Reviewer's report

**Title:** Prognostic benefit of surgical management in patients with renal cell carcinoma extending to renal vein and inferior vena cava: 17-year experience at a single center

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**Reviewer:** Yasushi Yoshino

**Reviewer's report:**

**General comment:**

This manuscript was designed by a retrospective study assessing clinical outcomes of renal cell carcinoma (RCC) with tumor thrombus undergoing surgery and finding prognostic factors due to comparison to the patient survival without surgery. Authors indicated surgical benefits of surgery for patients with tumor thrombus extending to the inferior vena cava (IVC). However, they could not find surgical advantages for patient with tumor thrombus extending only to the renal vein (RV) because the sample size especially in non-surgical group was small to distinguish the differences and patients with far advanced disease such as lymph node and other visceral metastasis also tended to undergo nephrectomy including tumor thrombus.

Their experiences did not differ to the acknowledgement previously reported. The largest series including 1122 patients with RV and IVC thrombus indicated that median overall survival (OS) was 33.8 months during median follow up period 24.7 months [1]. Even in this largest study, the role of surgical management is unclear because it has no data focusing on the outcomes comparing to those of RCC tumor thrombus without surgical treatment.

Prognostic significance of tumor thrombus level is controversial. Kim HL et al. reported the level of tumor thrombus was not a predictor of cancer specific survival (CSS) on multivariate analysis (HR: 0.95; p=0.872) [2]. On the contrary, Martinez-Salamanca JI et al. reported the level of tumor thrombus extending to supradiaphragmatic or atrial region was one of the independent predictors of CSS (HR: 2.10; p=0.00) as well as the tumor size greater than 7 cm, Furman grade, fat invasion, positive lymph node and metastatic disease[1].

Not all patients underwent surgery and/or tumor biopsy to reveal histopathology. Perhaps that is why histopathological factors were not assessed to distinguish the prognostic factors.

Anyway, most issues presented by Dr. Hatakeyama et al. in this manuscript are acceptable for some reasons as follows:
(1) Surgery is the curative approach for RCC extension to the IVC and long-term survival is possible in selected patients IVC thrombus treated with surgery.

(2) Five-year survival rate in surgically-treated patients without distant metastases is almost same as the data previously reported.

(3) Prognostic significance of level of tumor thrombus remains controversial.

Minor Essential Revisions seems to be required:

(1) The authors did not describe how many patients underwent surgical treatment (so called metastasectomy) for patient with lymph node disease and distant metastases and how many failed in the insufficient resection (positive surgical margin disease or remaining tumor) in surgery group. If most patients had untreated metastatic disease in surgery group, the significance of nephrectomy with tumor thrombus would be equaled to the cytoreductive surgery.

(2) Cardiopulmonary bypass was required in some patients. However, it is uncertain how many patients received renal artery embolization prior to the surgery. Subramanian VS et al reported increased risk of perioperative death in embolization group [3].

(3) Section of Background, Page 5, and Line 3: Another article should be considered to add the reference list which describes 4 to 15% of patients with RCC demonstrate direct tumor extension into the IVC [4].

(4) Section of Background: The first appearance in references was the surgery that Berg AA reported in 1913 [5]. It is only for author’s reference and recommendations for improvement but which the author can choose to ignore.

(5) Section of Background, Page 5, and Line 6: Perioperative mortality rates ranged from 2 to 9 % with my knowledge. Please consider to show the incidence of surgical mortalities to compare your intuitional experiences with early death caused by surgeries.

(6) Section of Follow-up schedule, Page 8, and Line 2: Did post-operative CT scan include chest and brain or only for abdominal check-up? Did you check chest X-ray for follow-up examinations?

(7) Section of Follow-up schedule: Did further treatment start from the first appearance of new metastatic regions or just after surgery as adjuvant therapy?

(8) Section of Statistical analysis and Discussion: The level of tumor thrombus had no impact on overall survival in this study. Where the thrombus levels were divided? Between RV thrombus and IVC thrombus or any other partition between suprahepatic thrombus and infrahepatic?

References:

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.