Original Study

Collecting Duct Carcinoma: Characteristics and Survival Outcomes From UroCCR Database (CDCSurv UroCCR n°141)

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Abstract

Renal collecting duct carcinoma is a rare and aggressive cancer with poor prognosis. This retrospective study analyzed 29 patients from the UroCCR database. Median cancer-specific survival was 21 months, with frequent early recurrences. Localized disease and smaller tumors were linked to better outcomes, highlighting the important need for improved management and innovative therapeutic approaches.

Objectives: To describe characteristics and survival outcomes of patients with renal collecting duct carcinoma (RCDC). **Methods:** We retrospectively analyzed data from patients treated for RCDC and included in the UroCCR database between 2007 and 2023. All tumors had a centralized pathological review by a CARARE network pathologist. Oncologic outcomes for cancer-specific survival (CSS) and progression-free survival (PFS) were estimated using the Kaplan-Meier method. **Results:** A total of 29 patients with RCDC were included. The prevalence of RCDC in the UroCCR database was 0.18% (29/16133). The median age was 63 years (45-81). At diagnosis, 20 (69%) patients were symptomatic and 9 (31%) had a metastatic disease. Partial and radical nephrectomy were performed in respectively 8 (29.6%) and 19 (70.4%) cases. The median CSS were 21 months (95% CI 9.6-32) and median PFS was 7 months (95% CI 3.6-10.3). In the nonmetastatic group, the median CSS was 22 months (95% CI: 6.2-37), and median PFS was 12 months (95% CI: 0-39). Two years estimated PFS and CSS rates were respectively 29.7% and 38%. A localized disease ($P = .012$) and a tumor size inferior to 4 cm ($P = .045$) were associated with better oncological outcomes. **Conclusion:** RCDC is a rare cancer with poor prognosis, and no treatment has demonstrated a significant improvement in survival. Recurrences

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are frequent and early. Management is heterogeneous and ineffective. These outcomes reinforce the need to better understand this tumor and evaluate alternative treatments.

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Keywords: Renal cancer, Nonclear renal cell carcinoma, CARARE network, Oncological outcomes, Patient characteristics

Introduction

The renal collecting duct carcinoma (RCDC), also known as Bellini carcinoma, is a rare malignant tumor of the kidney's collecting duct, distinct from clear cell renal cell carcinoma. It arises within the medullary collecting duct cells.[1–4]

Studies indicate its incidence among kidney tumors ranges from 0.6% to 2%.[5] The average age at diagnosis is 59 years, with a male-to-female sex ratio of 2.[2] Over two third of patients are smokers.[6] For less than 30% of patients, the tumor is incidentally discovered through imaging. Most patients present symptomatic tumors at the time of diagnosis. Common symptoms include gross hematuria (37%), abdominal pain, lumbar mass, weight loss, and asthenia.[7]

Diagnosis is typically guided by imaging, often using an abdomino-pelvic CT scan. There are no specific radiological signs of RCDC, but some characteristic features include its endophytic location within the renal medulla, infiltrating the renal sinus while respecting the renal cortex. On unenhanced scans, it shows spontaneous hyperdensity compared to surrounding healthy tissue. On contrast-enhanced scans, it shows heterogeneous low enhancement[2,8] (Figure 1).

RCDC is an aggressive tumor with a poor prognosis. Over 30% of the cases are diagnosed at a metastatic stage, often requiring systemic treatment.[2,9]

The diagnosis is confirmed through histological analysis based on WHO criteria[1] (Figure 2). The histological, clinical and radiological characteristics of RCDC place it in an intermediate position between renal cell carcinoma and urothelial carcinoma of the upper urinary tract. The RCDC should be considered as distinct entity among kidney tumors.[2]

Therapeutic management is not well established.[9,10] According to the Guidelines, localized renal cell carcinoma should be treated with surgery, while platinium-based chemotherapy may be considered for metastatic RCDC. Cabozantinib monotherapy is an alternative treatment.[6,11] Panunzio et al. reported from the SEER database that the median cancer specific survival (CSS) was 18 months in a retrospective study of 399 RCDC patients.[12] Xie et al. described, based on Mayo Clinic's nephrectomy registry, that operated RCDC patients had a median OS of 18 months and a median PFS of 6 months.[5] Zhou et al. reported, in a prospective study of 50 metastatic RCDC patients in Peking University Cancer Hospital, that those receiving gemcitabine, cisplatin, and sorafenib had a median OS of 12.6 months and a median PFS of 6.4 months.[4]

This study aimed to describe characteristics and survival outcomes of patients treated for RCDC and to identify prognostic factors.

Materials and Methods

Patients

This study included all confirmed cases of RCDC (metastatic or not) from the UroCCR database (NCT03293563, CNIL authorization number: DR-2013-206), from January 2007 to May 2023. UroCCR is a French national clinicobiological multidisciplinary database dedicated to Kidney Cancer. All patients underwent centralized review by an expert pathologist from the CARARE (CAncers RAres du REin) network. The 40 UroCCR centers were requested to update data retrospectively. Collected clinical-pathological features and follow-up data included age, sex, African phenotype, tobacco use, BMI, TNM stage, ECOG status, metastatic sites, surgery, histological diagnosis, imaging, systemic treatment, time between diagnosis and systemic treatment, biological markers, clinical presentation, RECIST v1.1 criteria, OS, CSS and PFS. The study obtained approval from Ethical Committee (DC 2012/108). Histological diagnoses were confirmed by pathologists using WHO criteria.[1]

PFS and CSS were calculated based on the Kaplan-Meier method with the Log Rank test. Recurrence and death risk factors were evaluated in patients with malignant pathology using a Cox regression analysis. The significance threshold P was set at .05.

Qualitative variables were described with absolute values and percentages, and quantitative values with median, first quartile, and third quartile. Statistical analyses were performed with SPSS® Version 15.0 Software.

Results

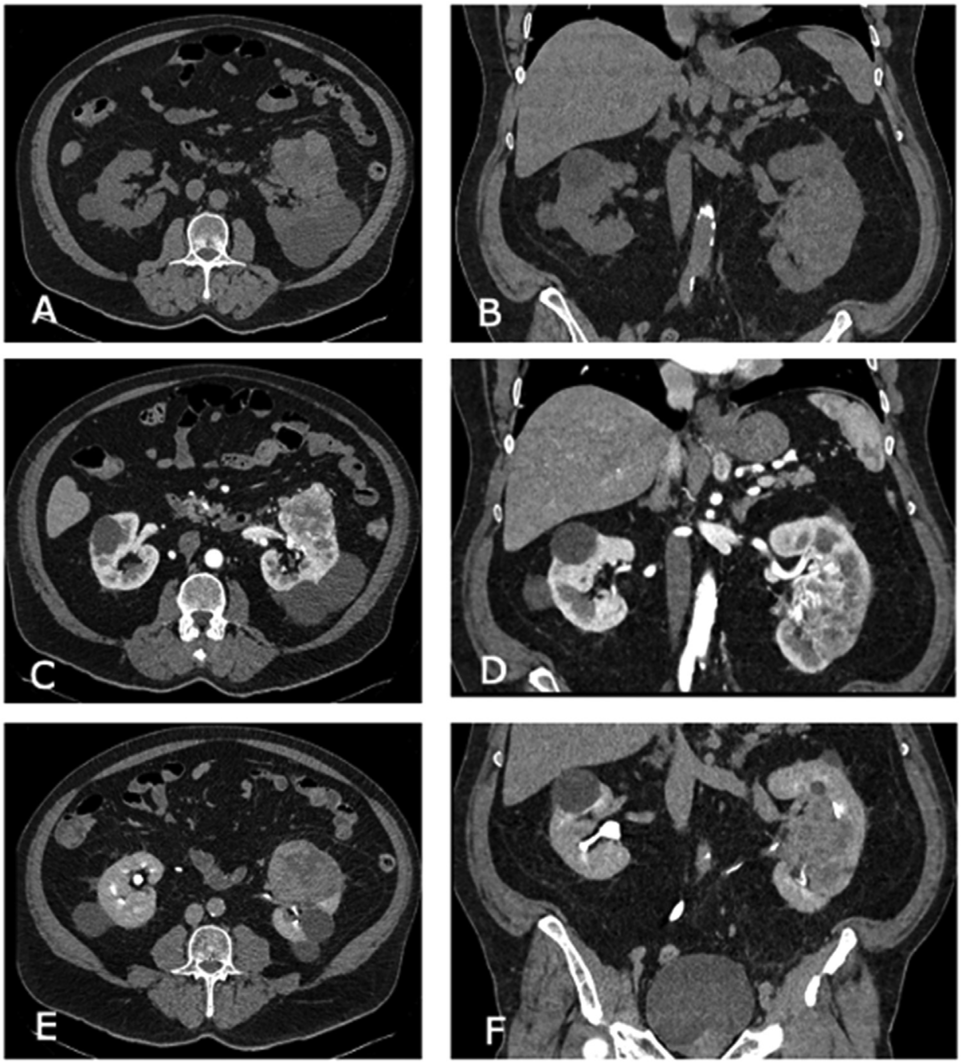
Patient Characteristics

A total of 29 patients with RCDC were included in our analysis. In the UroCCR database, there were 16 133 patients with renal cancer at the time of the study. The prevalence of RCDC in the UroCCR database was 0.18%. Patient characteristics are reported in Table 1.

The median age was 63 years (range 45-81). The male-to-female sex ratio was 2.22. There were 2 (7%) patients with African phenotype. There were 6 (20.7%) smokers. The median BMI was 26.2 kg/m² (range 19.5-41.6).

At diagnosis, 20 (69%) patients were symptomatic, and 27 (93%) patients had an ECOG performance status $\leq$1. At diagnosis, 14 patients underwent biopsy prior to treatment, and the correlation between the biopsy and the surgical specimen was 50%. There were 27 (93%) patients who underwent nephrectomy. Partial and radical nephrectomy were performed in respectively 8 (29.6%) and 19 (70.4%) cases. Among the patients who underwent partial nephrectomy, 6 had clear surgical margins, while 2 had in touch with tumor.

Figure 1 CT scan of left renal collecting duct carcinoma. (A) Unenhanced axial, (B) Unenhanced coronal, (C) Arterial enhanced axial, (D) Arterial enhanced coronal, (E) Delayed excretory-phase axial, (F) Delayed excretory-phase coronal. The tumor presents a solid appearance. On unenhanced imaging, it shows spontaneous hyperdensity compared to adjacent healthy tissues. On arterial enhanced imaging, it shows heterogeneous low enhancement. On delayed excretory-phase, it is endophytic within the renal medulla, infiltrating the renal sinus.



The tumor was localized in the upper-pole, in the median part and in the lower pole of the kidney in respectively 9 (31%), 12 (41%) and 8 (27%) cases. The tumor invaded the renal sinus in 11 (38%) cases. There were 17 (59%) patients classified as ≥ T3, and 9 (31%) patients classified metastatic at diagnosis. Among the 9 metastatic patients, 3 (33%) had more than 2 metastatic sites.

Survival Results

In the entire cohort, the median CSS was 21 months (95% CI 9.6-32) (Figure 3) and the median PFS was 7 months (95% CI 3.6-10.3) (Figure 4). In multivariate cox regression analysis, metastatic disease at diagnosis was the only predictive factor of specific death (Table 2).

For nonmetastatic patients, the median CSS was 22 months (95% CI: 6.2-37), and the median PFS was 12 months (95% CI: 0-39). Two years estimate PFS and CSS rates were respectively 29.7% and 38%. A tumor size inferior to 4 cm was associated with better outcomes ($P = .045$) (Figure 5).

For patients with metastatic RCDC, the median CSS was 4 months (95% CI: 1-6.9). There was a significant difference between the median CSS for nonmetastatic patients and for metastatic patients ($P = .012$) (Figure 6).

Management of metastatic patients is reported in Table 3.

Figure 2 Histopathologic features of the renal collecting duct carcinoma. (A) and (B) HES 5x, Tumor proliferation organized in tubes or cords (arrows) infiltrating the renal tissue with the presence of glomeruli (stars) and fibrous desmoplastic stromal (triangle). (C) HES 20x, Cuboidal cells with marked cytonuclear atypia and eosinophilic cytoplasm and numerous mitoses (arrows). (D) Neutrophil polymorphonuclear cells (arrows).

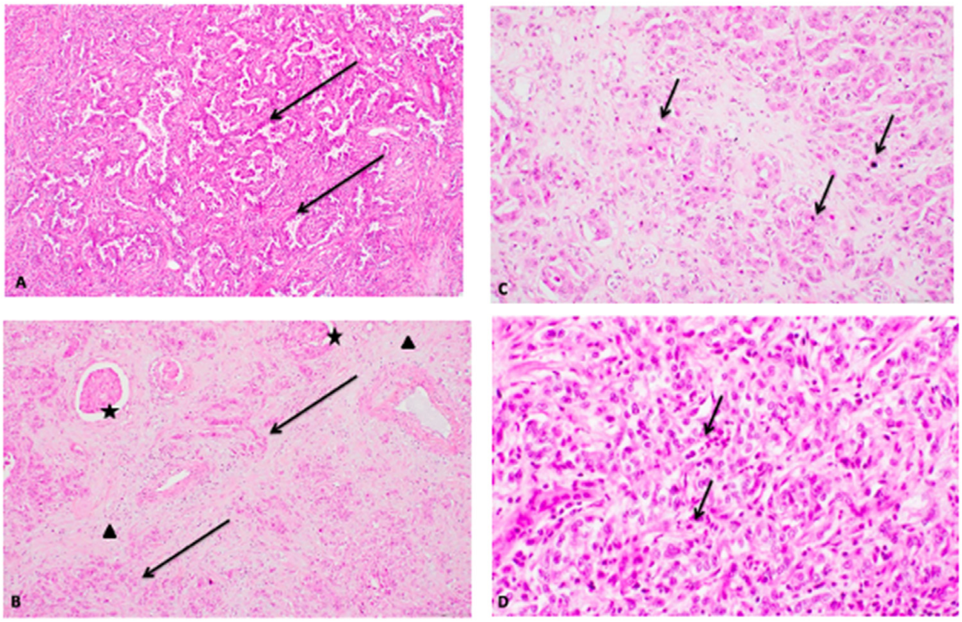


Figure 3 Kaplan-Meier curve of CSS for all RCDC.

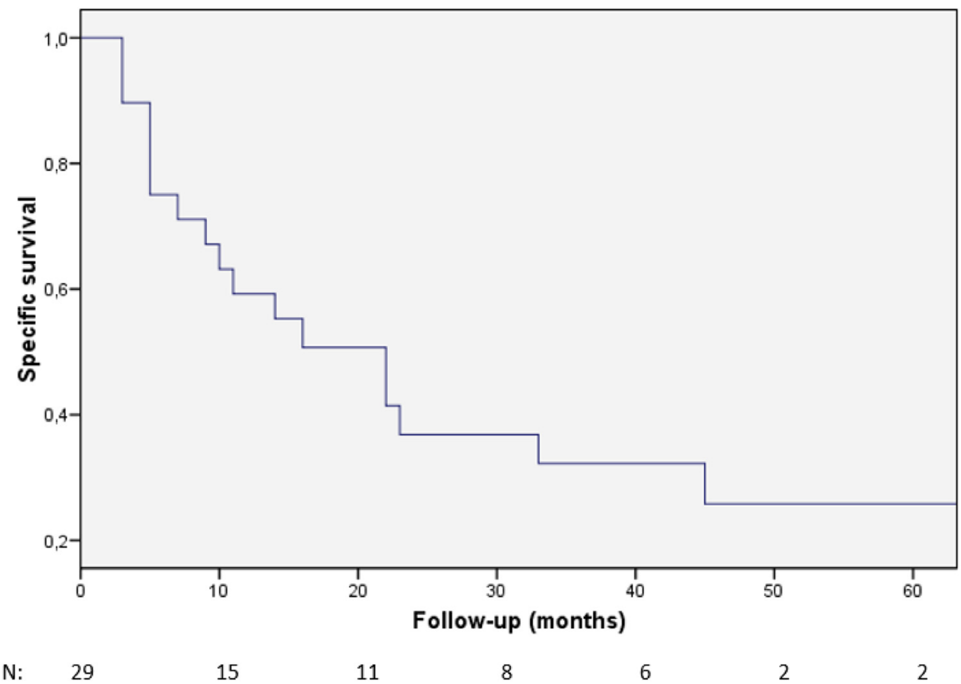


Table 1 Patient and Tumor Characteristics

Patients	*n* = 29
Median (range) age, years	63 (45-81)
Sex: male, n (%)	20 (69)
African phenotype, n (%)	2 (7)
Symptoms at diagnosis, n (%)	20 (69)
Chronic kidney disease at diagnosis, n (%)	2 (6.9)
Tobacco use, n (%)	6 (20.7)
Median (range) BMI, kg/m²	26.2 (19.5-41.6)
Median (range) hemoglobin at diagnosis, g/dL	12.6 (5.9-16)
ECOG-PS, n (%)	
≤1	27 (93)
>1	2 (7)
Median (range) platelets at diagnosis, G/L	292 (187-552)
Tumor localization, n (%)	
Upper-pole	9 (31)
Inter-pole	12 (41)
Lower-pole	8 (27)
Invasion of renal sinus, n (%)	11 (38)
Nephrectomy, n (%)	27 (93)
Tumor stage, n (%)	
T1	7 (24)
T2	5 (17)
T3	13 (44)
T4	4 (13.7)
N stage	
N0-X	16 (55.2)
N1-2	13 (44.8)
M stage, n (%)	
M0	20 (69)
M1	9 (31)
Median (range) follow-up (months)	8 (2-115)
Metastatic sites, n (%)	
1	6 (67)
≥ 2	3 (33)

Table 2 Multivariable Cox Regression Analysis for Predictive Factors of Cancer Specific Death

	H.R	95% C.I.	*P*
Tumor stage (T1-2 vs T3-4)	0.435	0.07 - 2.4	.435
N stage (N0-X vs N1-2)	1.45	0.37 - 5.6	.587
M stage (M1 vs M0)	5.868	1.6 - 20.5	.006
Gender (male vs female)	2.05	0.13 - 2.7	.273
Age at diagnosis (continuous)	0.96	0.94-1.05	.967

Discussion

In this study, the prevalence of RCDC among kidney cancers in the UroCCR database was 0.18%, which is lower than reported in the literature. According to Suarez et al., the prevalence among kidney cancers was close to 1%.[2] According to Cabanillas et al., the prevalence among kidney cancers was less than 2%.[10] However, Xie et al., described in their study that the prevalence of RCDC among nephrectomized patients was 0.2%. This lower prevalence can be explained by the use of a surgical database.[5] In our study, this low prevalence can also be explained by the inclusion of patients

Figure 4 Kaplan-Meier curve of PFS for all RCDC.

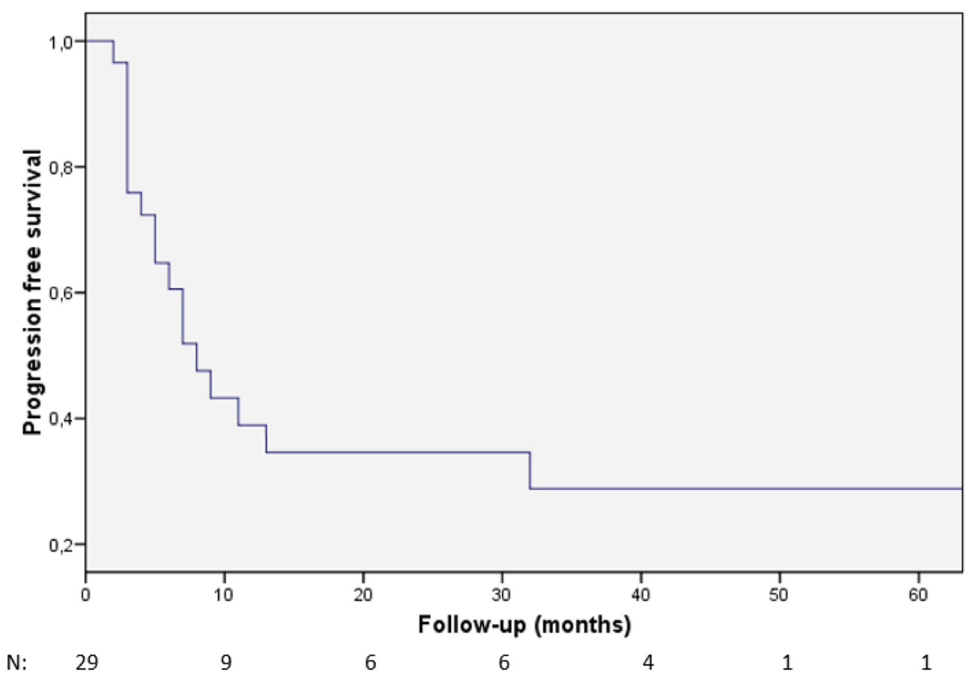


Table 3 Metastatic Patients Management and Survival

	Management	Survival (Months)
Patient 1	Nephrectomy	4
Patient 2	Nephrectomy	5
Patient 3	Nephrectomy	7
Patient 4	Nephrectomy	2
Patient 5	Nephrectomy + Metastasis surgery	79
Patient 6	Cisplatin + Gemcitabine + Bevacizumab	2
Patient 7	Cisplatin + Gemcitabine + Bevacizumab	2
Patient 8	Nephrectomy + Everolimus	4
Patient 9	Nephrectomy + MVAC	11

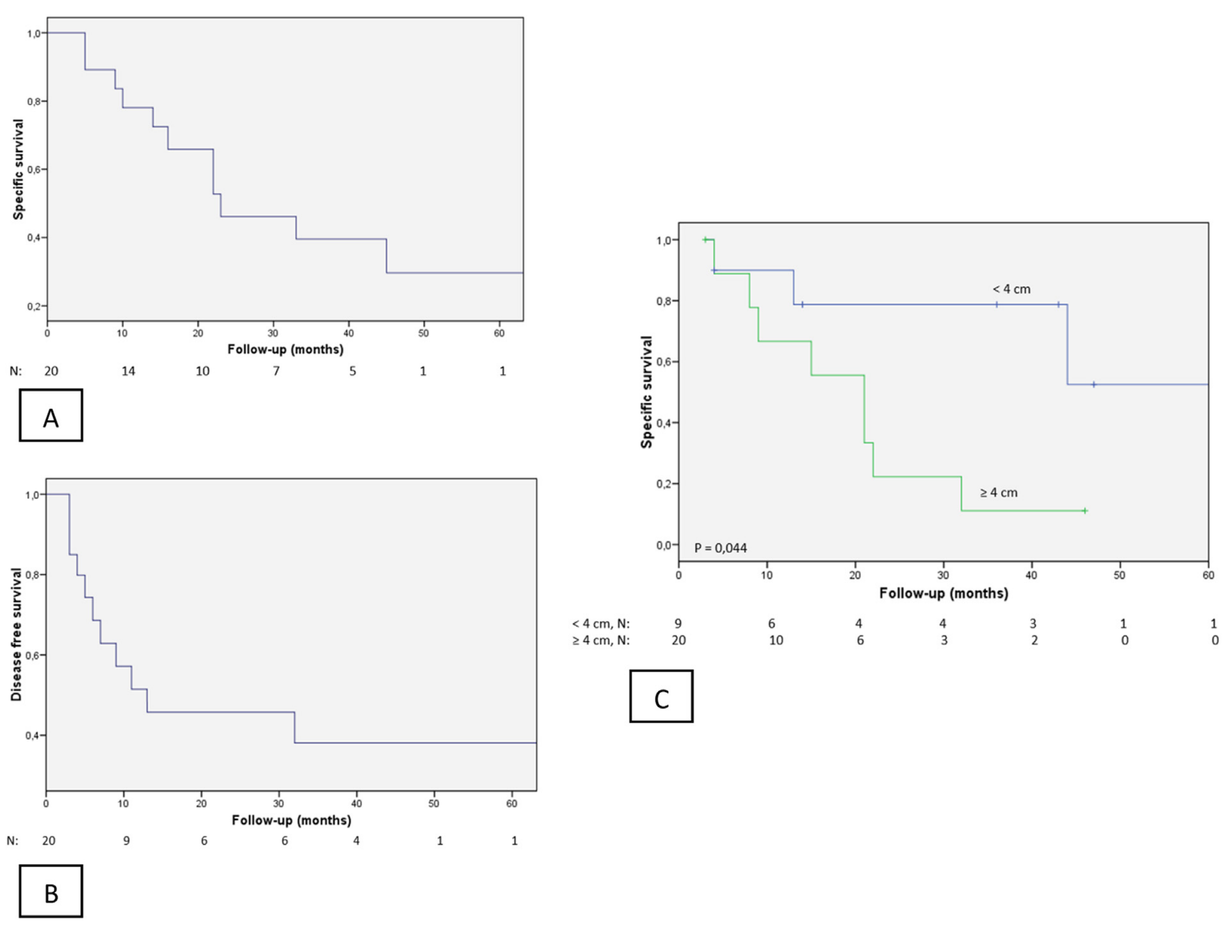
in UroCCR mainly by urologists. The incidence of RCDC showed a decreasing trend annually. The incidence went from 0.4580 per 1,000,000 people in 2004 to 0.1943 per 1,000,000 people in 2018 according to the study by Tang et al.[13] This change in prevalence over time may also reflect an improvement in the accuracy of pathological diagnosis.

The patient characteristics in our study appeared to be similar to previous studies in terms of age, sex ratio, BMI, and tobacco exposure.[4,5,14,15] At diagnosis, the proportion of symptomatic patients in our study was 69%, and the proportion of metastatic patients was 31%. These results were consistent with other studies which describe symptoms present at diagnosis in 50 to 90% of patients.[2,5,14] Also, patients were metastatic at diagnosis in 30 to 42% of cases.[4,15]

In our entire cohort, median CSS was 21 months and median PFS was 7 months. It was similar to previous studies which described a median OS of RCDC between 13 and 24 months.[5,10,13–16] Two older studies described a median OS of 30 months and 54.4 months.[17,18] While the median PFS of RCDC was around 6 months.[4,5,18]

We found that nonmetastatic RCDC ($P = .012$) and tumor size inferior to 4 cm ($P = .045$) were associated with better outcomes (Figures 3,6). As other studies, survival appeared to be better among nonmetastatic RCDC with a median OS between 34 months and 69.9 months; same as for small tumors.[2,13,14,18] The 5-year OS of nonmetastatic RCDC was 44%.[6,19] In several articles, the median OS was short for metastatic RCDC patients (less than 12 months).[2,4,9,13–15,18,20,21]

Figure 5 Kaplan-Meier curves for nonmetastatic RCDC. (A) CSS, (B) PFS and (C) CSS for tumor size <4 cm compared to tumor size ≥ 4cm.



The diagnosis of RCDC typically begins with a CT scan. Yoon et al. analyzed the CT scans of 18 patients with RCDC in a retrospective study. All tumors were solid with occasional cystic components, primarily located in the medulla. On contrast-enhanced CT scan, enhancement was low and heterogeneous. Renal sinus invasion was present in the majority of cases. The tumor often respected the renal contour and was not exophytic[8] (Figure 1).

Histological diagnosis is made through a renal biopsy in only 29.7% of cases.[14] Regarding histological analysis, it is important to exclude urothelial carcinoma or metastasis. RCDC presents a tubular and tubulopapillary appearance, irregular and infiltrating glands, and a desmoplastic stroma. There is usually significant inflammation around the tumor, including a neutrophil infiltrate around and within the tumor. Cells often exhibit high-grade nuclear characteristics with eosinophilic cytoplasm. They are cuboidal and line the tubules. There are commonly numerous abnormal mitoses (Figure 2).

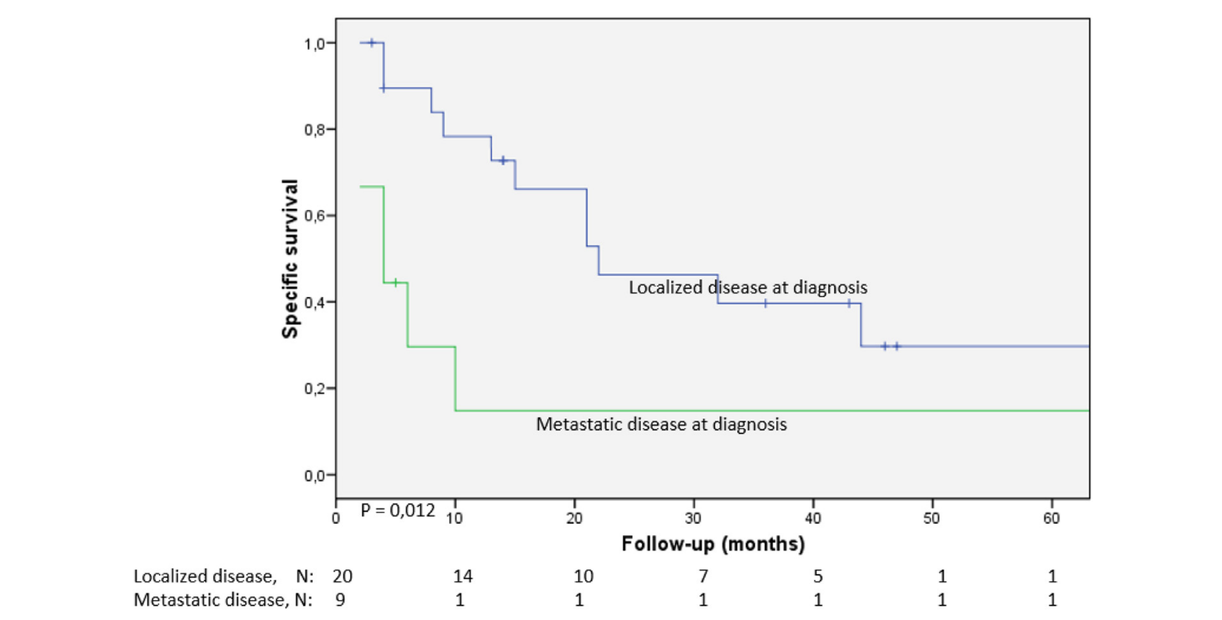
Due to the rarity of this tumor, there is limited data on the subject, and guidelines regarding management are not clear. In guidelines, it is specified that the gold standard for localized renal cancer is surgery, and the platinium-based chemotherapy may be considered for metastatic RCDC. Cabozantinib monotherapy is an alternative treatment.[6,11]

For patients with localized RCDC, surgical management is advisable. Considering early recurrences and low survival despite localized disease, it would be interesting to evaluate the role of neoadjuvant and adjuvant treatment. In the article by Zhou et al., it was suggested to consider adjuvant treatment following surgery for patients with localized T3-T4 RCDC to reduce the risk of recurrence and mortality.[4]

Regarding the management of patients with metastatic RCDC, the modalities are more heterogeneous. In several retrospective studies, the survival of patients with metastatic RCDC treated with systemic therapy and cytoreductive nephrectomy appears to be better.[4,13,15,16] In our study, 7 metastatic patients underwent nephrectomy.

A platinum-based chemotherapy is recommended as first-line treatment for patients with RCDC due to morphological and cytogenetic similarities with urothelial carcinoma.[6,9,11] The study by Oudard et al. reported that the combination of carbo-

Figure 6 Kaplan-Meier curve of CSS comparing nonmetastatic and metastatic RCDC.



platin/cisplatin and gemcitabine achieved an ORR of 26%.[20] In the literature, the effectiveness of several treatment combinations has been evaluated. The new generation of tyrosine kinase inhibitors, such as cabozantinib and lenvatinib, could enhance the efficacy of anti-angiogenics.[4]

The BONSAI study by Procopio et al. reported that using cabozantinib as a first-line treatment for patients with metastatic RCDC achieved an ORR of 35%. It suggested to consider cabozantinib as a therapeutic option in the first-line treatment for these patients.[9] The study by Sheng et al. reported that the combination of cisplatin, gemcitabine, and sorafenib as a first-line treatment for patients with metastatic RCDC resulted in an ORR of 30.8%.[21] In our study, 2 metastatic patients were treated with the combination of gemcitabine, cisplatin, and bevacizumab, and their OS was 2 months.

Immunotherapy has changed the prognosis of metastatic kidney cancer. Regarding patients with RCDC, 20% of them were PD-L1+, and PD-L1 expression was significantly associated with advanced stage and grade.[22] In the study by Zhou et al., 4 patients with metastatic RCDC were treated with an anti-PD-1 and axitinib, resulting in one patient showing a partial response and 2 with disease stability. The ORR was 25%.[4] In the article by Koshkin et al., among the 4 patients with metastatic RCDC, 75% showed disease progression with nivolumab.[23]

In the study by Albiges et al., the combination of lenvatinib and pembrolizumab as a first-line treatment for nonclear renal cell carcinomas was effective, with an ORR of 49%. The study recommended this combination as a first-line treatment for patients with nonclear renal cell carcinoma, regardless of histology. However, they excluded patients with RCDC due to the aggressiveness of the disease and its prognosis, opting to maintain platinum-based chemotherapy.[24] Therefore, the results of this study cannot be extrapolated to RCDC patients. Still, it would be interesting to evaluate this combination in patients with metastatic RCDC in a prospective study.

There is a lack of data in the literature concerning targeted therapy. Costantini et al. found that 8% of patients with RCDC (2/26 cases) were HER2 positive, according to the ASCO/CAP 2018 guidelines.[25] This promising therapeutic approach could be considered for patients with metastatic RCDC with HER2+ status.

Considering the results of this study and the lack of significant results in the literature, it is important to include in research protocols, patients with RCDC. A research protocol is currently underway, evaluating immunotherapy in patients with RCDC. It is important to test HER2 status in patients with RCDC to assess eligibility for targeted therapy and its effectiveness.

Nephrectomy is recommended for nonmetastatic patients. It would be interesting to evaluate the role of neoadjuvant and adjuvant treatment in these nonmetastatic patients in prospective studies. First-line treatment options should either be the combination of GC or cabozantinib. It would be interesting to evaluate the combination of Lenvatinib and Pembrolizumab in these metastatic patients in prospective studies.

Like previous studies on the subject, there were some similar limitations. The rarity of the pathology resulted in limited patient inclusion, leading to low statistical power. The study was retrospective and should be interpreted with caution due to inherent biases associated with retrospective data collection. There was likely a selection bias due to the inclusion of patients in the UroCCR database primarily by urologists. Indeed, it is possible that some metastatic patients who received only systemic therapy are not included in the surgical databases. There was likely a misclassification bias due to the new WHO Guidelines regarding the diagnosis of RCDC. In the study by Kiyozawa et al., 18 cases of RCDC were reclassified as SMARCB1/INI1-deficient carcinoma (2/18), FH-deficient carcinoma (7/18), and RCDC (9/18). Therefore, by testing the expression of SMARCB1 and FH, 50% of patients labeled as RCDC were ultimately not classified as such.[26] Some patients in the UroCCR database may be RCDC cases but were misclassified as RCC. Indeed, the CARARE network has only reviewed rare histologies within the UroCCR database and has not conducted a comprehensive review of all cases.

Despite these limitations, this study had strengths. It was a multicenter study and all patients underwent centralized review.

Conclusion

RCDC is a rare cancer with a poor prognosis, for which no treatment has definitively shown a significant improvement in survival. Patients with localized RCDC and a small tumor <4 cm appeared to have a better survival after nephrectomy. However, recurrences are frequent and early, even among nonmetastatic patients. Due to the rarity of the tumor and the lack of data in the literature, the management of RCDC remains heterogeneous and often ineffective. This article reinforces the need for further studies to better understand this tumor and evaluate alternative treatments.

Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Louis-Pacôme Le Mével: Writing – review & editing, Writing – original draft, Resources, Methodology, Formal analysis, Conceptualization. **Jean-Christophe Bernhard:** Validation, Resources. **Mokrane Yacoub:** Resources. **Thibaut Waeckel:** Resources. **Céline Bazille:** Resources. **Cécile Champy:** Resources. **Maria Mamodaly:** Resources. **Karim Bensalah:** Writing – review & editing, Validation, Resources. **Nathalie Rioux-Leclercq:** Resources. **Constance Michel:** Resources. **Ilhem Hergli:** Resources. **Louis Surlemont:** Resources. **Julie Leclerc:** Resources. **Morgan Roupret:** Resources. **Franck Bruyere:** Resources. **Gaëlle Fromont:** Resources. **Thibaut Tricard:** Resources. **Véronique Lindner:** Resources. **Bastien PARIER:** Resources. **Sophie Ferlicot:** Resources. **Jean-François Hermieu:** Resources. **Margot Bucau:** Resources. **Caroline Pettenati:** Resources. **Souhil Lebdai:** Writing – review & editing, Validation, Supervision, Resources, Methodology. **Thibaut Culty:** Writing – review & editing, Validation, Resources. **Cosmina Nedelcu:** Writing – review & editing, Validation, Resources. **Merzouka Zidane-Marinnes:** Writing – review & editing, Validation, Resources. **Pierre Bigot:** Writing – review & editing, Validation, Supervision, Resources, Methodology, Conceptualization.

Ethical Statement

All the procedures were in accordance with the ethical standards of the institutional and national research committee and with the Helsinki declaration. The study obtained approval from Ethical Committee (DC 2012/108).

References

1. Moch H, Amin MB, Berney DM, et al. The 2022 World Health Organization classification of tumours of the urinary system and male genital organs—Part A: renal, penile, and testicular tumours. *Eur Urol*. 2022;82(5):458–468.
2. Suarez C, Marmolejo D, Valdivia A, et al. Update in collecting duct carcinoma: current aspects of the clinical and molecular characterization of an orphan disease. *Front Oncol*. 2022;12:970199.
3. Bigot P, Barthelemy P, Boissier R, et al. French AFU Cancer Committee guidelines - update 2022-2024: management of kidney cancer. *Prog En Urol*. 2022;32(15):1195–1274.
4. Zhou L, Liu Y, Mo J, et al. Clinicopathological characteristics and prognosis of metastatic collecting duct carcinoma. *Urol Oncol Semin Orig Investig*. 2022;40(8):385.e1–385.e8.
5. Xie Z, Yadav S, Lohse CM, et al. Collecting duct carcinoma: a single-institution retrospective study. *Urol Oncol Semin Orig Investig*. 2022;40(1):13.e9–13.e18.
6. Ljunberg B, Albiges L, Bedke J, et al. *EAU Guidelines on Renal Cell Carcinoma*. EAU; 2023 *https://uroweb.org/guidelines/renal-cell-carcinoma*.
7. Tokuda N, Naito S, Matsuzaki O, et al. Collecting duct (Bellini Duct) renal cell carcinoma: a nationwide survey in Japan. *J Urol*. 2006;176(1):40–43.
8. Yoon SK, Nam KJ, Rha SH, et al. Collecting duct carcinoma of the kidney: CT and pathologic correlation. *Eur J Radiol*. 2006;57(3):453–460.
9. Procopio G, Sepe P, Claps M, et al. Cabozantinib as first-line treatment in patients with metastatic collecting duct renal cell carcinoma: results of the BONSAI trial for the Italian Network for Research in Urologic-Oncology (Meet-URO 2 Study). *JAMA Oncol*. 2022;8(6):910.
10. Cabanillas G, Montoya-Cerrillo D, Kryvenko ON, Pal SK, Arias-Stella JA. Collecting duct carcinoma of the kidney: diagnosis and implications for management. *Urol Oncol Semin Orig Investig*. 2022;40(12):525–536.
11. Powles T, Albiges L, Bex A, et al. Renal cell carcinoma: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol*. 2024;35(8):692–706.
12. Panunzio A, Tappero S, Hohenhorst L, et al. Collecting duct carcinoma: epidemiology, clinical characteristics and survival. *Urol Oncol Semin Orig Investig*. 2023;41(2):110.e7–110.e14.
13. Tang C, Zhou Y, Ge S, Yi X, Lv H, Zhou W. Incidence, clinical characteristics, and survival of collecting duct carcinoma of the kidney: a population-based study. *Front Oncol*. 2021;11:727222.
14. Chen J, Cai D, Gong K, Zhu S. Collecting duct carcinoma of the kidney: analysis of 74 cases from multiple centers. *Urology*. 2022;164:163–168.
15. Sui W, Matulay JT, Robins DJ, et al. Collecting duct carcinoma of the kidney: disease characteristics and treatment outcomes from the National Cancer Database. *Urol Oncol Semin Orig Investig*. 2017;35(9):540 e13-540.e18.
16. Qian X, Xu J, Liu C, et al. Impact of treatment modalities on prognosis in patients with renal collecting duct carcinoma: a population-based study. *Front Oncol*. 2022;12:810096.
17. Abern MR, Tsivian M, Polascik TJ, Coogan CL. Characteristics and outcomes of tumors arising from the distal Nephron. *Urology*. 2012;80(1):140–146.
18. Kwon KA, Oh SY, Kim HY, et al. Clinical features and treatment of collecting duct carcinoma of the kidney from the Korean Cancer Study Group Genitourinary and Gynecology Cancer Committee. *Cancer Res Treat*. 2014;46(2):141–147.
19. An J, Packiam VT, Chennamadhavuni A, et al. Patient characteristics and survival outcomes of non-metastatic, non-clear cell renal cell carcinoma. *Front Oncol*. 2022;11:786307.
20. Oudard S, Banu E, Vieillefond A, et al. Prospective multicenter phase II study of Gemcitabine plus platinum salt for metastatic collecting duct carcinoma: results of a GETUG (Groupe d'Etudes des Tumeurs Uro-Génitales) study. *J Urol*. 2007;177(5):1698–1702.
21. Sheng X, Cao D, Yuan J, et al. Sorafenib in combination with gemcitabine plus cisplatin chemotherapy in metastatic renal collecting duct carcinoma: a prospective, multicentre, single-arm, phase 2 study. *Eur J Cancer*. 2018;100:1–7.
22. Choueiri TK, Fay AP, Gray KP, et al. PD-L1 expression in nonclear-cell renal cell carcinoma. *Ann Oncol*. 2014;25(11):2178–2184.
23. Koshkin VS, Barata PC, Zhang T, et al. Clinical activity of nivolumab in patients with non-clear cell renal cell carcinoma. *J Immunother Cancer*. 2018;6(1):9.
24. Albiges L, Gurney H, Atduev V, et al. Pembrolizumab plus lenvatinib as first–line therapy for advanced non-clear-cell renal cell carcinoma (KEYNOTE-B61): a single-arm, multicentre, phase 2 trial. *Lancet Oncol*. 2023;24(8):881–891.
25. Costantini M, Amoreo CA, Torregrossa L, et al. Assessment of HER2 protein overexpression and gene amplification in renal collecting duct carcinoma: therapeutic implication. *Cancers*. 2020;12(11):3345.
26. Kiyozawa D, Kohashi K, Takamatsu D, et al. Approach for reclassification of collecting duct carcinoma and comparative histopathological analysis with SMARCB1/INI1-deficient renal cell carcinoma and fumarate hydratase-deficient renal cell carcinoma. *Hum Pathol*. 2022;124:36–44.