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Does Biopsy Before Partial Nephrectomy Influence the Operative Outcome?

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Abstract

Background: Partial Nephrectomy (PN) is the gold standard for patients with cT1 renal lesions. 20% of those lesions are benign. The concordance rate between tumor histotype on percutaneous Renal Tumor Biopsy (RTB) and on the surgical specimen of the following PN is 90%.

Objective: To evaluate the impact of previous RTB on surgical outcomes and Perioperative Complications (POC) for PN. Design, setting, and participants: Our study included 164 patients from the Urology Department of the Paris Institute Mutualiste Montsouris (IMM).

Measurements: Perioperative complications included operative time, clamping time and blood loss, perioperative complications were assessed by Clavien-Dino classification. In addition, the histological outcome from RTB and PN were registered.

Results and Limitations: The number of benign lesions differed significantly between patients with and without prior RTB: respectively 7% (4/56) and 20% (22/107), p=0.03. No significant difference was found in perioperative complication. No significant difference in Clavien >2 POC rate was observed with respectively 7% (4/57) and 10% (11/107).

Conclusion: This study shows a significant reduction of benign lesions in PN after RTB. RTB do not increase the amount or severity of POC.

Keywords: Benign; Biopsy; Nephrectomy; Renal cell carcinoma; Small renal mass

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Introduction

Although abdominal imaging (Computed Tomography or MRI) allows accurate diagnosis of Renal Cell Cancer (RCC), it cannot reliably distinguish oncocytoma and fat-free angiomyolipoma from malignant lesions [1-4].

On the other hand, the sensitivity (97.5%), specificity (96.2%), and positive predictive value (99.8%) of RTB are very high showing that it is reliable for the diagnosis of a malignant lesion. Furthermore, histologic determination of RCC subtype is highly accurate [5,6].

Percutaneous samplings are performed under local anesthesia with eighteen-gauge needle core biopsy, using US or CT guidance, with a similar diagnostic yield. Recent studies showed that at least two good quality cores should be obtained, and necrotic areas should be avoided to maximize diagnostic yield [6-10].

Overall, percutaneous biopsies have a low morbidity. The most common complications are renal hematoma (4.9%), clinically significant pain (1.2%), gross hematuria (1.0%), pneumothorax (0.6%) and hemorrhage requiring transfusion (0.4%). Tumor seeding along the needle tract has been considered anecdotal, especially when using coaxial technique [5,6,11-13].

A recent study showed that benign findings at pathology is significantly lower in centers where biopsies are performed (5% *vs.* 16%), suggesting that biopsies can reduce unnecessary surgery for benign tumors and therefore the morbidity associated with these procedures [14].

Until yet, the latest guidelines (AUA, EAU and NCCN) do not recommend a systematic RTB before surgery in patients with a contrast-enhancing solid renal mass.

Indeed, certain concerns remain among urologists regarding RTB's safety and its ability to impact the management of renal masses, because of its significant Negative Predictive Value (NPV). As a result, a non-malignant biopsy result may not be reliable. A systematic review estimated the NPV at 63%, meaning that 37% of the patients undergoing surgery after a negative biopsy had a malignant disease on final pathology.

I have been shown that in the cases where radiologic findings were suspicious for malignancy and a first biopsy was non-diagnostic, repeated biopsies were reported to be diagnostic in a high proportion of cases (83% to 100%) [5,6,15-17].

In this monocentric study, we aimed to compare histological outcome of PN in patients with or without prior RTB and the rate of per-operative and peri-operative complications between those two groups.

Patients and Methods

Patients selection

Data from patients who underwent laparoscopic or robotic-assisted PN between January 2012 and December 2019 at IMM were prospectively recorded in the IMM database and retrospectively reviewed. Patients with a cT1 lesion and available pathological tissue diagnosis (diagnostic biopsy and/or extirpative surgery) were selected for analysis. Inclusion criteria were laparoscopic PN with or without prior RTB. Exclusion criteria were cystic lesions, prior history of ablative treatment for kidney lesion, or radical nephrectomy due to perioperative considerations. A total of 163 patients have been included (56 with prior RTB and 107 without).

Data recording

Indications for RTB and PN have been discussed during the uro-oncology multi-disciplinary weekly meeting. All RTBs were performed at the IMM Radiology Department under local anesthesia. Eighteen-gauge needles with coaxial technique under CT guidance were used. Minimum two samples were taken for anatomopathological analysis. Both RTBs and surgical specimen were analyzed at the IMM Anatomopathology Department. Preoperative data such as age, Hemoglobin (Hb), Tumor Size (TS) and RENAL score were recorded by the patient's urologist. Perioperative data such as duration of surgery, ischemia time and blood loss were recorded by the surgeon. Perioperative complications were recorded by the Urology Department's MD using the Clavien-Dino classification; Clavien 1 and 2 were considered as minor complications whereas 3 and more were considered as major complications.

Statistical analysis

The quantitative variables were described using the usual position and dispersion statistics, i.e., mean median, variance, minimum, maximum and quantiles. Qualitative variables were described using the numbers and proportions of each modality. The characteristics of patients and histological findings were compared between RTB and non-RTB groups using the Wilcoxon rank-sum test for continuous variables and the Chi2 parametric test for proportions if the conditions were met or Fisher's exact test. Univariable and multivariable logistic regressions models were generated to test for an association between patient (age, hemoglobin), lesion (size, RENAL score), procedure-related characteristics (blood loss, ischemia time, operating time, Clavien-Dino complication) and the histological outcome of PN. A sensitivity analysis was also performed to identify the odds of finding a benign histology at surgery based on pretreatment RTB status. The first alpha species risk was set at 5% for all analyses. All the analyses were performed on the R software in its version 3.1, R Development Core Team (2008). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria *via* the GMRC Shiny Stat application of the Strasbourg University Hospital (2017).

Results

Patient characteristics are detailed in Table 1. Overall characteristics did not differ significantly except for the tumor size which was higher in the patient group without prior RTB. Benign lesions were significantly lower in the RTB group with 7% (4/56) compared to 20% (22/107) in the non RTB group, p=0.03 IC 95% [1.05; 14.09] (Table 2). We show no significant difference between the two groups concerning the occurrence of complications in Clavien-Dino group 1 and 2 and Clavien 3 and more (Table 3); in the same way, no significant difference was found regarding operative time, ischemia time and blood loss.

We then analyzed the RTB group comparing histological findings from RTB and PN samples (Table 4). Sensitivity of RTB was 92% and Specificity was 100%. Among the 7 RTB with no histological conclusion, 3 turned out to be oncocytoma, 3 Clear Cell RCC and 1 Chromophobe RCC. Furthermore, 3 Papillary RCC were reconsidered Clear Cell RCC. Overall, the concordance rate between tumor histotype on RTB and on the surgical specimen of PN was 83% (including 7 Non-Diagnostic).

Discussion

Over the last decades, preventing treatment of benign lesions has been a growing concern in health care. To that end, the strategy for the management of renal masses have changed with an increase of active surveillance and new tools such as RTB that have been developed

Table 1: Characteristics of the two cohorts of men with and without RTB.

	With Prior RTB	Without Prior RTB	p value
Total number of included patients	56	107	
Age (median, years)	61	62.5	0.9
Hemoglobin (median, g/dl)	14.24	14.08	0.5
Tumor Size (median, cm)	28.2	35.2	0.00044
RENAL Score:			
4	34% (19)	37% (40)	0.90
5	21% (12)	16% (17)	0.44
6	13% (7)	12% (13)	1
7	9% (5)	10% (11)	0.97
8	7% (4)	15% (16)	0.21
9	7% (4)	9% (9)	0.77
10 and more	9% (5)	1% (1)	0.019
Robotic Laparoscopy	43% (24)	51% (55)	0.87

Table 2: Anatomopathology' results of surgical specimen after PN.

	With Prior RTB	Without Prior RTB	RR	p value
Total number of included patients	56	107		
Benign Lesions	7.1 % (4)	20.6 % (22)	3.34 IC 95% [1.05; 14.09]	0.03
Malign Lesions	92.9 % (52)	79.4 % (85)		

Table 3: Results of peri-operative Clavien-Dino complications.

	With Prior RTB	Without Prior RTB	RR	p value
Total number of included patients	56	107		
Per-Operative				
Operative Time (median, min)	93	85		0.81
Ischemia Time (median, min)	14	11		0.07
Blood Loss (median, mL)	317	344		0.13
Peri-Operative				
No complication	80.4% (45)	85% (91)		
Complication :	19.6% (11)	15% (16)	1.39 IC 95% [0.53; 3.49]	0.51
Clavien 1 and 2	12.5% (7)	4.7% (5)		0.14
Clavien 3 and more	7.1% (4)	10% (11)		0.57

Table 4: Comparison between RTB and PN histological results.

Histological Type	RTB	PN
Clear Cell RCC	46% (26)	57% (32)
Papillary RCC	30% (17)	25% (14)
Chromophe RCC	9% (5)	11% (6)
Oncocytoma	2% (1)	7% (4)
ND*	13% (7)	0

*ND: Non-Diagnostic: Doubt between oncocytic neoplasms (Oncocytoma) and malignant ones (Chromophobe or Clear Cell Carcinoma)

to separate benign and malign lesions. Although RTB is the only diagnostic test which can provide histological proof of malignancy, it is also safe with a very low risk of complications [11].

Currently, the use of RTB is still not widespread among urologists and takes a secondary place in the management of renal masses for which surgical treatment is possible according to the current recommendations. This can be related to the thought that RTB does not alter management of such masses, or that it is not safe enough regarding the insight it can provide.

Thus, we intended to study the impact RTB could have on our management of renal masses. Our results showed that the number of benign masses was significantly lower in the group with prior RTB (7% *vs.* 20%, p=0.03), as showed by Richard PO et al. [14] with a significantly lower rate of benign histology in the biopsy group (5% *vs.* 16%, p<0.001).

It has been shown that an increase of tumor size was associated with a low risk of benign tumor by Frank et al. with a percentage of benign tumors of 46.3% for tumors of less than 1cm *vs.* 6.3% for those of 7 cm or greater [18,19].

In our findings, the median size of tumor was superior in the group without prior RTB (35.2 *vs.* 28.2 cm, p<0.01). This could represent a potential bias by increasing the number of benign histology in the group with prior RTB. Nevertheless, the amount of benign histology remained higher in the group without RTB. This suggests that RTB could be useful in the management of renal masses regardless of their size.

In addition, we showed that the median age of patients with benign lesions was higher than the one of patients with malign lesions (66.7 *vs.* 61.1; p=0.03). Although this has already been shown in other studies, this association still remain controversial in the literature [18,20,21].

Nonetheless, these patients would certainly benefit the most from avoiding useless surgical treatment as they are more fragile. Our results are in favor of using RTB in the management of renal masses, in order to reduce the number of unnecessary surgically removed benign masses.

Overall, RTB itself has a low comorbidity [11]. To the best of our knowledge, no study has yet compared the impact of RTB on the complication rate of the following surgical extirpation. Our results showed no significant difference between the two groups regarding the Clavien-Dino complication rate of PN, and this rate was consistent with the literature [22]. The same goes for blood loss, with no significant difference between the two groups, under 0.5l [23,24]. Operative time and ischemia time were not different between the two groups with a median ischemia time similar to the one reported by Thompson et al. [25]. Therefore, there seems to be little impact from RTB on the following surgical treatment.

However, RTB has limitations. Although coaxial technique allows quality tissue samples, they remain insufficient in some cases for pathologists to distinguish benign from malignant lesions [26]. In our study, 7/54 RTB could not separate oncocytic neoplasms (Oncocytoma) from malignant ones (Chromophobe or Clear Cell Carcinoma). There are evidences in the literature supporting that a second RTB could reduce this number [6,15,17]. Another concern is the significant predictive negative value (63%) of RTB, meaning that a benign biopsy doesn't ensure the absence of malignancy [5]. Furthermore, our study has also some limitations. Firstly, most of the renal masses were initially assed using abdominal Computed Tomography. The use of MRI in addition might have enhanced the characterization of some renal masses before biopsy, even though it is less likely to have changed the management of such masses [1-4]. Secondly, we could not assess RTB's predictive negative value in our study since we only gathered data from patients who underwent partial nephrectomy, an unknown portion of patient having otherwise been treated with active surveillance or ablative treatments after RTB. As a result, there might have been some false negative biopsies among those patients who could have benefited from surgery.

Nevertheless, active surveillance of these small lesions can be considered safe at least over the short term [27]. RTB could therefore still play a part in this active surveillance by allowing a better selection of patients.

Conclusion

The present study shows that RTB adds value to abdominal imaging by increasing the predictive value and specificity for RCC, without increasing the complication rate of surgical ablative treatment. As a result, the use of RTB could potentially lower the number of patients undergoing ablative treatment and could favor active surveillance management of small masses.

Author's Contribution

D Pasquier: Data analysis, Manuscript righting F Rozet: Project development, Manuscript Righting A Fregeville: Data collection E Barret: Data analysis R Sanchez salas: Data analysis A Mombet: Data collection N Cathala: Data collection X Cathelineau: Project development.

Ethics Approval

The study was approved by the Institutional Review Board (ref

CEPAR: 2020-03) and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

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