Original Article

The association of body composition with postoperative complications and length of hospital stay after radical or partial nephrectomy in patients with renal cell cancer: a multicenter population-based cohort study

Jake S. F. Maurits[1], J. P. Michiel Sedelaar[2], Katja K. H. Aben[1,3], Lambertus A. L. M. Kiemeney[1,2], Alina Vrieling[1]

[1]Department for Health Evidence, Radboud University Medical Center, Nijmegen, The Netherlands; [2]Department of Urology, Radboud University Medical Center, Nijmegen, The Netherlands; [3]Department of Research and Development, Netherlands Comprehensive Cancer Organisation, Utrecht, The Netherlands

Contributions: (I) Conception and design: JSF Maurits, A Vrieling; (II) Administrative support: JSF Maurits, A Vrieling; (III) Provision of study materials or patients: JSF Maurits, KKH Aben; (IV) Collection and assembly of data: JSF Maurits; (V) Data analysis and interpretation: JSF Maurits, JPM Sedelaar, A Vrieling; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Dr. Alina Vrieling. Radboud University Medical Center, Department for Health Evidence (Mailbox 133), P.O. Box 9101, 6500 HB Nijmegen, The Netherlands. Email: Alina.Vrieling@radboudumc.nl.

Background: Body mass index (BMI) and body composition have been associated with postoperative outcomes in oncological surgery. Evidence in renal cell cancer (RCC) is limited and inconsistent. Therefore, we examined BMI and body composition in relation to postoperative outcomes in patients with RCC.

Methods: We conducted a multicenter population-based historical cohort study including 801 patients with RCC treated with radical (79%) or partial (21%) nephrectomy between 2008–2012. Computed Tomography images at third lumbar vertebrae were assessed for skeletal muscle (SM) index, SM density, visceral adipose tissue (VAT) index and subcutaneous adipose tissue index (SATI). Multivariable multilevel logistic regression analyses were used to examine associations between BMI, body composition and (major) postoperative complications and extended length of hospital stay (LOHS) (≥7 days). Discrimination of models for major complications was compared using receiver operating characteristics (ROC) curves.

Results: In total, 19.6% of the patients had postoperative complications (6.2% Clavien grade ≥III) and 24.1% had extended LOHS. A 10-unit increase in SM density was inversely associated with extended LOHS [odds ratio (OR) 0.58; 95% confidence interval (95% CI): 0.44–0.78]. Associations of high BMI and lower SM density with risk of major complications and of higher VAT index with extended LOHS were also observed but statistical significance differed according to surgical procedure. Models predicting major complications with or without body composition parameters were not different.

Conclusions: Lower SM density was associated with extended LOHS and non-significantly associated with higher risk of major postoperative complications. High BMI was associated with higher risk of major postoperative complications. Higher VAT was non-significantly associated with higher risk of extended LOHS. Results by surgical procedure were in the same direction but were only statistically significant for some subgroups. Validation of these results and investigation of the added value of body composition parameters to anatomic classification systems is needed.

Keywords: Renal cell cancer (RCC); surgery; body composition; complications; length of hospital stay (LOHS)

Submitted May 20, 2022. Accepted for publication Oct 14, 2022.
doi: 10.21037/tau-22-367
View this article at: https://dx.doi.org/10.21037/tau-22-367

© Translational Andrology and Urology. All rights reserved.

Introduction

Renal cell cancer (RCC) is the 16th most common cancer worldwide with an estimated 431,000 new cases and 179,000 deaths in 2020 (1). Most stage I–III patients are treated with radical or partial nephrectomy. Cytoreductive nephrectomy was standard practice among low volume stage IV patients and is still being used (2). Patients treated with partial nephrectomy experience less complications than those treated with radical nephrectomy (3). Postoperative complications may require reoperation and reduce patients' quality of life (4). Therefore, it is important to identify factors that are associated with postoperative complications. Currently, anatomic classification systems (e.g., PADUA, R.E.N.A.L.) are advised to predict outcomes. This enables comparisons between partial nephrectomy and other tumor ablation options and helps in treatment planning and patient counseling. However, surgeon experience and other patient features should also be considered (2).

Body mass index (BMI) and body composition features have been hypothesized to be associated with postoperative outcomes. Excess adipose tissue reduces the visual field and operating space, complicating dissection of perinephric fat from the renal capsule (5). Low skeletal muscle (SM) mass and density impairs the immune system, resulting in more (severe) inflammation increasing the risk of postoperative infectious complications (6). Body composition information in cancer patients can be obtained from routinely made CT scans (7). This information includes quantitative measures, i.e., cross-sectional areas of SM, visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT), as well as qualitative measures, i.e., skeletal muscle radiodensity (SMD).

Meta-analyses showed that preoperative CT-determined sarcopenia is related to major postoperative complications in surgical oncological patients (7). However, evidence on body composition and postoperative outcomes in RCC is limited and inconsistent due to high heterogeneity in assessment of body composition parameters, outcomes and effect estimates (5). Therefore, we examined the association of BMI and body composition parameters with postoperative outcomes in patients with RCC in a Dutch multicenter historical cohort study. We present the following article in accordance with the STROBE reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-22-367/rc).

Methods

Study population

A population-based historical cohort study on body composition parameters in relation to postoperative outcomes and survival was conducted in 7 Dutch hospitals. Results on survival have already been published elsewhere (8) and this analysis is focused on postoperative outcomes. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was approved by the Committee for Human Research region Arnhem-Nijmegen (No. CMO 2015-1822), which waived the need for informed consent. All local ethics committees from the participating hospitals provided permission for data collection.

Urologists and radiologists were asked for permission to identify patients in their hospital diagnosed with RCC from the Netherlands Cancer Registry (NCR), held by the Netherlands Comprehensive Cancer Organisation (IKNL). Permission was also asked for collecting CT images obtained preferably before renal surgery and for retrospectively collecting information from medical records by IKNL personnel. Inclusion criteria were as follows: patients should have primary stage I–IV RCC, be diagnosed between 2008 and 2012 and be 18 years of age or older at time of diagnosis. Patients were excluded if they had invasive cancer in the five years preceding RCC diagnosis due to its potential effects on body composition. Unidentifiable patients, duplicate patients and those without any or with unanalyzable CT scan (e.g., too much graining/low contrast or artefacts) were excluded. We also excluded patients without surgical treatment or treated with cryosurgery or radiofrequency ablation, due to small numbers of patients receiving these treatments.

Body composition analysis

A single axial CT image at the third lumbar vertebra (L3) was used to examine body composition parameters (9). Body composition parameters were quantified using Slice-O-Matic 5.0 software (TomoVision), based on density thresholds in Hounsfield units (HU); 29 to +150 for SM, −190 to −30 for SAT, and −150 to −50 for VAT. Total cross-sectional areas were measured in cm^2 for SM, VAT and SAT and mean HU densities were reported for SMD. Incomplete cross-sectional areas of SM and SAT in CT scans (e.g., due to poor positioning or large body size of the patient)

© Translational Andrology and Urology. All rights reserved.

were estimated in MATLAB. Cross-sectional areas were normalized for height squared (m^2) to obtain SMI (cm^2/m^2), subcutaneous adipose tissue index (SATI, cm^2/m^2) and VAT index (VATI, cm^2/m^2) (10). All CT scan analyses were performed by one trained researcher (J.S.F.M.) following a standardized protocol. A small subset (n=30) was analyzed by a second researcher to assess interrater reproducibility by calculating intraclass correlation coefficients (0.992 for SMI, 0.999 for VAT and 0.979 for SAT).

Clinical data collection

Tumor characteristics (clinical and post-surgical tumor, node and metastasis (TNM) stage, Fuhrman grade, morphology) and treatment data (type and date of surgery) were derived from the NCR. Preoperative information [body weight, height, smoking status, American Society of Anesthesiologists (ASA) score] and perioperative information (complications, Clavien Grade classification, date of surgery and date of discharge, surgical blood loss and surgical time) were extracted from medical records by IKNL data managers.

Outcomes

The primary outcome was postoperative complications, categorized as any (Clavien grade ≥II) and major (Clavien grade ≥III) postoperative complications. The secondary outcome was extended length of hospital stay (LOHS). LOHS was calculated as the date from surgery until discharge date, and extended LOHS was categorized at the 75th percentile into <7 and ≥7 days (11).

Statistical analysis

Study population characteristics are presented by type of nephrectomy. Means and standard deviations (SD), medians and interquartile ranges (IQR), or total numbers and percentages are presented where appropriate.

Univariable and multivariable multilevel logistic regression analyses were used to assess the associations of BMI and body composition parameters with any complications (yes *vs.* no), major complications (Clavien grade ≥3 *vs.* no) and LOHS (≥7 *vs.* <7 days).

Associations for BMI were assessed per 1-unit increase and categorized with BMI between 25–30 and >30 kg/m^2 versus BMI <25 kg/m^2. Associations for SMI, SMD, SATI and VATI were assessed per 10-unit increase (continuous model) and using sex-specific medians (dichotomous model). Continuous and dichotomous models were compared using Akaike's Information Criterion (AIC). The combination of having high SMD/high SMI versus having low SMD/low SMI was examined in a subset of patients. Multilevel analyses with random effects for hospitals were used to adjust for cluster effects of the hospital performing the surgery. Since random effects models for major complications did not converge, multilevel analyses with fixed effects for hospitals were used. Multivariable analyses were adjusted for age at diagnosis, sex, stage, ASA score, smoking and mutually adjusted for other body composition parameters. We created receiver operating characteristic (ROC) curves with area under curves (AUC) to assess predictive values of adding body composition parameters to a prediction model (i.e., age, sex, stage and ASA score) for major complications. We used bootstrapping (n=2,000) to obtain 95% confidence intervals (CIs) for the AUCs and bootstrap tests (n=2,000) for testing differences. Multiple imputation was used for missing data, except for ROC curve analyses where a single imputed dataset and a sensitivity analysis on several single imputed datasets was used. We performed three sensitivity analyses. First, we included only stage I–III RCC patients because stage IV *vs.* stage I–III surgeries might be more complicated. Sensitivity analysis including only patients with stage IV was not possible due to the small number of events. Second, we included only patients treated with radical nephrectomy as these might have a higher risk of postoperative complications and extended LOHS compared to patients treated with partial nephrectomy. Third, we performed sensitivity analyses for open and laparoscopic + robot-assisted nephrectomy, separately, as minimally invasive surgery can reduce LOHS, regardless of body composition.

Analyses were executed in R (Windows version 3.6.2, packages "RMS", "pROC", "MICE", "ggplot2").

Results

Study population characteristics

Overall, 801 patients were included (*Figure 1*) of which 630 patients (78.7%) received radical nephrectomy and 171 (21.3%) partial nephrectomy (*Table 1*). Mean age was 63±11.3 years and 499 patients (62.3%) were male. Altogether, 157 patients (19.6%) had postoperative complications, consisting of 107 (68.2%) Clavien grade II and 50 (31.8%) Clavien grade III–V (major) complications. Median LOHS was 4 (IQR 3–6) days and 193 patients

© Translational Andrology and Urology. All rights reserved.

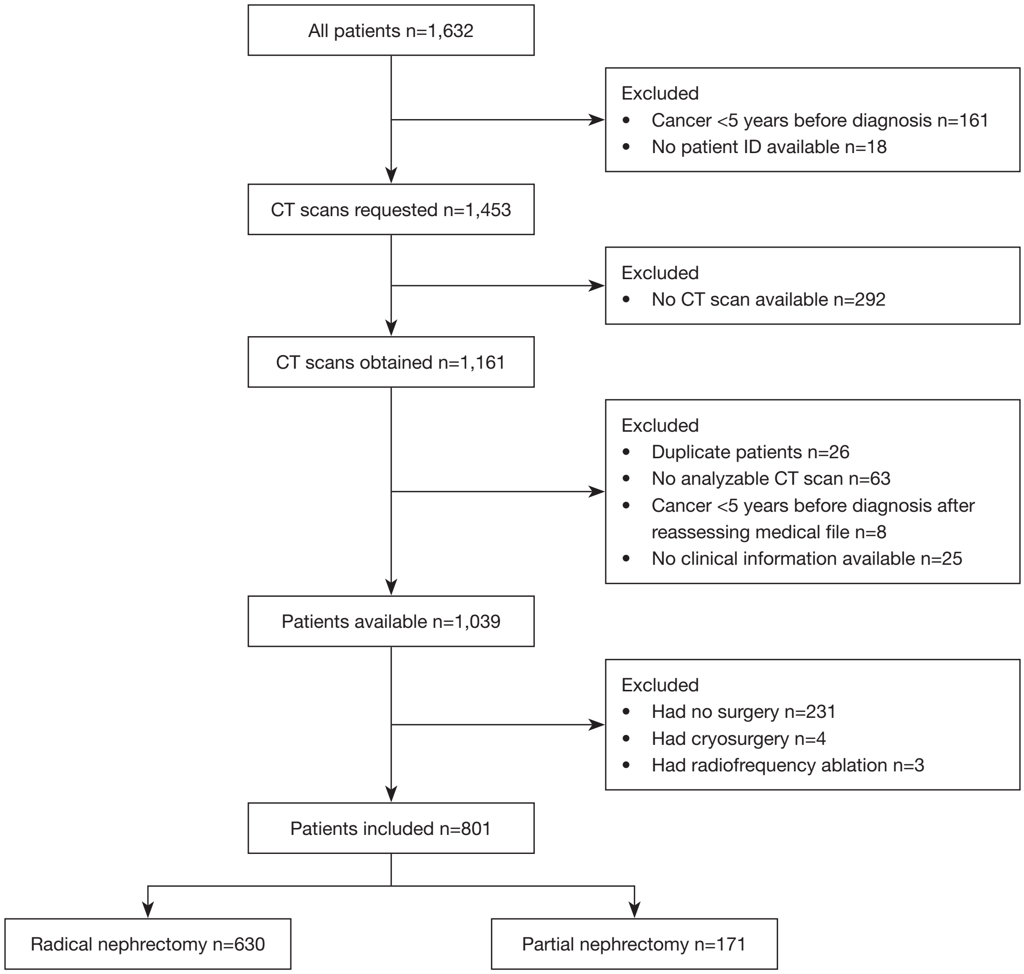

Figure 1 Flowchart of included patients with renal cell cancer. CT, computed tomography.

(24.1%) had a LOHS ≥7 days.

Postoperative complications

Multivariable analyses showed that BMI >30 *vs.* <25 kg/m^2 was statistically significantly associated with higher risk of major postoperative complications [odds ratio (OR) 2.87; 95% confidence interval (95% CI) 1.11–7.40; *Table 2*]. A 10-unit increase in SMD was not statistically significantly associated with lower risk of major postoperative complications (OR 0.66; 95% CI: 0.41–1.05). Results were similar for high *vs.* low SMD and for high SMD/high SMI combined *vs.* low SMD/low SMI combined (OR 0.46; 95% CI: 0.21–1.00 and OR 0.51; 95% CI: 0.18–1.45, respectively). No multivariable associations for VATI, SATI and SMI were found. AICs for continuous and dichotomous multivariable model indicated no difference in fit (372.53 *vs.* 373.17 for VATI/SATI/SMI/SMD and 368.79 *vs.* 367.80 for BMI, respectively).

The AUC of the ROC curve for a model with age, sex, stage and ASA score was 0.71 (95% CI: 0.65–0.77). The AUC non-significantly increased to 0.74 (95% CI: 0.68–0.80) after adding VATI, SATI, SMI and SMD ($P_{difference}$=0.26; *Figure 2*) and to 0.73 (95% CI: 0.67–0.79) after adding BMI to the model ($P_{difference}$=0.34; *Figure 2*). Sensitivity analysis using single imputed datasets showed ignorable differences in the AUC.

Results for any complications were similar to those for major complications (*Table 3*). However, BMI >30 *vs.* <25 kg/m^2 was not statistically significantly associated with an increased risk of any complications (OR 1.71; 95% CI: 0.98–2.97). A 10-unit increase in SMD, high *vs.* low SMD, and high SMD/high SMI *vs.* low SMD/low SMI were inversely but not statistically significantly associated with

© Translational Andrology and Urology. All rights reserved.

Table 1 Study sample characteristics of patients with RCC by types of surgery

Characteristics	Radical nephrectomy (N=630)	Partial nephrectomy (N=171)	Overall (N=801)
Age at diagnosis (years), mean (SD)	63.5±11.4	61.1±11.1	63.0±11.3
Sex, n (%)			
Male	389 (61.7)	110 (64.3)	499 (62.3)
Female	241 (38.3)	61 (35.7)	302 (37.7)
ASA score, n (%)			
I	96 (15.2)	34 (19.9)	130 (16.2)
II	299 (47.5)	76 (44.4)	375 (46.8)
III	101 (16.0)	27 (15.8)	128 (16.0)
IV	4 (0.6)	0 (0)	4 (0.5)
Missing	130 (20.6)	34 (19.9)	164 (20.5)
BMI category (kg/m^2), n (%)			
<18.5	4 (0.6)	0 (0)	4 (0.5)
18.5–24.9	225 (35.7)	50 (29.2)	275 (34.3)
25.0–29.9	231 (36.7)	84 (49.1)	315 (39.3)
≥30.0	97 (15.4)	27 (15.8)	124 (15.5)
Missing	73 (11.6)	10 (5.8)	83 (10.4)
Smoking, n (%)			
Current smoker	130 (20.6)	38 (22.2)	168 (21.0)
Non-current smoker	382 (60.6)	110 (64.3)	492 (61.4)
Missing	118 (18.7)	23 (13.5)	141 (17.6)
Hypertension, n (%)			
No	274 (43.5)	76 (44.4)	350 (43.7)
Yes	310 (49.2)	83 (48.5)	393 (49.1)
Missing	46 (7.3)	12 (7.0)	58 (7.2)
Diabetes, n (%)			
No	515 (81.7)	152 (88.9)	667 (83.3)
Yes	115 (18.3)	19 (11.1)	134 (16.7)
Tumor stage[†], n (%)			
I	264 (41.9)	152 (88.9)	416 (51.9)
II	85 (13.5)	3 (1.8)	88 (11.0)
III	158 (25.1)	9 (5.3)	167 (20.8)
IV	122 (19.4)	5 (2.9)	127 (15.9)
Missing	1 (0.2)	2 (1.2)	3 (0.4)
Nephrectomy procedure, n (%)			
Open	198 (31.4)	36 (21.1)	234 (29.2)
Laparoscopic	410 (65.1)	77 (45.0)	487 (60.8)
Robot-assisted	14 (2.2)	56 (32.7)	70 (8.7)
Missing	8 (1.3)	2 (1.2)	10 (1.2)

Table 1 (*continued*)

© Translational Andrology and Urology. All rights reserved.

Table 1 (*continued*)

Characteristics	Radical nephrectomy (N=630)	Partial nephrectomy (N=171)	Overall (N=801)
Postoperative complications, n (%)			
No	501 (79.5)	143 (83.6)	644 (80.4)
Yes	129 (20.5)	28 (16.4)	157 (19.6)
Complication grade (Clavien-Dindo), n (%)			
Grade II	87 (13.8)	20 (11.7)	107 (13.4)
Grade III	23 (3.7)	7 (4.1)	30 (3.7)
Grade IV	11 (1.7)	1 (0.6)	12 (1.5)
Grade V	8 (1.3)	0 (0)	8 (1.0)
No complication	501 (79.5)	143 (83.6)	644 (80.4)
Surgical blood loss (mL)			
Median [Q1, Q3]	200 [50.0, 750]	200 [100, 500]	200 [60.0, 650]
Missing, n (%)	147 (23.3)	44 (25.7)	191 (23.8)
Surgical time (minutes)			
Median [Q1, Q3]	160 [126, 205]	188 [160, 230]	168 [131, 210]
Missing, n (%)	50 (7.9)	28 (16.4)	78 (9.7)
Length of hospital stay (days)			
Median [Q1, Q3]	4.00 [3.00, 7.00]	4.00 [3.00, 6.00]	4.00 [3.00, 6.00]
Missing, n (%)	11 (1.7)	2 (1.2)	13 (1.6)
Length of hospital stay			
<7 days	459 (72.9)	136 (79.5)	595 (74.3)
≥7 days	160 (25.4)	33 (19.3)	193 (24.1)
Missing, n (%)	11 (1.7)	2 (1.2)	13 (1.6)
VATI (cm^2/m^2)			
Median [Q1, Q3]	48.9 [23.6, 73.8]	55.6 [34.4, 75.3]	51.1 [26.9, 74.2]
Missing, n (%)	55 (8.7)	6 (3.5)	61 (7.6)
SATI (cm^2/m^2)			
Median [Q1, Q3]	51.6 [35.1, 73.0]	54.6 [38.2, 80.6]	52.5 [35.8, 74.7]
Missing, n (%)	55 (8.7)	6 (3.5)	61 (7.6)
SMI (cm^2/m^2)			
Median [Q1, Q3]	45.6 [39.1, 52.5]	49.1 [41.4, 54.1]	46.6 [39.8, 52.9]
Missing, n (%)	55 (8.7)	6 (3.5)	61 (7.6)
SMD (cm^2/m^2)			
Median [Q1, Q3]	35.1 [27.8, 41.5]	34.6 [29.7, 42.2]	35.0 [28.2, 41.6]

†, tumor staging based on pathological TNM classification, complemented with clinical TNM classification used in the year of incidence (6th edition up to and including 2009, 7th edition from 2010–2012). RCC, renal cell cancer; SD, standard deviation; ASA, American Society of Anesthesiologists; BMI, body mass index; Q1, 25% percentile; Q3, 75% percentile; VATI, visceral adipose tissue index; SATI, subcutaneous adipose index; SMI, skeletal muscle index; SMD, skeletal muscle density; TNM, tumor, nodes and metastases.

© Translational Andrology and Urology. All rights reserved.

Table 2 Logistic regression for body composition parameters and major postoperative complications (Clavien-Grade ≥3 *vs.* no)

Factors modelled	Univariable†, odds ratio (95% CI)	Multivariable‡, odds ratio (95% CI)
BMI per 1 unit	1.05 (0.98–1.11)	1.07 (0.99–1.15)
BMI 25.0–29.9 *vs.* <25	1.90 (0.91–3.98)	2.01 (0.93–4.32)
BMI >30 *vs.* <25	2.49 (1.03–6.00)*	2.87 (1.11–7.40)*
VATI per 10 units	1.10 (1.01–1.19)*	1.02 (0.91–1.15)
VATI high *vs.* low	1.40 (0.77–2.53)	1.03 (0.52–2.04)
SATI per 10 units	0.99 (0.91–1.08)	0.99 (0.86–1.13)
SATI high *vs.* low	1.21 (0.67–2.18)	1.09 (0.55–2.17)
SMI per 10 units	0.89 (0.64–1.23)	0.94 (0.57–1.53)
SMI high *vs.* low	0.74 (0.41–1.35)	1.02 (0.52–1.99)
SMD per 10 units	0.57 (0.42–0.78)*	0.66 (0.41–1.05)
SMD high *vs.* low	0.30 (0.15–0.59)*	0.46 (0.21–1.00)
High SMD/high SMI *vs.* low SMD/low SMI§	0.28 (0.12–0.69)*	0.51 (0.18–1.45)

The Akaike information criterion was 372.53 for the multivariable continuous model and 373.17 for the dichotomous model for VATI/SATI/SMI and SMD, and for BMI 368.79 and 367.80, respectively. *, significant at P<0.05; †, with fixed effects for hospital of diagnosis; ‡, adjusted for sex, age at diagnosis, stage, American Society of Anesthesiologists score, smoking, mutually adjusted for the other body composition parameters (except for BMI) and fixed effects for hospital of diagnosis; §, based on a subset of patients with both high SMD and high SMI, and patients with both low SMD and low SMI. Patients with either high/low combination were excluded. CI, confidence interval; BMI, body mass index; VATI, visceral adipose tissue index; SATI, subcutaneous adipose index; SMI, skeletal muscle index; SMD, skeletal muscle density.

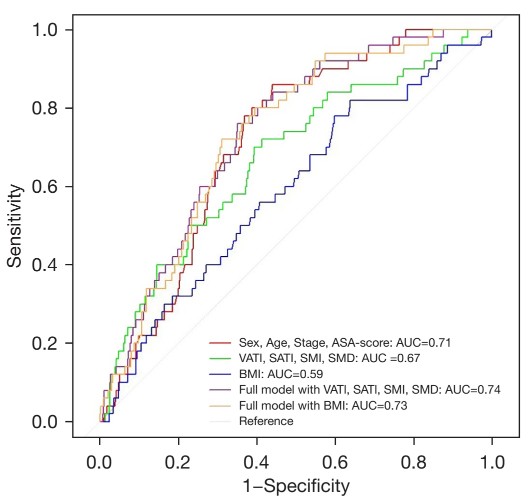

Figure 2 Areas under the receiver operating characteristics curve for major complications. ASA, American Society of Anesthesiologists; AUC, area under curve; VATI, visceral adipose tissue index; SATI, subcutaneous adipose index; SMI, skeletal muscle index; SMD, skeletal muscle density; BMI, body mass index.

risk of any complications There was no difference in fit between continuous and dichotomous models (AICs 742.09 *vs.* 741.44 for VATI/SATI/SMI/SMD and 738.07 *vs.* 738.91 for BMI, respectively). No associations with VATI, SATI and SMI were found.

LOHS

A 10-unit increase in SMD was statistically significantly associated with lower risk of extended LOHS (OR 0.58; 95% CI: 0.44–0.78; *Table 4*). Results were similar for high *vs.* low SMD and for high SMD/high SMI *vs.* low SMD/low SMI. The continuous model had a better model fit than the dichotomous model (762.63 *vs.* 776.97, respectively). A 10-unit increase in VATI was not statistically significantly associated with higher risk (OR 1.07; 95% CI: 1.00–1.16) and a 10-unit decrease in SATI was not statistically significantly associated with lower risk of extended LOHS (OR 0.92; 95% CI: 0.84–1.00). No associations for BMI or SMI were found.

© Translational Andrology and Urology. All rights reserved.

Table 3 Logistic regression analyses for body composition parameters and postoperative complications (any *vs.* no)

Factors modelled	Univariable[†], odds ratio (95% CI)	Multivariable[‡], odds ratio (95% CI)
BMI per 1 unit	1.04 (1.00–1.08)	1.04 (0.99–1.09)
BMI 25.0–29.9 *vs.* <25	1.11 (0.74–1.68)	1.09 (0.71–1.68)
BMI >30 *vs.* <25	1.79 (1.07–2.99)*	1.71 (0.98–2.97)
VATI per 10 units	1.08 (1.02–1.14)*	1.00 (0.93–1.08)
VATI high *vs.* low	1.23 (0.85–1.76)	0.86 (0.55–1.33)
SATI per 10 units	1.02 (0.97–1.07)	1.02 (0.94–1.10)
SATI high *vs.* low	1.39 (0.96–1.99)	1.37 (0.89–2.09)
SMI per 10 units	1.01 (0.83–1.24)	1.10 (0.81–1.49)
SMI high *vs.* low	0.84 (0.59–1.21)	1.02 (0.68–1.54)
SMD per 10 units	0.68 (0.56–0.83)*	0.79 (0.59–1.06)
SMD high *vs.* low	0.48 (0.33–0.70)*	0.70 (0.45–1.11)
High SMD/high SMI *vs.* low SMD/low SMI[§]	0.45 (0.27–0.75)*	0.70 (0.37–1.33)

The Akaike information criterion was 742.09 for the multivariable continuous model and 741.44 for the dichotomous model for VATI/SATI/SMI and SMD, and for BMI 738.07 and 738.91, respectively. *, significant at P<0.05; †, with random effects for hospital of diagnosis; ‡, adjusted for sex, age at diagnosis, stage, American Society of Anesthesiologists score, smoking, mutually adjusted for the other body composition parameters (except for BMI) and random effects for hospital of diagnosis; §, based on a subset of patients with both high SMD and high SMI and patients with both low SMD and low SMI. Patients with either high/low combination were excluded. CI, confidence interval; BMI, body mass index; VATI, visceral adipose tissue index; SATI, subcutaneous adipose index; SMI, skeletal muscle index; SMD, skeletal muscle density.

Table 4 Logistic regression for body composition parameters and length of hospital stay (≥7 *vs.* <7 days)

Factors modelled	Univariable[†], odds ratio (95% CI)	Multivariable[‡], odds ratio (95% CI)
BMI per 1 unit	1.02 (0.98–1.06)	1.03 (0.99–1.08)
BMI 25.0–29.9 *vs.* <25	1.24 (0.84–1.81)	1.34 (0.88–2.03)
BMI >30 *vs.* <25	1.38 (0.82–2.30)	1.47 (0.84–2.57)
VATI per 10 units	1.11 (1.05–1.16)*	1.07 (1.00–1.16)
VATI high *vs.* low	1.56 (1.10–2.20)*	1.40 (0.92–2.14)
SATI per 10 units	0.99 (0.94–1.04)	0.92 (0.84–1.00)
SATI high *vs.* low	0.98 (0.70–1.38)	0.87 (0.58–1.32)
SMI per 10 units	0.86 (0.71–1.04)	1.06 (0.80–1.42)
SMI high *vs.* low	0.64 (0.45–0.90)*	0.83 (0.56–1.23)
SMD per 10 units	0.51 (0.42–0.62)*	0.58 (0.44–0.78)*
SMD high *vs.* low	0.39 (0.27–0.56)*	0.62 (0.40–0.96)*
High SMD/high SMI *vs.* low SMD/low SMI[§]	0.26 (0.15–0.45)*	0.47 (0.25–0.89)*

The Akaike information criterion was 762.63 for the multivariable continuous model and 776.97 for the dichotomous model for VATI/SATI/SMI and SMD, and for BMI 777.47 and 778.80, respectively. *, significant at P<0.05; †, with random effects for hospital of diagnosis; ‡, adjusted for sex, age at diagnosis, stage, American Society of Anesthesiologists score, smoking, mutually adjusted for the other body composition parameters (except for BMI) and random effects for hospital of diagnosis; §, based on a subset of patients with both high SMD and high SMI and patients with both low SMD and low SMI. Patients with either high/low combination were excluded. CI, confidence interval; BMI, body mass index; VATI, visceral adipose tissue index; SATI, subcutaneous adipose index; SMI, skeletal muscle index; SMD, skeletal muscle density.

© Translational Andrology and Urology. All rights reserved.

Sensitivity analyses

BMI was no longer statistically significantly associated with major complications while SMD remained statistically significantly associated with extended LOHS for stage I–III patients, patients treated with radical nephrectomy, with open nephrectomy, and with laparoscopic or robot-assisted nephrectomy (Tables S1,S2). Higher VATI became significantly associated with extended LOHS and higher SMD with lower risk of major complications in patients treated with radical nephrectomy and with laparoscopic or robot-assisted nephrectomy.

Discussion

This multicenter population-based historical cohort study showed that higher SMD was associated with extended LOHS. High BMI and lower SMD may be associated with major complications and higher VATI with extended LOHS, depending on surgical procedure. Adding body composition parameters to a model consisting of age, sex, tumor stage and ASA score did not significantly improve prediction of major postoperative complications.

Comparison with other studies

Our findings for higher SMD and lower risk of extended LOHS and a potential lower risk of major complications are contrary to a small French study (12). Darbas *et al.* included 96 patients with localized RCC receiving partial or radial nephrectomy and found no difference in occurrence of post-surgical infections or LOHS according to SMD (12). Nevertheless, this study may have been underpowered and only included overweight and obese patients. In colorectal cancer, however, low SMD was significantly associated with higher risk of (major) postoperative complications (11,13-15) and longer LOHS (11,13,16). One potential explanation is that low SMD is characterized by secretion of inflammatory adipokines from adipocytes surrounding muscle fibers, which impairs the body's defense (17). Low SMD might also be a marker of overall frailty or higher susceptibility towards stressors, i.e., surgeries (13,17).

We found that high BMI was associated with higher risk of major complications in patients treated with laparoscopic or robot-assisted nephrectomy. This is in accordance with a meta-analysis where obese versus non-obese patients treated with laparoscopic partial nephrectomy had significantly more Clavien III complications (18). Other studies found no relationship between obesity and any complications (19-21) or major complications (22). Kott *et al.* found in 251 patients treated with robot-assisted partial nephrectomy that increasing BMI decreased complications rates up till an inflection point of 30 kg/m^2, while above that point higher BMI was associated with higher complication rates (23). The precise relationship remains to be investigated.

No significant association was observed between SMI and (major) complications or LOHS. This is in accordance with Darbas *et al.* who showed no association of SMI with LOHS (12). However, Peyton *et al.* reported that low *vs.* high total psoas area was associated with higher risk of major complications but not minor complications or LOHS in 137 patients with stage III and IV RCC who underwent radical nephrectomy (24). Sharma *et al.* found that low *vs.* high SMI was associated with longer LOHS but not with postoperative complications in 105 patients with metastatic renal cell cancer treated with cytoreductive nephrectomy (25). All three studies conducted no multivariable analyses thus results may be confounded. Meta-analyses including patients undergoing abdominal surgery showed that preoperative CT-determined sarcopenia was significantly related to (major) postoperative complications and frequently (6 out of 10 studies) associated with increased LOHS (7).

The combination of high SMD/high SMI versus low SMD/high SMI was associated with shorter LOHS but not with lower risk of complications. This effect seemed mainly due to SMD, in contrast to a USA-based study including 1,630 stage I–III colon cancer patients undergoing colon resection showing an additive effect (11). To our knowledge, no other study investigated this in patients with RCC.

Higher VATI was associated with extended LOHS in stage I–III patients and in patients treated with radical nephrectomy and with minimally invasive nephrectomy while no associations with (major) complications were found. Ioffe *et al.* reported no significant association of VAT with complications or LOHS in a US study including 118 patients with RCC treated with minimally invasive partial nephrectomy (26). Darbas *et al.* showed no association between VATI and LOHS (12,26). A Chinese study in 76 patients with stage I–III RCC treated with laparoscopic radical nephrectomy showed that higher VAT was associated with postoperative complications and extended LOHS, unadjusted for potential confounders (27). Higher VAT has been associated with longer operation time and more blood loss and could thereby contribute to complications and extended LOHS (11). We found that higher VATI

© Translational Andrology and Urology. All rights reserved.

was associated with longer operation time as reported in literature (28,29), but not with increased blood loss (data not shown). This may partially explain why we did not detect a significant association between VATI and (major) complications.

We found no statistically significant association between SATI and risk of (major) complications or extended LOHS which is in line with three other studies (12,26,30).

Sensitivity analyses in patients with stage I–III RCC, or with different surgical procedures showed similar associations for SMD and VATI as observed in the complete group of patients. Nevertheless, not all associations were found to be statistically significant. This is probably a power issue due to the small number of patients within each subgroup. Especially for partial nephrectomy, results may also be invalid due to overfitting. Given the low power, no interaction hypothesis could be statistically tested.

Strengths

This is the largest study to date that investigated associations between body composition and postoperative outcomes in patients with RCC. We studied multiple outcomes in multivariable models correcting for confounders (5). Moreover, we examined body composition components continuously per 10 units and dichotomously using sex-specific medians.

Limitations

This study had several limitations. First, given the observational and retrospective nature, this study depended on data from medical records and is susceptible to residual confounding. Especially for associations with extended LOHS, other factors related to LOHS could not be retrieved from medical files (e.g., contraindications for discharge or carrying the discharge day over the weekend). Second, since this study was part of a larger study to examine body composition in relation to survival outcomes (8), requiring a long follow-up time, the surgical data are relatively old and indications and techniques may have changed over time. However, sensitivity analyses for open nephrectomy *vs.* laparoscopic and robot-assisted nephrectomy showed similar results for all body composition parameters indicating that these results are still relevant today. Third, 24% of the identified patients had no suitable CT scan. Reasons were unavailable CT scans (e.g., no diagnostic scan made or at a different hospital) or poor quality scans (e.g., low contrast, graining or artifacts). About 38% of those with no suitable CT scan were not treated with nephrectomy and the remaining patients were similar with respect to age, sex and tumor stage, indicating selection bias is likely to be limited. Fourth, no technical parameters from CT scans could be retrieved from medical files. It is unlikely that these parameters are related to surgical complications or LOHS. However, they may have introduced random variability to our assessment of SMD, potentially weakening observed associations. Around 77% of the CT scans were contrast-enhanced, which may increase SMD compared to non-contrast use (31-33). Sensitivity analyses for contrast-enhanced CT scans did not alter our conclusions (data not shown). Fifth, we could not examine added effects of body composition parameters to prognostic scores since information on the required prognostic parameters was poorly documented. Sixth, we could not obtain characteristics regarding the surgeon performing the nephrectomy. As a proxy we performed multilevel analyses taking into account that patients underwent surgery within the same hospital. Nevertheless, differences within hospitals due to differences between surgeons may still exist which we could not adjust for. We included hospital of surgery as a fixed cluster effect in the analysis for major complications because of non-converging random intercept models. However, since the hospitals are a random sample of large community and university hospitals in the Netherlands, results are generalizable to other hospitals. Last, some CT scans had incomplete cross-sectional areas of SM and SAT due to an inadequate CT scanning protocol. We estimated missing areas and adjusted body composition values accordingly. The impact on our results for SMD is expected to be minimal since SM areas were incomplete for only 6.5% of the patients.

Conclusions

Lower SMD was associated with higher risk of extended LOHS and showed non-significant associations with higher risk of major postoperative complications. High BMI was associated with higher risk of major postoperative complications. Higher VAT was non-significantly associated with higher risk of extended LOHS. Results for both SMD and LOHS by surgical procedure were in the same direction but differed in statistical significance between subgroups. SMD and VATI can be determined on diagnostic CT scans and may provide additional information over BMI. This information could be used for patient risk stratification and

© Translational Andrology and Urology. All rights reserved.

pre-surgical interventions aimed at improving postoperative outcomes. The predictive value of BMI, SMD and VATI for postoperative outcomes and their added value to anatomic classification systems needs to be validated.

Acknowledgments

We thank the following hospitals and urologists for allowing us to use their hospital data: Radboud university medical center, Nijmegen; Amphia Hospital, Breda/Oosterhout (Dr. DKE van der Schoot); Catharina Hospital, Eindhoven (Dr. EL Koldewijn); Meander Medical Centre, Amersfoort (Dr. FS van Rey); Rijnstate Hospital, Arnhem (Dr. GAHJ Smits); Slingeland Hospital, Doetinchem (Dr. ADH Geboers); Ziekenhuisgroep Twente, Almelo and Hengelo (Dr. SP Stomps). We thank the registration team of the Netherlands Comprehensive Cancer Organisation (IKNL) for the collection of data for the Netherlands Cancer Registry as well as IKNL staff for scientific advice. We thank the radiology departments of the involved hospitals for providing the CT scans.

Funding: This work was supported by a research grant (KUN 2015-7948) from the Dutch Cancer Society. This funding source had no role in the design, data collection, analyses and interpretation of the data, writing the report, or decision to submit the article for publication.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-22-367/rc

Data Sharing Statement: Available at https://tau.amegroups.com/article/view/10.21037/tau-22-367/dss

Peer Review File: Available at https://tau.amegroups.com/article/view/10.21037/tau-22-367/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-22-367/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was approved by the Committee for Human Research region Arnhem-Nijmegen (No. CMO 2015-1822), which waived the need for informed consent. All local ethics committees from the participating hospitals provided permission for data collection.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-49.
2. EAU Guidelines. Edn. presented at the EAU Annual Congress Amsterdam 2022. ISBN 978-94-92671-16-5: EAU Guidelines Office, Arnhem, The Netherlands. Available online: https://uroweb.org/guidelines/compilations-of-all-guidelines/
3. Gupta K, Omil-Lima D, Sheyn D, et al. Temporal improvements in renal surgery outcomes across surgical approaches. Int Urol Nephrol 2021;53:1311-6.
4. 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.
5. Vrieling A, Kampman E, Knijnenburg NC, et al. Body Composition in Relation to Clinical Outcomes in Renal Cell Cancer: A Systematic Review and Meta-analysis. Eur Urol Focus 2018;4:420-34.
6. Xu J, Zheng B, Zhang S, et al. Effects of preoperative sarcopenia on postoperative complications of minimally invasive oesophagectomy for oesophageal squamous cell carcinoma. J Thorac Dis 2019;11:2535-45.
7. Jones K, Gordon-Weeks A, Coleman C, et al. Radiologically Determined Sarcopenia Predicts

Morbidity and Mortality Following Abdominal Surgery: A Systematic Review and Meta-Analysis. World J Surg 2017;41:2266-79.
8. Maurits JSF, Sedelaar JPM, Mulders PFA, et al. Skeletal muscle radiodensity and visceral adipose tissue index are associated with survival in renal cell cancer - A multicenter population-based cohort study. Clin Nutr 2022;41:131-43.
9. Mourtzakis M, Prado CM, Lieffers JR, et al. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab 2008;33:997-1006.
10. Ebadi M, Martin L, Ghosh S, et al. Subcutaneous adiposity is an independent predictor of mortality in cancer patients. Br J Cancer 2017;117:148-55.
11. Xiao J, Caan BJ, Cespedes Feliciano EM, et al. Association of Low Muscle Mass and Low Muscle Radiodensity With Morbidity and Mortality for Colon Cancer Surgery. JAMA Surg 2020;155:942-9.
12. Darbas T, Forestier G, Leobon S, et al. Impact of Body Composition in Overweight and Obese Patients With Localised Renal Cell Carcinoma. In Vivo 2020;34:2873-81.
13. van Vugt JLA, Coebergh van den Braak RRJ, Lalmahomed ZS, et al. Impact of low skeletal muscle mass and density on short and long-term outcome after resection of stage I-III colorectal cancer. Eur J Surg Oncol 2018;44:1354-60.
14. Margadant CC, Bruns ER, Sloothaak DA, et al. Lower muscle density is associated with major postoperative complications in older patients after surgery for colorectal cancer. Eur J Surg Oncol 2016;42:1654-9.
15. Boer BC, de Graaff F, Brusse-Keizer M, et al. Skeletal muscle mass and quality as risk factors for postoperative outcome after open colon resection for cancer. Int J Colorectal Dis 2016;31:1117-24.
16. Malietzis G, Currie AC, Athanasiou T, et al. Influence of body composition profile on outcomes following colorectal cancer surgery. Br J Surg 2016;103:572-80.
17. Aleixo GFP, Shachar SS, Nyrop KA, et al. Myosteatosis and prognosis in cancer: Systematic review and meta-analysis. Crit Rev Oncol Hematol 2020;145:102839.
18. Aboumarzouk OM, Stein RJ, Haber GP, et al. Laparoscopic partial nephrectomy in obese patients: a systematic review and meta-analysis. BJU Int 2012;110:1244-50.
19. Abdullah N, Dalela D, Barod R, et al. Robotic partial nephrectomy for renal tumours in obese patients: Perioperative outcomes in a multi-institutional analysis. Can Urol Assoc J 2015;9:E859-62.
20. Sharma V, Aggarwal A, McGuire BB, et al. Open vs Minimally Invasive Partial Nephrectomy: Assessing the Impact of BMI on Postoperative Outcomes in 3685 Cases from National Data. J Endourol 2015;29:561-7.
21. Sperling CD, Xia L, Berger IB, et al. Obesity and 30-Day Outcomes Following Minimally Invasive Nephrectomy. Urology 2018;121:104-11.
22. Hua X, Ying-Ying C, Zu-Jun F, et al. Obesity, hypertension and diabetes mellitus affect complication rate of different nephrectomy techniques. Actas Urol Esp 2014;38:640-6.
23. Kott O, Golijanin B, Pereira JF, et al. The BMI Paradox and Robotic Assisted Partial Nephrectomy. Front Surg 2020;6:74.
24. Peyton CC, Heavner MG, Rague JT, et al. Does Sarcopenia Impact Complications and Overall Survival in Patients Undergoing Radical Nephrectomy for Stage III and IV Kidney Cancer? J Endourol 2016;30:229-36.
25. Sharma P, Zargar-Shoshtari K, Caracciolo JT, et al. Sarcopenia as a predictor of overall survival after cytoreductive nephrectomy for metastatic renal cell carcinoma. Urol Oncol 2015;33:339.e17-23.
26. Ioffe E, Hakimi AA, Oh SK, et al. Effect of visceral obesity on minimally invasive partial nephrectomy. Urology 2013;82:612-8.
27. Zhai T, Zhang B, Qu Z, et al. Elevated visceral obesity quantified by CT is associated with adverse postoperative outcome of laparoscopic radical nephrectomy for renal clear cell carcinoma patients. Int Urol Nephrol 2018;50:845-50.
28. Yuge K, Miyajima A, Jinzaki M, et al. How does visceral obesity affect surgical performance in laparoscopic radical nephrectomy? Jpn J Clin Oncol 2015;45:373-7.
29. Hagiwara M, Miyajima A, Hasegawa M, et al. Visceral obesity is a strong predictor of perioperative outcome in patients undergoing laparoscopic radical nephrectomy. BJU Int 2012;110:E980-4.
30. Gorin MA, Mullins JK, Pierorazio PM, et al. Increased intra-abdominal fat predicts perioperative complications following minimally invasive partial nephrectomy. Urology 2013;81:1225-30.
31. Paris MT, Furberg HF, Petruzella S, et al. Influence of Contrast Administration on Computed Tomography-Based Analysis of Visceral Adipose and Skeletal Muscle Tissue in Clear Cell Renal Cell Carcinoma. JPEN J Parenter Enteral Nutr 2018;42:1148-55.
32. van Vugt JLA, Coebergh van den Braak RRJ, Schippers HJW, et al. Contrast-enhancement influences skeletal

© Translational Andrology and Urology. All rights reserved.

muscle density, but not skeletal muscle mass, measurements on computed tomography. Clin Nutr 2018;37:1707-14.
33. Rollins KE, Javanmard-Emamghissi H, Awwad A, et al. Body composition measurement using computed tomography: Does the phase of the scan matter? Nutrition 2017;41:37-44.

Cite this article as: Maurits JSF, Sedelaar JPM, Aben KKH, Kiemeney LALM, Vrieling A. The association of body composition with postoperative complications and length of hospital stay after radical or partial nephrectomy in patients with renal cell cancer: a multicenter population-based cohort study. Transl Androl Urol 2022;11(12):1667-1679. doi: 10.21037/tau-22-367

© Translational Andrology and Urology. All rights reserved.