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Original article

Is imperative partial nephrectomy feasible for kidney cancer with venous thrombus involvement? Outcomes of 42 cases and matched pair analysis with a large radical nephrectomy cohort

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Abstract

Background: Radical nephrectomy (RN) with/without (±) thrombus excision (ThE) is the undisputed standard treatment for kidney cancer (KC) with renal or caval thrombus (Th). However, partial nephrectomy (PN) ± ThE may be considered in rare cases due to imperative (I) indications.

Objective: To evaluate the efficacy of IPN ± ThE and to compare it with RN ± ThE for KC with Th.

Design, setting, and participants: Records of 2,549 patients undergoing surgery for KC with Th at 24 institutions between 1971 and 2014 were retrospectively reviewed.

Outcome measurements and statistical analysis: Primary outcomes were overall survival (OS) and cancer specific survival (CSS), renal function variation after surgery and complications. Secondary outcomes were predictors of OS and CSS for IPN cases. To reduce bias IPN group was matched with RN using a propensity score with greedy algorithm on the basis of age, gender, tumor size, TNM, and histology.

Results and limitations: Forty-two patients underwent IPN ± Th. All thrombi were ≥level I; 5 patients experienced Clavien ≥ 3 complications with 2 complications-related deaths. At 27.3 (interquartile range: 7.1–47.7) months OS and CSS were 54.8% and 78.6%, respectively whereas at 9.7 (interquartile range: 1.4–43.7) months eGFR change was −17.3 ± 27.0 ml/min. On univariate analysis tumour size, preoperative eGFR, transfusions, hospital stay, high serum creatinine, operating time, complications, lymphadenectomy, and metastases related to an increased risk of death.

After matching ($n = 38$ per arm) no significant differences were present except for tumor necrosis (IPN = 39.5%; 15.8%; $P = 0.01$), thrombus level ($P = 0.02$), so as for operating time ($P = 0.27$), perioperative transfusions ($P = 0.74$) and complications ($P = 0.35$).

A 5-year OS and CSS for IPN were 57.9% and 73.7%, respectively with no significant differences with RN (OS = 63.2, $P = 0.611$; CSS = 68.4, $P > 0.99$). After 14.9 months creatinine and eGFR changes were (+0.4 ± 0.6 mg/dl and −23.2 ± 37.3 ml/min; $P = 0.2879$).

Conclusions: In selected cases due to imperative indications PN ± ThE is a complex procedure and may be an alternative to RN ± ThE for KC with Th yielding noninferior oncological outcomes, functional outcomes, and complications. Further studies are needed to determine the role of PN ± ThE for KC with Th.

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1. Introduction

Despite the recent stage migration towards the diagnosis of earlier stage disease, up to 30% of renal cell carcinomas present at an advanced stage including venous thrombus involvement with renal or caval extension. Even higher percentages are reported when considering more aggressive histological subtypes [1–3]. Due to the higher risk of recurrence and disease-related deaths of this subgroup radical treatment is highly warranted making radical nephrectomy (RN) with or without thrombus excision the undisputed gold standard.

Meanwhile partial nephrectomy (PN) is gaining popularity with the aim of preserving renal function, and avoiding renal insufficiency related comorbidities. Current guidelines favor nephron sparing surgery for localized neoplasms below 7 cm, and in the absence of technical contraindications [4]; although not recommended, increasing evidence is also showing PN feasibility in case of larger tumors; in the setting of T2 RCC *nephron sparing surgery* yields higher blood loss and complication rates compared to RN but seems to be oncologically safe, not adversely affecting overall survival (OS) and cancer specific survival (CSS) [5].

Nonetheless, *thrombus* presence remains an absolute contraindication for PN [4]. Even following RN survival is poor and approximately 1 of 2 patients will recur within 5 years even if no metastases or positive nodes are present at the time of surgery [1,6]. Furthermore, surgical risk for patients with *thrombus* is much greater compared to lower stages; the surgery increases in complexity depending on the thrombus level and so do complications, affecting up to 1 of 3 patients in the immediate postoperative period for thrombi extending above the diaphragm. Overall, intraoperative and perioperative deaths reach almost 2% [2].

However, in some conditions including—solitary kidneys, bilateral cancers, or baseline poor renal function, PN may be envisioned as imperative (I) reasons. Not surprisingly these cases are extremely rare, accounting approximately for 1% of surgeries for *KC* with *venous thrombus* [7]. To date only a few small series described PN in patients with renal vein involvement, yielding conflicting results [8–10] and raising significant scepticism [11]. This holds true to a greater degree for thrombi extending into the IVC with PN descriptions being limited to case reports [8,12,13].

Indeed absence of data raises oncological, technical and ethical issues concerning PN feasibility in locally advanced KCs. First, oncological safety has to be proven, and (that the risk of sparing nephrons will not cause increased local recurrence, and or impair oncologic outcomes). Second, technical feasibility of this challenging procedure cannot be stated at present, apart from personal surgeon's experiences. Third, even if demonstrated oncologically effective and relatively safe, whether excision of relatively large masses allows renal function preservation compared to standard treatment needs to be verified. The aim to preserve renal function must not expose the patient to an increased risk of cancer recurrence and progression, high-grade complications and death.

Therefore, we performed a multicentre study to evaluate IPN with/without *thrombus excision*; oncological outcomes, functional outcomes and complications, and also to compare IPN with RN ± *thrombus excision* in patients with *KC* and Th.

2. Materials and methods

2.1. Institutions, patients, and study variables

We retrospectively reviewed the data of 2549 patients who underwent surgical treatment for *KC* with *venous thrombus involvement* from 1971 to 2014 at 24 International Institutions (Supplementary Material 1), included in the central database from the International Renal Cell Carcinoma-Venous Thrombus Consortium (IRCC-VTC) as previously described [14]. IPN were performed at 7 centres. Institutions who performed IPN were contacted to retrieve and update patients' records for central data storage, with the last follow-up data available as of December 2016.

Collected variables are listed in Tables 1 and 2. Fuhrman system was used for histological grading when appropriate and pathologic staging was performed according to the 2009 TNM classification [15]. Complications were graded using the Clavien-Dindo Classification and comorbidities were reported using Charlson Comorbidity Index following EAU Guidelines recommendations [16]. Renal function was evaluated through serum creatinine levels and eGFR. Thrombus level was defined according to the Mayo Clinic Classification based on preoperative computed tomography or magnetic resonance imaging scans [2].

Follow-up was performed according to institutional protocols. Patients were generally followed every 3 months for the first year, semiannually for the second year, and annually thereafter. Diagnostic imaging included ultrasonography and computed tomography abdomen/pelvis. Cause of death was determined by the treating physician or by chart review. Perioperative mortality (death within 30 days of surgery) was censored at time of death for cancer-specific survival analyses.

2.2. Statistical analysis

Data are presented as mean and standard deviation, or median (interquartile range). Comparison between IPN and RN groups was made using the Wilcoxon-Mann-Whitney