

ORIGINAL RESEARCH REPORT

Demographic trends in clear cell renal cell carcinoma: insights from tertiary hospital in Surabaya

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ABSTRACT

Background: Clear cell renal cell carcinoma (ccRCC) is the most common renal malignancy, with distinct clinicopathological features. Despite established global patterns, regional characteristics in Indonesia remain understudied. This study describes ccRCC profiles at a tertiary Indonesian hospital, focusing on demographic trends, tumor characteristics, and staging patterns to enhance local diagnostic and management approaches. **Objective:** This study aims to describe the characteristics of ccRCC in Dr. Soetomo General Academic Hospital from 2014-2022. **Material and Method:** This is a retrospective descriptive study using secondary data including age, sex, tumor size, and pathological grade. **Result:** There were 50 patients of ccRCC throughout 9 years, most of them were male (70%), and 30% were female. Age group span between 31-80, with 51-60 age group being the most dominant (18%). Tumor sizes were grouped by <7 cm (40%) and >7 cm (60%), with 14 cm being the biggest size. The most common histopathology stage was T2 (42%), followed by T3 (32%), T1 (14%), and T4 (12%). **Conclusion:** The most common patients of ccRCC in Dr. Soetomo General Academic Hospital Surabaya were male patients, aged 51-60, with mostly > 7cm tumor size and in stage T2.



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Highlights

1. This study provides profile of ccRCC patients in an Indonesian tertiary hospital, filling a vital gap in regional oncological data from a resource-limited setting where such evidence is scarce.



2. The predominance of advanced-stage tumors contrasts sharply with Western cohorts, underscoring the interplay of healthcare access, awareness, and potential biological factors in driving aggressive disease presentations in Indonesia.

BACKGROUND

Renal cell carcinoma (RCC), a malignant neoplasm arising from the renal tubular epithelium, ranks as the third most prevalent genitourinary cancer and the thirteenth most frequent cause of global cancer mortality (Fiebig and Kraywinkel, 2019; Hsieh et al., 2017), with more than 10 subtype based on histology and molecular (Hsieh et al., 2017), with different prognosis, imaging characteristics and morbidities (Ng et al., 2008). Epidemiological data demonstrate a consistent year-over-year increase in its incidence rates worldwide (Bukavina et al., 2022; Gürsoy et al., 2020), with variations incidence across time, geography and sex (Bukavina et al., 2022). The major subtypes, counting 5% incidence, including clear cell RCC (ccRCC), papillary RCC and chromophobe (Kanwal, 2023). ccRCC represents the predominant histological variant (Kase et al., 2023), comprising 75-85% of all RCC cases (Gkolfinopoulos et al., 2020; Naghdibadi et al., 2023). This subtype demonstrates particularly aggressive biological behavior, evidenced by its dismal prognosis - metastatic cases show a strikingly low 5-year survival rate of just 8% (Weaver et al., 2022). A study found age-adjusted incidence were increased almost 4-times during the last 17 years (2000 to 2017), with significantly improvement of overall survival during 2009-2017 (Liao et al., 2025). The metastasis this neoplasm including the liver, bone, lungs, and brain (Kase et al., 2023). Immunotherapy is one of medical option for treating metastatic renal cell cancer (Gkolfinopoulos et al., 2020), beside single targeted therapy targeting specific molecular pathway (Gkolfinopoulos et al., 2020), cytoreductive nephrectomy and radiation therapy (Kase et al., 2023).

Epidemiological and pathological data on ccRCC in Indonesia are still limited despite its clinical importance (Rahaju et al., 2024). The majority of studies on this disease focus on Western populations, where risk factors and diagnostic processes may differ (Barrera-Juarez et al., 2024). In environments with variable resources, such as Indonesia, this gap restricts evidence-based approaches for early detection and management. The previous study to conduct the characteristics of ccRCC at 2010-2014 in Bandung summarized a total of 12 ccRCC cases out of 25 RCC subjects that predominant on male with a wide range of age, from pediatric to adult population (Suryana Putra et al., 2016).

OBJECTIVE

This study aims to describe the characteristics of ccRCC in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

MATERIAL AND METHODS

Study design

This is a descriptive retrospective study, using secondary data of all radical nephrectomy patients with ccRCC diagnosis at Dr. Soetomo General Academic Hospital's Anatomical Pathology Laboratory (January 2014-June 2022).

Data collection

Medical records and histopathology forms were reviewed. Sex and age data were collected. To ensure diagnostic accuracy, all ccRCC slides underwent blinded re-evaluation by anatomical pathologists to verify the primary diagnosis and tumor stage. We excluded specimens showing additional malignant diagnoses.

Data analysis

Categorical variables were presented as frequencies and percentages.

RESULTS

The study included 50 ccRCC cases with a male predominance (70%, n=35) and a male-to-female ratio of 2.3:1. The mean patient age was 57.4 years (range: 32-75), with age distribution peaking in the 51-60 year group (38%, n=19), followed by 61-70 years (30%, n=15), 41-50 years (20%, n=10), 71-80 years (8%, n=4), and 31-40 years (4%, n=2), as showed in table 1.

Table 1. Age distribution in ccRCC patients

Age category	n	%
31-40	2	4
41-50	10	20
51-60	19	38
61-70	15	30
71-80	4	8
Total	50	100

Pathological staging (American Joint Committee on Cancer and American College of Surgeons, 2018; Amin et al., 2017) revealed T2 tumors as most common (42%, n=21), particularly among males (24%, n=12) and the 51-60 year group (18%, n=9). T3 cases comprised 32% (n=16), with highest frequency in 51-60 year-olds (14%, n=7). T1 tumors (14%, n=7) occurred most frequently in 41-50 year-olds (6%, n=3), while T4 (12%, n=6) predominated in 61-70 year-olds (6%, n=3). Staging criteria followed: T1 (≤ 7 cm, organ-confined), T2 (> 7 cm, organ-confined), T3 (perirenal extension), and T4 (Gerota's fascia invasion).

Table 2. Pathology T stage distribution across ccRCC patients

T stage	Male (n)	Female (n)	Total (n)
T1	6	1	7
T2	12	9	19
T3	12	4	16
T4	5	1	6
Total	35	15	50

DISCUSSION

Globally, renal cell carcinoma remains a significant public health concern, currently ranking as the 12th most common cancer worldwide (Cirillo et al., 2024). The observed increase in incidence rates, particularly in developing nations like Indonesia, may be attributed to multiple factors including advancements in diagnostic imaging technologies that have improved detection rates, as well as the rising prevalence of modifiable risk factors such as tobacco use, obesity, and hypertension (Dumith et al., 2012; Makino et al., 2022). These findings are particularly relevant to our Indonesian context, where previous multicenter data from nine major hospitals (2013-2017) documented 635 cases of renal cancer, with ccRCC representing 42% of these cases (Rahaju et al., 2024). The identification of 50 ccRCC cases at our institution during the study period suggests a potentially increasing disease burden that merits continued surveillance. Two recent study investigating the clinical profile of ccRCC have been conducted during 2014 to 2020 in the same hospital center, with the finding: male predominant, high grade (pT2), with metastase stage of N0 during 2016-2020 (Thaib and Rahaju, 2022), while the older study taking during 2014-2017 involving renal cell carcinoma patients stated similar study: male predominant with age of 50-56 years-old, stage 2 tumor and mostly ccRCC subtype receiving radical nephrectomy (Rusdhy et al., 2019).

Age

Our demographic analysis revealed a mean patient age of 57.3 years (range: 32-75 years), with the highest proportion of cases (18%) occurring in the 51-60 year age group. This finding aligns with

previous reports from Hasan Sadikin Hospital in Bandung that identified peak incidence between 51-65 years (mean age 58 years) (Suryana Putra et al., 2016). However, it is noteworthy that our patients presented at a younger average age compared to Western populations, where studies of over 87,000 American patients reported a mean diagnosis age of 62 years (Liao et al., 2025). This discrepancy may reflect regional differences in risk factor profiles, genetic predisposition, or healthcare access patterns. The presence of two early-onset cases (ages 35 and 36 years) in our series suggests the possible contribution of genetic factors such as von Hippel-Lindau (VHL) syndrome (Vocke et al., 2022; Zhang et al., 2024) or Xp11.2 translocation in these younger patients (Gopee-Ramanan et al., 2022; Wang et al., 2020). A study highlight that during the period of 1990-2000, the patient's age of RCC were 61.1 years-old, while during 2017-2021, the age were younger (53.7 years-old), meaning there were a significantly lower mean age, with a significant increment in female, with male-to-female ratio of 3.4:1 to 1.9:1 (Al Azab et al., 2024).

Sex

The male predominance observed in our study (70% male, 30% female; ratio 2.3:1) is consistent with global patterns which show a 1.5-fold higher incidence in males (Ning et al., 2023; Peired et al., 2021; Schiavoni et al., 2023). This gender disparity may be partially explained by lifestyle factors more prevalent among Indonesian males, particularly tobacco use - a well-established risk factor for ccRCC. Striking gender disparities exist in smoking prevalence among Indonesian adults, with 67.2% of working-age men being active smokers compared to only 2.16% of women. Given the well-established association between tobacco use and renal carcinogenesis, this substantial difference in smoking rates likely contributes to the observed male predominance in ccRCC cases in our population (Holipah et al., 2020; Satyana et al., 2020). Tobacco smoking significantly elevates hypertension risk through multiple pathophysiological mechanisms. Nicotine induces acute blood pressure elevation via sympathetic nervous system activation and systemic vasoconstriction, while chronic smoking promotes endothelial dysfunction, arterial stiffness, and oxidative stress - all contributing to sustained hypertension development. Epidemiological studies demonstrate smokers have 1.5-2 times greater hypertension risk compared to non-smokers, with risk correlating to smoking intensity and duration (Klein, 2022; Kshatri et al., 2022). Additionally, the relative risk of ccRCC in individuals with hypertension is estimated to be 1.2 to 1.71-times higher compared to those without hypertension (Yang et al., 2024). The observed male predominance in ccRCC may be driven, in part, by sex-specific genomic and immunomodulatory pathways. Studies suggest that the androgen-androgen receptor (AR) axis promotes a permissive tumor microenvironment (TME) in males, potentially through transcriptional regulation of immune checkpoint molecules (e.g., PD-L1) or T-cell exhaustion pathways (Ning et al., 2023). Specifically, male ccRCC tumors exhibit higher infiltration of dysfunctional CD8⁺ T-cells, which show upregulated exhaustion markers (e.g., PD-1, TIM-3) and impaired cytotoxic activity—a phenotype linked to AR-mediated suppression of T-cell effector genes.

Stage

Consistent with global patterns, the cited multicenter study (Chen et al., 2017; Fateh et al., 2023; Lai et al., 2022) identified T1 as the most common stage at RCC diagnosis (60-70% of cases), particularly T1a tumors (≤ 4 cm). However, our study exhibited a higher prevalence of advanced-stage tumors (T2/T3). The predominance of larger tumors at diagnosis in our study population may reflect disparities in healthcare access, as evidenced by comparative data from regions with robust private healthcare sectors. Studies demonstrate that in systems with widespread availability of private medical services (Barrera-Juarez et al., 2024), renal tumors are more frequently detected at smaller sizes and earlier stages—likely due to higher utilization of routine imaging and preventive care. This contrasts with our findings, suggesting that limited access to diagnostic resources in Indonesia's predominantly public healthcare system may contribute to delayed detection. A case study underlined a late diagnostic resulting with giant renal cell carcinoma (Rahmatika et al., 2024). This might be answered why our findings contrasting others. A study also highlight socioeconomic factors reagrding on tumor size (Hellenthal and Bermejo, 2012), and surprisingly, this factor also became an independent predictive factor of short-survival (Danzig et al., 2014).

The clinical implications of our findings are several-fold. First, the relatively young age at diagnosis compared to Western populations suggests the need for heightened clinical suspicion for ccRCC in younger Indonesian patients with relevant symptoms or risk factors. Second, the strong male predominance and association with modifiable risks like smoking and hypertension highlight important opportunities for preventive interventions and public health education. Finally, the predominance of larger tumors at diagnosis underscores the need for strategies to improve early detection in our healthcare setting, possibly through targeted imaging in high-risk populations or enhanced physician awareness.

Limitations

This study has several limitations, including its retrospective design, which may lead to missing or incomplete data, and its single-center nature, limiting generalizability to other healthcare settings in Indonesia. Despite these constraints, the findings provide valuable insights into ccRCC characteristics in an understudied population.

CONCLUSION

This study characterizes ccRCC in an Indonesian tertiary hospital, confirming global patterns of male predominance and late-middle-age onset while revealing regional distinctiveness through younger presentation ages and larger tumor sizes at diagnosis. These findings underscore the need for tailored early detection strategies and highlight opportunities for preventive interventions.

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Conflict of Interest

The author declares no conflict of interest.

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Ethical Clearance

This research received ethical clearance from the Institutional Review Board of Dr. Soetomo General Academic Hospital, complying with OHRP regulations (Approval No. 1197/LOE/301.4.2/I/2023; January 24, 2023).

Author Contribution

ASS: writing, curation, translating, data analysis, funding; ASR: conceptualizing, review, editing; NK: writing, translating, review, editing.

REFERENCES

- Al Azab, R.S., Al-Zubi, M.T., Aladaileh, M.A.A., Darwazeh, H., Alshboul, M., Khader, Y.S., Ghalayini, I.F., Mustafa Ali, M.A., Al Demour, S., 2024. Renal cell carcinoma: an overview of the epidemiology, presentation, histopathological characteristics, and surgical treatment variation between old and new era – a cross-sectional study. *Int. J. Surg. Open* 62, 140–143.
- American Joint Committee on Cancer, American College of Surgeons, 2018. *AJCC Cancer staging manual*, 8th ed, Atlas of Cross-Sectional and Projective MR Cholangiopancreatography. Springer, Chicago, US.
- Amin, M.B., Greene, F.L., Edge, S.B., Compton, C.C., Gershenwald, J.E., Brookland, R.K., Meyer, L., Gress, D.M., Byrd, D.R., Winchester, D.P., 2017. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more “personalized” approach to cancer staging. *CA. Cancer J. Clin.* 67, 93–99.
- Barrera-Juarez, E., Halun-Trevino, A.N., Ruelas-Martinez, M., Madero-Frech, A., Camacho-Trejo, V., Estrada-Bujanos, M., Bojorquez, D., Uribe-Montoya, J., Rodriguez-Covarrubias, F., Villarreal-Garza, C., 2024. Prognosis impact and clinical findings in renal cancer patients: comparative analysis between public and private health coverage in a cross-sectional



- and multicenter context. *Cancer Causes Control* 36, 265–273.
- Bukavina, L., Bensalah, K., Bray, F., Carlo, M., Challacombe, B., Karam, J.A., Kassouf, W., Mitchell, T., Montironi, R., O'Brien, T., Panebianco, V., Scelo, G., Shuch, B., van Poppel, H., Blosser, C.D., Psutka, S.P., 2022. Epidemiology of Renal Cell Carcinoma: 2022 Update. *Eur. Urol.* 82, 529–542.
- Chen, L., Ma, X., Li, H., Gu, L., Li, X., Gao, Y., Xie, Y., Zhang, X., 2017. Influence of tumor size on oncological outcomes of pathological T3aN0M0 renal cell carcinoma treated by radical nephrectomy. *PLoS One* 12, 2–11.
- Cirillo, L., Innocenti, S., Becherucci, F., 2024. Global epidemiology of kidney cancer. *Nephrol. Dial. Transplant.* 39, 920–928.
- Danzig, M.R., Weinberg, A.C., Ghandour, R.A., Kotamarti, S., McKiernan, J.M., Badani, K.K., 2014. The association between socioeconomic status, renal cancer presentation, and survival in the United States: A survival, epidemiology, and end results analysis. *Urology* 84, 583–589.
- Dumith, S.C., Garcia, L.M.T., Da Silva, K.S., Menezes, A.M.B., Hallal, P.C., 2012. Predictors and health consequences of screen-time change during adolescence - 1993 Pelotas (Brazil) birth cohort study. *J. Adolesc. Heal.* 51, S16–S21.
- Fateh, S., Arkawazi, L., Tahir, S., Rashid, R., Rahman, D., Aghaways, I., Kakamad, F., Salih, A., Bapir, R., Fakhraddin, S., Fattah, F., Abdalla, B., Mohammed, S., 2023. Renal cell carcinoma T staging: Diagnostic accuracy of preoperative contrast-enhanced computed tomography. *Mol. Clin. Oncol.* 18, 1–7.
- Fiebig, J., Kraywinkel, K., 2019. Epidemiology of renal cell carcinoma in Germany. *Onkologie* 25, 483–487.
- Gkolfinopoulos, S., Psyri, A., Bamias, A., 2020. Clear-cell renal cell carcinoma - A comprehensive review of agents used in the contemporary management of advanced/metastatic disease. *Oncol. Rev.* 20.
- Gopee-Ramanan, P., Chin, S., Lim, C., Shanbhogue, K.P., Schieda, N., Krishna, S., 2022. Renal Neoplasms in Young Adults. *Radiographics* 42, 433–450.
- Gürsoy, D., Seçinti, İ.E., Hakverdi, S., Görür, S., 2020. Renal Cell Carcinoma : Epidemiological Profile and Histopathological Features. *Bull Urooncol* 19, 68–73.
- Hellenthal, N.J., Bermejo, C.E., 2012. The role of socioeconomic status in renal cell carcinoma. *Urol. Oncol. Semin. Orig. Investig.* 30, 89–94.
- Holipah, H., Sulistomo, H.W., Maharani, A., 2020. Tobacco smoking and risk of all-cause mortality in Indonesia. *PLoS One* 15, 1–12.
- Hsieh, J.J., Purdue, M.P., Signoretti, S., Swanton, C., Albiges, L., Schmidinger, M., Heng, D.Y., Larkin, J., Ficarra, V., 2017. Renal cell carcinoma. *Nat. Rev. Dis. Prim.* 3.
- Kanwal, R., 2023. Metastasis in renal cell carcinoma: Biology and treatment. *Adv. Cancer Biol. - Metastasis* 7, 100094.
- Kase, A.M., George, D.J., Ramalingam, S., 2023. Clear Cell Renal Cell Carcinoma: From Biology to Treatment. *Cancers (Basel)* 15, 1–15.
- Klein, L.W., 2022. Pathophysiologic Mechanisms of Tobacco Smoke Producing Atherosclerosis. *Curr. Cardiol. Rev.* 18.
- Kshatri, J.S., Satpathy, P., Sharma, S., Bhoi, T., Mishra, S.P., Sahoo, S.S., 2022. Health research in the state of Odisha, India: A decadal bibliometric analysis (2011–2020). *J. Fam. Med. Prim. Care* 6, 169–170.
- Lai, G.S., Li, J.R., Wang, S.S., Chen, C.S., Yang, C.K., Hung, S.C., Cheng, C.L., Ou, Y.C., Chiu, K.Y., 2022. Tumor Size Significantly Affects Prognosis in Pathological T3a Renal Cell Carcinoma. *Anticancer Res.* 42, 2185–2191.
- Liao, Z., Cui, L., Pai, P., Lu, Y., Li, X., Wang, G., Huang, W., Wang, D., Shaikh, N., Peng, Zhangzhe, Peng, Zhuoming, He, H., Liao, Z., 2025. Incidence and survival patterns of clear cell renal cell carcinoma from 2000 to 2017, based on A SEER Database. *J. Cancer* 16, 1591–1597.
- Makino, T., Kadomoto, S., Izumi, K., Mizokami, A., 2022. Epidemiology and Prevention of Renal Cell Carcinoma. *Cancers (Basel)* 14, 1–20.
- Naghdibadi, M., Momeni, M., Yavari, P., Gholaminejad, A., Roointan, A., 2023. Clear Cell Renal Cell Carcinoma: A Comprehensive in silico Study in Searching for Therapeutic Targets. *Kidney Blood Press. Res.* 48, 135–150.
- Ng, C.S., Wood, C.G., Silverman, P.M., Tannir, N.M., Tamboli, P., Sandler, C.M., 2008. Renal cell carcinoma: Diagnosis, staging, and surveillance. *Am. J. Roentgenol.* 191, 1220–1232.
- Ning, K., Peng, Y., Jiang, Y., Li, Z., Luo, X., Lin, L., Deng, M., Wu, Y., Huang, T., Huang, Y., Xie, Y., Yang, X., Zhang, M., Xiong, L., Zou, X., Zhou, Z., Zhou, F., Dong, P., Yu, C., Zhang, Z., 2023. Sex differences in renal cell carcinoma: a single-cell analysis reveals exhausted CD8⁺ T-cells highly infiltrated in males. *Biol. Sex Differ.* 14, 1–16.
- Peired, A.J., Campi, R., Angelotti, M.L., Antonelli, G., Conte, C., Lazzeri, E., Becherucci, F., Calistri, L., Serni, S., Romagnani, P., 2021. Sex and gender differences in kidney cancer: Clinical and experimental evidence. *Cancers (Basel)* 13, 1–22.
- Rahaju, A.S., Rahniayu, A., Kusumastuti, E.H., Wiratama, P.A., Thaib, P.K.P., Takaria, M., 2024. Correlation between PD-

- L1 and Ki-67 Expression at various T-stage Clear Cell Renal Cell Carcinomas. *Res. J. Pharm. Technol.* 17, 109–114.
- Rahmatika, N., Wirjopranoto, S., Azmi, Y.A., Putra, A.G.P., Soetanto, K.M., 2024. Outcome of delayed presentation in patients with giant renal cell carcinoma: A case report. *Int. J. Surg. Case Rep.* 125, 110541.
- Rusdhy, F., Djatisoesanto, W., Erawati, D., Fauziah, D., 2019. Characteristics of Renal Cell Carcinoma Patients in RSUD Dr Soetomo Surabaya in 2014-2017 486 | Publisher : Humanistic Network for Science and Technology Health Notions , Volume 3 Number 12 (December 2019) ISSN 2580-4936 487 | Publisher : Humanistic Net. *Heal. Notions* 3, 486–489.
- Satyana, R.P.U., Uli, R.E., Magliano, D., Zomer, E., Liew, D., Ademi, Z., 2020. Assessing the impact of smoking on the health and productivity of the working-age Indonesian population using modelling. *BMJ Open* 10, 1–12.
- Schiavoni, V., Campagna, R., Pozzi, V., Cecati, M., Milanese, G., Sartini, D., Salvolini, E., Galosi, A.B., Emanuelli, M., 2023. Recent Advances in the Management of Clear Cell Renal Cell Carcinoma: Novel Biomarkers and Targeted Therapies. *Cancers (Basel)*. 15.
- Suryana Putra, D., Suryanti, S., Sihombing, A.T., 2016. Characteristics of Renal Cell Carcinoma in Dr. Hasan Sadikin General Hospital Bandung, 2010–2014. *Althea Med. J.* 3, 644–648.
- Thaib, P.K.P., Rahaju, A.S., 2022. Clinicopathological profile of clear cell renal cell carcinoma. *Int. J. Heal. Med. Sci.* 5, 91–100.
- Vocke, C.D., Ricketts, C.J., Metwalli, A.R., Pinto, P.A., Gautam, R., Raffeld, M., Merino, M.J., Ball, M.W., Linehan, W.M., 2022. Differential VHL Mutation Patterns in Bilateral Clear Cell RCC Distinguishes Between Independent Primary Tumors and Contralateral Metastatic Disease. *Urology* 165, 170–177.
- Wang, Yuxiong, Wang, Yuantao, Feng, M., Lian, X., Lei, Y., Zhou, H., 2020. Renal cell carcinoma associated with Xp11.2 translocation/transcription factor E3 gene fusion: an adult case report and literature review. *J. Int. Med. Res.* 48.
- Weaver, C., Bin Satter, K., Richardson, K.P., Tran, L.K.H., Tran, P.M.H., Purohit, S., 2022. Diagnostic and Prognostic Biomarkers in Renal Clear Cell Carcinoma. *Biomedicines* 10.
- Yang, G., Wang, Y., Lai, Z.W., Zhang, H., Zhang, Y., Song, F., 2024. Renin-angiotensin-system and clear cell renal carcinoma: research advances and future perspectives. *J. Cancer Metastasis Treat.* 10.
- Zhang, S., Fang, T., He, Y., Feng, W., Yu, Z., Zheng, Y., Zhang, C., Hu, S., Liu, Z., Liu, J., Yu, J., Zhang, H., He, A., Gong, Y., He, Z., Yang, K., Xi, Z., Yu, W., Zhou, L., Yao, L., Yue, S., 2024. VHL mutation drives human clear cell renal cell carcinoma progression through PI3K/AKT-dependent cholesteryl ester accumulation. *eBioMedicine* 103, 105070.