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Extreme obesity does not predict poor cancer outcomes after surgery for renal cell cancer

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Abstract

Objective—To assess whether extreme obesity (body mass index [BMI] ≥ 40 kg/m²) is associated with peri-operative outcomes, overall survival (OS), cancer-specific survival (CSS), or recurrence-free survival (RFS) after surgical treatment for renal cell carcinoma (RCC).

Patients and Methods—After institutional review board approval, we used an institutional database to identify patients treated surgically between January 2000 and December 2014 with a pathological diagnosis of RCC. Comprehensive clinical and pathological data were reviewed. Kaplan–Meier analyses were used to estimate OS, RFS and CSS. Univariate and multivariate Cox proportional hazards analysis was used to evaluate associations with OS, CSS and RFS in patients with extreme obesity, among other known predictive variables.

Results—In all, 100 patients (11.9%) with a BMI ≥ 40 kg/m² and 743 patients (88.1%) with a BMI < 40 kg/m² who were treated surgically for RCC were identified. Morbid obesity was not associated with an increased risk of blood transfusion (odds ratio [OR] 1, 95% confidence interval [CI] 0.587–1.70; $P = 1.0$). The median (interquartile range) length of hospital stay (LOS) was 4 (3–6) days. Morbid obesity was not associated with longer LOS ($P = 0.26$) or 30-day hospital readmission rates ($P = 1.0$). Major complications (Clavien $\geq 3a$) were recorded in 67 patients (7.95%). BMI ≥ 40 kg/m² was not a predictor of major complications (OR 0.58, 95% CI 0.227–1.47; $P = 0.251$) or 90-day mortality ($P = 0.4067$). BMI ≥ 40 kg/m² was not associated with worse OS ($P = 0.7$), CSS ($P = 0.2$) or RFS ($P = 0.5$). BMI ≥ 35 kg/m² was also not associated with worse OS, CSS or RFS ($P = 0.3, 0.1, 0.5$, respectively). The 5-year OS rate was 68.9% for the entire cohort, including 69 and 70% for patients with BMI < 40 kg/m² and BMI ≥ 40 kg/m², respectively ($P = 0.69$). The 5-year CSS was 79.5% for the entire cohort, including 78.4 and 87.9% ($P = 0.16$) for patients with BMI < 40 kg/m² and BMI ≥ 40 kg/m², respectively. The 5-year RFS rates for BMI < 40 kg/m² and BMI ≥ 40 kg/m² were 84.1 and 90.6%, respectively ($P = 0.48$).

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Conflict of Interest

None declared.

Conclusions—Extreme obesity is not associated with worse peri-operative or cancer outcomes after surgery for RCC. Surgery should remain a standard treatment option in well selected morbidly obese patients.

Keywords

renal cell carcinoma; morbid obesity; class 3 obesity; obesity

Introduction

Obesity has been suggested as a risk factor for developing RCC because of the high prevalence of obesity in patients with RCC compared with the general population [1]. In addition, a large prospective cohort study identified obesity as a risk factor for increased cancer mortality in many types of cancer, including RCC [2]; however, recent studies have suggested that moderate obesity and higher visceral fat percentages in patients with RCC may actually be associated with improved outcomes [3,4]. Although the relationship between obesity and survival in RCC remains poorly understood, evidence from multiple studies suggests that overweight (body mass index [BMI] 25–29.9 kg/m²) or mildly obese (BMI 30–34.9 kg/m²) patients with RCC have better survival rates when compared with patients with ideal body mass (BMI 20–24.9 kg/m²) [5–7], but few studies have evaluated survival in patients with the most extreme obesity (BMI ≥ 40 kg/m²), despite significant research showing that these patients have the highest prevalence of medical comorbidities and the shortest life expectancies [8].

The overall incidence of morbid obesity (BMI ≥ 40 kg/m²) is rising rapidly in the USA [9], and surgeons will increasingly be faced with the challenges of surgical treatment in extremely obese patients [10]; however, the benefits of surgical RCC treatment must be evaluated carefully in extremely obese patients who potentially may benefit less from more aggressive treatments if survival after surgery is poor. In addition, surgeons must consider that morbidly obese patients may be at higher risk of major complications or mortality after surgery [11,12]. The objective of the present study was to evaluate if morbid obesity (BMI ≥ 40 kg/m²) was associated with worse recurrence, survival or peri-operative outcomes after surgical treatment for RCC.

Materials and Methods

After institutional review board approval, an institutional database was used to identify patients treated surgically between January 2000 and December 2014 who had a pathological diagnosis of RCC. Comprehensive patient information was collected including Charlson comorbidity index CCI (excluding points for age or RCC diagnosis), RENAL nephrometry score [13], 2009 American Joint Committee on Cancer TMN stage, and pathological variables according to International Society of Urological Pathology definitions [14]. BMI definitions for ideal, overweight and obese patients were defined according to previous studies [15]. Overall survival (OS) was measured from the time of RCC surgery until death from any cause. Cancer-specific survival (CSS) was measured as the time interval from surgery until death for all patients diagnosed with metastatic RCC. Recurrence-free

survival (RFS) was defined as the period from surgery until local or as distant disease recurrence. Peri-operative mortality and complications occurring within 90 days of surgery were classified according to the Clavien–Dindo system [16] (major complications designated as 3a). Peri-operative transfusions and hospital readmission were defined as occurring within 30 days after surgery.

Kaplan–Meier analyses were used to estimate OS, RFS and CSS. Univariate and multivariate Cox proportional hazards models were used to evaluate the associations of each prognostic variable with OS, RFS and CSS. Univariate and multivariate logistic regression was used to evaluate associations of prognostic variables with major complications. Predictors of hospital readmission and length of hospital stay (LOS) were evaluated using Wilcoxon rank-sum tests and Spearman correlation coefficients, and a general linear model was used to perform multivariate analysis when appropriate. A P value < 0.05 was considered to indicate statistical significance and SAS 9.4 software (SAS Institute, Cary, NC, USA) was used for all analyses.

Results

A total of 843 patients were treated surgically for RCC during the study period, including 100 patients (11.9%) with a BMI ≥ 40 kg/m². Clinical and pathological characteristics for all patients are shown in Table 1. Morbidly obese patients were more likely to be younger ($P = 0.001$), have lower grade tumours ($P < 0.001$) and less likely to have distant metastatic disease at presentation ($P = 0.02$). For the entire cohort, the median (interquartile range [IQR]) nephrometry score was 9 (7–10), and the median CCI was 2 (1–3). Laparoscopic or robot-assisted approaches were used in 395 patients (46.9%), while 448 patients (53.1%) were treated using open surgical approaches. Lymph node dissection was performed in 84 patients (10.0%). A greater number of patients were treated in the more recent 7 years (2008–2014) than in the first 8 years (2000–2007) of the study period (459 vs 384 patients; $P = 0.01$). The median (IQR) follow-up was 26.8 (7.6–65.2) months.

Mortality from RCC was identified in 127 patients (15.1%). The 5-year CSS was 79.5% for the entire cohort, including 78.4 and 87.9% ($P = 0.16$) for patients with BMI < 40 kg/m² and BMI ≥ 40 kg/m² respectively (Fig. 1). BMI ≥ 40 kg/m² was not associated with worse CSS, $P = 0.16$ (Table 2). Independent predictors of CSS included metastatic RCC at presentation (hazard ratio [HR] 7.4, 95% CI 4.0–13.3; $P < 0.0001$) and tumour grade 4 (HR 3.0, 95% CI 1.1–8.4; $P = 0.03$).

Mortality from any cause was identified in 225 patients (26.8%). The 5-year OS was 68.9% for the entire cohort including 69 and 70%, for patients with BMI < 40 kg/m² and BMI ≥ 40 kg/m², respectively ($P = 0.69$). Morbid obesity was not associated with worse OS ($P = 0.69$; [Table 3]).

Independent predictors of OS included: age (HR 1.04, 95% CI 1.02–1.05; $P < 0.001$), distant metastases (HR 3.2, 95% CI 2.0–5.3; $P < 0.001$), tumour grade (HR 1.7, 95% CI 0.9–3.0; $P = 0.03$) and CCI (HR 1.1, 95% CI 1.0–1.2; $P = 0.007$).

Of 725 patients without evidence of nodal or distant metastases at the time of surgery, 74 (10.2%) subsequently developed cancer recurrence. The 5-year RFS rates for BMI < 40 kg/m² and BMI ≥ 40 kg/m² were 84.1 and 90.6%, respectively ($P = 0.48$ [Fig. 2]). Multivariate analysis identified tumour grade (HR 4.7, 95% CI 1.4–16.4; $P = 0.01$), the presence of tumour thrombus (HR 4.6, 95% CI 1.3–15.9; $P = 0.02$), and RENAL nephrometry score (HR 1.3, 95% CI 1.0–1.6; $P = 0.02$) as independent predictors of RCC recurrence (Table 4).

Extended evaluation of BMI and survival outcomes

We also evaluated BMI as a continuous variable and it was not associated with cancer-specific mortality ($P = 0.08$), any-cause mortality ($P = 0.35$) or cancer recurrence ($P = 0.46$). Defining extreme obesity as BMI ≥ 35 kg/m² ($n = 200$, 23.7%) was not associated with worse cancer mortality ($P = 0.11$), any-cause mortality ($P = 0.69$) or cancer recurrence ($P = 0.76$). Finally, three cohorts BMI < 25 kg/m², BMI 25–29.9 kg/m², and BMI ≥ 30 kg/m² were compared and there was no association with cancer mortality ($P = 0.06$), any-cause mortality ($P = 0.15$), or cancer recurrence ($P = 0.36$). Patient characteristics and peri-operative outcomes for these cohorts are shown in Supporting Information Tables 1 and 2.

Peri-operative outcomes

Overall, 160 patients (19.1%) received peri-operative blood transfusion; 10.7% for 682 patients without venous thrombus. Morbid obesity was not associated with an increased risk of transfusion (OR 1, 95% CI 0.587–1.70; $P = 1.0$). After multivariate analysis, a laparoscopic or robot-assisted approach (OR 0.16, 95% CI 0.085–0.296; $P < 0.001$), stage T4 (OR 9.4, 95% CI 2.01–43.74; $P < 0.001$), presence of tumour thrombus (OR 3.2, 95% CI 1.58–6.54; $P = 0.001$), and age (OR 1.04, 95% CI 1.01–1.06; $P = 0.001$) were associated with risk of receiving blood transfusion.

The median (IQR) LOS was 4 (3–6) days. Morbid obesity was not associated with longer LOS ($P = 0.26$). Independent predictors of LOS after multivariate analysis included open surgical approach ($P < 0.001$), extended lymph node dissection ($P = 0.01$), age ($P < 0.001$) and tumour thrombus ($P = 0.003$). A total of 42 patients (5.0%) were readmitted to the hospital within 30 days of surgical discharge. Morbid obesity was not associated with higher readmission rates ($P = 1.0$). A greater number of comorbidities measured using CCI was the only predictive factor for hospital readmission on multivariate analysis (OR 1.2, 95% CI 1.08–1.39; $P = 0.001$).

Major complications and peri-operative mortality

Major complications (Clavien ≥ 3a) were recorded in 67 patients (7.95%). The most common major complications were cardiac (2.1%), pulmonary (1.9%) and renal (1.3%). BMI ≥ 40 kg/m² was not a predictor of major complications (OR 0.58, 95% CI 0.227–1.47; $P = 0.251$). After multivariable analysis, independent predictors of major complications (Table 4) included the presence of tumour thrombus (OR 2.9, 95% CI 1.72–5.01; $P < 0.001$) and CCI (OR 1.2, 95% CI 1.08–1.32; $P = 0.001$). There was no difference in 90-day mortality ($P = 0.407$) for patients with BMI ≥ 40 kg/m² (3/100; 3.0%) vs patients with BMI < 40 kg/m² (12/743; 1.6%).

Peri-operative outcomes were also considered using a threshold of BMI ≥ 35 kg/m² (200 patients) vs <35 kg/m² (643 patients). Similarly, there was no association with BMI ≥ 35 kg/m² and risk of major complications, peri-operative transfusion, LOS or hospital readmission ($P = 0.57$, $P = 0.67$, $P = 0.25$ and $P = 0.14$, respectively).

Discussion

Patients with extreme obesity (BMI ≥ 40 kg/m²) have a high incidence of major medical comorbidities and shortened life expectancy [9,17]. Given that the incidence of both RCC [18] and extreme obesity [9] are increasing, urologists will increasingly have to consider the potential benefits of treatment vs the higher risk of surgical and anaesthetic complications in very obese patients [19]. Recent studies have suggested that obesity increases the risk of developing RCC [1], although mild or moderate obesity is not necessarily associated with worse outcomes [4–7, 19–22]. In the present study, we evaluated the largest series to date of RCC patients with extreme obesity, and found similar CSS and recurrence rates when compared with patients with lower body mass. Obesity was not associated with cancer recurrence or mortality using multivariate analysis to consider differences in known predictive factors between groups. Importantly, there was also no difference in peri-operative blood transfusion rate, LOS, readmission rate or major complications after surgery; therefore, surgery should continue to be a standard treatment option for RCC in well selected morbidly obese patients.

The majority of studies that evaluate RCC in obese patients have defined obesity as having a BMI ≥ 30 kg/m² [5,6,21], but this definition may not accurately reflect some patient's overall health or expected longevity [23]. In 2013, a meta-analysis of 2.9 million patients evaluated the association of all-cause mortality with BMI. Interestingly, the authors found no differences in mortality in patients of ideal body weight (BMI 20–24.9 kg/m²) compared with those described as overweight (BMI 25–29.9 kg/m²), or in patients with class 1 obesity (BMI 30–34.9 kg/m²), while mortality rates were higher only in patients with BMI ≥ 35 kg/m² [24]. Life expectancy is clearly shortened in morbidly obese patients, with an estimated 6–14 years of life lost for an individual with BMI ≥ 40 kg/m² [8]; however, previous studies examining the effects of obesity on patients with RCC have not separately analysed morbidly obese patients [4,6], or contain only a small number of patients with BMI ≥ 40 kg/m². Of 1338 patients with RCC, Waalkes et al. [25] reported only 18 patients (1.3%) who had a BMI ≥ 40 kg/m², and Isac et al. [20] only identified 28 morbidly obese patients of 250 obese patients treated with robot-assisted partial nephrectomy. In the present study, 100 patients (11.9%) with BMI ≥ 40 kg/m² were identified, despite a statewide morbid obesity incidence of only 2.8% [26]. This large cohort of morbidly obese patients with RCC provides a unique opportunity for further analysis of the prognostic value of extreme obesity for RCC recurrence and survival.

Multiple studies, including a recent meta-analysis, have suggested that having a higher BMI is associated with improved outcomes in RCC [4,19]; however, the perception of improved survival may be a result of obese patients presenting with more favourable disease characteristics. In the present study, morbidly obese patients with RCC treated with surgery were younger, had lower grade tumours, and were less likely to have metastatic RCC at

presentation, similar to other studies [6,21]. Multivariate analysis was used to independently evaluate predictors of cancer outcomes and the present study did not identify obesity as a predictor of recurrence or cancer mortality, despite considering multiple BMI definitions of obesity and other known predictive variables. Predictors of all-cause and cancer mortality in the present study included the presence of distant metastases and tumour grade, similar to other studies [27]. The presence of venous thrombus, tumour grade and RENAL nephrometry score were independent predictors of cancer recurrence in patients without metastatic disease at presentation. As suggested in previous studies, higher nephrometry scores may be associated with more complex tumours and more aggressive tumour biology [28].

The present study showed no differences in postoperative outcomes, including blood transfusion rates, major complications, hospital readmission within 30 days, and LOS. Importantly, multivariable models were used to evaluate the association of BMI with each outcome to adjust for differences in the baseline characteristics between cohorts, but failed to show worse outcomes in morbidly obese patients. Other studies have reported worse peri-operative outcomes in obese patients [10–12], especially when patients have multiple comorbidities [29]. Although severe obesity is associated with medical comorbidities and shortened life-span [8], obesity itself is not independently predictive of worse peri-operative outcomes. Morbidly obese patients without serious comorbidities, therefore, can be expected to have equivalent major peri-operative outcomes compared with other patients with RCC treated surgically.

The presence of extreme obesity is rapidly rising in the USA [8,9]. The present study shows that patients with BMI ≥ 40 kg/m² do not necessarily have worse outcomes when treated surgically for RCC. Although multivariate models were used to evaluate differences between patient cohorts, it is certainly possible an unmeasured bias exists because surgeons are likely to select healthier patients for surgery. Other limitations include the retrospective nature of this analysis and possible biases related to study design. More contemporary metrics to measure preoperative fitness, such as frailty index [30], may be more useful but are difficult to measure retrospectively. Finally, it is possible that the outcomes observed in the present study will not be generalizable to a community setting because of the significant experience at our institution with treatment of patients with a high BMI.

In conclusion, extreme obesity was not associated with worse survival or recurrence after surgery for RCC. Surgical treatment of RCC is feasible in well selected patients with BMI ≥ 40 kg/m², and RCC treatment outcomes are similar to those in patients with a lower BMI.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations:

BMI	body mass index
OS	overall survival

CSS	cancer-specific survival
RFS	recurrence-free survival
OR	odds ratio
LOS	length of hospital stay
CCI	Charlson comorbidity index
IQR	interquartile range
HR	hazard ratio

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Fig. 1.

(a) Cancer mortality for 843 patients treated surgically for RCC. (b) Cancer mortality for 843 patients treated surgically for RCC, ideal BMI (BMI 20–25) vs BMI ≥ 40 .

Fig. 2.
 (a) Disease recurrence after surgery for 725 non-metastatic RCC patients. (b) Disease recurrence after surgery for 725 non-metastatic RCC patients, ideal BMI (BMI 20–25) vs BMI ≥40.

Table 1

Patient and disease characteristics.

	BMI < 40 kg/m² N = 743	BMI > 40 kg/m² N = 100	P
Median (IQR) age, years	60.3 (51.6–68.9)	56.5 (50–62.6)	0.001
Median BMI, kg/m ²	28.6 (25.3–32.4)	44.3 (41.1–48.9)	
Median CCI	1 (0–2)	1 (0–2)	0.89
Median RENAL nephrometry score	9 (7–10)	9 (7–10)	0.60
Smoking history, <i>n</i> (%)			
Current	140 (19.4)	23 (23.2)	0.50
Never	303 (41.9)	43 (43.4)	
Previous	280 (38.7)	33 (33.3)	
Approach			
Minimally invasive, including laparoscopic and robot-assisted	352 (47.4)	43 (43)	0.46
Open	391 (52.6)	57 (57)	
Type of nephrectomy			
Partial nephrectomy	183 (24.6)	23 (23)	0.80
Radical nephrectomy	560 (75.4)	77 (77)	
Pathological T stage			
T1	428 (57.6)	57 (57)	0.26
T2	85 (11.4)	17 (17)	
T3	216 (29.1)	26 (26)	
T4	14 (1.9)	0	
Tumour nuclear grade			
1	114 (16.2)	24 (25)	0.007
2	316 (44.8)	51 (53.1)	
3	190 (27)	16 (16.7)	
4	85 (12.1)	5 (5.2)	
M1	97 (13.1)	5 (5)	0.02
N1	41 (5.5)	5 (5)	0.30
M0N0	632 (85.1)	93 (93)	0.03
Perinephric/sinus fat invasion	134 (18)	15 (15)	0.58
RCC subtype			
Clear	590 (79.4)	86 (86)	0.14
Non-clear	153 (20.6)	14 (14)	
Venous thrombus			
None	597 (80.4)	85 (85)	0.46
Renal vein	86 (11.6)	9 (9)	
IVC < 2 cm	13 (1.8)	1 (1)	
IVC > 2 cm	28 (3.8)	1 (1)	
IVC below diaphragm	9 (1.2)	1 (1)	
IVC above diaphragm	10 (1.4)	3 (3)	

	BMI < 40 kg/m² N = 743	BMI > 40 kg/m² N = 100	P
2000–2007	340 (45.8)	44 (44)	0.75
2008–2014	403 (54.2)	56 (56)	

BMI, body mass index; CCI, Charlson comorbidity index; IQR, interquartile range; IVC, inferior vena cava.

Table 2
Clinical and pathological variables associated with cancer mortality for 843 patients treated surgically for RCC.

Variable	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
Age	1.01	0.9–1.02	0.06			
CCI	1.4	1.3–1.5	<0.0001	1.03	0.9–1.1	0.4
Smoking status						
Never	Reference					
Prior	1.2	0.8–1.7	0.3			
Current	0.9	0.6–1.5	0.8			
Approach						
Open	Reference			Reference		
Minimally invasive	0.3	0.2–0.5	<0.0001	0.6	0.4–1.1	0.09
Nephrectomy type						
Radical	Reference			Reference		
Partial	0.2	0.1–0.3	<0.0001	0.6	0.2–1.6	0.3
Pathological T stage						
T1	Reference			Reference		
T2	3.9	2.1–7.5		2.1	0.84–5.2	
T3	10.1	6.3–16.2		2.1	0.85–5.9	
T4	22.9	10.5–49.9	<0.0001	2.2	0.69–7.2	0.3
Tumour grade						
1	Reference			Reference		
2	2.2	0.9–4.9		1.3	0.5–3.8	
3	6.6	2.9–14.7		1.9	0.7–5.1	
4	16.9	7.6–38.2	<0.0001	3.3	1.2–9.1	0.01
Tumour thrombus						
None	Reference			Reference		
Present	6.3	4.4–8.9	<0.0001	1.8	1.6–3	0.02
Nodal status						
N0/Nx	Reference			Reference		

Variable	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
N1	8.2	5.3–12.7	<0.0001	1.4	0.8–2.4	0.3
Metastases						
M0	Reference			Reference		
M1	19.9	13.7–29.1	<0.0001	8.9	5.1–15.8	<0.0001
Year of surgery						
2000–2007	Reference					
2008–2014	0.7	0.5–1.1	0.09			
RCC histology						
Clear-cell	Reference					
Non-clear-cell	0.9	0.6–1.5	0.8			
BMI 40 kg/m ²						
No	Reference					
Yes	0.6	0.3–1.2	0.2			
RENAL score	1.4	1.3–1.5	<0.0001	1.03	0.9–1.1	0.4

BMI, body mass index; CCI, Charlson comorbidity index; HR, hazard ratio.

Table 3

Clinical and pathological variables associated with any cause mortality for 843 patients treated surgically for RCC.

Variable	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
Age	1.04	1.02–1.05	<0.0001	1.03	1.01–1.04	<0.0001
CCI	1.3	1.2–1.4	<0.0001	1.1	1.04–1.2	0.002
Smoking status						
Never	Reference					
Prior	1.2	0.9–1.6	0.2			
Current	0.9	0.7–1.3	0.7			
Approach						
Open	Reference			Reference		
Minimally invasive	0.5	0.4–0.7	<0.0001	0.7	0.5–1.1	0.09
Nephrectomy type						
Radical	Reference			Reference		
Partial	0.4	0.3–0.6	<0.0001	0.8	0.5–1.4	0.4
Pathologic T stage						
T1	Reference			Reference		
T2	1.9	1.2–2.9		1.3	0.74–2.4	
T3	3.9	2.9–5.3		1.3	0.8–2.2	
T4	8.1	4.2–15.7	<0.0001	1.4	0.6–3.3	0.7
Tumour grade						
1	Reference			Reference		
2	0.85	0.6–1.3		0.8	0.5–1.3	
3	2.01	1.4–3		1.1	0.7–1.9	
4	4.02	2.6–6.3	<0.0001	1.7	0.9–3.1	0.02
Tumour thrombus						
None	Reference			Reference		
Present	3.8	2.9–4.9	<0.0001	1.6	1.03–2.4	0.03
Nodal status						
N0/Nx	Reference			Reference		

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Variable	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
N1	5.5	3.7–8.1	<0.0001	1.3	0.8–2.2	0.3
Metastases						
M0	Reference			Reference		
M1	7.5	5.6–10.1	<0.0001	3.6	2.2–5.8	<0.0001
Year of surgery						
2000–2007	Reference					
2008–2014	0.8	0.6–1.1	0.2			
RCC histology						
Clear-cell	Reference					
Non-clear-cell	0.9	0.6–1.2	0.5			
BMI < 40 kg/m ²						
No	Reference					
Yes	0.9	0.6–1.4	0.7			
RENAL score	1.2	1.1–1.3	<0.0001	1.02	0.9–1.1	0.6

BMI, body mass index; CCI, Charlson comorbidity index; HR, hazard ratio.

Table 4

Clinical and pathological variables associated with cancer recurrence for 725 non-metastatic patients treated surgically for RCC.

Variable	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
Age	1.02	1–1.04	0.05	1.01	0.9–1.04	0.3
CCI	0.9	0.8–1.1	0.7			
Smoking status						
Never	Reference					
Prior	1.6	0.9–2.5	0.07			
Current	1.5	0.9–2.5	0.14			
Approach						
Open	Reference			Reference		
Minimally invasive	0.6	0.4–0.9	0.03	0.8	0.04–1.5	0.5
Nephrectomy type						
Radical	Reference			Reference		
Partial	0.4	0.2–0.7	0.004	0.8	0.3–2.1	0.6
Pathological T stage						
T1	Reference			Reference		
T2	1.8	0.86–3.9		1.1	0.48–2.7	
T3	5.4	3.3–8.9		0.84	0.25–2.9	
T4	5.6	0.7–41.4	<0.0001	5.6	0.7–46.4	0.4
Tumour grade						
1	Reference			Reference		
2	2.3	0.9–5.9		1.6	0.5–4.6	
3	7	2.7–18.1		3.6	1.2–10.8	
4	11.3	3.9–33.3	<0.0001	4.7	1.3–15.4	0.01
Tumour thrombus						
None	Reference			Reference		
Present	7.9	4.9–12.7	<0.0001	4.8	2.5–9.2	<0.0001
Year of surgery						
2000–2007	Reference					

Variable	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
2008–2014	0.8	0.5–1.4	0.5			
RCC histology						
Clear cell	Reference					
Non-clear-cell	0.8	0.4–1.4	0.4			
BMI 40 kg/m ²						
No	Reference					
Yes	0.8	0.3–1.6	0.5			
RENAL score	1.4	1.3–1.8	<0.0001	1.2	0.9–1.5	0.05

BMI, body mass index; CCI, Charlson comorbidity index; HR, hazard ratio.