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DE DOCTEUR EN MÉDECINE

Assessment of the prevalence and predictive factors for renal cancer local recurrence after nephron sparing surgery with negative margins (R0).

Évaluation de la prévalence des récidives locales du cancer du rein ainsi que des facteurs prédictifs après chirurgie par néphrectomie partielle avec marges négatives (R0).

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Par Lucas Deluegue

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JURY

Président :

Monsieur le Professeur Arnauld Villers

Assesseurs :

Monsieur le Professeur Philippe Puech

Monsieur le Professeur Xavier Leroy

Monsieur le Docteur Jonathan Olivier

Directeur de Thèse :

Monsieur le Docteur Jean-Christophe Fantoni

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Liste des abréviations

NSS :	Nephron sparing surgery
RCC :	Renal cell carcinoma
IQ :	Interquartile
HR :	Hazard ratio
CPP :	Committee for the Protection of Persons
BMI :	Body mass index
ECOG :	Eastern Cooperative Oncology Group
WHO :	World Health Organization
RFS :	Recurrence free survival
TTR :	Time to recurrence
CCC :	Clear cell carcinoma
TP 1 :	Tubulopapillary type 1
TP 2 :	Tubulopapillary type 2

NP :	Néphrectomie partielle
CCR :	Carcinome à cellules rénales
CNIL :	Commission Nationale de l'Informatique et des Libertés
CPP :	Comité de Protection des Personnes
IMC :	Indice de masse corporelle
OMS :	Organisation Mondiale de la Santé
SSR :	Survie sans récidive
CCC :	Carcinome à cellules claires
TP 1 :	Tubulo-papillaire de type 1
TP 2 :	Tubulo-papillaire de type 2

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ABSTRACT

Introduction:

Local recurrence following partial nephrectomy with negative surgical margins (R0) remains a clinical concern in renal cell carcinoma (RCC).

This study aims to determine the rate of local recurrence after R0 partial nephrectomy and identify the predictive factors associated with this recurrence.

Patients and Method:

A multicentric retrospective study was conducted in France (URO CCR n°140), including all patients who underwent partial nephrectomy between April 2007 and November 2022 for stage cT1-cT3a/N0/M0 RCC with negative surgical margins.

Exclusion criteria included a history of renal cancer, multifocal tumors, benign tumor and renal metastasis from another primary cancer.

Outcomes:

A total of 2438 patients met the inclusion criteria. Local recurrence occurred in 97 patients (3.9%) after a median follow-up of 29 months (IQ: 26;86). Multivariate analysis identified several risk factors for recurrence including an open surgical approach (HR 4.694 [2.020;10.856]), the occurrence of intraoperative complications, (HR 3.306 [1.292;8.460], delay between diagnosis and surgery (HR 1.021 [1.006;1.037]), and the presence of vascular emboli (HR 3.787 [1.543;9.294]) and necrosis (HR 2.634 [1.485;4.672]) on pathological analysis.

Conclusion:

This study found a 3.9% rate of local recurrence after partial nephrectomy for RCC with R0 margins.

Key risk factors for local recurrence include the open surgical approach, delays between diagnosis and surgery, intra-operative complications and adverse pathological features such as vascular emboli and necrosis.

RESUME

Introduction :

La récidive locale après néphrectomie partielle en marges chirurgicales négatives (R0) reste un problème clinique dans le cancer du rein.

Cette étude vise à déterminer le taux de récidives locales après une néphrectomie partielle R0 et à identifier les facteurs prédictifs associés à cette récidive.

Patients et méthode :

Une étude rétrospective multicentrique a été menée en France (URO CCR n°140), portant sur des patients ayant subi une néphrectomie partielle entre avril 2007 et novembre 2022 pour un cancer du rein de stade cT1-cT3a/N0/M0 avec des marges chirurgicales négatives.

Les critères d'exclusion comprenaient les antécédents de cancer du rein, les tumeurs multifocales, les tumeurs bénignes et les métastases rénales d'un autre cancer primaire.

Résultats :

Au total, 2 438 patients ont été inclus. Une récidive locale est survenue chez 97 patients (3,9 %) après un suivi médian de 29 mois (IQ : 26;86). L'analyse multivariée a identifié plusieurs facteurs de risque de récidive, notamment une approche chirurgicale ouverte (HR 4.694 [2.020;10.856]), la survenue de complications peropératoires (HR 3.306 [1.292;8.460], le délai entre le diagnostic et la chirurgie (HR 1.021 [1.006;1.037]), la présence d'emboles vasculaires (HR 3.787 [1.543;9.294]) et de nécrose (HR 2.634 [1.485;4.672]) à l'analyse anatomo-pathologique.

Conclusion :

Cette étude a révélé un taux de récidive locale de 3,9 % après chirurgie par néphrectomie partielle pour un cancer du rein avec des marges négatives.

Les principaux facteurs de risque de récidive locale comprennent l'approche chirurgicale ouverte, le délai entre le diagnostic et la chirurgie, les complications peropératoires et les caractéristiques anatomopathologiques défavorables telles que les emboles vasculaires et la nécrose.

INTRODUCTION

Renal cell carcinoma (RCC) is the 6th most commonly diagnosed cancer in men and 10th in women worldwide (1).

The incidence of RCC is rising, due to advances in imaging techniques and the incidental detection of tumors during abdominal imaging for nonspecific musculoskeletal or gastrointestinal complaints (2).

Surgical resection remains the gold standard for the management of localized RCC (3). When technically feasible, nephron-sparing surgery (NSS) has been shown to provide equal oncologic outcome compared with radical nephrectomy for small tumor (4).

Several studies have demonstrated that NSS offers improved functional outcomes in the treatment of small lesions and reduces the risk of cardiovascular events (5). Regarding surgical approaches, there is no significant difference in oncologic outcomes including disease-specific survival and overall survival (6).

Given the importance of accurately predicting recurrence risk, identifying reliable predictive factors is essential for selecting the optimal surgical approach and informing patients preoperatively. While numerous studies have explored these factors, most have included patients with positive surgical margins (R1) after NSS. In this study, we aim to determine the rate of recurrence following R0 partial nephrectomy and identify predictive factors for recurrence in this population.

INTRODUCTION

Le cancer du rein est le sixième cancer le plus fréquemment diagnostiqué chez l'homme et le dixième chez la femme dans le monde (1). Son incidence est en augmentation, en raison des progrès des techniques d'imagerie et de la détection fortuite de tumeurs lors d'une imagerie abdominale pour des troubles musculo-squelettiques ou gastro-intestinaux non spécifiques (2).

La résection chirurgicale reste le traitement de référence du cancer du rein localisé (3). Lorsque cela est techniquement possible, il a été démontré que la chirurgie d'épargne néphronique donnait des résultats oncologiques équivalents à ceux de la néphrectomie totale pour les petites tumeurs (4).

Plusieurs études ont démontré que la néphrectomie partielle (NP) offre de meilleurs résultats fonctionnels dans le traitement des petites lésions (5). En ce qui concerne les approches chirurgicales, il n'y a pas de différence significative dans les résultats oncologiques, que ce soit en termes de la survie spécifique ou de survie globale (6).

Il est important de prédire avec précision le risque de récidive. L'identification de facteurs prédictifs fiables est donc essentielle pour choisir l'approche chirurgicale optimale et informer les patients en pré-opératoire. Bien que de nombreuses études aient exploré ces facteurs, la plupart ont inclus des patients avec des marges chirurgicales positives (R1) après NP.

Dans cette étude, nous cherchons à déterminer le taux de récidive après une néphrectomie partielle R0 et à identifier les facteurs prédictifs de récidive dans cette population.

PATIENTS AND METHOD

Study design and patient population:

All patients were prospectively enrolled in the UroCCR multicentric database: UroCCR project (NCT03293563), which is IRB-approved and obtained the CNIL authorization number DR-2013-206.

A favorable opinion has been received from the Committee for the Protection of persons (CPP) for UroCCR: “Comité de Protection des Personnes Sud-Ouest et Outre-mer III: num de décision DC 2012/108 et l’avis du CCTIRS”. All patients received oral and written information about the objectives and methodology of the UroCCR project and written consent was obtained.

We conducted a retrospective analysis of patients who underwent NSS for RCC across 24 urology departments in France between April 2007 and November 2022.

The inclusion criteria were patients aged 18 years or older, with clinical stage cT1-cT3a RCC and with no lymph node involvement (N0) and no distant metastasis (M0), who underwent NSS with negative surgical margins (R0) confirmed by the final pathology report.

Exclusion criteria included a history of surgery for an ipsilateral or contralateral renal tumor, previous renal cancer follow-up, multifocal tumors, benign lesion or renal metastasis from another cancer, unavailable radiological data or lack of follow up.

After applying these criteria, a total of 2,438 patients were included in the final analysis (Fig. 1).

Data collection:

We collected patients demographic data including age, sex, body mass index (BMI), smoking status, past medical history, renal function, Eastern Cooperative Oncology Group Performance Status (ECOG). We also looked at surgical and pathological data including surgical approach, biopsy status, tumor histology, tumor location and pathological findings.

Tumor stage was determined according to the 2017 TNM Classification of Malignant Tumors (7) and pathological diagnosis was based on the 2016 World Health Organization (WHO) classification (8).

Post-operative follow-up was conducted according to the recommendations of the French society of Urology and consisted of a contrast-enhanced computed tomography (CT) every 6 months for the first 3 years post-surgery, followed by annual scans.

Recurrence was confirmed by pathological analysis (biopsy or additional surgery).

Surgery:

The surgical approaches included open surgery or laparoscopic surgery with or without robotic assistance. The choice of approach depended on tumor size, location, complexity and surgeon expertise.

Outcome measure:

The primary outcome was to determine the rate of recurrence following R0 partial nephrectomy.

The secondary outcome was the evaluation of predictive factors for local recurrence after NSS for Renal cell carcinoma with negative margin (R0), It was defined as tumor bed recurrence or recurrence in the ipsilateral kidney.

Recurrence free survival (RFS) was defined as the time from surgery to the recurrence of tumor, death, or end of follow-up. Time to recurrence (TTR) was calculated as follows: “date of recurrence event – date of Surgery”.

Prognostic factors evaluated:

Based on the available literature, we included the following prognosis factors in a univariate analysis: age, tumor size, surgery delay, estimated blood less during surgery, intraoperative complication, surgical approach (open or laparoscopic), robotic assistance, histology, Fuhrman grade, vascular emboli, biopsy, tumor location, necrosis and sarcomatoid component, papillary and microcystic architecture, renal score, ECOG.

Afterwards, the significant prognosis factors were included in multivariable analysis.

Robotic assistance, Fuhrman grade, microcystic component and blood loss were not included in the multivariate analysis because of the lack of sufficient data to be statistically feasible.

Statistical analysis:

Qualitative variables were described in terms of frequencies and percentages. Quantitative variables were described by the mean and standard deviation, or by the median and interquartile range in the case of a non-Gaussian distribution. The normality of the distributions was verified graphically and using the Shapiro-Wilk test.

The cumulative incidence of recurrence was estimated and plotted using the Kalbfleisch and Prentice method, considering death as a concurrent event. The search for risk factors for recurrence was carried out using a Fine and Gray model for quantitative variables, and a Gray test for qualitative variables. The log-linearity assumption was tested for quantitative variables using cubic spline functions. Variables not meeting this assumption were categorized. The proportional hazards hypothesis was verified graphically using Schoenfeld residuals and by testing the interaction with time. In the event of non-proportionality, the time was divided into two periods (≤ 60 months and > 60 months). Factors with a p-value of less than 0.05 that were clinically relevant were entered into a multivariate Fine and Gray model. Factors with too much missing data (>10%) were not selected for the multivariate model. The search for risk factors for tumor bed recurrence, considering death as a concurrent event, was carried out using the same methodology as that described above.

The significance level was set at 5%. Statistical analyses were performed using SAS software (SAS Institute version 9.4).

RESULTS

According to our study criteria, 2438 patients were included in the analysis with median follow-up of 29 months (IQ: 26;86). 97 patients (3.9%) presented a local recurrence with average recurrence time at 76 months. Of these recurrences, 30 (30.9%) occurred within the first five years and 67 (69.1%) more than five years after surgery. Patient characteristics are shown in Table 1.

Among these patients, 1655 (67.9%) were men. The median patient age was 61 years (IQ: 51;69), and the median BMI was 26.7 kg/m2 (IQ: 23.9;30.1). Open surgery and mini-invasive surgery (MIS) were performed in 304 (12.5%) and 2134 (87.5%), respectively. 78.7% of the surgery was made with robotic assistance. The average time between diagnosis and surgery was 3 months.

The median tumor size was 3.2 cm with interquartile [2.3;4.5], and most tumors (66.8%) were clinical T1a lesions. There are also 20.3% T1b, 2.7% T2a, 0.8% T2b and 9.4% of patients with T3a. 41.1% of patients had high blood pressure, 19.8% had dyslipidemia, 14.8% had diabetes. 458 Patients (18.8%) receive biopsy.

Histological findings wer clear cell RCC for 1714 patients (70.3%), type 1 papillary RCC for 270 (11.1%), type 2 papillary RCC for 102 (4.2%), chromophobe RCC for 234 (9.6%). A cystic component was found in 19.5% of cases, 60 (2.5%) tumors had a sarcomatoid component, 385 (15.8%) had a necrosis component and 116 (4.8%) had vascular micro emboli. Intraoperative complications occurred in102 Patients (4.2%) with 24 (1%) conversions to open surgery. Finally, 61 patients (2.5%) died during follow up.

Univariate Analysis:

Some of Univariate analysis returned statistically significant (table 3), some of them seems to be risk factors for recurrence: tumor size with HR for five first years after surgery is 2.412 [1.595;3.646], p<0.0001 and after 2.523 [1.153;5.521], p=0.0206. Necrosis with HR 2.782 [1.843;4.200], p<0.0001 (fig 2). Sarcomatoid with HR 4.602 [2.187;9.682], p<0.0001 (fig 3). Delay between diagnosis and surgery with HR 1.020 [1.007;1.033], p=0.0031.

Vascular emboli and intra operative complication are statistically significant only in the five first years after surgery. Vascular emboli HR for five first years after surgery is 6.276 [2.684;14.675], p<0.0001 (fig 4) and after he is 1.715 [0.803;3.664], p=0.1635. Intra operative complication HR for five first years after surgery is 6.578 [2.806;15.419], p<0.0001 (fig 5) and after he is 1.384 [0.500;3.830], p=0.5314.

Renal score was classified in light, moderate or high risk, more the renal score is important, more the risk of recurrence is high with HR for five first years after surgery 1.854 [1.142;3.012], p=0.0126 and after 2.948 [1.646;5.283], p=0.0003 (fig 6).

Some of them seems to be protector factor: Robotic assistance with HR 0.240 [0.155;0.371], p<0.0001 (fig 7). Microcyst architecture with HR 0.504 [0.269;0.943], p=0.0321 (fig 8).

About surgical approach, open surgery is statistically significant in increasing the risk of recurrence within five years after surgery with HR 4.548 [2.181;9.480], p<0.001 but after five years, this difference is not significant with HR 0.536 [0.271;1.060], p=0.0732 (fig 9).

Concerning Histology subtype of tumor: CCC is a statistically significant risk factor for recurrence with HR 2.126 [1.247;3.624], p=0.0056 (fig 10). Tubulopapillary carcinoma is not a significant factor in our study, TP1 with HR 0.414[0.171;1.002], p=0.0506 and TP2 with HR 1.606 [0.703;3.666], p=0.2609. About Chromophobe lesion and oncocytoma, there are not enough patients with recurrence in our study to realize statistical analysis.

For Fuhrman grade, is it only statistically significant for grade 4 with HR 6.270 [1.846;21.298], p= 0.033, other grade are not statistically significant in our study (fig 11).

Concerning biopsy, our study shows that do not significantly increase the risk of recurrence with HR 1.135 [0.698;1.844], p=0.6100 (fig 12).

Other Univariate analysis returned non statistically significant: Intrahilar tumor with HR 0.984 [0.399;2.426], p=0.9712. ECOG with HR 1.267 [0.644;2.494], p=0.4935. Cystic component with HR 0.923 [0.552;1.543], p=0.7598. Papillary architecture with HR 0.911 [0.538;1.543], p=0.7290. Symptom at diagnosis with HR 1.066 [0.620;1.835], p= 0.8171. Exophytic or endophytic tumor with HR 0.663 [0.349;1.259], p=0.2088.

Multivariate Analysis (Table 3):

We performed a multivariate analysis including all univariate analysis statistically significant.

Nine variables were including in the model: surgical approach, tumor size, necrosis, sarcomatoid content, histology CCC, renal score, delay between diagnosis and surgery, intra operative complication and vascular emboli.

We excluded age, robotic assistance, Fuhrman grade and microcyst architecture because on a statistical level, these criteria distorted the results of the analysis.

After this multivariate analysis, only six variables were statistically significant: Surgical approach in five first year after surgery with HR 4.694 [2.030;10.856], p= 0.0003. Necrosis with HR 2.634 [1.485;4.672], p= 0.0009. Delay between diagnosis and surgery with HR 1.021 [1.006;1.037], p= 0.0064.

Intra operative complication in five first years after surgery with HR 3.306 [1.292;8.460], p= 0.0126 and vascular emboli with HR 3.787 [1.543;9.294], p= 0.0036. CCC histology with HR 2.261 [1.114;4.588], p= 0.0239.

Renal score, tumor size and sarcomatoid content are significant in univariate analysis but not in multivariate analysis (table 3).

DISCUSSION

In this study, we aimed to assess the recurrence rate and identify predictive factors for local recurrence in a population with negative surgical margins following nephron-sparing surgery.

Our findings revealed a recurrence rate of 3.9%, which, while consistent with other studies (9), may be considered relatively high given that our cohort exclusively included patients with negative margins (10). This highlights the necessity of identifying additional risk factors that contribute to recurrence despite the achievement of R0 margins.

Our results align with current literature (11), particularly regarding the impact of **necrosis and sarcomatoid features as risk factors for recurrence (12,13)**. These factors were also found to be significant in our study. The association between vascular emboli and recurrence has been well-documented in the literature (14), and our study further corroborates this link, **finding an elevated risk of recurrence in the presence of vascular emboli.**

Pre-operative analysis of presence of necrosis, sarcomatoid content and vascular emboli could guide management. However, imaging remains an unreliable examination for detecting these elements and biopsy (15), despite very good agreement for the histological subtype, is much less effective for necrosis (16).

Interestingly, our research did not demonstrate a significant increase in recurrence rates following preoperative biopsy. Although some studies have reported cases of needle tract seeding leading to recurrences(17,18), our findings align with larger studies that have shown no significant increase in recurrence risk after biopsy (19).

Additionally, we observed that **perioperative complication increased the risk of recurrence within the first five years**, potentially due to tumor dissemination during complex surgical procedures. Previous research by Wood and al supports this finding, demonstrating a higher recurrence rate associated with longer surgical duration and greater blood loss (20).

Regarding the surgical approach, our study diverges from the findings of Peyronnet and al who reported comparable oncologic outcomes between open and laparoscopic approaches (21). **Contrary to their study, our results suggest that robotic assisted surgery is associated with a lower recurrence rate compared to non-robotic approaches**. We also observed a higher risk of recurrence with open surgery compared to laparoscopic techniques. However, these results should be interpreted with caution, as the observed difference may be influenced by the median tumor size which was larger in patients undergoing open surgery (4.40cm) compared to those undergoing laparoscopic surgery (3.48cm). Additionally, the choice of open surgery may reflect more complex cases, potentially explaining the observed differences in recurrence rates.

Tumor location within the kidney (hilar, exophytic or endophytic) did not seem to impact recurrence rates in our cohort. Similarly, tumor size was not significant in our multivariate analysis, contrary to what might be expected given that larger tumors can complicate surgery. However, **we did find that a longer time interval between diagnosis and surgery increased the risk of recurrence**, underscoring the importance of timely intervention.

Our findings emphasize the necessity for prolonged follow-up after surgery, even in cases where negative surgical margins are achieved. Although guidelines typically recommend a follow-up period of 5 years post R0 partial nephrectomies, our data show almost 70% of recurrences occurred more than five years after surgery. This suggests that extended surveillance may be warranted.

The strengths of our study include its multicentric design, with, patients data collected from twenty-four French hospitals, allowing for a robust sample size. Furthermore, by focusing exclusively on patients with R0 margins, we were able to isolate other parameters, as positive margins are a well-established risk factor for recurrence (22). Notably, few studies have reported such a large cohort of patients with recurrences following NSS in the context of negative margins.

However, our study has limitations, primarily due to its retrospective design. Some patients were lost to follow-up, limiting our ability to conduct long-term evaluations. In addition, patients included later in the data collection period had shorter follow-up times.

The retrospective nature of the study also led to missing data, particularly in follow-up and histopathological records, partly due to the absence of centralized reviews for imaging and histology. Furthermore, the lack of a standardized protocol may impact reproducibility, although the adherence to guidelines from the French association of urology and the European association of urology provide several reliable points of comparison.

In view of our results, renal cell carcinoma should be treated early to reduce the risk of recurrence. A preoperative detection of necrosis or vascular emboli could lead us to perform a total nephrectomy, particularly if the size of the lesion or the surgery appears complex.

CONCLUSION

In our large multicentric cohort, the recurrence rate after partial nephrectomy for renal cell carcinoma with negative surgical margins (R0) was 3.9%.

The open surgical approach, the delay between diagnosis and surgery, intra-operative complications, clear cell renal carcinoma histology, presence of vascular emboli and necrosis on pathology were found to be independent predictive factors for local recurrence.

DISCUSSION

Dans cette étude, nous avons cherché à évaluer le taux de récidive et à identifier les facteurs prédictifs de récidive locale dans une population ayant des marges chirurgicales négatives après néphrectomie partielle.

Nos résultats ont révélé un taux de récidive de 3,9 % qui, bien que cohérent avec d'autres études (9), peut être considéré comme relativement élevé étant donné que notre cohorte comprenait exclusivement des patients avec des marges négatives (10). Cela souligne la nécessité d'identifier d'autres facteurs de risque contribuant à la récidive malgré l'obtention de marges négatives après chirurgie.

Nos résultats sont conformes à la littérature actuelle (11), **notamment concernant l'impact de la nécrose et d'une composante sarcomatoïde en tant que facteurs de risque de récidive (12,13).** Ces facteurs se sont également révélés significatifs dans notre étude. L'association entre les emboles vasculaires et la récidive est bien documentée dans la littérature (14), **notre étude corrobore ce lien, en constatant un risque plus élevé de récidive en présence d'emboles vasculaires.**

L'analyse pré-opératoire de la présence de nécrose, de contenu sarcomatoïde et d'emboles vasculaires pourrait guider la prise en charge chirurgicale. Cependant, l'imagerie reste un examen peu fiable pour détecter ces éléments (15) et la biopsie, malgré une très bonne concordance pour le sous-type histologique, est beaucoup moins performante pour la nécrose (16).

Il est intéressant de noter que notre étude n'a pas mis en évidence d'augmentation significative du taux de récidive après biopsie pré-opératoire. Bien que certaines études aient rapporté des cas d'ensemencement de l'aiguille conduisant à des récidives (17,18), nos résultats s'alignent sur des études plus larges qui n'ont pas montré d'augmentation significative du risque de récidive après la biopsie (19).

En outre, nous avons observé que les complications per-opératoires augmentaient le risque de récidive au cours des cinq premières années, ce qui pourrait être dû à la dissémination de la tumeur au cours d'interventions chirurgicales complexes. Des recherches antérieures menées par Wood et son équipe appuient ce résultat, démontrant un taux de récidive plus élevé associé à une durée chirurgicale plus longue et à une perte sanguine plus importante (20).

Concernant l'approche chirurgicale, notre étude diverge des résultats de Peyronnet et son équipe qui ont rapporté des résultats oncologiques comparables entre les approches ouvertes et laparoscopiques (21). **Contrairement à leur étude, nos résultats suggèrent que la chirurgie assistée par robot est associée à un taux de récidive plus faible que les approches non robotisées.** Nous avons également observé un risque de récidive plus élevé avec la chirurgie ouverte qu'avec les techniques laparoscopiques. Cependant, ces résultats doivent être interprétés avec prudence, car la différence observée peut être influencée par la taille médiane de la tumeur, qui était plus importante chez les patients ayant subi une chirurgie ouverte (4.40 cm) que chez ceux ayant subi une chirurgie laparoscopique (3.48cm). De plus, le choix de la chirurgie ouverte peut refléter des cas plus complexes et pourrait expliquer les différences observées dans les taux de récidive.

La localisation de la tumeur dans le rein (hilaire, exophytique ou endophytique) ne semble pas avoir d'impact sur le taux de récidive dans notre cohorte. De même, la taille de la tumeur n'est pas revenue significative dans notre analyse multivariée, contrairement à ce que l'on pourrait attendre étant donné que les tumeurs plus grosses peuvent rendre la chirurgie plus complexe. Cependant, nous avons constaté qu'un intervalle de temps plus long entre le diagnostic et l'intervention chirurgicale augmentait le risque de récidive, ce qui souligne l'importance de réaliser une intervention dans un délai raisonnable.

Nos résultats soulignent la nécessité d'un suivi prolongé après l'opération, même dans les cas où les marges chirurgicales sont négatives. Bien que les recommandations préconisent habituellement une période de suivi de cinq ans après les néphrectomies partielles R0, nos données montrent que près de 70 % des récidives se sont produites plus de cinq ans après l'opération. Cela suggère qu'une surveillance prolongée pourrait être justifiée.

Les points forts de notre étude sont sa conception multicentrique, avec des données sur les patients recueillies dans vingt-quatre hôpitaux français, ce qui permet d'avoir un échantillon de taille importante. De plus, en nous concentrant exclusivement sur les patients avec des marges négatives, nous avons pu isoler d'autres paramètres, les marges positives étant un facteur de risque de récidive bien établi (22). De plus, peu d'études ont rapporté une cohorte aussi importante de patients présentant des récidives locales après une chirurgie par néphrectomie partielle avec des marges négatives.

Cependant, notre étude présente des limites, principalement en raison de sa conception rétrospective. Certains patients ont été perdus de vue, ce qui a limité notre capacité à mener des évaluations à long terme. Par ailleurs, les patients inclus plus tardivement dans l'étude ont été suivis moins longtemps.

La nature rétrospective de l'étude a également conduit à des données manquantes, en particulier pour le suivi et les données anatomo-pathologiques, en partie à cause de l'absence de relecture centralisée pour l'imagerie et l'anatomo-pathologie. En outre, l'absence de protocole standardisé peut avoir un impact sur la reproductibilité, bien que l'adhésion aux lignes directrices de l'Association française d'Urologie et de l'Association Européenne d'Urologie fournisse plusieurs points de comparaison fiables.

Au vu de nos résultats, le cancer du rein doit être traité précocement pour réduire le risque de récidive. La détection pré-opératoire de nécrose ou d'emboles vasculaires pourrait nous amener à réaliser une néphrectomie totale, en particulier si la taille de la lésion ou la chirurgie semble complexe.

CONCLUSION

Dans notre étude, le taux de récidive après néphrectomie partielle pour carcinome à cellules rénales avec marges chirurgicales négatives (R0) est de 3,9 %.

L'approche chirurgicale ouverte, le délai entre le diagnostic et la chirurgie, les complications per-opératoires, l'histologie carcinome rénal à cellules claires, la présence d'emboles vasculaires et de nécrose à l'anatomo-pathologie sont des facteurs de risque de récidive locale.

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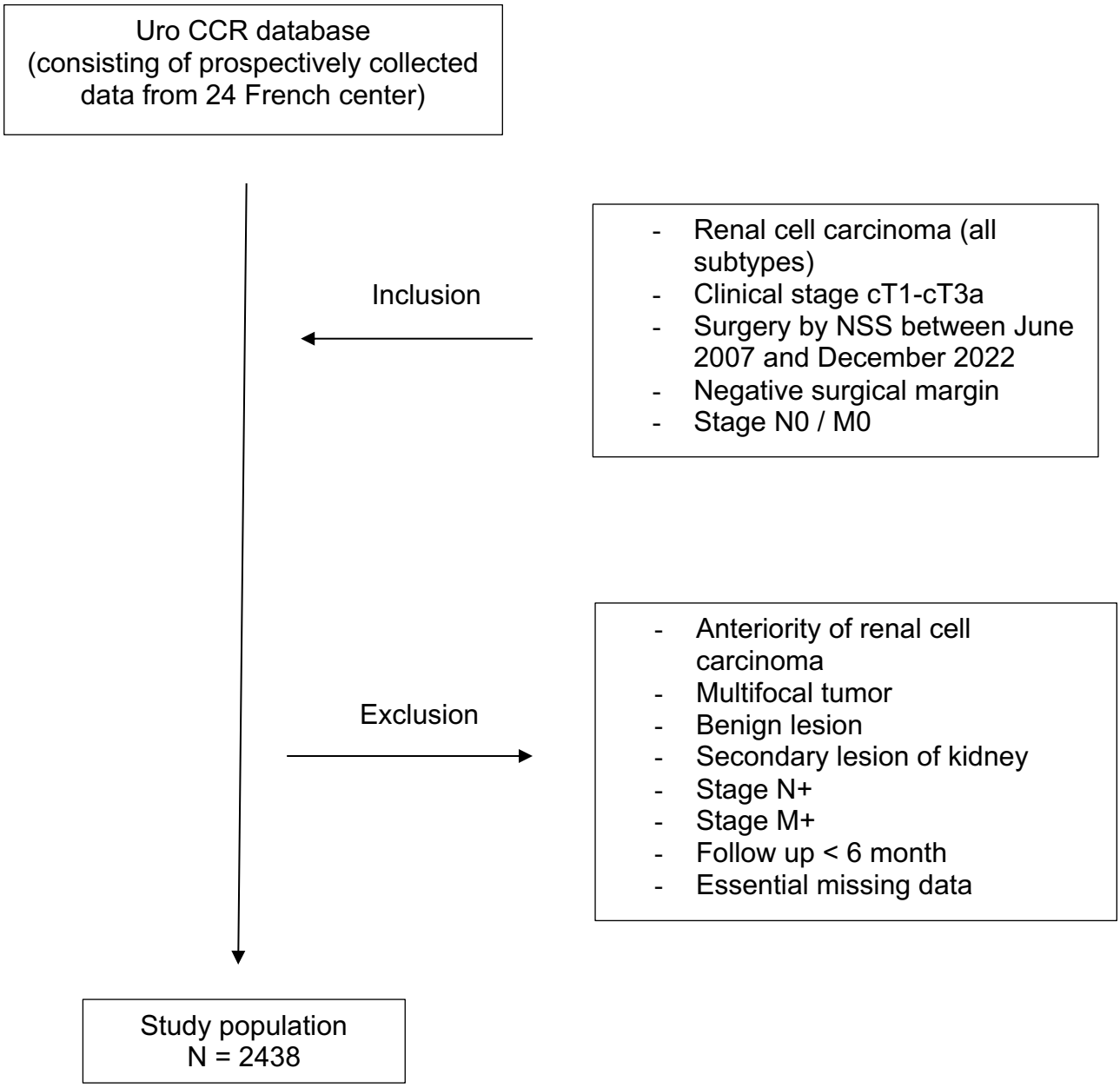
ANNEXES

Figure 1 – Flowchart demonstrating the inclusion and exclusion criteria for the present study.



NSS = Non sparing surgery

Table 1: population characteristic

Variable			Description
Name	Unit	Modality	N=2438
Age at diagnosis		Mean +/- ecart deviation Median (Q1 ;Q3)	59.2 +/- 12.7 61 (51 ; 69)
Sex	N(%)	Men Women	1655 (67.9) 783 (32.1)
BMI		Mean +/- ecart deviation Median (Q1 ;Q3)	27.4 +/- 5.2 26.7 (23.9 ; 30.1)
Diabete	N(%)	No Yes	2076 (85.2) 362 (14.8)
High blood pressure	N(%)	No Yes	1436 (58.9) 1002 (41.1)
Smoker	N(%)	No Yes	1951 (80) 487 (20)
Dyslipidemia	N(%)	No Yes	1955 (80.2) 483 (19.8)
Chronic kidney disease	N(%)	No Yes	2353 (96.5) 85 (3.5)
Surgical approach	N(%)	MIS Open surgery	2134 (87.5) 304 (12.5)
Robotic assistance	N(%)	No Yes Miss data	236 (9.7) 1917 (78.7) 285 (11.6)
Tumor size	cm	Mean +/- ecart deviation Median (Q1 ;Q3)	3.6 +/- 1.9 3.2 (2.3 ; 4.5)
T stage	N(%)	T1a T1b T2a T2b T3a	1628 (66.8) 494 (20.3) 65 (2.7) 19 (0.8) 232 (9.4)
Biopsy	N(%)	No Yes	1980 (81.2) 458 (18.8)
Histology	N(%)	CCC TP1 TP2 Chromophobe Oncocytoma Others	1714 (70.3) 270 (11.1) 102 (4.2) 234 (9.6) 13 (0.5) 105 (4.3)
Cystic component	N(%)	No Yes Miss data	1941 (79.6) 473 (19.5) 24 (0.9)
Necrose content	N(%)	No Yes Miss data	1958 (80.3) 385 (15.8) 95 (3.9)

Sarcomatoid component	N(%)	No Yes Miss data	2212 (90.7) 60 (2.5) 166 (6.8)
Vascular embolus	N(%)	No Yes Miss data	2190 (89.8) 116 (4.8) 132 (5.4)
Intraoperative complication	N(%)	No Yes Miss Data	2328 (95.5) 102 (4.2) 8 (0.3)
Blood less	ml	Mean +/- ecart deviation Median (Q1 ;Q3)	239 +/- 310 150 (50 ; 300)
Conversion	N(%)	No Yes	2414 (99) 24 (1)
Margin resection	N(%)	R0 R1 R2	2438 (100) 0 (0) 0 (0)
Symptom at diagnosis	N(%)	Asymptomatic Local sign General sign	1956 (80.2) 396 (16.2) 86 (3.5)
Renal score	N(%)	Light Moderate Elevate	915 (37.5) 1203 (49.3) 320 (13.1
Fuhrman grade	N(%)	1 2 3 4 Miss data	162 (6.6) 1293 (53.1) 608 (24.9) 103 (4.2) 272 (11.2)
Delay between diagnosis and surgery	month	Mean +/- ecart deviation Median (Q1 ;Q3)	3.7 +/- 7.2 2 (1.0 ; 4.0)
Death (overall)	N(%)	No Yes	2377 (97.5) 61 (2.5)

Table 1: population characteristic (following part)

Figure 2 – Cumulative incidence functions for recurrence with death as a concurrent event

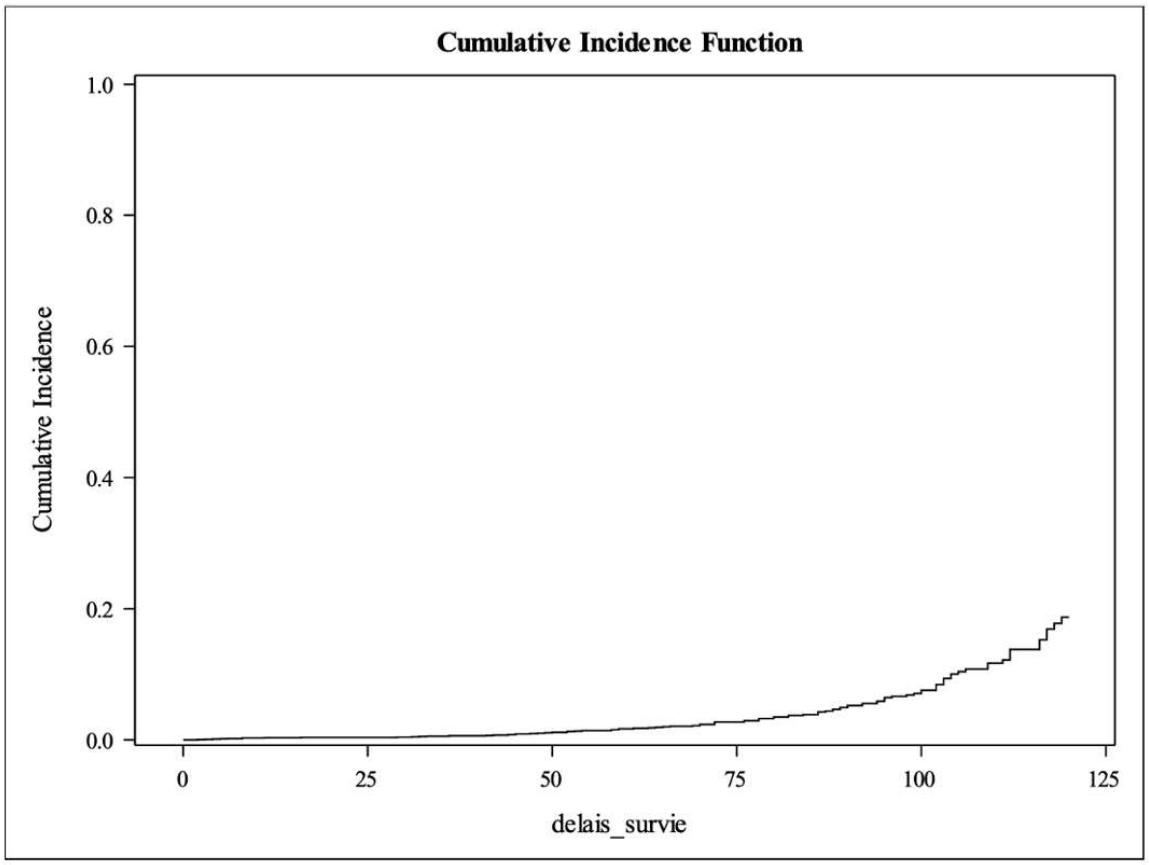
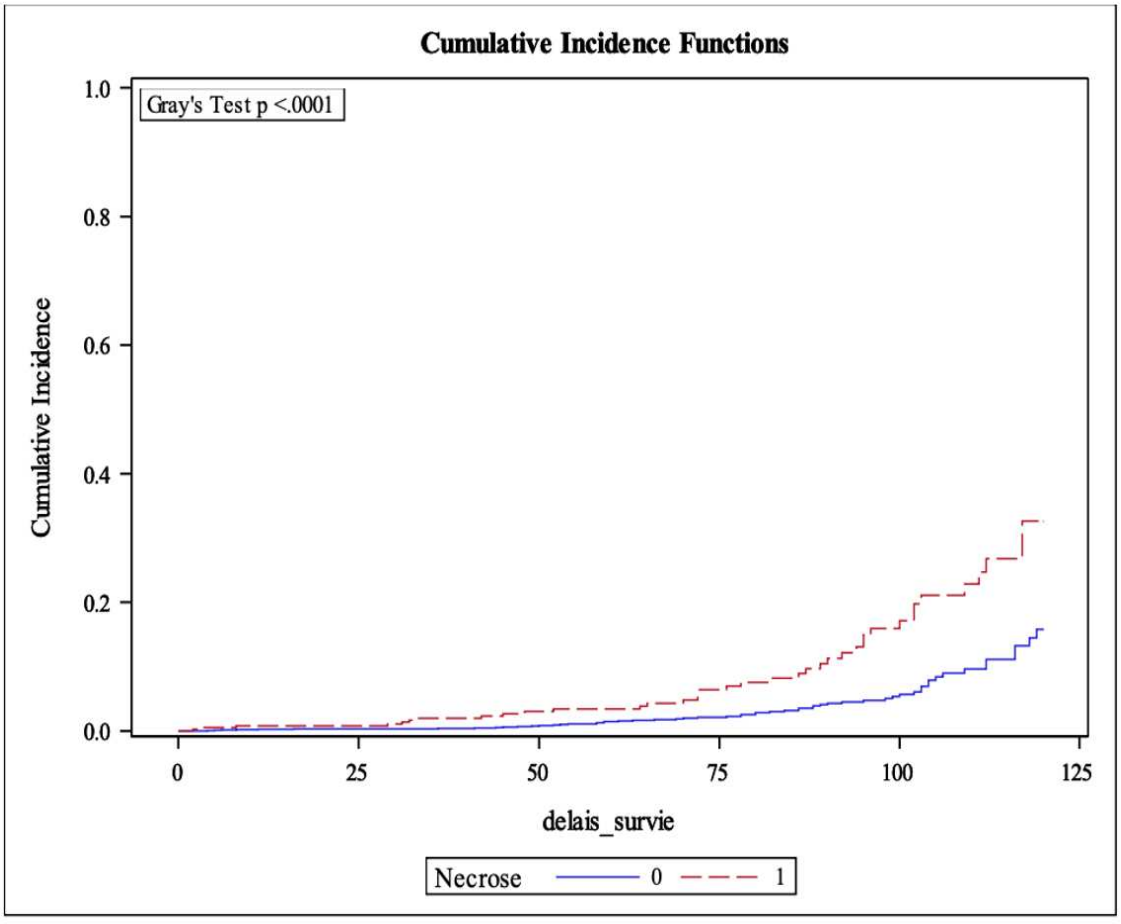
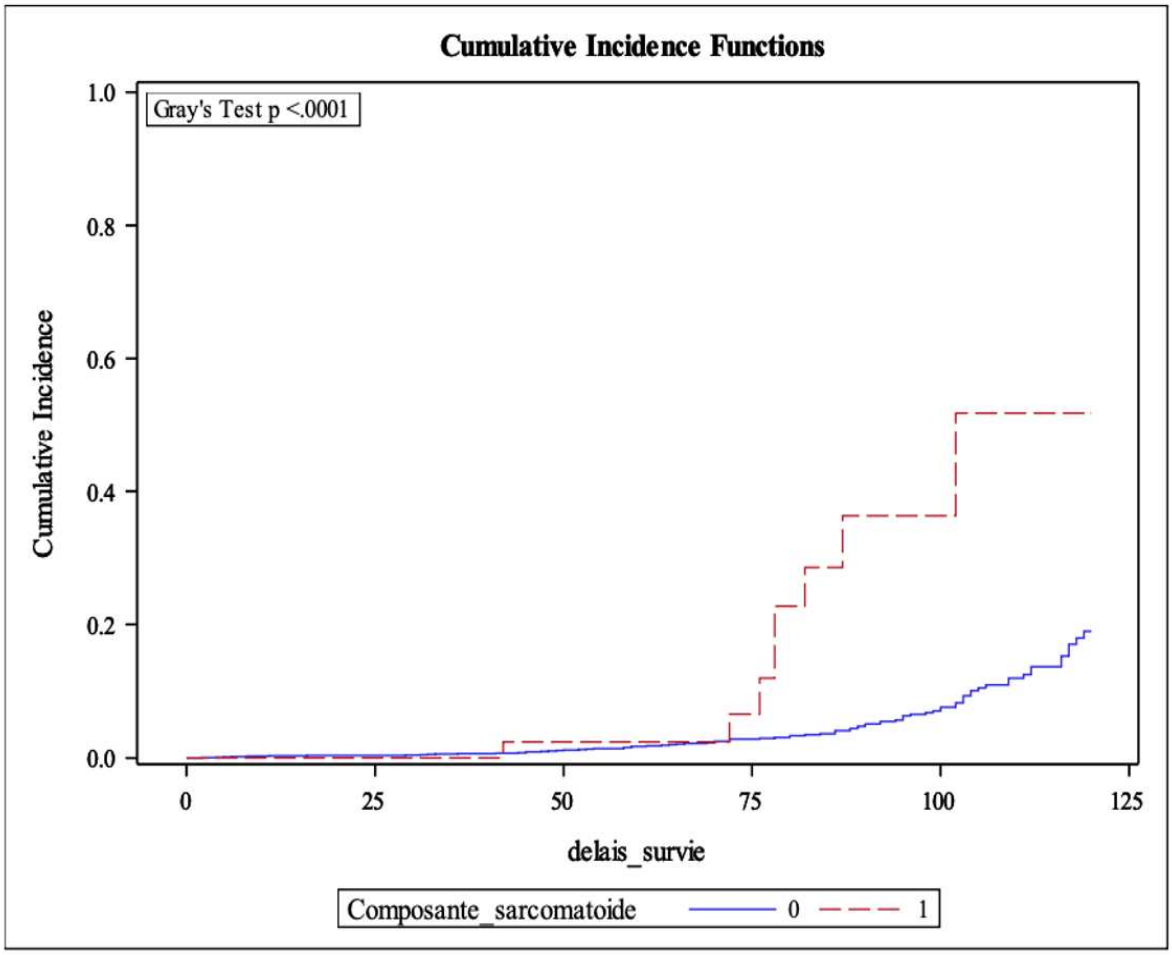


Figure 3 – Cumulative incidence functions for recurrence with or without intra tumoral necrosis.



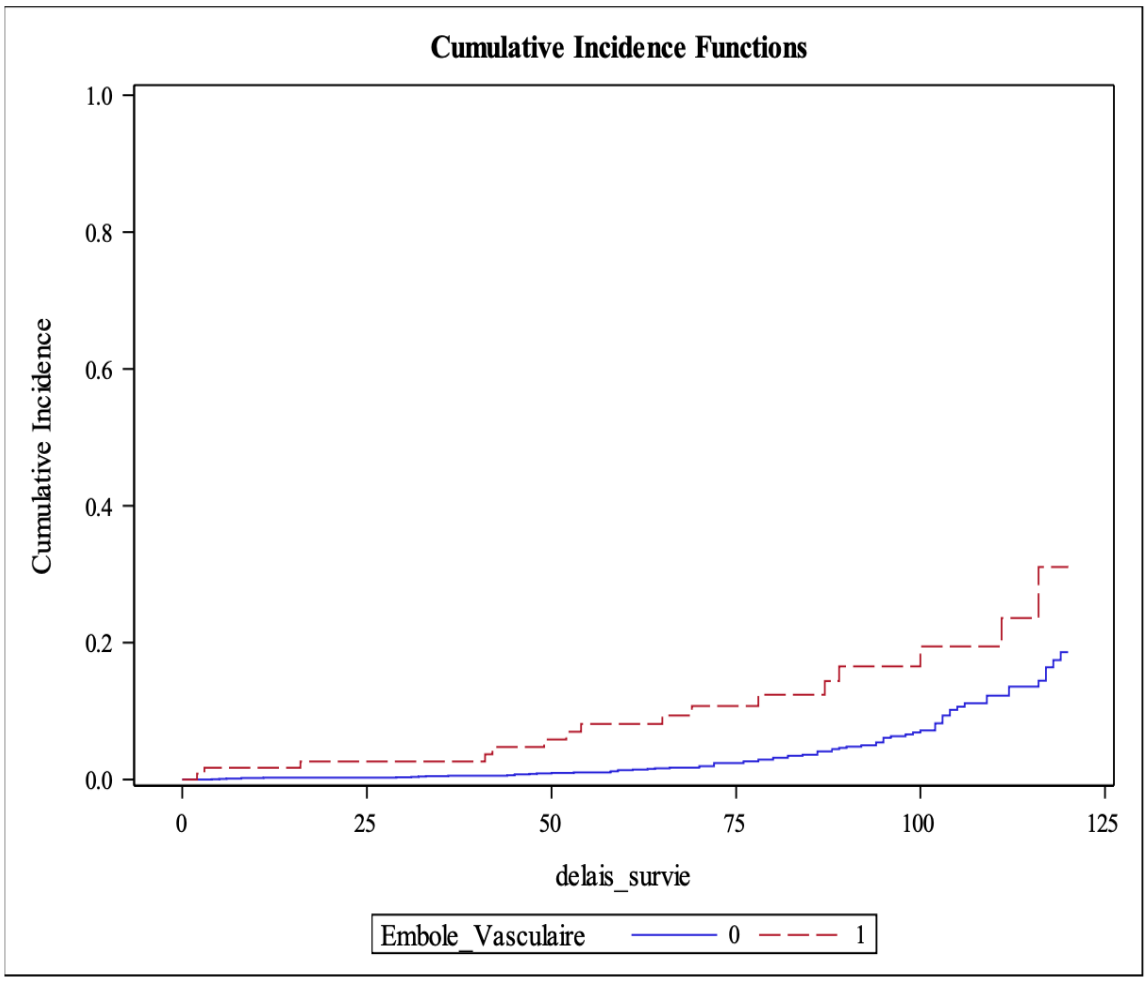
0 = without necrosis
1 = with necrosis

Figure 4 – Cumulative incidence functions for recurrence with or without sarcomatoid content.



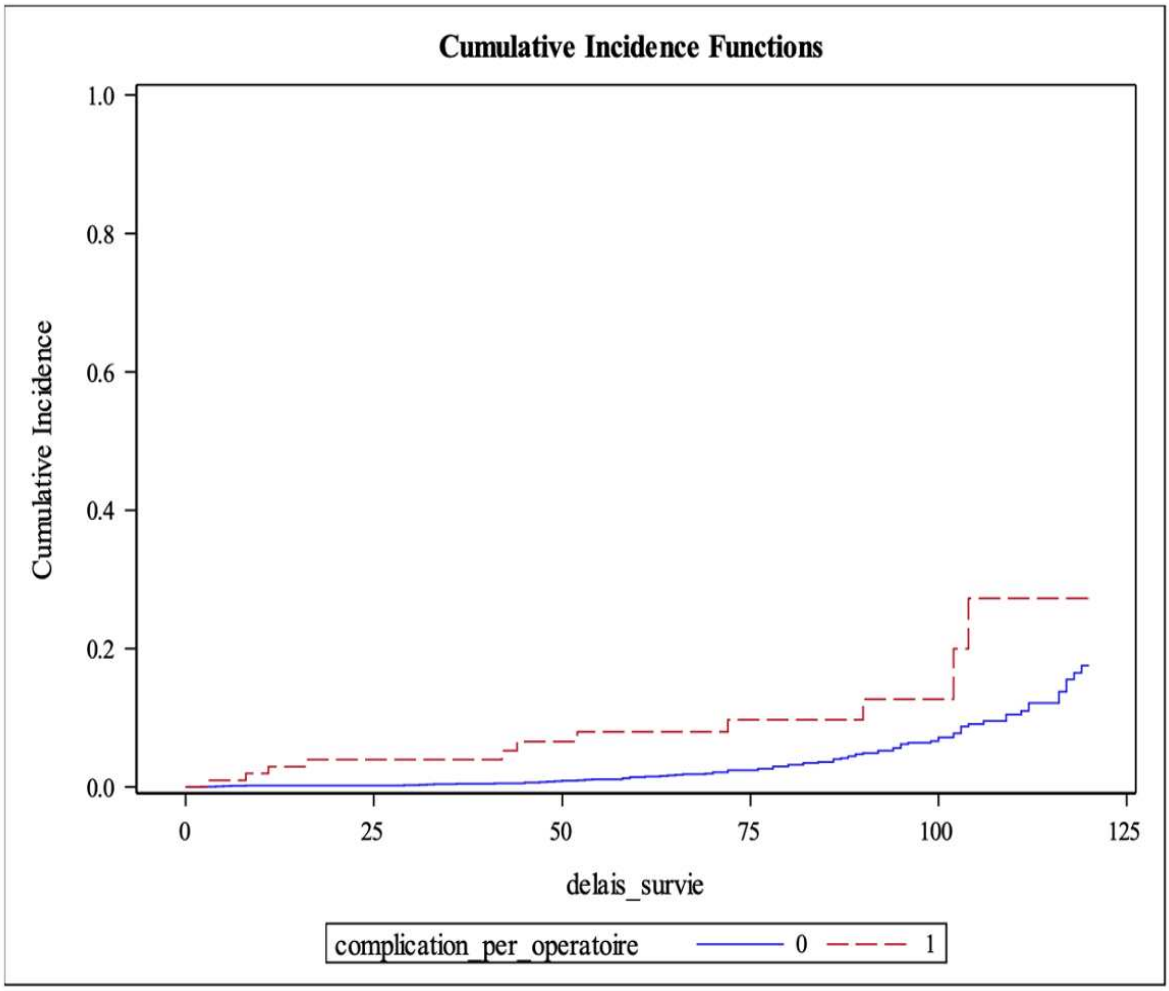
0 = without sarcomatoid content
1 = with sarcomatoid content

Figure 5 – Cumulative incidence functions for recurrence with or without vascular embolus.



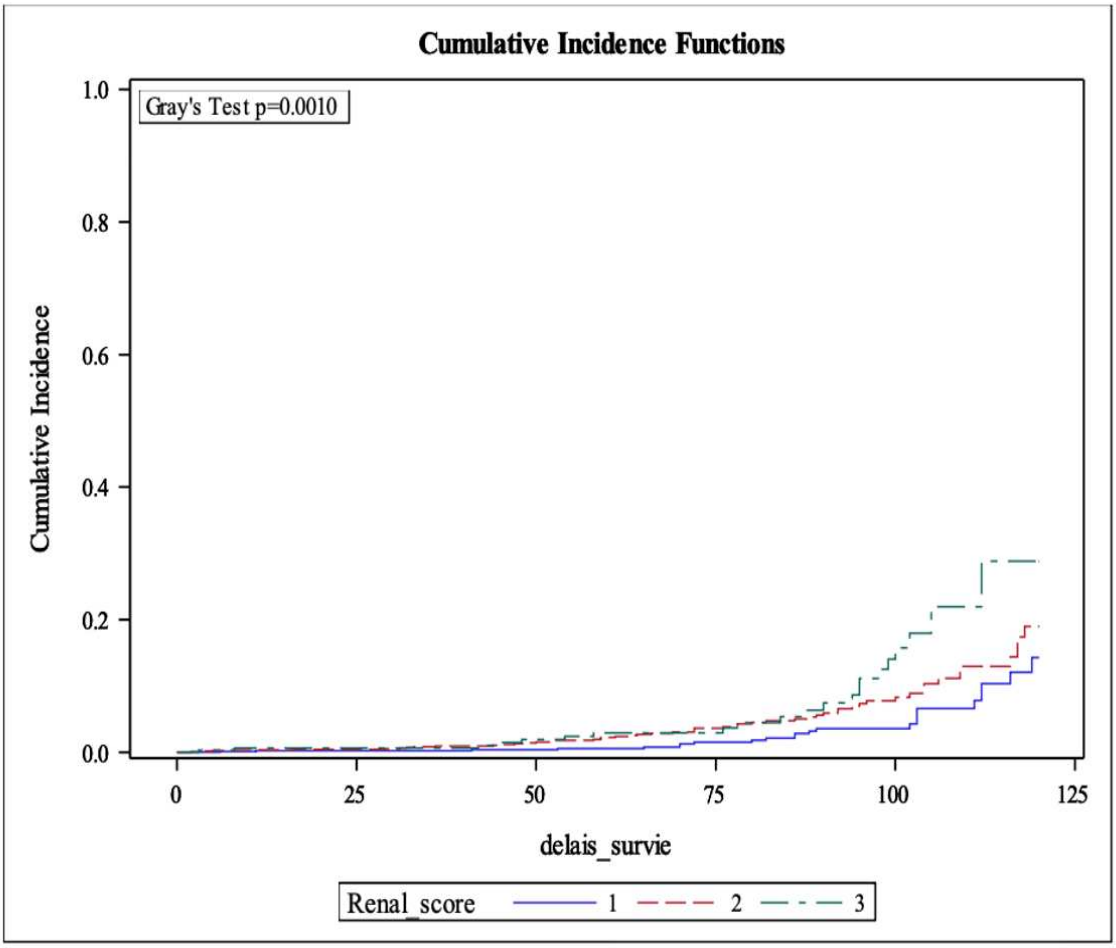
0 = No vascular embolus
1 = Vascular embolus

Figure 6 – Cumulative incidence functions for recurrence with or without intra operative complication.



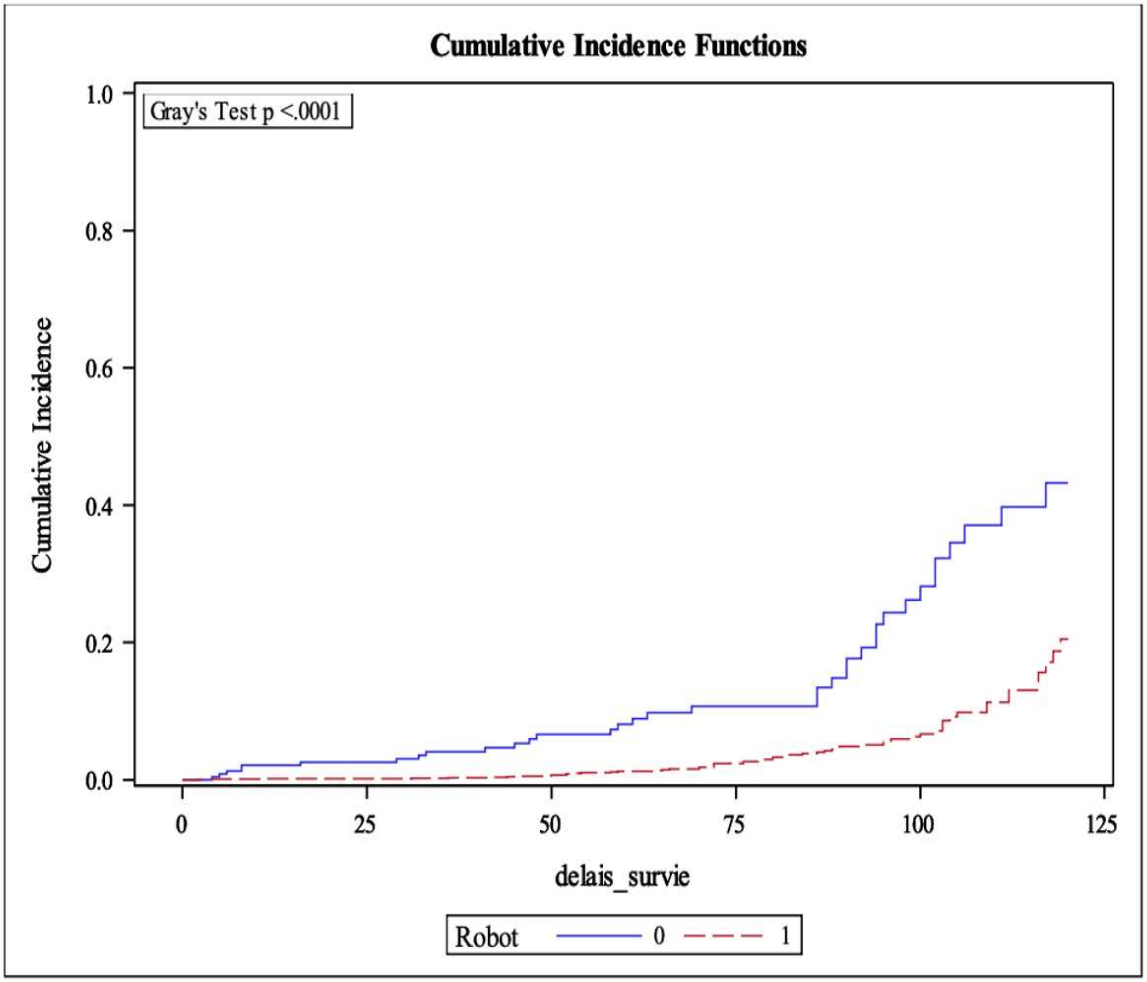
0 = No intra operative complication
1 = Intra operative complication

Figure 7 – Cumulative incidence functions for recurrence according to the renal score.



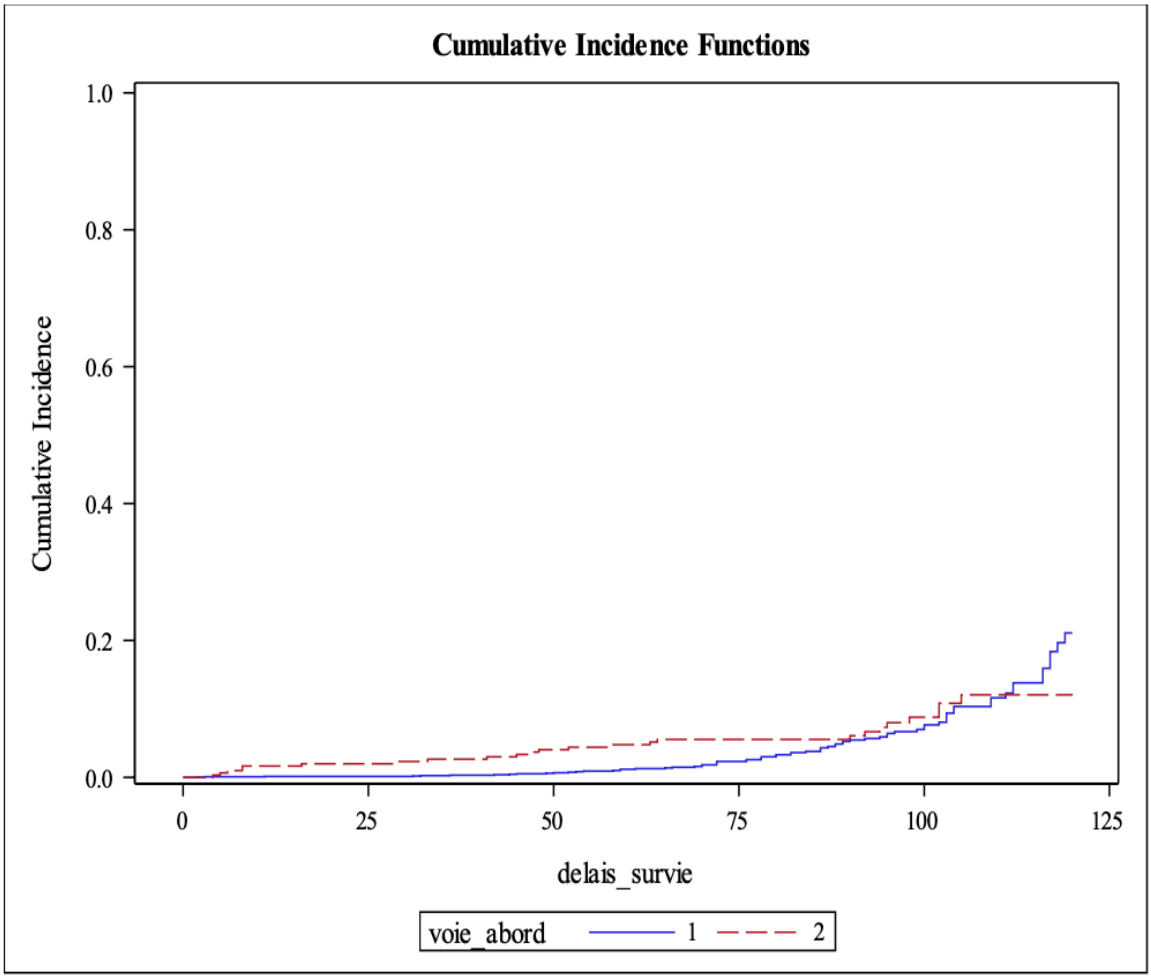
1 = Renal score light
2 = Renal score moderate
3 = Renal score high

Figure 8 – Cumulative incidence functions for recurrence with or without robotic assistance.



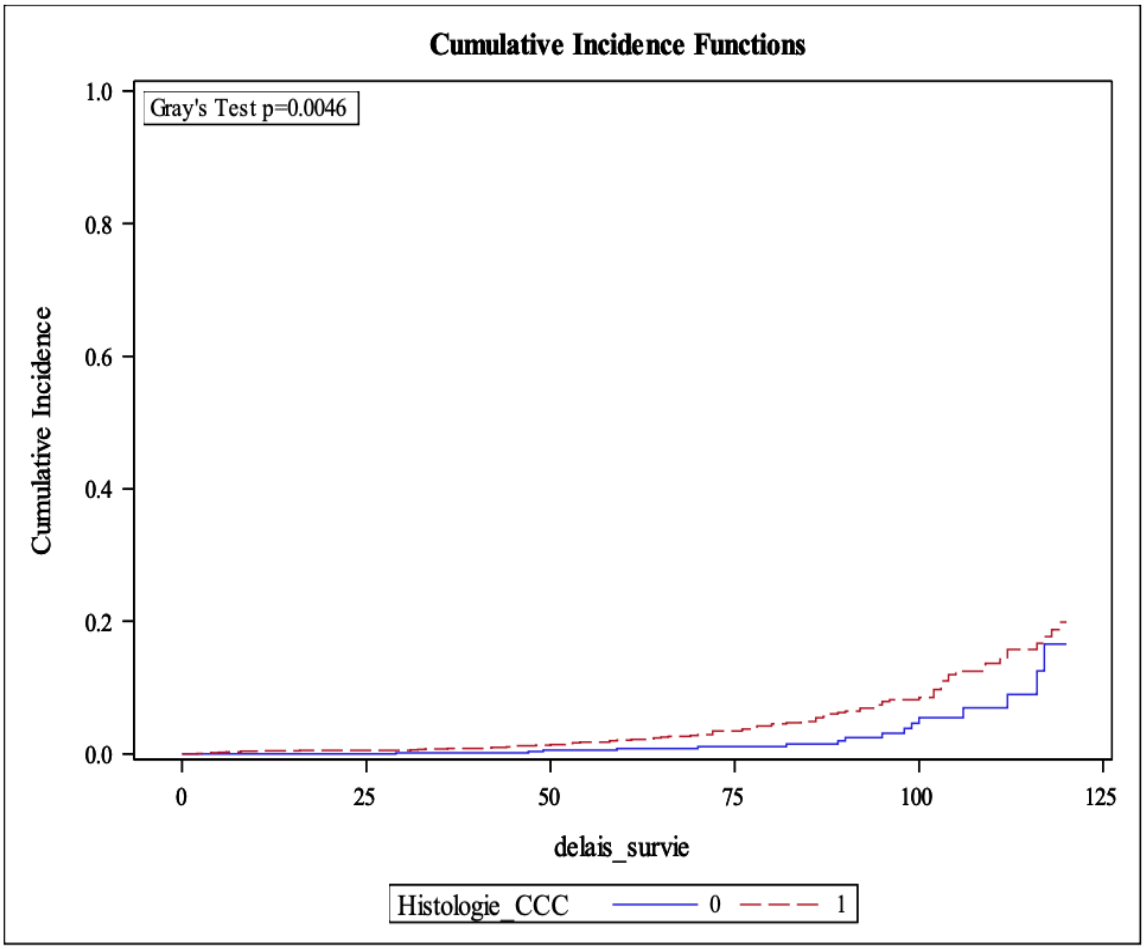
0 = without robotic assistance
1 = with robotic assistance

Figure 9 – Cumulative incidence functions for recurrence with laparoscopic surgery or open surgery.



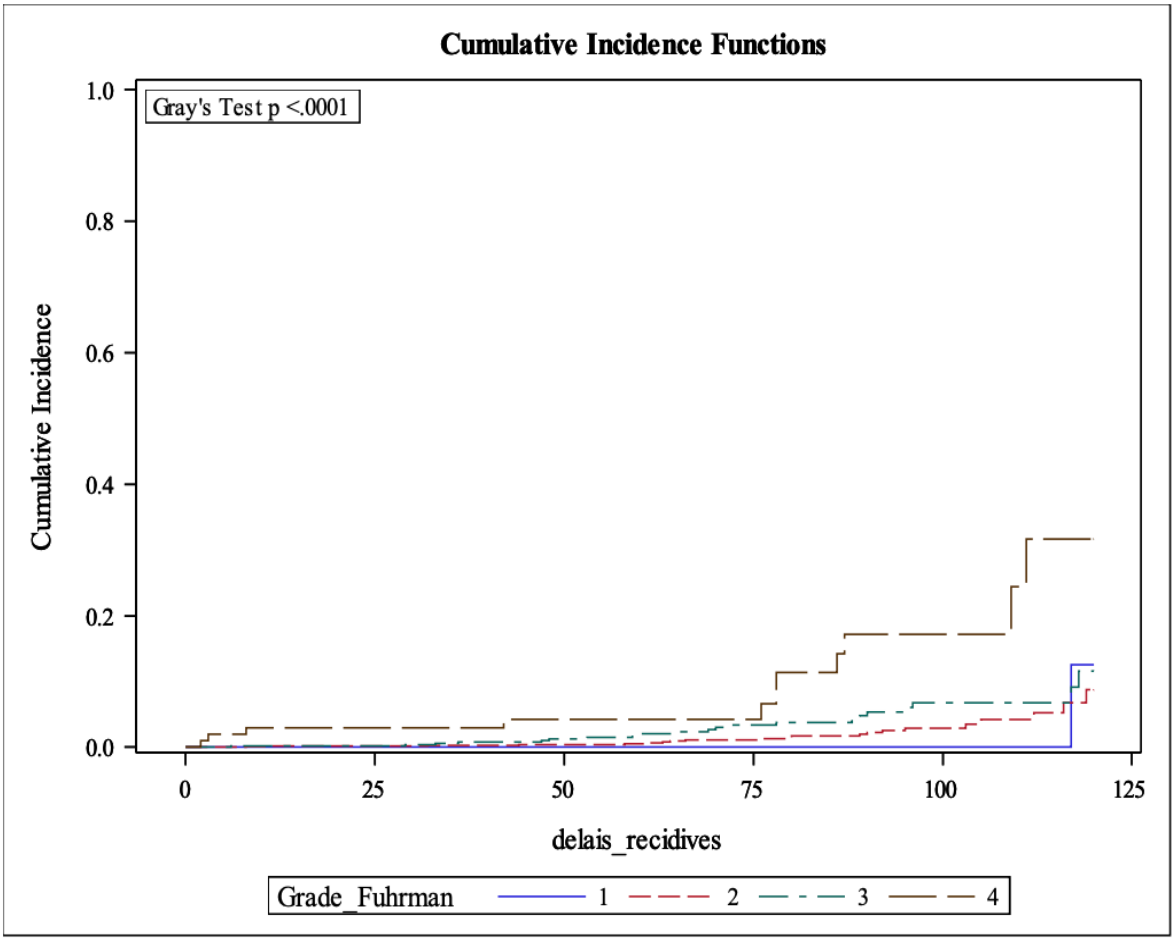
1 = laparoscopic surgery
2 = Open surgery

Figure 10 – Cumulative incidence functions for recurrence for CCC histology.



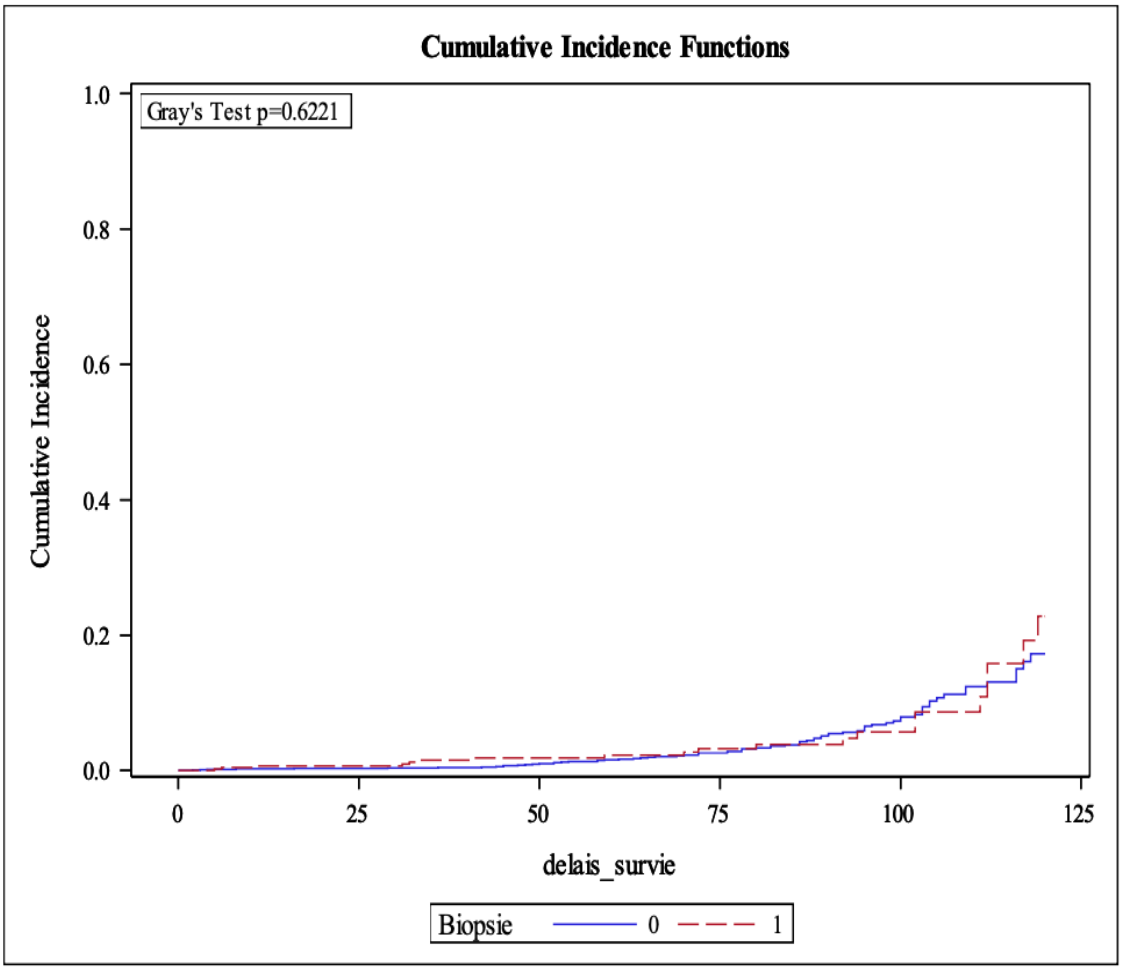
0 = Without CCC histology biopsy
1 = With CCC Histology

Figure 11 – Cumulative incidence functions for recurrence for different Fuhrman grade.



1 = Grade 1
2 = Grade 2
3 = Grade 3
4 = Grade 4

Figure 12 – Cumulative incidence functions for recurrence with or without biopsy.



0 = Without biopsy
1 = With biopsy

Tableau 3 – Multivariate analysis result.

	Univariate analysis				Multivariate analysis			
Variable name	Hazard Ratio	Confidence interval 95% HR		P-value	Hazard Ratio	Confidence interval 95% HR		P-value
Tumor size	***2.523***	***1.153***	**5.521**	***0.0206***	***1.855***	***0.662***	***5.196***	***0.2395***
Necrosis	***2.782***	***1.843***	**4.200**	***<0.0001***	***2.634***	***1.485***	***4.672***	***0.0009***
Sarcomatoid content	***4.602***	***2.187***	**9.682**	***<0.0001***	***1.384***	***0.538***	***3.557***	***0.5004***
Delay between diagnosis and surgery	***1.020***	***1.007***	**1.033**	***0.0031***	***1.021***	***1.006***	***1.037***	***0.0064***
Vascular emboli	***6.276***	***2.684***	**14.675**	***<0.0001***	***3.787***	***1.543***	***9.294***	***0.0036***
Per operative complications	***6.578***	***2.806***	**15.419**	***<0.0001***	***3.306***	***1.292***	***8.460***	***0.0126***
Renal score	***1.854***	***1.142***	**3.012**	***0.0126***	***1.592***	***0.913***	***2.774***	***0.1011***
Robotic assistance	***0.240***	***0.155***	**0.371**	***<0.0001***				
Microcystic architecture	***0.504***	***0.269***	**0.943**	***0.0321***				
Open surgery vs laparoscopy	***4.548***	***2.181***	**9.480**	***<0.0001***	***4.694***	***2.030***	***10.856***	***0.0003***
Histology: CCC	***2.126***	***1.247***	**3.624**	***0.0056***	***2.261***	***1.114***	***4.588***	***0.0239***
Histology: TP1	*0.414*	*0.171*	1.002	*0.0506*				
Histology: TP2	*1.606*	*0.703*	3.666	*0.2609*				
Grade Fuhrman 4	***6.270***	***1.846***	**21.298**	***0.033***				
Biopsy before surgery	*1.135*	*0.698*	1.844	*0.6100*				
Intra hilar tumor	*0.984*	*0.399*	2.426	*0.9712*				
ECOG	*1.267*	*0.644*	2.494	*0.4935*				
Cystic component	*0.923*	*0.552*	1.543	*0.7598*				
Symptoms at diagnosis	*1.066*	*0.620*	1.835	*0.8171*				
Papillary Architecture	*0.911*	*0.538*	1.543	*0.7290*				

AUTEUR : Nom : DELUEGUE **Prénom : LUCAS**

Date de Soutenance : 17 octobre 2024

Titre de la Thèse : Évaluation de la prévalence des récidives locales du cancer du rein ainsi que des facteurs prédictifs après chirurgie par néphrectomie partielle avec marges négatives (R0).

Thèse - Médecine - Lille 2024

Cadre de classement : Urologie

DES + spécialité : DES Urologie

Mots-clés : Cancer, rein, récidive, locale, néphrectomie partielle, prévalence et facteurs prédictifs.

Introduction :
La récidive locale après néphrectomie partielle en marges chirurgicales négatives (R0) reste un problème clinique dans le cancer du rein.
Cette étude vise à déterminer le taux de récidive locale après une néphrectomie partielle R0 et à identifier les facteurs prédictifs associés à cette récidive.

Patients et méthode :
Une étude rétrospective multicentrique a été menée en France (URO CCR n°140), portant sur des patients ayant subi une néphrectomie partielle entre avril 2007 et novembre 2022 pour un cancer du rein de stade cT1-cT3a/N0/M0 avec des marges chirurgicales négatives.
Les critères d'exclusion comprenaient les antécédents de cancer du rein, les tumeurs multifocales, les tumeurs bénignes et les métastases rénales d'un autre cancer primaire.

Résultats :
Au total, 2 438 patients ont été inclus. Une récidive locale est survenue chez 97 patients (3,9 %) après un suivi médian de 29 mois (IQ : 26;86). L'analyse multivariée a identifié plusieurs facteurs de risque de récidive, notamment une approche chirurgicale ouverte (HR 4.694 [2.020;10.856]), la survenue de complications peropératoires (HR 3.306 [1.292;8.460], le délai entre le diagnostic et la chirurgie (HR 1.021 [1.006;1.037]), la présence d'emboles vasculaires (HR 3.787 [1.543;9.294]) et de nécrose (HR 2.634 [1.485;4.672]) à l'analyse anatomopathologique.

Conclusion :
Cette étude a révélé un taux de récidive locale de 3,9 % après chirurgie par néphrectomie partielle pour un cancer du rein avec des marges négatives.
Les principaux facteurs de risque de récidive locale comprennent l'approche chirurgicale ouverte, le délai entre le diagnostic et la chirurgie, les complications peropératoires et les caractéristiques anatomo-pathologiques défavorables telles que les emboles vasculaires et la nécrose.

Composition du Jury :

Président : Pr Arnauld Villers.

Assesseurs : Pr Philippe Puech, Pr Xavier Leroy, Dr Jonathan Olivier.

Directeur de thèse : Dr Jean-Christophe Fantoni.