Observational Study

Medicine®

OPEN

Surgical treatment for Xp11.2 translocation renal cell carcinoma with venous thrombus

A STROBE-compliant study

Liyuan Ge, MD[a], Xiaojun Tian, MD[a], Jing Ma, MD[b], Guojiang Zhao, MD[a], Yimeng Song, PhD[a], Shudong Zhang, MD[a,*], Lulin Ma, MD[a,*]

Abstract

The aim of the study was to report the experience and outcomes of Xp11.2 translocation renal cell carcinoma (tRCC) patients with tumor thrombus undergoing radical nephrectomy and thrombectomy.

Between January 2017 and December 2017, 66 consecutive patients with RCC and venous thrombus involvement received surgical treatment at Peking University Third Hospital. Of which, 5 patients were confirmed of Xp11.2 tRCC, 61 patients were diagnosed of non-tRCC subtypes including 45 ccRCCs, 10 pRCCs, and 6 other subtypes. Demographic, clinical, operation, pathological and follow-up data were extracted for analysis. Prognostic factors were identified by Cox regression analysis.

All the patients received radical nephrectomy and thrombectomy successfully. During a median follow-up of 18 months, 5 patients in non-tRCC group and 1 patient in tRCC group died of disease progression. Survival analysis revealed that Xp11.2 tRCC patients experienced shorter DFS than non-tRCC patients, however, there is no significant difference in OS between two groups. Xp11.2 tRCC histological subtype and presence of metastasis at diagnosis were identified as independent negative factors of DFS by multivariate analysis.

Radical nephrectomy with thrombectomy provides an acceptable efficacy for tRCC patients with tumor thrombus extending into the venous system. In addition, multimodality treatment should be considered for advanced Xp11.2 RCCs as this subtype was a negative prognostic factor of DFS.

Abbreviations: ccRCC = clear-cell renal cell carcinoma, DFS = disease free survival, IVC = inferior vena cava; OS = overall survival; pRCC = papillary renal cell carcinoma; RCC = renal cell carcinoma; tRCC = translocation renal cell carcinoma.

Keywords: kidney cancer, radical nephrectomy, targeted therapy, thrombectomy, venous thrombus, Xp11.2 translocation renal cell carcinoma

1. Introduction

Renal cell carcinoma (RCC) is the most lethal urological malignancy, accounting for 2% to 3% of all kinds of adult malignancies.[1] With technological improvements and genetic profiling, its classification has been expanded. Xp11.2 translocation renal cell carcinoma (tRCC) represents a rare subtype of renal cell carcinoma (RCC) and was included as a separate entity since 2004.[2] Xp11.2 tRCCs occupies one-third of pediatric RCCs, whereas only account for 1.6% to 4.2% of adult RCCs.[3] In 4% to 10% of patients, RCC forms a venous tumor thrombus and invades the inferior vena cava (IVC).[4] Multidisciplinary treatment has been applied to this particular type. Surgical resection in the form of radical nephrectomy and thrombectomy was reported to be the only way to obtain satisfactory local control.[5] Recently, stereotactic ablative radiation therapy was reported to be a potentially safe treatment option in the unresectable setting for RCC patients with tumor thrombus.[6] With further study on the pathogenesis of RCC, more and more targeted agents and biomarkers are developed for cancer management.[7–9] Although it was reported of limited efficacy in shrinking thrombus level preoperatively or prolonging survival time by postoperative adjuvant therapy, part of the patients does benefit from targeted therapy.[10–12] On the other hand, because of the relatively high prevalence of clear cell RCC, clinical trials of targeted agents have mainly focused on this population while excluding those non-clear cell subtypes.[13] Half of the Xp11.2 tRCCs were reported to have more aggressive clinicopathologic features such as venous system tumor thrombus invasion.[14–16] Moreover, histological subtype has been identified as an important prognostic factor, few studies compared surgical outcomes between different pathological subtypes in RCC

Editor: Vito Mancini.

LG, XT, and JM contributed equally to this work.

This study was approved by the Medical Ethics Committee for Human Experiments of Peking University Third Hospital.

This work was supported by the National Natural Science Foundation of China [grant No.81500189] and Beijing Municipal Science & Technology Commission [grant No. Z161100000116037, 2017].

The authors have no conflicts of interest to declare.

[a] Department of Urology, [b] Department of Ultrasonography, Peking University Third Hospital, Haidian District, Beijing, PR China.

[*] Correspondence: Lulin Ma, Shudong Zhang, Department of Urology, Peking University Third Hospital, 49 North Garden Road, Haidian District, Beijing 100191, PR China (e-mail: doctor.lulin.ma@gmail.com, shudong_zhang@126.com).

How to cite this article: Ge L, Tian X, Ma J, Zhao G, Song Y, Zhang S, Ma L. Surgical treatment for Xp11.2 translocation renal cell carcinoma with venous thrombus: A STROBE-compliant study. Medicine 2019;98:37(e17172).

Received: 7 February 2019 / Received in final form: 22 July 2019 / Accepted: 20 August 2019

http://dx.doi.org/10.1097/MD.0000000000017172

patients with tumor thrombus.[17–19] It is less clear if it applies to patients with tRCCs, therefore, we reviewed our database to assess the treatment outcome of this particular subtype for the purpose of better management.

2. Methods

2.1. Study population

Following approved by the Medical Ethics Committee for Human Experiments of Peking University Third Hospital (M2017147), the database of RCC with thrombus was queried to identify Xp11.2 tRCC patients received radical nephrectomy and thrombectomy in the Department of Urology, Peking University Third Hospital from Jan 2017 to Dec 2017. Patients with bilateral renal tumors or refused surgical treatment were excluded. Clinical information extracted included age at surgery, gender, symptoms at diagnosis, body mass index, tumor size, side. The thrombus level was stratified by Mayo staging system.[20] Pathologic features were retrospectively reviewed by one genitourinary pathologist (Min Lu, Peking University Third Hospital), included surgical margin status, histologic subtype, thrombus presence/level, lymph node status, and metastasis. A dual-color, break-apart FISH assay for TFE3 gene rearrangement was performed to confirm the diagnosis.

2.2. Surgical procedures

Surgical details are as follows. For laparoscopic radical nephrectomy with thrombectomy: First, the patients were positioned in the right lateral decubitus position, then the left renal artery was ligated, followed by isolating the renal vein to the IVC. Then, the patients were positioned in the left lateral decubitus position, and the IVC, right renal artery and vein were isolated, followed by sequentially clamping of the IVC below the renal vein, right renal artery, and vein. After elevating pneumoperitoneum pressure to 20 to 25 mmHg, the junction of the renal vein and IVC was curvilinearly incised, and the tumor thrombus was pulled out when it was confirmed that the tumor thrombus was completely isolated. Then, clamped the upper incision of IVC and flushed the lumen of vena cava with heparin saline, followed by continuous suture of the IVC. For open surgery, patients were positioned in a supine position and an incision under the costal margin was chosen. Upon entry into retroperitoneal, structures around IVC were exposed including renal artery and vein. After then, the junction of the renal vein and IVC was curvilinearly incised, and the tumor thrombus was pulled out by a milking way.[21] After that, the lumen of the vena cava was constructed as mentioned above.

2.3. Follow-up

All patients were regularly followed in our hospital every 3 months during the first year, every 6 months for the following year, and then annually. Creatinine level, chest X-ray and abdominal computed tomography imaging were done at regular intervals to monitor renal function and to evaluate any evidence of local recurrence or distant metastasis.

2.4. Statistical analysis

Due to the relatively small sample size, data were presented as median values and wide ranges. SPSS 24.0 (SPSS Inc., Chicago, IL) was used for statistical analyses. The differences between groups were evaluated using the log-rank test. Variables were compared between groups using the Student's t test. Kaplan–Meier method was used for generating survival curves. A P value $< .05$ was considered significant. Prognostic factors were identified by univariable and multivariable analysis using Cox regression models.

3. Results

General characteristics of the whole cohort were listed in Table 1. During the period, 66 patients with RCC and venous involvement received surgical treatment at our department were identified. Of these patients, 5 (7.6%) patients were confirmed of Xp11.2 tRCC by FISH assay. For the other 61 non-tRCC patients, 45 (68.2%) patients had clear-cell renal cell carcinoma (ccRCC), 10 (15.2%) patients were diagnosed of papillary renal cell carcinoma (pRCC) and 6 (9.1%) of other subtypes. The prevalence of metastases in tRCC and non-tRCC group was 20% and 13.1%, respectively. The prevalence of lymph node invasion in 2 cohorts was 20% and 8.2%, respectively. Postoperative adjuvant targeted therapy was adopted in 25 patients, of which 22 patients in non-tRCC cohort and 3 patients in tRCC cohort. The patients in tRCC cohort were significantly younger than patients in non-tRCC cohort ($P = .001$). The rest of the parameters showed no significant differences between the two cohorts. More detailed information is available upon request.

The tRCC cohort encompassing 2 males and 3 females with a median age of 25 (15–54) years old. The median BMI was 24.2 (17.3–26.5) kg/m^2. Two of 5 patients' tumors were located in the left renal and the median tumor size was 13.0 (6.8 to 17.0) cm. RCC presented with painless gross hematuria in 1 patient, abdominal mass in 1, flank pain in 1 and 2 cases were found incidentally during an ultrasound examination. According to the classification criteria of Mayo clinic, the thrombus was classified as level 0, 1, 3 in 3 patients, 1 patient, and 1 patient, respectively. Postoperative pathology outcomes showed that all the surgical margins were negative. One case was classified as ISUP nuclear grade 2, 1 case was classified as grade 4 and the others was classified as grade 3. Postoperative recurrence occurred in 2 cases (Patient 2# and Patient 5#). Patient2# was diagnosed with liver and retroperitoneal lymph node progression at the 5th postoperative month. Upon progression, Patient 2# chose supportive treatment rather than specific cancer treatment and died at the 11th postoperative month. For Patient 5#, he started adjuvant targeted therapy 2 months after surgery and was diagnosed with left anterior superior iliac spine metastasis at the 3rd postoperative months. Upon progression, the patient continued sunitinib (6-week cycles including 4 weeks' treatment followed by 2 weeks off, 37.5 mg daily dose) and received local radiotherapy (Stereotactic radiotherapy, 50Gy, 10 fractions) for oligo metastasis at the same time. After radiotherapy, the patient continues maintenance sunitinib (6-week cycles, 37.5 mg daily dose). Until the last follow-up, Patient 5# was still alive and the bone metastasis was stable without evidence of disease progression. The other 3 patients were alive until the last follow-up, and no one has evidence of disease recurrence. Characteristics and outcomes of tRCC patients were summarized in Table 2.

For the whole cohort, all the patients were followed up continually, except 3 cases in non-tRCC cohort lost follow up. During a median follow-up period of 18 months (range 4–25 months), there were 6 deaths, of which 5 patients in

Table 1

Characteristics of the whole cohort patients.

	tRCC Group (n = 5)	Non-tRCC Group (n = 61)	*P* Value
Age, years, median, interquartile range	25 [15–54]	59 [17–82]	.001
Gender (F/M)	3/2	18/43	.316
Side (L/R)	2/3	20/41	.333
Body mass index	24.2 [17.3–26.5]	23.4 [17.3–30.5]	.532
Size	13.0 [6.8–17.0]	8.7 [3.8–20.0]	.149
Clinical TNM			/
cT3	4	57	/
cT4	0	4	/
Lymph Node invasion	1	5	.531
Metastasis	1	8	.389
Mayo level			/
0	3	9	/
1	1	21	/
2	0	12	/
3	1	15	/
4	0	4	/
Histology	Xp11.2	ccRCC:45; pRCC:10; other:6	/
ISUP grade			.641
Low (1–2)	1	25	
High (3–4)	4	36	
Operation time (minutes)	299 [125–372]	332 [135–541]	.136
Postoperative targeted therapy	3	22	.359
Deceased	1	5	.404

F = female, M = male, L = left, R = right.

non-tRCC cohort and 1 patient in tRCC cohort. Overall survival and disease-free survival curves were generated (Fig. 1A and B). Despite the relatively small sample size, disease free survival (DFS) of tRCC cohort is significantly shorter than non-tRCC cohort (Fig. 1B, $P = .008$). There is no significant difference in overall survival between the 2 groups (Fig. 1A, $P = .425$). Owing to relatively short follow-up time, median DFS and OS were not reached. Cox regression analysis reveals that Xp11.2 tRCC histological subtype and presence of metastasis at diagnosis were independent factors for shorter DFS (Table 3).

4. Discussion

Surgical management is currently the only chance for RCC patients with venous thrombus. Although several studies reported benefits associated with surgical treatment in such patients, there is no specific study concerning outcomes of Xp11.2 tRCC with venous thrombus.[17,22] In this study, we identified 5 Xp11.2 tRCC patients from a single central database of RCC patients with venous thrombus. Comparing with non-tRCCs, there is no significant difference in OS between the 2 groups. However, this rare subtype was identified as an independent adverse prognostic factor in DFS analysis. Therefore, close follow-up and systematic therapies should be offered for tRCC patients with venous thrombus after surgery if necessary.

Given the aggressive and invasive biological behavior of adult Xp11.2 translocation RCCs, a few patients of Xp11.2 tRCC will be diagnosed with venous thrombus invasion. Approximately 4% to 10% patients of RCC have tumor thrombus invading renal vein or IVC at diagnosis.[23,24] In our study, tRCC account for 7.6% of total RCC patients with thrombus, which makes up a substantial portion of RCC patients with venous thrombus extension. Xp11.2 tRCC mainly occurs in children and young adults, presenting a different incidence of age comparing with conventional clear-cell RCC.[25] Choo et al reported that Xp11.2 tRCCs showed a bimodal incidence of age distribution with the larger peak at 31 to 40 years and the smaller peak at 61 to

Table 2

Characteristics and outcomes of tRCC patients.

Patient Number	Age years	Sex	BMI kg/m2	Symptoms	Side	Size cm	Mayo level	TNM stage	Surgical approach	ISUP grade	Adjuvant therapy	Follow-up month	Current Status
1	25	F	21.6	Symptomless	R	8.5	0	T3aN0M0	ORNT	2	No	21	Alive, NED
2	22	M	24.6	Abdominal mass	L	14.5	0	T3aN0M0	ORNT	3	No	11	Dead, progressed at 5 months after surgery
3	15	F	17.3	Flank pain	R	13.0	3	T3bN1M0	ORNT	4	Sunitinib	16	Alive, NED
4	51	F	24.2	Symptomless	L	6.8	0	T3aN0M0	LRNT	3	Sunitinib	17	Alive, NED
5	54	M	26.5	Hematuria	R	17.0	1	T3aN0M1	ORNT + HCLR	3	Sunitinib	20	Alive, progressed at 3 months after surgery

HCLR = hepatic caudate lobe resection, LRNT = laparoscopic radical nephrectomy + thrombectomy, NED = no evidence of disease, ORN = open radical nephrectomy + thrombectomy, SD = stable disease.

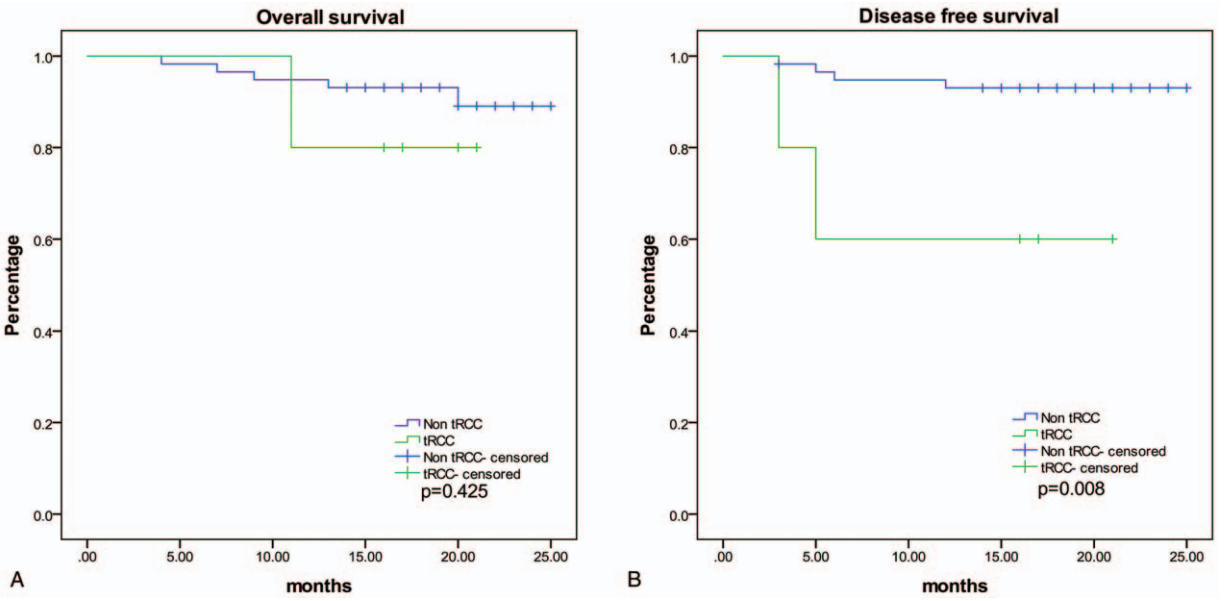

Figure 1. A: Overall survival analysis for whole cohort. B: Disease free survival analysis for whole cohort.

70 years while the conventional clear-cell RCC showed a peak at 51 to 60 years.[26] In our study, the median age of tRCC cohort is significantly younger than the non-tRCC cohort, which is consistent with works of literature mentioned above.

Owing to the low incidence of this unique subtype and tumor thrombus, no effective treatments with good evidence were established for this rare type, only some single case reports.[27] With the development of surgical equipment and perioperative intensive monitoring, aggressive surgical attempts have been expanded to such RCC patients with comparatively low mortality and morbity.[28] Most of the studies favoring surgical intervention were based on large series ccRCC patients with tumor thrombus.[18,29] Comparing with non-tRCC group, our analysis demonstrated a comparable OS rate in tRCC patients. It suggests that aggressive surgery could be offered for tRCC patients with thrombus.

Frédéric et al summarized that aggressive surgical management may achieve satisfactory survival outcome for nonmetastatic disease, while the metastatic disease is an indicator of poor survival outcome.[30] In our analysis, despite the small number of patients, we also identified the presence of metastatic disease at diagnosis as a negative marker of shorter DFS. However, a recent study suggested that radical nephrectomy and thrombectomy also is beneficial for metastatic patients.[31] In our study, Patient 5# was diagnosed of liver metastasis and received complete surgical resection including primary tumor, thrombus and liver metastasis. Unfortunately, the patient experienced single site bone metastasis at the 3rd postoperative month. Upon progression, he received local radiotherapy for bone metastasis and postoperative targeted therapy. During a 20 months follow-up, the man is still alive and disease is stable without evidence of progression. Although it was just a single case, it gives us inspiration for managing metastatic Xp11.2 tRCC.

With the efficacy of targeted molecular medicines have been validated in reducing the size of primary tumors and metastases, more and more clinicians begun to explore the clinical benefits of targeted molecular medicines in RCCs with tumor thrombus. Although several single case reports demonstrated the down-

Table 3

DFS survival in whole cohort by COX survival analysis.

	Univariable Analysis			Multivariable Analysis		
	HR	95%CI	*P* Value	HR	95%CI	*P* Value
Gender (Female vs Male)	0.027	0.000–37.364	.328	–		
Age (≥58 vs <58)	0.871	0.176–4.316	.866	–		
Side (Left vs Right)	0.946	0.173–5.164	.948	–		
Size (≥7 cm vs <7 cm)	33.993	0.019–62086.34	.357	–		
TNM (High vs Low)	0.046	0.000–253238.2	.697	–		
ISUP grade (High vs Low)	3.480	0.407–29.797	.255	–		
Lymph node invasion (Yes vs No)	2.204	0.257–18.866	.257	–		
Adjuvant therapy (Yes vs No)	3.241	0.593–17.706	.175	–		
Metastasis at diagnosis (Yes vs No)	8.006	1.602–40.023	.011	10.327	1.863–57.255	.008
Subtype (tRCC vs non-tRCC)	7.130	1.298–39.174	.024	9.939	1.589–62.162	.014

CI = confidence interval, HR = hazard ratio, tRCC = translocation renal cell carcinoma.

staging efficacy in patients with thrombus, minimal clinical effect on RCC tumor thrombus was confirmed by subsequent large series reports.[10,32–35] For postoperative adjuvant therapy, Gu et al reported that adjuvant treatment postoperatively showed no survival benefit for patients with thrombus in a prospective cohort study.[36] Although targeted therapy did not improve OS or DFS in our analysis, 3 tRCC patients received postoperative targeted molecular medicines showed a satisfactory oncological control.

There are still some limitations to our study. One major drawback of this study is that the sample size was insufficient due to the low incidence. Another problem is that it was a retrospective research, the results should be confirmed in larger prospective settings. Besides, the follow-up time is relatively short, more long-term scale observation should be conducted.

5. Conclusions

Taken together, these results suggest that radical nephrectomy and thrombectomy provide an acceptable efficacy for Xp11.2 tRCC patients with venous tumor thrombus. Being limited to small sample size and short follow-up time, more research using controlled trials is needed to be conducted in the future study.

Acknowledgments

The authors thank Hongxian Zhang, Lei Zhao, Guoliang Wang (Department of Urology, Peking University Third Hospital) for providing patients' information. The authors thank Kaiwen Ni (Department of Epidemiology and Hygienic Statistics,) for helping us with statistical analysis. The authors thank Min Lu (Department of Pathology) for reviewing all the pathology results.

Author contributions

Conceptualization: Lulin Ma.
Data curation: Xiaojun Tian.
Formal analysis: Jing Ma, Guojiang Zhao.
Funding acquisition: Yimeng Song, Shudong Zhang.
Writing – original draft: Liyuan Ge, Xiaojun Tian.
Writing – review & editing: Guojiang Zhao, Shudong Zhang.
Lulin Ma orcid: 0000-0002-9283-5931.

References

[1] Znaor A, Lortet-Tieulent J, Laversanne M, et al. International variations and trends in renal cell carcinoma incidence and mortality. Eur Urol 2015;67:519–30.
[2] Lopez-Beltran A, Scarpelli M, Montironi R, et al. 2004 WHO classification of the renal tumors of the adults. Eur Urol 2006;49:798–805.
[3] Ross H, Argani P. Xp11 translocation renal cell carcinoma. Pathology 2010;42:369–73.
[4] Bissada NK, Yakout HH, Babanouri A, et al. Long-term experience with management of renal cell carcinoma involving the inferior vena cava. Urology 2003;61:89–92.
[5] Psutka SP, Leibovich BC. Management of Inferior Vena Cava Tumor Thrombus in Locally Advanced Renal Cell Carcinoma. London, England: SAGE Publications; 2015. 7, 216–229.
[6] Hannan R, Margulis V, Chun SG, et al. Stereotactic radiation therapy of renal cancer inferior vena cava tumor thrombus. Cancer Biol Ther 2015;16:657–61.
[7] Escudier B, Eisen T, Stadler WM, et al. Sorafenib in advanced clear-cell renal-cell carcinoma. N Engl J Med 2007;356:125–34.
[8] de Martino M, Gigante M, Cormio L, et al. JAK3 in clear cell renal cell carcinoma: mutational screening and clinical implications. Urol Oncol 2013;31:930–7.
[9] Gnarra JR, Tory K, Weng Y, et al. Mutations of the VHL tumour suppressor gene in renal carcinoma. Nat Genet 1994;7:85–90.
[10] Cost NG, Delacroix SE, Sleeper JP, et al. The impact of targeted molecular therapies on the level of renal cell carcinoma vena caval tumor thrombus. Eur Urol 2011;59:912–8.
[11] Cai W, Huang J, Yuan Y, et al. Sunitinib or sorafenib as neoadjuvant therapy may not improve the survival outcomes of renal cell carcinoma with tumor thrombus. Urol Int 2018;101:391–9.
[12] Kakoki K, Miyata Y, Mochizuki Y, et al. Long-term treatment with sequential molecular targeted therapy for Xp11.2 translocation renal cell carcinoma: a case report and review of the literature. Clin Genitourin Cancer 2017;15:e503–6.
[13] Bellmunt J, Dutcher J. Targeted therapies and the treatment of non-clear cell renal cell carcinoma. Ann Oncol 2013;24:1730–40.
[14] Malouf GG, Camparo P, Molinié V, et al. Transcription factor E3 and transcription factor EB renal cell carcinomas: clinical features, biological behavior and prognostic factors. J Urol 2011;185:24–9.
[15] Song HC, Sun N, Zhang WP, et al. Biological characteristics of pediatric renal cell carcinoma associated with Xp11.2 translocations/TFE3 gene fusions. J Pediatr Surg 2014;49:539–42.
[16] Classe M, Malouf GG, Su X, et al. Incidence, clinicopathological features and fusion transcript landscape of translocation renal cell carcinomas. Histopathology 2017;70:1089–97.
[17] Miyake H, Terakawa T, Furukawa J, et al. Prognostic significance of tumor extension into venous system in patients undergoing surgical treatment for renal cell carcinoma with venous tumor thrombus. Eur J Surg Oncol 2012;38:630–6.
[18] Hatakeyama S, Yoneyama T, Hamano I, et al. Prognostic benefit of surgical management in renal cell carcinoma patients with thrombus extending to the renal vein and inferior vena cava: 17-year experience at a single center. BMC Urol 2013;13:47.
[19] Mancini V, Battaglia M, Ditonno P, et al. Current insights in renal cell cancer pathology. Urol Oncol 2008;26:225–38.
[20] Blute ML, Leibovich BC, Lohse CM, et al. The Mayo Clinic experience with surgical management, complications and outcome for patients with renal cell carcinoma and venous tumour thrombus. BJU Int 2004;94:33–41.
[21] Ciancio GVAS. Management of renal cell carcinoma with level III thrombus in the inferior vena cava. J Urol 2002;168:1374–7.
[22] Haferkamp A, Bastian PJ, Jakobi H, et al. Renal cell carcinoma with tumor thrombus extension into the vena cava: prospective long-term followup. J Urol 2007;177:1703–8.
[23] Abbasi A, Johnson TV, Ying K, et al. Duplicated vena cava with tumor thrombus from renal cancer: use of venogram for safer operative planning. Urology 2012;79:e57–8.
[24] Woodruff DY, Van Veldhuizen P, Muehlebach G, et al. The perioperative management of an inferior vena caval tumor thrombus in patients with renal cell carcinoma. Urol Oncol 2013;31:517–21.
[25] Kang HW, Seo SP, Kim WT, et al. Impact of young age at diagnosis on survival in patients with surgically treated renal cell carcinoma: a multicenter study. J Korean Med Sci 2016;31:1976.
[26] Choo MS, Jeong CW, Song C, et al. Clinicopathologic characteristics and prognosis of Xp11.2 translocation renal cell carcinoma: multicenter, propensity score matching analysis. Clin Genitourin Cancer 2017;15: e819–25.
[27] Zhu G, Qiu X, Chen X, et al. Cardiopulmonary bypass-assisted surgery for the treatment of Xp11.2 translocation/TFE3 gene fusion renal cell carcinoma with a tumor thrombus within the inferior vena cava: a case report. Oncol Lett 2015;10:3532–4.
[28] Xu B, Zhao Q, Jin J, et al. Laparoscopic versus open surgery for renal masses with infrahepatic tumor thrombus: the largest series of retroperitoneal experience from china. J Endourol 2014;28:201–7.
[29] Berczi A, Flasko T, Szerafin T, et al. Surgical management and outcome of renal cell carcinoma with inferior vena cava tumor thrombus. Urol Int 2017;99:267–71.
[30] Pouliot F, Shuch B, Larochelle JC, et al. Contemporary management of renal tumors with venous tumor thrombus. J Urol 2010;184:833–41.
[31] Manso M, Pacheco-Figueiredo L, Santos-Silva A, et al. Renal cell carcinoma with venous thrombus: should surgery be offered when metastasis is present at diagnosis? Urol Int 2018;101:387–90.
[32] Karakiewicz PI, Suardi N, Jeldres C, et al. Neoadjuvant sutent induction therapy may effectively down-stage renal cell carcinoma atrial thrombi. Eur Urol 2008;53:845–8.

[33] Robert G, Gabbay G, Bram R, et al. Complete histologic remission after sunitinib neoadjuvant therapy in T3b renal cell carcinoma. Eur Urol 2009;55:1477–80.
[34] Harshman LC, Srinivas S, Kamaya A, et al. Laparoscopic radical nephrectomy after shrinkage of a caval tumor thrombus with sunitinib. Nat Rev Urol 2009;6:338–43.
[35] Bigot P, Fardoun T, Bernhard JC, et al. Neoadjuvant targeted molecular therapies in patients undergoing nephrectomy and inferior vena cava thrombectomy: is it useful? World J Urol 2014;32:109–14.
[36] Gu L, Li H, Chen L, et al. Postoperative adjuvant sorafenib or sunitinib for nonmetastatic renal cell carcinoma with venous tumor thrombus: a prospective cohort study. Transl Oncol 2017;10:949–55.