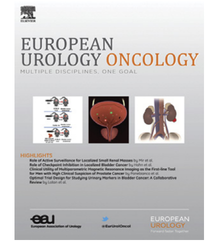
EUROPEAN UROLOGY ONCOLOGY 1 (2018) 252–261

available at www.sciencedirect.com
journal homepage: euoncology.europeanurology.com



European Association of Urology

National Norwegian Practice Patterns for Surgical Treatment of Kidney Cancer Tumors ≤7 cm: Adherence to Changes in Guidelines May Improve Overall Survival

Karin M. Hjelle [a,b,*], *Tom B. Johannesen* [c], *Leif Bostad* [d], *Lars A.R. Reisæter* [b,e], *Christian Beisland* [a,b]

[a] *Department of Urology, Haukeland University Hospital, Bergen, Norway;* [b] *Department of Clinical Medicine, University of Bergen, Bergen, Norway;* [c] *Cancer Registry of Norway, Oslo, Norway;* [d] *Department of Pathology, Haukeland University Hospital, Bergen, Norway;* [e] *Department of Radiology, Haukeland University Hospital, Bergen, Norway*

Article info

Article history:
Accepted April 10, 2018

Associate Editor:
Gianluca Giannarini

Keywords:
Guidelines
Kidney cancer
Partial nephrectomy
Population-based
Radical nephrectomy
Surgery
Survival

Abstract

Background: Guidelines on surgical treatment for kidney cancer (KC) have changed over the last 10 yr. We present population-based data for patients with KC tumors ≤7 cm from 2008 to 2013 to investigate whether surgical practice in Norway has changed according to guidelines.

Objective: To assess the predictors of treatment and survival after KC surgery.

Design, setting, and participants: We identified all surgically treated KC patients with tumors ≤7 cm without metastasis diagnosed during 2008–2013 (2420 patients) from the Cancer Registry of Norway.

Outcome measurements and statistical analysis: Relationships with outcomes were analyzed using joinpoint regression, multivariate logistic regression, Kaplan-Meier survival estimates, Cox regression, relative survival (RS), and competing-risk analyses.

Results and limitations: The mean follow-up was 5.2 yr. There was a 28% increase in the number of patients undergoing surgical treatment over the study period. Joinpoint regression revealed a significant annual increase in partial nephrectomy (PN) and a small reduction in radical nephrectomy (RN). PN increased from 43% to 66% for tumors ≤4 cm and from 10% to 18% for tumors of 4.1–7 cm. Minimally invasive (MI) RN increased from 53% to 72% and MI PN from 25% to 64%, of which 55% of procedures were performed with robotic assistance in 2013. The geographical distribution of treatment approaches differed significantly. Both PN and MI approaches were more frequent in high-volume hospitals. Cox regression analysis revealed that PN, age, and Fuhrman grade and stage were independent predictors of survival. There were no significant differences in cancer-specific survival ($p = 0.8$). The 5-yr RS for T1a disease was higher after PN than after RN.

Conclusions: The rate of PN for tumors ≤7 cm increased in the 6-yr study period. MI approaches increased for both RN and PN. This treatment shift coincides with the new guideline recommendations in 2010. The possible better survival for patients undergoing PN compared to RN indicates the importance of following evidence-based guidelines.

Patient summary: The use of partial nephrectomy and minimally invasive surgery for kidney cancer tumors increased in Norway from 2008 to 2013 according to population-based data, coinciding with guideline changes. The study illustrate that adherence to guidelines may improve patient outcomes.

* Corresponding author. Department of Urology, Haukeland University Hospital, P.O. Box 1400, Bergen N-5021, Norway. Tel.: +47 55 972383; Fax: +47 55 972050.
E-mail address: karin.margrethe.hjelle@helse-bergen.no (K.M. Hjelle).

https://doi.org/10.1016/j.euo.2018.04.001
2588-9311/

Check for updates

1. Introduction

In Norway, the incidence of kidney cancer (KC) increased by 52% over the course of one decade (2007–2016) [1], with similar observations in Europe and worldwide [2]. Surgical treatment is still the mainstay of intervention for localized KC. Partial nephrectomy (PN) has oncological outcomes similar to radical nephrectomy (RN) for tumors ≤7 cm [3]. Furthermore, several retrospective studies have suggested that PN patients may achieve better overall survival (OS) [4–7], most likely attributed to lower impairment of renal function. However, recent publications have challenged this possible OS gain for PN over RN, claiming that it is caused by selection bias [8]. Since the early 1990s, the "pure" laparoscopic and later the robot-assisted laparoscopic approach to kidney surgery evolved to complement the RN and PN open approaches. It has been shown that minimally invasive methods (MIMs) have equivalent oncological outcomes to open surgery [9] and add benefits such as less surgical trauma, lower morbidity, and shorter hospital stays [10].

From 2006, the European Association of Urology (EAU) guidelines recommended PN as the standard of care for tumors ≤4 cm and as an option in experienced centers for selected patients with tumors of 4.1–7 cm [11]. In 2010, the EAU recommendation changed significantly, as PN then became the standard of care for all tumors ≤7 cm. Moreover, a laparoscopic approach was recommended for RN if PN was not indicated [12].

On this basis, we aimed to establish updated population-based Norwegian data on KC surgery for tumors ≤7 cm. Furthermore, we evaluated adherence to changing guidelines and the implementation of MIMs and PN. Finally, predictors for treatment and survival after surgery were assessed.

2. Patients and methods

2.1. *Data source, data extraction, exclusions, and quality assurance*

Data sets for all 4465 kidney cancer patients in Norway (ICD-10 code C64) diagnosed during the 6-yr period from 2008 to 2013 were extracted from the Cancer Registry of Norway (CRN) database. Information on reporting and the CRN is provided in the Supplementary material. The data sets consist of demographic, tumor-related, treatment-related, and follow-up (FU)-related variables. Information on kidney function, comorbidity, and complication rates was not available. Data quality assurance and removal of erroneously registered patients ($n = 16$) was performed at the CRN, and has been previously described [13]. Thereafter, data sets for 4449 patients were transferred to an anonymous database for subsequent analyses. Of these, 2420 patients aged >18 yr with N0M0 KC ≤7 cm and surgically treated with PN or RN remained within the data set. Figure 1 shows details for the inclusion and exclusion of patients. In accordance with national regulations, the study did not require informed consent from the patients when performed at the CRN.

2.2. *Definitions used for analyses*

Patients were classified as N0M0 if they had no nodal or distant metastasis at the time of surgery or within 4 mo thereafter. Details on staging and follow-up are described in the Supplementary material. For tumor staging, the 2009 version of the TNM classification was used [14]. Tumor size was based on the histology report, whereas survival and FU were estimated from data received from the Norwegian Cause of Death Registry dated December 31, 2016. Open operations were classified as those that started as open or were converted from a MIM approach to open surgery. Procedures classified as RN started as RNs or were PNs converted to RN during surgery. MIMs included pure laparoscopy, hand-assisted laparoscopy, and robot-assisted laparoscopy.

Norway is subdivided into 19 counties and the health care system is organized in four regional health authorities (HAs): the Northern (NHA), Central (CHA), Western (WHA), and South-Eastern (SHA) HAs. Hospitals performing KC surgery were divided into two groups on the basis of national volume recommendations according to their mean annual surgical volume: low-volume hospitals (LVH) performed <20 KC operations/yr, while high-volume hospitals (HVH) performed ≥20 KC operations/yr [13,15]. Hospitals performing fewer than four KC surgeries during the study were excluded.

2.3. *Statistical analysis*

Standard descriptive statistics were used, with results presented as the mean ± standard error of the mean (SEM). The median and interquartile range (IQR) were used for descriptions of variation within groups. We used *t* tests and χ^2 tests for comparisons of continuous and categorical variables, respectively.

Multiple logistic regression models were established without any preselection of the variables. Survival estimates, OS and cancer-specific survival (CSS) were calculated using the Kaplan-Meier method. Relative survival (RS) was calculated using the Pohar-Perme method [16]. Cox regression was performed to identify predictors of OS, with the hazard ratio (HR) and 95% confidence interval (CI) reported. Conditional probability estimates for death were calculated for different groups with competing risks. Joinpoint regression analysis was carried out using Joinpoint Regression v.4.5.0.1 (https://surveillance.cancer.gov/joinpoint) [17]. Statistical significance was set at $p < 0.05$. Calculations were performed using SPSS v.24.0 (IBM, Armonk, NY, USA) or R software v.3.3.0 (www.r-project.org).

3. Results

3.1. *Patient characteristics*

The mean observation time from surgery to death or last FU was 5.2 yr (median 5.0, range 3.8–6.6). Patients undergoing RN were older (64.8 vs 61.2 yr; $p < 0.001$) and had larger tumors (4.3 ± 0.04 vs 2.7 ± 0.04 cm; $p < 0.001$) than those undergoing PN.

The male/female ratio was 1.9:1. There was no difference between the RN and PN groups for gender ($p = 0.23$) or tumor size ($p = 0.1$). Table 1 lists patient, tumor (including stage, grade, and histopathological subtypes), and treatment characteristics for the whole cohort.

3.2. *Treatment status and changes*

3.2.1. *Nationwide*

There was a 28% overall increase in surgical treatment of patients with a KC tumor ≤7 cm. The number of patients who underwent RN yearly was stable, while the number of patients undergoing PN doubled from 2008 to 2013 (Supplementary Table 1). Joinpoint regression analysis

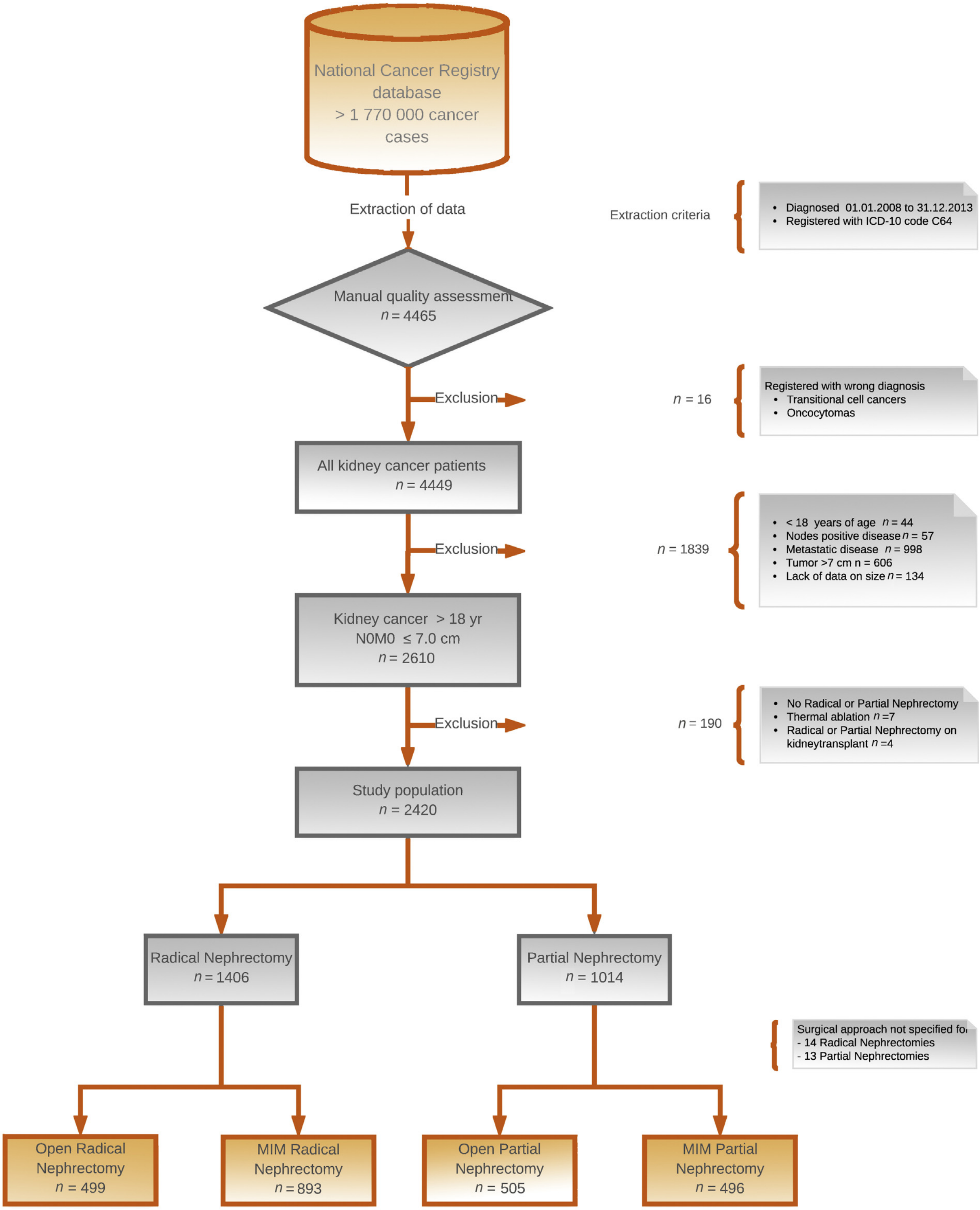


Fig. 1 – Flowchart for data extraction from the main database of the Cancer Registry of Norway according to the inclusion and exclusion criteria. MIM = minimally invasive method.

revealed an increase in the use of PN and a decrease in the use of RN (Fig. 2). Throughout the study period, 58% of tumors ≤4 cm were treated with PN and a significant increase was observed from 2008 to 2013 (43% vs 66%). For tumors of 4.1–7 cm, only 14% were treated with PN, but with an increase from 10% in 2008 to 18% in 2013. The distribution of treatments and time trends are illustrated in Figure 3 and Supplementary Figure 1. In the RN group,

Table 1 – Characteristics of patients with a kidney cancer tumor ≤7 cm (N0M0) surgically treated during 2008–2013

	Overall	RN	PN	*p* value
Patients, *n* (%)	2420 (100)	1406 (58.1)	1014 (41.9)	
Age (yr)				<0.001 [a]
Mean ± SEM	63.3 ± 0.2	64.8 ± 0.3	61.2 ± 0.4	
Median (range)	65 (18–92)	66 (18–92)	63 (18–89)	
Gender, *n* (%)				0.2 [b]
Female	845 (35)	505 (36)	340 (34)	
Male	1575 (65)	901 (64)	674 (66)	
Side, *n* (%)				0.03 [b]
Right	1225 (51)	706	523	
Left	1178 (49)	697	482	
Bilateral	10 (0)	5	5	
Not specified	7 (0)	2	5	
Tumor size (cm)				
Mean ± SEM (median)	3.6 ± 0.03 (3.5)	4.3 ± 0.04 (4.4)	2.65 ± 0.04 (2.5)	<0.001 [a]
≤4 cm (*n* = 1553)	2.6 ± 0.02 (2.5)	3.0 ± 0.03 (2.2)	2.3 ± 0.03 (3.0)	<0.001 [a]
>4 to ≤7 cm (*n* = 867)	5.5 ± 0.03 (5.3)	5.6 ± 0.03 (5.5)	5.0 ± 0.07 (5.0)	<0.001 [a]
Subtype, *n* (%)				<0.001 [b]
Clear cell	1701 (70)	1028 (73)	673 (66)	
Papillary	407 (17)	197 (14)	210 (21)	
Chromophobe	149 (6)	85 (6)	64 (6)	
Multicystic clear cell	76 (3)	35 (2)	41 (4)	
Other kidney cancers	87 (4)	61 (4)	26 (3)	
Fuhrman grade, *n* (%)				<0.001 [b]
1	269 (11)	124 (9)	145 (14)	
2	1314 (54)	742 (53)	572 (56)	
3	544 (23)	366 (26)	178 (18)	
4	61 (2)	50 (3)	11 (1)	
Not specified	232 (10)	124 (9)	108 (11)	
T stage, *n* (%)				<0.001 [b]
pT1a	1497 (62)	614 (44)	883 (87)	
pT1b	716 (30)	604 (43)	112 (11)	
pT3a	193 (8)	174 (12)	19 (2)	
pT3b	9 (0)	9 (1)	0 (0)	
pT4	5 (0)	5 (0)	0 (0)	

RN = radical nephrectomy; PN = partial nephrectomy; SEM = standard error of the mean.
[a] According to a *t* test between the RN and PN groups.
[b] Exact ^{2} test for comparison between the RN and PN groups.

MIM use increased from 52% in 2008 to 72% in 2013. Figure 3 demonstrates the shift in 2010 towards more MIMs. For PN, MIM use increased from 25% to 64% during the study period, and 55% of PNs in 2013 were performed with robotic assistance (vs 7% in 2008). The major shift in the use of PN occurred from 2010 onwards, including a gradual increase in MIM. In 2013, the use of robot-assisted laparoscopic PN (RALPN) surpassed pure laparoscopic PN (Supplementary Table 1). The use of MIM-PN and open partial nephrectomy (OPN) was similar between the age groups (<65 vs ≥65 yr); by contrast, MIM-RN was used significantly more often than open radical nephrectomy (ORN) for patients <65 yr (70% vs 60%; $p = 0.004$).

3.2.2. Regional and county trends

The geographic distribution of PN versus RN and open versus MIMs differed significantly between the regions, as illustrated in Supplementary Figure 2 ($p < 0.001$). RN was used more frequently for patients within the SHA (62%) and NHA (63%) compared to the CHA (55%) and WHA (45%). The most frequent procedure was laparoscopic RN (LRN) in the SHA and OPN in the WHA. In each region, PN increased significantly from the first to the second half of the study period, but differences persisted ($p < 0.03$). The distribution of treatment types by HA and year is shown in Supplementary Figure 2. Patients living in the 19 counties experienced divergent treatment strategies, although with a trend towards an increase in PN use for all counties, as shown in Figure 4.

3.2.3. Hospital trends

The tumor size distribution did not differ between HVHs and LVHs, although HVHs used PN for KC surgery more often than LVHs (44% vs 33%; $p < 0.001$). This was particularly evident for tumors ≤4 cm ($p < 0.001$) but was less pronounced for tumors of 4.1–7 cm ($p = 0.295$). PN use increased from the first to the second period at both HVHs (from 36% to 51%) and LVHs (from 24% to 38%), despite no change in tumor size.

3.3. *Predictors of treatment*

To identify predictors of PN, several factors were entered into a multivariate logistic regression model (Table 2). Younger age, smaller tumor size, HVH, second half of the study period, and WHA and CHA remained independent predictors. Furthermore, the independent predictors of undergoing MIM surgery were female gender, HVH, second half of the study period, and SHA.

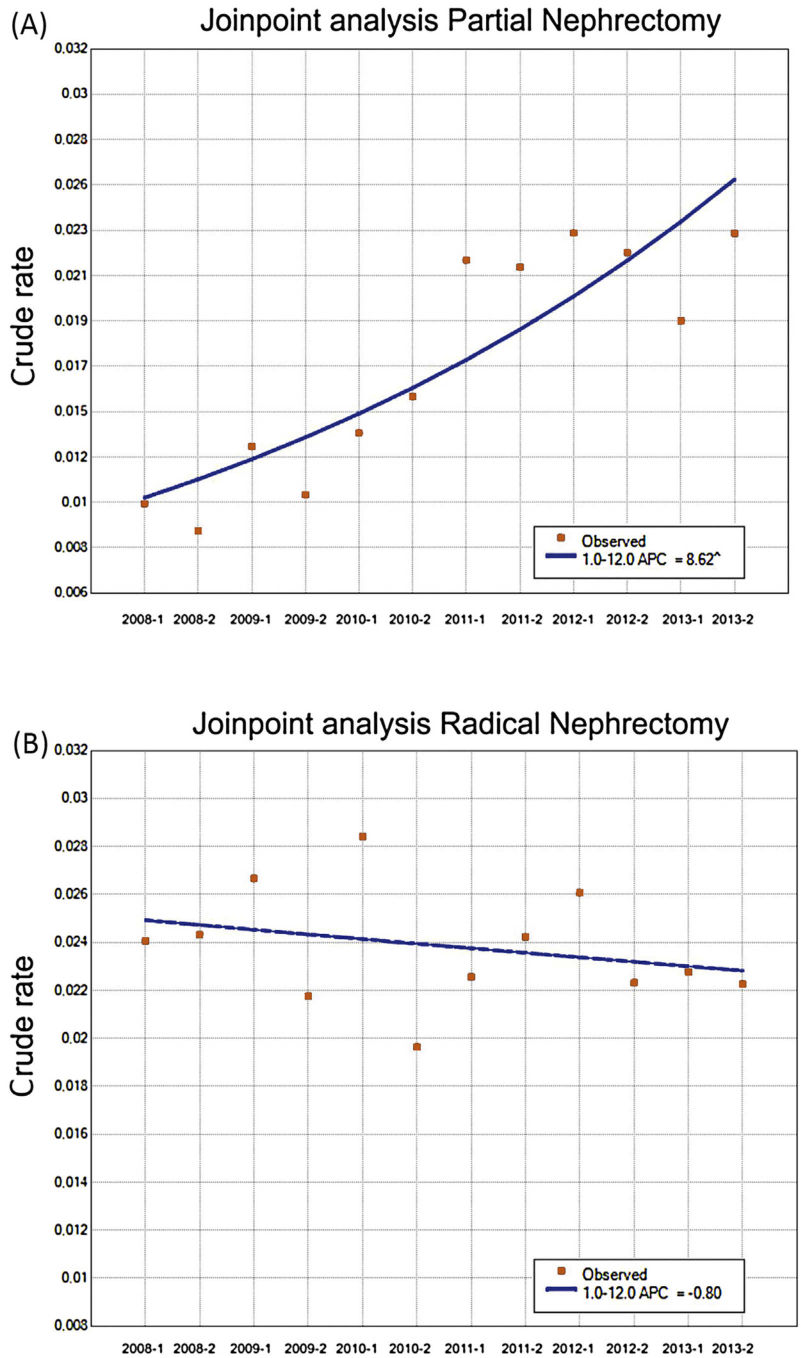


Fig. 2 – Temporal trends in the use of (A) partial nephrectomy and (B) radical nephrectomy for 2420 patients. Data points show the annual frequencies and the trend line demonstrates the joinpoint regression results. The annual percentage change (APC) was significantly different from zero at $\alpha = 0.05$ for partial nephrectomy, indicating a significant increase in this procedure. The small decrease in radical nephrectomy was not statistically significant.

3.4. Survival analyses

Kaplan-Meier plots showed an OS benefit for patients undergoing PN compared to RN (Supplementary Figs. 3 and 4). On Cox regression analysis, PN was an independent predictor of OS, as were age, Fuhrman grade, and T stage (Supplementary Table 2). There was no difference in CSS between PN and RN when stratified for stage ($p = 0.8$). Although the difference is not significant, the 5-yr RS was higher for the PN group (98.1, 95% CI 94.0–99.4) than for the RN group (92.8, 95% CI 88.1–95.7). For T1b tumors the 5-yr RS was 98.8 (95% CI 16.3–100.0) after PN and 90.0 (95% CI 85.1–93.3) after RN. Competing-risks analysis (Fig. 5A) revealed a higher probability of death from competing risks in the RN group, with early separation of the curves for RN and PN. However, after splitting other-cause deaths into other cancers and noncancerous conditions (Fig. 5B), PN and RN patients had a similar probability of death from a

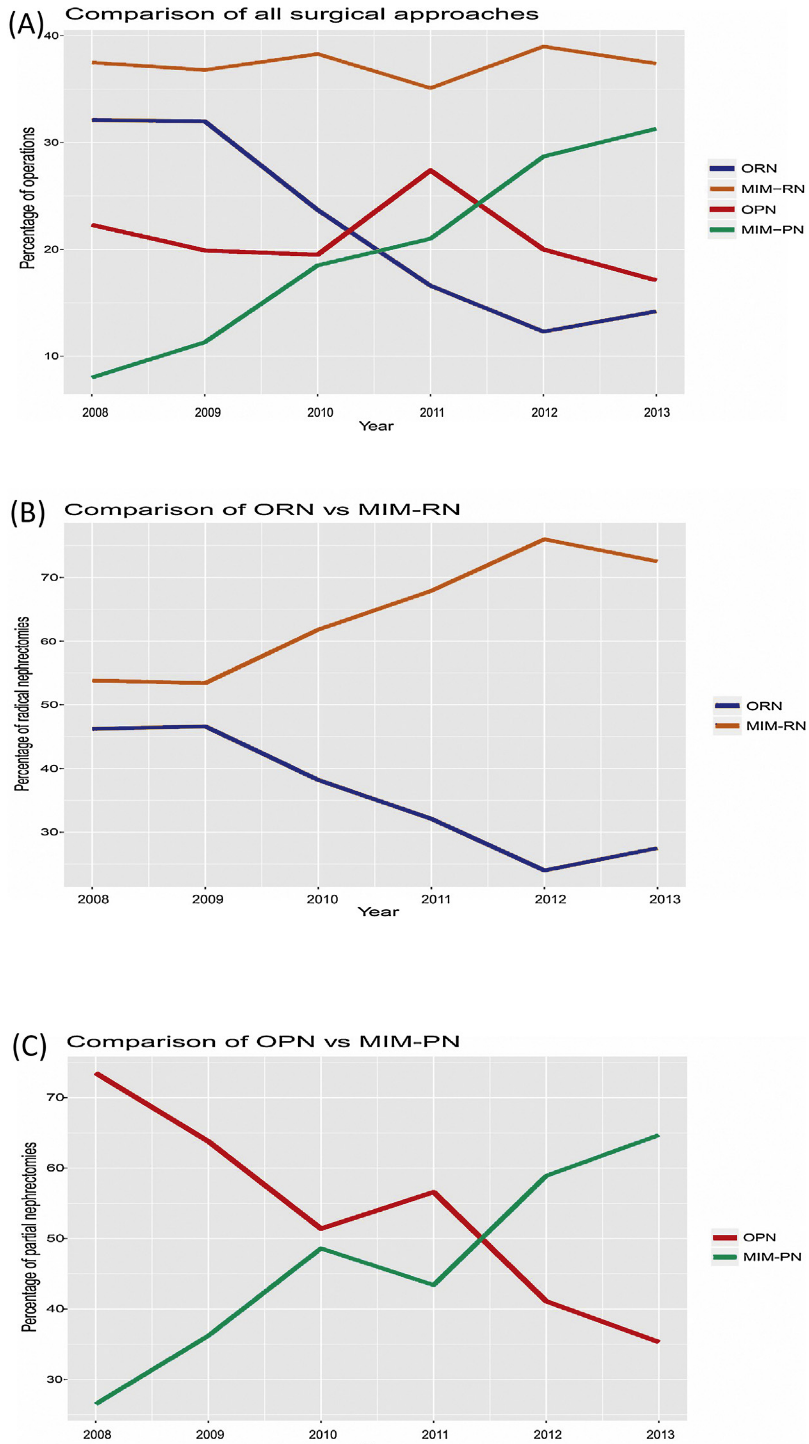


Fig. 3 – Comparison of treatments in terms of percentage of procedures per year. (A) All approaches investigated. (B) Open radical nephrectomy (ORN) versus minimally invasive radical nephrectomy (MIM-RN). (C) Open partial nephrectomy (OPN) versus minimally invasive partial nephrectomy (MIM-PN).

noncancerous condition the first 2 yr before the curves separate, and the competing risks increase for RN patients. Figure 5C shows similar separation of the curves comparing death from all cancers to death for noncancerous conditions.

4. Discussion

The present study clearly demonstrates that the field of KC surgical care and management is rapidly changing. Over the past 20 yr the toolbox for personalized surgical treatment of

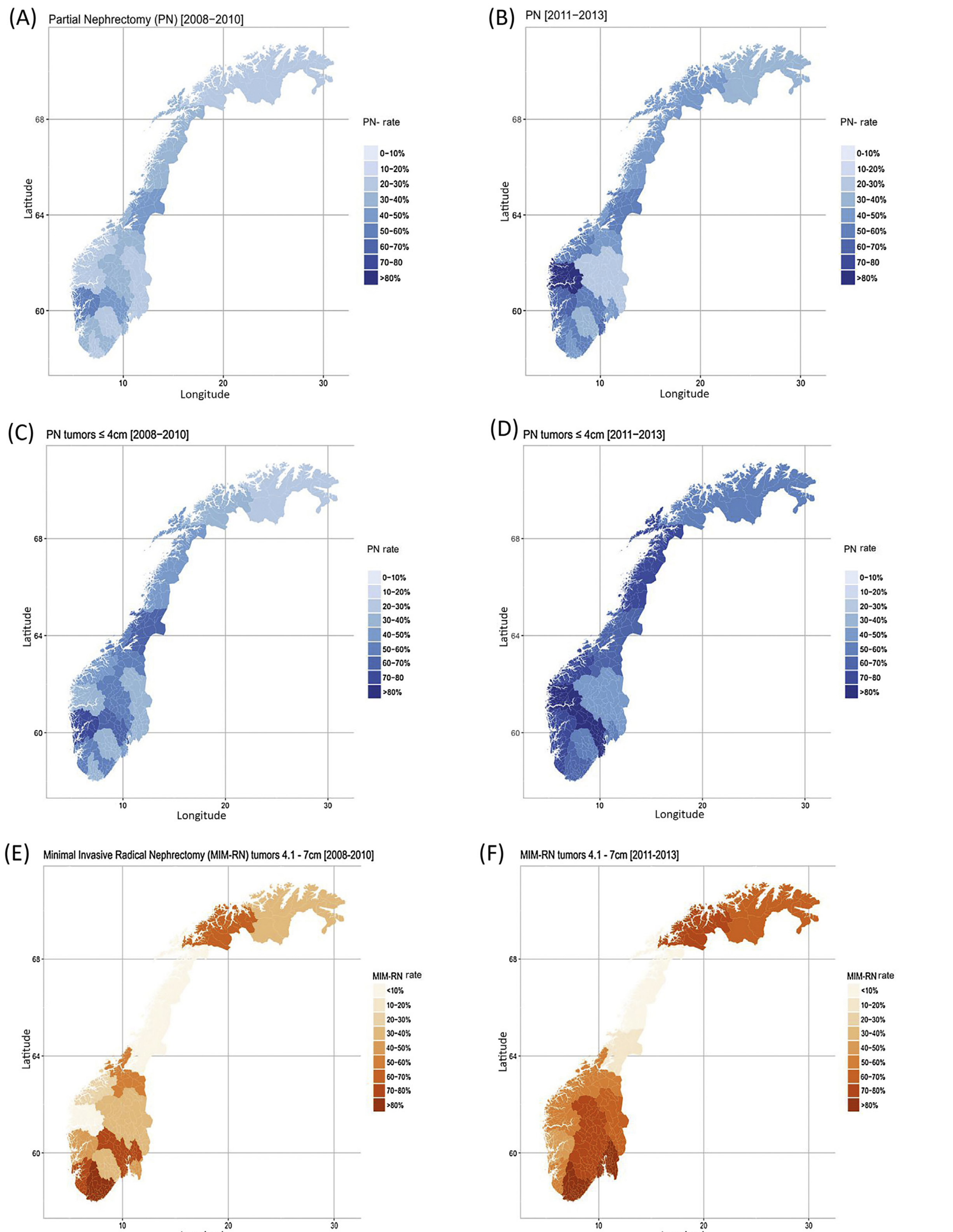


Fig. 4 – Distribution and changes in treatment in the 19 counties in Norway in the first half (2008–2010) and second half (2011–2013) of the study period. PN during (A) 2008–2010 and (B) 2011–2013. (C) PN for tumors ≤4 cm during (C) 2008–2010 and (D) 2011–2013. MIM-RN for tumors of 4.1–7 cm during (E) 2008–2010 and (F) 2011–2013. MIM includes pure laparoscopic, hand-assisted, and robot-assisted laparoscopic methods. Overall, the variation in PN among counties ranged from 26% to 59%. The variation in PN rate ranged from 36% to 77% for tumors ≤4 cm and from 2% to 28% for tumors of 4.1–7 cm (data not shown). Counties with a PN rate of <25% PN in 2008 doubled the PN rate in 2013, whereas counties with a PN rate of 25–40% in 2008 increased this to approximately 60% in 2013. Four of the 19 counties generally used PN more often than RN during the study period. From the first to the second half of the study, the use of MIM-RN for tumors of 4.1–7 cm became more widespread. PN = partial nephrectomy; MIM-RN = minimally invasive radical nephrectomy.

Table 2 – Multiple logistic regression analyses to predict PN and MIM in surgically treated kidney cancer patients

Variable	PN vs RN (n = 2420)		MIM vs open (n = 2396)	
	OR (95% CI)	p value	OR (95% CI)	p value
Age (continuous in years)	0.97 (0.96–0.98)	<0.001	0.99 (0.99–1.00)	0.6
Gender (male vs female)	1.20 (0.97–1.39)	0.20	0.81 (0.67–0.98)	0.03
Tumor size (continuous in cm)	0.42 (0.39–0.45)	<0.001	1.02 (0.96–1.07)	0.6
Year of diagnosis		<0.001		<0.001
2008–2010	1.00 (reference)		1.00 (reference)	
2011–2013	2.17 (1.73–2.58)	<0.001	1.93 (1.61–2.31)	<0.001
Hospital volume		<0.001		<0.001
<20 procedures per year	1.00 (reference)		1.00 (reference)	
≥20 procedures per year	1.87 (1.45–2.46)	<0.001	2.2 (1.78–2.88)	<0.001
Regional Health Authority		<0.001		<0.001
South-Eastern	1.00 (reference)		1.00 (reference)	
Western	3.0 (2.26–3.89)	<0.001	0.20 (0.16–0.25)	<0.001
Central	2.1 (1.55–2.75)	<0.001	0.44 (0.34–0.56)	<0.001
Northern	1.2 (0.84–1.73)	0.3	0.13 (0.09–0.18)	<0.001

PN = partial nephrectomy; RN = radical nephrectomy; MIM = minimally invasive method; OR = odds ratio; CI = confidence interval.

renal tumors has expanded. In the past, most urology surgeons had one standard open surgical procedure for all, but today urologists face multiple choices regarding both the surgical approach (standard, single site, hand-assisted, or robot-assisted laparoscopy) and tumor removal (RN vs PN). Moreover, ablative treatments and surveillance could be appropriate alternatives. In this changing landscape, evidence-based guidelines are important contributors in helping to choose the best treatment for individual KC patients. One of the important changes demonstrated in this study is the marked increase in PN following the major change in the EAU recommendation for PN in 2010. The overall use of PN in Norway increased from 31% to 49% between 2008 and 2013. The implementation was greatest for tumors ≤4 cm (66% in 2013), but was also substantial for tumors of 4.1–7 cm (18% in 2013). This is in line with current evidence-based knowledge on the surgical treatment of localized KC tumors of ≤7 cm, which advocates PN rather than RN whenever feasible [12]. The current data show that use of PN in Norway is comparable to recent Dutch and Swedish population-based data. In the Dutch study, the use of PN was 62% for T1a and 30% for T1b tumors in 2014, while in the Swedish study it was 53% for T1a and 9% T1b tumors in 2011 [18,19]. Similar data are also available from the USA [20,21].

Similar to the more widespread adoption of PN, MIM use has also increased. This trend is evident for both MIM-RN and MIM-PN. MIM is popular among patients because of lower perioperative morbidity and better cosmetic results [22]. In studies on quality of life after KC surgery, laparoscopic procedures performed better than open surgery [23]. Pure laparoscopic PN is a more challenging procedure than LRN. It requires considerable surgical expertise, which may have limited its implementation. The learning curve for RALPN seems shorter than for pure laparascopic PN [24], and RALPN is also favorable in terms of complications, conversions, and ischemia time [25]. Costs for the purchase and maintenance of the robotic platform are considerable, and therefore acquisition is not warranted in every hospital [26,27]. However, when RALPN is available, it increases the adoption of PN [27,28].

The data from the first half of the present study reflect the EAU recommendation of PN as an established treatment, and national guidelines calling for all tumors ≤4 cm to be evaluated for PN before treatment [11,29]. These guidelines offer great latitude for individual surgeons to decide on

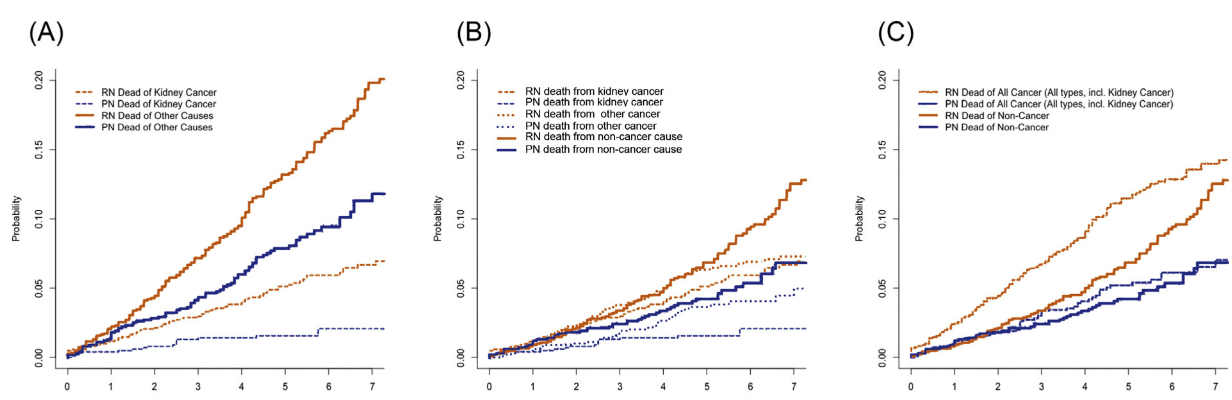


Fig. 5 – Competing-risks analysis for partial nephrectomy (PN) and radical nephrectomy (RN). Probability of death (A) from kidney cancer versus death from all other causes; (B) from kidney cancer versus other cancers and noncancerous conditions; and (C) from all cancers (including kidney cancers) versus noncancerous conditions.

treatment according to their own preferences. The important change in the 2010 edition of the EAU guidelines was the recommendation of PN "whenever possible" and of whether or not to perform LRN on T1 tumors suitable for PN [12]. This recommendation probably made the decision to continue performing open RN for all tumors more difficult for LVHs. The present study demonstrates that regional discrepancies were less pronounced in 2013 than earlier, and that the regional treatment patterns seem to have equalized. More imperative recommendations might have been a key to this change. It has been demonstrated that surgeons interpret terms such as "if technically feasible" differently. In a survey among American urologists, the willingness to offer PN depended on the surgeon's preferences, skill, experience, practice setting, renal tumor caseload, and percentage PN, rather than just on tumor size and complexity [30]. In a Canadian study, high-volume surgeons predicted MIM and academic status predicted PN [31]. Our study lacks data at the surgeon level, but obviously more imperative guidelines force changes in management. This could occur with uptake of new methods or referral to larger centers. The hospital volume effect has been discussed in several publications, and influences the type of surgery, perioperative complications, morbidity, and mortality [19,30–32]. In our study, we also found that HVHs were independent predictors of PN. Overall, the present study indicates that the Norwegian urology community seems to have adapted relatively quickly to changing guidelines.

In line with other authors [7,19], we found that Norwegian patients treated with PN experienced better OS and RS and that PN independently predicted OS.

Earlier publications have partly related this to better preserved renal function, as chronic renal insufficiency represents a dose-dependent risk factor for cardiovascular diseases and events, risk of hospitalization, and mortality from any cause [4]. However, a meta-analysis by Wang et al [33] did not indicate that PN reduced the rate of cardiovascular events.

Newer findings indicate that only selected groups of patients presenting with preoperative chronic kidney disease (CKD) or concomitant comorbidity benefit from PN [34,35] and that worsening of already existing CKD is faster and more pronounced after RN than after PN, possibly leading to more subsequent deaths among RN patients. The additional contribution of medically induced CKD to outcome when compared to surgically induced CKD is also important [36].

There is an ongoing debate on whether the OS gain after PN is caused by selection bias [37]. Even though our study is population-based, selection bias and unmeasured confounders might be present, and should be kept in mind when considering the degree of survival benefit for PN, as discussed by others [8,37]. However, our competing-risks analysis demonstrates that it takes approximately 2 yr before the noncancer mortality rates for PN and RN separate, indicating a lesser degree of selection bias in this group of patients. On the basis of our data, we cannot rule out that the less steep noncancer mortality rate is partly due to improved renal function, but further research is warranted.

The present study is not without limitations. The CRN register data do not include information about tumor localization and complexity, renal function, or clinical data such as Charlson comorbidity scores and postoperative complications. Since hospitals were anonymous, as was surgeon experience, practice setting, and annual caseload, their influence on selection and diffusion of treatment could not be evaluated.

5. Conclusions

In Norway, the rate of PN for KC tumors $\leq$7 cm increased over the study period. For both RN and PN, the rates of open surgery decreased while the rate of MIM approaches increased. The rise in PN observed coincides with the new guidelines recommendations in 2010.

In general, KC treatment practice in Norway is comparable to that in other countries, but with divergent regional practice patterns. Patients undergoing PN for KC tumors $\leq$7 cm may have better OS and RS compared to similar RN patients, which supports the importance of following evidence-based guidelines.

Author contributions: Karin M. Hjelle had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Hjelle, Beisland, Johannesen.
Acquisition of data: Hjelle, Johannesen.
Analysis and interpretation of data: Hjelle, Beisland, Reisæter.
Drafting of the manuscript: Hjelle.
Critical revision of the manuscript for important intellectual content: Hjelle, Beisland, Bostad, Johannesen.
Statistical analysis: Hjelle, Beisland, Johannesen, Reisæter.
Obtaining funding: None.
Administrative, technical, or material support: None.
Supervision: Beisland, Johannesen.
Other: None.

Financial disclosures: Karin M. Hjelle certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.eururo.2016.04.035.

References

[1] Cancer Registry of Norway. Cancer in Norway 2016—cancer incidence, mortality, survival and prevalence in Norway. www.kreftregisteret.no/globalassets/cancer-in-norway/2016/cin-2106.pdf.

[2] Bray F, Ferlay J, Laversanne M, et al. Cancer incidence in five continents: inclusion criteria, highlights from volume X and the global status of cancer registration. Int J Cancer 2015;137:2060–71.

[3] MacLennan S, Imamura M, Lapitan MC, et al. Systematic review of oncological outcomes following surgical management of localised renal cancer. Eur Urol 2012;61:972–93.
[4] Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004;351:1296–305.
[5] Ljungberg B, Hedin O, Lundstam S, et al. Nephron sparing surgery associated with better survival than radical nephrectomy in patients treated for unforeseen benign renal tumors. Urology 2016;93(Suppl C):117–23.
[6] Capitanio U, Terrone C, Antonelli A, 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;67:683–9.
[7] Mashni JW, Assel M, Maschino A, et al. New chronic kidney disease and overall survival after nephrectomy for small renal cortical tumors. Urology 2015;86:1137–45.
[8] Shuch B, Hanley J, Lai J, et al. Overall survival advantage with partial nephrectomy: a bias of observational data? Cancer 2013;119:2981–9.
[9] Lane BR, Gill IS. 7-Year oncological outcomes after laparoscopic and open partial nephrectomy. J Urol 2010;183:473–9.
[10] MacLennan S, Imamura M, Lapitan MC, et al. Systematic review of perioperative and quality-of-life outcomes following surgical management of localised renal cancer. Eur Urol 2012;62:1097–117.
[11] Ljungberg B, Hanbury DC, Kuczyk MA, et al. EAU guidelines on renal cell carcinoma 2006. European Association of Urology 2006;1–26.
[12] Ljungberg B, Cowan NC, Hanbury DC, et al. EAU guidelines on renal cell carcinoma: the 2010 update. Eur Urol 2010;58:398–406.
[13] Hjelle K, Johannesen T, Beisland C. Postoperative 30-day mortality rates for kidney cancer are dependent on hospital surgical volume: results from a Norwegian population-based study. Eur Urol Focus 2017;3:300–7.
[14] Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. AJCC cancer staging manual. ed 7. New York, NY: Springer-Verlag; 2010.
[15] Gard M, Tveit K, Hafstad A. Kreftkirurgi i Norge (Cancer Surgery in Norway). Oslo, Norway: Helsedirektoratet (The Norwegian Directorate of Health); 2015.
[16] Perme MP, Stare J, Estève J. On estimation in relative survival. Biometrics 2012;68:113–20.
[17] Kim H, Fay M, Feuer E, Midthune D. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 2000;19:335–51.
[18] Aben KKH, Osanto S, Hulsbergen-van de Kaa CA, Soetekouw PM, Stemkens D, Bex A. Adherence to guideline recommendations for management of clinical T1 renal cancers in the Netherlands: a population-based study. World J Urol 2016;34:1053–60.
[19] Ljungberg B, Gudmundsson E, Christensen S, Lundstam S. Practice patterns for the surgical treatment of T1 renal cell carcinoma: a nationwide population-based register study. Scand J Urol 2014;48:445–52.
[20] Yang G, Villalta JD, Meng MV, Whitson JM. Evolving practice patterns for the management of small renal masses in the USA. BJU Int 2012;110:1156–61.
[21] Dulabon LM, Lowrance WT, Russo P, Huang WC. Trends in renal tumor surgery delivery within the United States. Cancer 2010;116:2316–21.
[22] Gill IS, Kavoussi LR, Lane BR, et al. Comparison of 1,800 laparoscopic and open partial nephrectomies for single renal tumors. J Urol 2007;178:41–6.
[23] Beisland E, Beisland C, Hjelle KM, Bakke A, Aarstad AK, Aarstad HJ. Health-related quality of life, personality and choice of coping are related in renal cell carcinoma patients. Scand J Urol 2015;49:282–9.
[24] Hanzly M, Frederick A, Creighton T, et al. Learning curves for robot-assisted and laparoscopic partial nephrectomy. J Endourol 2015;29:297–303.
[25] Choi JE, You JH, Kim DK, Rha KH, Lee SH. Comparison of perioperative outcomes between robotic and laparoscopic partial nephrectomy: a systematic review and meta-analysis. Eur Urol 2015;67:891–901.
[26] Wallis CJD, Garbens A, Chopra S, Gill IS, Satkunasivam R. Robotic partial nephrectomy: expanding utilization, advancing innovation. J Endourol 2017;31:348–54.
[27] Kardos SV, Gross CP, Shah ND, et al. Association of type of renal surgery and access to robotic technology for kidney cancer: results from a population-based cohort. BJU Int 2014;114:549–54.
[28] Sivarajan G, Taksler GB, Walter D, Gross CP, Sosa RE, Makarov DV. The effect of the diffusion of the surgical robot on the hospital-level utilization of partial nephrectomy. Med Care 2015;53:71–8.
[29] Beisland C, Bostad L, Klepp O, Heinrich D. Nasjonalt handlingsprogram og oppfølging av pasienter med nyrecellekreft (Norwegian national guidelines for patients with kidney cancer). Oslo, Norway: Sosial- og Helsedirektoratet; 2007.
[30] Weight CJ, Crispen PL, Breau RH, et al. Practice-setting and surgeon characteristics heavily influence the decision to perform partial nephrectomy among American Urologic Association surgeons. BJU Int 2013;111:731–8.
[31] Yap SA, Alibhai SMH, Margel D, Abouassaly R, Timilshina N, Finelli A. A population-based study of surgeon characteristics associated with the uptake of contemporary techniques in renal surgery. Can Urol Assoc J 2013;7:E576–81.
[32] Patel MI, Strahan S, Bang A, Vass J, Smith DP. Predictors of surgical approach for the management of renal cell carcinoma: a population-based study from New South Wales. ANZ J Surg 2017;87:E193–8.
[33] Wang Z, Wang G, Xia Q, et al. Partial nephrectomy vs. radical nephrectomy for renal tumors: a meta-analysis of renal function and cardiovascular outcomes. Urol Oncol 2016;34, 533.e511–9.
[34] Woldu SL, Weinberg AC, Korets R, et al. Who really benefits from nephron-sparing surgery? Urology 2014;84:860–8.
[35] Larcher A, Capitanio U, Terrone C, et al. Elective nephron sparing surgery decreases other cause mortality relative to radical nephrectomy only in specific subgroups of patients with renal cell carcinoma. J Urol 2016;196:1008–13.
[36] Lane BR, Campbell SC, Demirjian S, Fergany AF. Surgically induced chronic kidney disease may be associated with a lower risk of progression and mortality than medical chronic kidney disease. J Urol 2013;189:1649–55.
[37] Tobert CM, Riedinger CB, Lane BR. Do we know (or just believe) that partial nephrectomy leads to better survival than radical nephrectomy for renal cancer? World J Urol 2014;32:573–9.