancer. J Clin Oncol. 2018 Oct;36(Oct):JCO2018791905. http://dx.doi.org/10.1200/JCO.2018.79.1905. PubMed. 1527-7755
4. 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. 11 2018;103:356-387. doi: http://dx.doi.org/10.1016/j.ejca.2018.07.005.
5. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin. 2017 Jan;67(1):7–30. http://dx.doi.org/10.3322/caac.21387. PubMed. 1542-4863
6. Ljungberg B, Hanbury DC, Kuczyk MA, Merseburger AS, Mulders PF, Patard JJ, et al.; European Association of Urology Guideline Group for renal cell carcinoma. Renal cell carcinoma guideline. Eur Urol. 2007 Jun;51(6):1502–10. http://dx.doi.org/10.1016/j.eururo.2007.03.035. PubMed. 0302-2838
7. MacLennan S, Imamura M, Lapitan MC, Omar MI, Lam TB, Hilvano-Cabungcal AM, et al.; UCAN Systematic Review Reference Group; EAU Renal Cancer Guideline Panel. Systematic review of oncological outcomes following surgical management of localised renal cancer. Eur Urol. 2012 May;61(5):972–93. http://dx.doi.org/10.1016/j.eururo.2012.02.039. PubMed. 1873-7560
8. Janzen NK, Kim HL, Figlin RA, Belldegrun AS. Surveillance after radical or partial nephrectomy for localized renal cell carcinoma and management of recurrent disease. Urol Clin North Am. 2003 Nov;30(4):843–52. http://dx.doi.org/10.1016/S0094-0143(03)00056-9. PubMed. 0094-0143
9. Janowitz T, Welsh SJ, Zaki K, Mulders P, Eisen T. Adjuvant therapy in renal cell carcinoma-past, present, and future. Semin Oncol. 2013 Aug;40(4):482–91. http://dx.doi.org/10.1053/j.seminoncol.2013.05.004. PubMed. 1532-8708
10. Haas NB, Manola J, Uzzo RG, Flaherty KT, Wood CG, Kane C, et al. Adjuvant sunitinib or sorafenib for high-risk, non-metastatic renal-cell carcinoma (ECOG-ACRIN E2805): a double-blind, placebo-controlled, randomised, phase 3 trial. Lancet. 2016 May;387(10032):2008–16. http://dx.doi.org/10.1016/S0140-6736(16)00559-6. PubMed. 1474-547X
11. Ravaud A, Motzer RJ, Pandha HS, et al. Adjuvant Sunitinib in High-Risk Renal-Cell Carcinoma after Nephrectomy. N Engl J Med. 12 2016;375(23):2246-2254. doi: http://dx.doi.org/10.1056/NEJMoa1611406.
12. Motzer RJ, Haas NB, Donskov F, Gross-Goupil M, Varlamov S, Kopyltsov E, et al.; PROTECT investigators. Randomized Phase III Trial of Adjuvant Pazopanib Versus Placebo After Nephrectomy in Patients With Localized or Locally Advanced Renal Cell Carcinoma. J Clin Oncol. 2017 Dec;35(35):3916–23. http://dx.doi.org/10.1200/JCO.2017.73.5324. PubMed. 1527-7755
13. A Study Comparing Nivolumab, Nivolumab in Combination With Ipilimumab and Placebo in Participants With Localized Kidney Cancer Who Underwent Surgery to Remove Part of a Kidney (CheckMate 914). https://clinicaltrials.gov/ct2/show/NCT03138512?cond=NCT03138512&draw=2&rank=1
14. Mickisch GH, Garin A, van Poppel H, de Prijck L, Sylvester R; European Organisation for Research and Treatment of Cancer (EORTC) Genitourinary Group. Radical nephrectomy plus interferon-alfa-based immunotherapy compared with interferon alfa alone in metastatic renal-cell carcinoma: a randomised trial. Lancet. 2001 Sep;358(9286):966–70. http://dx.doi.org/10.1016/S0140-6736(01)06103-7. PubMed. 0140-6736
15. Flanigan RC, Salmon SE, Blumenstein BA, Bearman SI, Roy V, McGrath PC, et al. Nephrectomy followed by interferon alfa-2b compared with interferon alfa-2b alone for metastatic renal-cell cancer. N Engl J Med. 2001 Dec;345(23):1655–9. http://dx.doi.org/10.1056/NEJMoa003013. PubMed. 0028-4793
16. Méjean A, Ravaud A, Thezenas S, et al. Sunitinib Alone or after Nephrectomy in Metastatic Renal-Cell Carcinoma. N Engl J Med. 08 2018;379(5):417-427. doi: http://dx.doi.org/10.1056/NEJMoa1803675.
17. Ljungberg B, Albiges L, Abu-Ghanem Y, et al. European Association of Urology Guidelines on Renal Cell Carcinoma: The 2019 Update. Eur Urol. 05 2019;75(5):799-810. doi: http://dx.doi.org/10.1016/j.eururo.2019.02.011.
18. Escudier B, Porta C, Schmidinger M, et al. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. Ann Oncol. 05 01 2019;30(5):706-720. doi: http://dx.doi.org/10.1093/annonc/mdz056.
19. Cancer Registry Of Eastern Switzerland Krebsregister-ost.ch
20. Organization WH. International Classification of Diseases for Oncology – Third Edition. 2000.
21. James D. Brierley (Editor) MKGE, Christian Wittekind (Editor). TNM Classification of Malignant Tumours, 8th Edition. 2016.
22. https://www.stata.com
23. Waterhouse JA, Correa P, Powell J. Cancer incidence in five continents. Lyon: IARC; 1976.
24. Dickman PW, Coviello E. Estimating and Modeling Relative Survival. Stata J. 2015;15(1):186–215. http://dx.doi.org/10.1177/1536867x1501500112. http://dx.doi.org/10.1177/1536867X1501500112. 1536-867X
25. Padala SA, Barsouk A, Thandra KC, Saginala K, Mohammed A, Vakiti A, et al. Epidemiology of Renal Cell Carcinoma. World J Oncol. 2020 Jun;11(3):79–87. http://dx.doi.org/10.14740/wjon1279. PubMed. 1920-454X
26. Akhtar M, Al-Bozom IA, Al Hussain T. Papillary Renal Cell Carcinoma (PRCC): an Update. Adv Anat Pathol. 2019 Mar;26(2):124–32. http://dx.doi.org/10.1097/PAP.0000000000000220. PubMed. 1533-4031
27. Patel HD, Gupta M, Joice GA, et al. Clinical Stage Migration and Survival for Renal Cell Carcinoma in the United States. Eur Urol Oncol. 07 2019;2(4):343-348. doi: http://dx.doi.org/10.1016/j.euo.2018.08.023.
28. Capitanio U, Terrone C, Antonelli A, Minervini A, Volpe A, Furlan M, et al. Nephron-sparing techniques independently decrease the risk of cardiovascular events relative to radical nephrectomy in patients with a T1a-T1b renal mass and normal preoperative renal function. Eur Urol. 2015 Apr;67(4):683–9. http://dx.doi.org/10.1016/j.eururo.2014.09.027. PubMed. 1873-7560
29. Miller DC, Schonlau M, Litwin MS, Lai J, Saigal CS; Urologic Diseases in America Project. Renal and cardiovascular morbidity after partial or radical nephrectomy. Cancer. 2008 Feb;112(3):511–20. http://dx.doi.org/10.1002/cncr.23218. PubMed. 0008-543X