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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Diagnostic accuracy of percutaneous core biopsy before cryoablation for small-sized renal cell carcinoma

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PURPOSE

To retrospectively determine the diagnostic accuracy of a percutaneous core biopsy performed before cryoablation for small-sized renal cell carcinoma.

METHODS

In this study, 216 patients underwent a percutaneous core biopsy for 242 renal lesions suspected to be renal cell carcinoma on image findings before cryoablation at Kyushu University Hospital. We calculated the success rate of the histological diagnosis and investigated factors that may have contributed to the diagnostic success. Complications caused by the biopsy procedure were also evaluated.

RESULTS

The histological diagnosis was successful in 203 lesions (82.8%). The success rate of the histological diagnosis was 65.4% (34/52 cases) for tumors with a diameter of ≤15 mm and 88.9% (169/190 cases) for those >15 mm. Therefore, tumor diameter was a factor contributing to the histological diagnosis success rate in both univariate and multivariable analyses ($P < 0.001$). For lesions with a tumor diameter ≤15 mm, the histological diagnosis success rates increased from 50.0% to 76.2% in the presence of pre-lipiodol marking and to 85.7% when the biopsy procedure was performed separately from cryoablation; the latter was statistically significant ($P = 0.039$). Major complications that may have been caused by the biopsy procedure were grade 3 bleeding and tract seeding (one case each).

CONCLUSION

Percutaneous core biopsy in cryoablation for small-sized renal cell carcinoma had a high diagnostic rate and was safely performed. For lesions with a tumor diameter ≤15 mm, a separate biopsy procedure and pre-lipiodol marking may improve the diagnostic accuracy.

KEYWORDS

Ablation, biopsy, cryotherapy, CT, malignancy, renal

Cryoablation for renal cell carcinoma is a minimally invasive treatment that has become well established in recent years. Studies report that it provides a high degree of local control, preserves renal function comparable to surgical resection, and is suitable for elderly patients and patients with comorbidities or multiple lesions.[1-3] With the development of diagnostic imaging equipment, the incidental detection of small-sized renal cell carcinoma is increasing,[4,5] and cryoablation as a minimally invasive treatment for this small-diameter renal cell carcinoma is considered useful.

Prior to cryoablation for renal cell carcinoma, obtaining a histological diagnosis to clarify the medical evidence for the application of this technique is desirable. Most imaging diagnoses are accurate but not complete, and benign lesions may be present, although not frequently.[6,7]

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Percutaneous biopsy is necessary to obtain a histological diagnosis, but biopsy is not always easy. The level of difficulty varies depending on the size and location of the lesion, and there is a risk of complications such as bleeding and seeding.[8,9] In addition, the protocol for percutaneous biopsy in cryoablation has not been fully established, such as when to perform the biopsy, whether to perform it at the same time as cryoablation or separately, and the relationship with lipiodol marking, which is widely performed in Japan before cryoablation to improve the visibility of the lesion in computed tomography (CT) fluoroscopic images.[10,11]

Therefore, the purpose of this study is to retrospectively evaluate the diagnostic accuracy of percutaneous biopsy performed before cryoablation for renal cell carcinoma.

Methods

All the procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. This study has obtained approval from the Institutional Review Board of Kyushu University Hospital (no: 21109-00), and the need for informed consent was waived.

Participants

At our institution, 258 renal lesions of 221 patients were subjected to cryoablation between April 2014 and September 2019. All patients were given information about the indications for treatment by both our team and a urologist from our institution or elsewhere before agreeing to the cryoablation treatment. Percutaneous biopsies for histological diagnosis were performed on 216 patients with 242 lesions, excluding those with multiple lesions or patients who refused biopsy. The patient demographic data and lesion characteristics are detailed in Table 1.

Main points

- Tumor diameter was a factor contributing to the diagnostic accuracy of a percutaneous core biopsy performed before cryoablation for small-sized renal cell carcinoma.
- A biopsy performed in a separate session from cryoablation elevated the histological diagnostic rate for tumors <15 mm.
- Pre-lipiodol marking also improved the histological diagnostic rate of tumors <15 mm.

Flow of the procedure for biopsy, cryoablation, and lipiodol marking

This study had three different procedural flows. One hundred and twenty-eight lesions underwent biopsy and cryoablation in a single session, and 68 lesions were subjected to lipiodol marking as a pretreatment and underwent biopsy and cryoablation in the same session the next day. In 48 cases, the biopsy was performed the day before, with cryoablation performed separately. In 37 of these cases, lipiodol marking was performed after the biopsy. These processes are summarized in Figure 1.

Percutaneous core biopsy

All percutaneous biopsy procedures were performed under local anesthesia and CT fluoroscopy using an interventional radiology (IVR)-CT system (Aquilion One, Canon, Tokyo, Japan) while the patient was in a prone or oblique-prone position. An 18-gauge (G) core biopsy needle using a 17-G introducer (TEMNO evolution, Merit Medical, Tokyo, Japan) was inserted into the renal lesion, and the tissue was evaluated by an experienced histopathologist for histological diagnosis.

Cryoablation

All cryoablation procedures were performed with the patient under local anesthesia and in a prone or oblique-prone position using the cryoablation (CryoHit, Galil Medical, MN, USA) and IVR-CT systems. Subsequently, 17-G cryoprobes (IceRod, IceSeed, Galil Medical, MN, USA) were inserted into the tumors using CT fluoroscopy to surround them. The tumors were frozen twice for 10 min by passing argon gas through the probes with a 5-min interval for thawing between the two 10-min freezing periods. Unenhanced CT was obtained to confirm the extension of the ablation area, the so-called "ice ball," at least 5 mm beyond the tumor margin.

Transarterial lipiodol marking

Transarterial lipiodol marking was performed before cryoablation to improve the contrast between the tumor and normal parenchyma during the CT-guided procedure. Digital subtraction and CT angiography of the renal artery and branches were obtained to identify the tumor through a transfemoral approach using a 3–4F sheath (Super sheath, Medikit, Tokyo, Japan). Selective catheterization of the tumor's feeding artery, injection of lipiodol (Guerbet, Paris, France), and embolization with a small gelatin sponge (Serescue, Nihon Kayaku, Tokyo, Japan) were then performed. Unenhanced CT was obtained to confirm the deposition of lipiodol throughout the tumor.

Statistical analysis

First, the biopsy results and diagnostic success rate were evaluated. We considered those with a specific histological diagnosis, such as clear cell carcinoma, papillary renal carcinoma, angiomyolipoma, and oncocytoma, to be diagnostic, whereas those with no malignant tissue or with atypical cells were considered non-diagnostic. Second, risk factors associated with histological diagnosis were analyzed. These included age, sex, tumor size, tumor location, biopsy procedure, and pre-lipiodol marking. Continuous variables (e.g., age, tumor size) were compared between diagnostic and non-diagnostic groups using the Student's *t*-test and categorical variables (e.g., sex, tumor size divided

Table 1. Demographic data and lesion characteristics in all patients undergoing a percutaneous core biopsy for suspected renal cell carcinoma

Patient characteristics (n = 216)	
Age, years, median (minimum–maximum)	71 (30–91)
Sex, n (%)	
Male/female	160 (74.1)/56 (25.9)
Number of lesions, n (%)	
1/2/3/4	195 (90.2)/17 (7.9)/3 (1.4)/1 (0.4)
Lesion characteristics (n = 242)	
Size, mm, mean ± SD (minimum–maximum)	23.2 ± 7.98 (8–40) ≤15 (n = 52)/>15 (n = 190)
Location, n (%)	
Exophytic/endophytic/hilum	122 (50.4)/103 (42.6)/17 (7.0)
Upper/middle/lower	71 (29.3)/111 (45.9)/60 (24.8)
Anterior/posterior/X	96 (39.7)/120 (49.6)/26 (10.7)

SD, standard deviation.

into two groups with a 15 mm diameter, tumor location, biopsy procedure, and pre-lipiodol marking) were compared using the chi-square test. Significant differences identified by univariate analysis were then analyzed through multivariate analysis using logistic regression with forward selection. Variables assessed to be $P < 0.10$ in the univariate analysis were entered into a multivariable logistic regression analysis. A comparison of the diagnostic rates from the different procedures was performed for large and small tumor sizes using the chi-square test, with $P < 0.05$ considered a statistically significant difference. Complications were graded according to the Common Terminology Criteria for Adverse Events (version 5), published by the National Cancer Institution in 2017, and complications of grade 3 or higher were examined. All statistical analyses were performed using JMP Pro (version 14; SAS Institute). Descriptive statistics are presented as mean ± standard deviation and frequencies are presented as percentages.

Results

The results of the biopsy and diagnosis rate assessments are presented in Table 2. The most common type was clear cell carcinoma (179 cases), followed by papillary carcinoma (16 cases). A small number of benign lesions such as oncocytoma and angiomyolipoma were also identified. The overall diagnostic rate was 82.8%. In the analysis of risk factors involved in histological diagnosis, there was a significant difference in the diagnostic rates according to tumor size in the univariate analysis ($P < 0.001$). A significant difference in the diagnostic rate for tumor size ≤15 or >15 mm ($P < 0.001$) was also detected. No significant difference was observed in tumor location (exophytic/endophytic/hilum: $P = 0.336$; upper/middle/lower: $P = 0.078$; anterior/posterior/X: $P = 0.575$) (Table 3). A multivariable analysis was performed on factors achieving P values < 0.1 in the univariate analysis, and in this analysis, a significant difference was observed for tumor size ≤15 and >15 mm ($P < 0.001$) (Table 4).

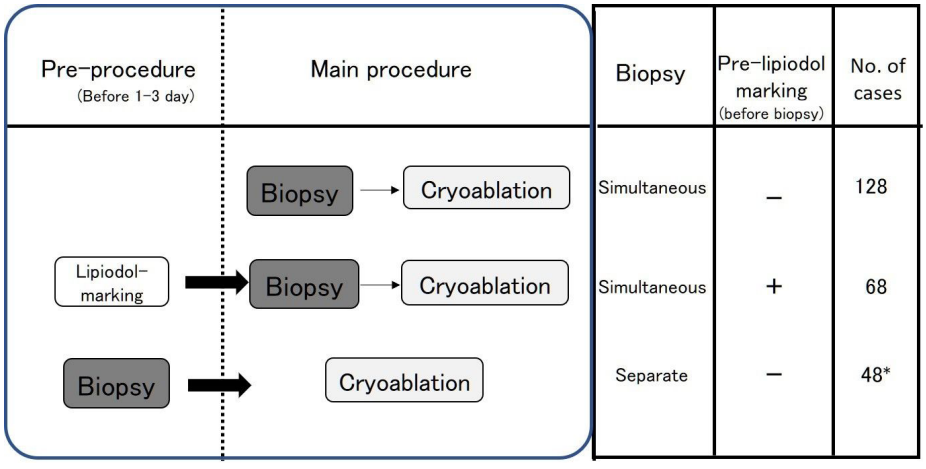

Figure 1. Flow of the procedure for biopsy, cryoablation, and lipiodol marking. *Lipiodol marking was performed immediately after the biopsy in 37 of the 48 cases.

Table 2. Biopsy results and diagnostic rates

Biopsy results		No of cases (%)
Diagnostic	Clear cell carcinoma	179 (74.0)
	Papillary carcinoma	16 (6.6)
	Chromophobe carcinoma	1 (0.4)
	Metastatic carcinoma	1 (0.4)
	Oncocytoma	4 (1.7)
	Angiomyolipoma	2 (0.8)
	Total	203 (82.8)
Non-diagnostic	No malignant tissue	25 (10.3)
	Atypical cell	14 (5.8)
	Total	39 (17.2)

In the comparison of diagnostic rates according to procedures, the diagnostic rate of the biopsy increased with the addition of pre-lipiodol marking compared with simultaneous biopsy and cryoablation; the diagnostic rates increased further by performing biopsy and cryoablation in separate sessions. This was more pronounced for tumors <15 mm in diameter, for which the diagnostic rate was only 50% in cases where biopsy and cryoablation were performed simultaneously but increased to 76.2% when pre-lipiodol marking was performed; it increased significantly to 85.7% when biopsy and cryoablation were performed in separate sessions ($P = 0.039$) (Figure 2).

The only grade 3 or higher complications were one case of hemorrhage and one of seeding of the puncture site.

Discussion

Percutaneous biopsy of renal tumors is a well-established technique that has been reported extensively.[8,9,12] However, biopsy of small renal cell carcinoma, which is an indication for cryoablation, is often difficult because of tumor size and location. In addition, it is difficult to determine when to perform a biopsy in cryoablation, and this has not been established. Therefore, we investigated the diagnostic performance of percutaneous biopsy in the cryoablation of renal cell carcinoma.

In the present study, the overall diagnostic rate of biopsy was 82.8%, and the diagnostic rate was higher when cryoablation and biopsy were performed in separate sessions than when they were performed simultaneously. Other authors have reported that the diagnostic rate of biopsy for renal masses is generally around 90%[8,9,12,13] and that the diagnostic performance of radiofrequency ablation and biopsy for renal cell carcinoma is 68%.[14] These suggest that performing a biopsy at the same time as cryoablation decreases the histological diagnostic performance of the biopsy. The reason may be that when a biopsy is performed in the same session as cryoablation, the priority is inevitably given to cryoablation as the treatment, and the biopsy and diagnosis are neglected. In addition, if a biopsy is performed with a cryoprobe inserted into the lesion, the recognition and identification of the lesion may be inadequate because of the artifacts caused by the cryoprobes, thereby affecting the diagnostic performance of the biopsy.

The risk factor involved in the histological diagnostic rate is tumor size. In this

Table 3. Univariate analysis of the risk factors associated with histological diagnosis

Factor		Diagnostic (n = 203)	Non-diagnostic (n = 39)	*P* value
Age, years	Mean ± SD	69.9 ± 11.9	67.1 ± 15.1	0.101
Sex, n (%)	Male/female	135/51 (82.1/91.1)	29/5 (17.9/8.9)	0.212
Size, mm	Mean ± SD	24.0 ± 7.75	19.0 ± 7.98	<0.001
n (%)	>15 mm	169 (88.9)	21 (11.1)	<0.001
	≤15 mm	34 (65.4)	18 (34.6)	
Location, n (%)	Exophytic/endophytic/hilum	99/88/16 (81.1/79.3/94.1)	23/15/1 (18.9/20.7/5.9)	0.336
	Upper/middle/lower	60/98/45 (84.5/88.3/75.0)	11/13/15 (15.5/11.7/25.0)	0.078
	Anterior/posterior/X	82/101/20 (85.4/87.8/76.9)	14/19/6 (14.6/12.1/23.1)	0.575
Biopsy procedure, n (%)	Simultaneous/separate	161/42 (82.1/91.3)	35/4 (17.9/8.7)	0.128
Pre-lipiodol marking, n (%)	+/–	59/144 (86.8/82.8)	9/30 (13.2/17.2)	0.446

SD, standard deviation.

Table 4. Multivariable logistic analysis of the risk factors associated with histological diagnosis

Factor		Odds ratio	95% Confidence interval	*P* value
Size	≤15 mm/>15 mm (reference)	4.04	1.92, 8.50	<0.001
Location	Upper/middle/lower (reference)	0.70 0.45	0.28, 1.73 0.19, 1.10	0.192

Factors with *P* values <0.1 in the univariate analysis (Table 3) were extracted and subjected to multivariable logistic analysis. *P* value of the entire logistic model was <0.001. McFaden R-squared was 0.121.

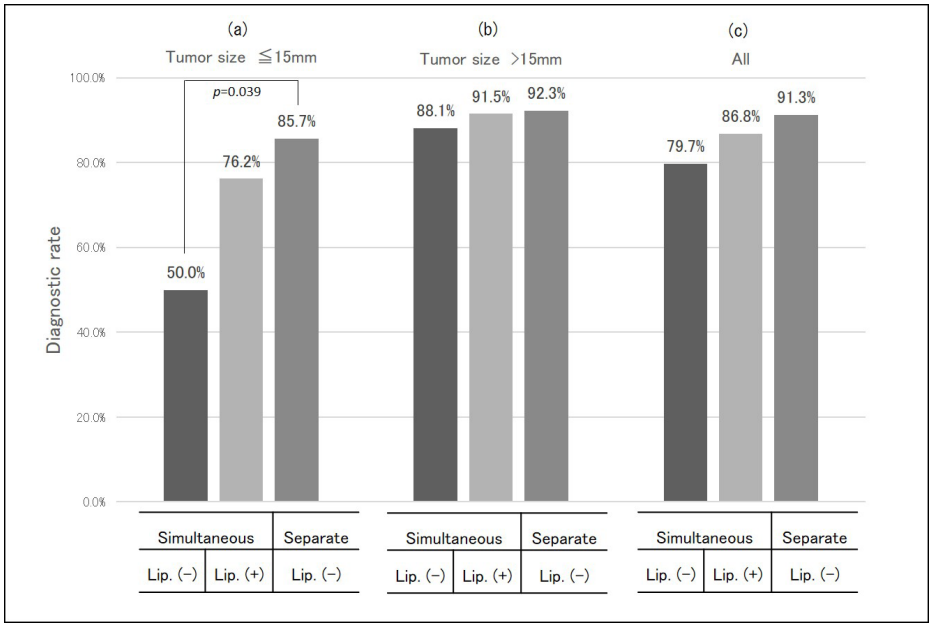

Figure 2. Comparison of the diagnostic rates of the biopsies between procedures by tumor size. (a) The diagnostic rate of the biopsy for the tumors with a diameter ≤15 mm increased from 50.0% to 76.2% in the presence of pre-lipiodol-marking and to 85.7% with a biopsy procedure performed separately from the cryoablation, with the latter being statistically significant ($P < 0.05$, chi-square test). There was a similar but not statistically significant difference in the diagnostic rates for tumors >15 mm (b) and all tumors **(c).** Lip, pre-lipiodol marking.

study, for tumors <15 mm in diameter, the diagnostic rate was 50% when the biopsy was performed at the same time as cryoablation, increasing to 76.2% when lipiodol marking was performed the day before and further to 85.7 % when the biopsy and cryoablation were performed in separate sessions. This suggests that pre-lipiodol marking and separate sessions of biopsy and cryoablation may be useful for increasing the histological diagnostic rate of lesions with small tumor sizes. Pre-lipiodol marking certainly increases the visibility of the lesion; in addition, performing cryoablation and a biopsy in separate sessions improves the operator's concentration during each procedure (Figures 3, 4). In the present study, pre-lipiodol marking followed by cryoablation and biopsy was not performed in separate sessions, but it is highly likely that this would further increase the histological diagnostic rate.

In the present study, the location of the lesion did not affect the histological diagnostic rate. Studies have reported that exophytic lesions have a high diagnostic rate[15] and that lesions in the hilar region of the kidney also have a high diagnostic rate;[16] thus, the effect of the location of the lesion on the histological diagnostic rate of biopsy is uncertain. At this stage, there is no need to change the biopsy procedure according to the location of the lesion.

Serious complications were not frequent, with one case of hemorrhage and one of seeding of the puncture site; these complications are similar to those previously reported in biopsy and cryoablation studies.[1,2,9] Percutaneous biopsies for renal lesions, including cryoablation and lipiodol marking performed concurrently or in separate sessions, seem to be well tolerated.

In the present study, the imaging modality used for the biopsy of renal lesions was CT. In other imaging modalities, ultrasound allows convenient biopsy from any angle, and magnetic resonance imaging provides better soft-tissue resolution and recognition of target lesions. However, the diagnostic rate of biopsies for renal lesions with these imaging modalities is comparable to that of CT usage in this study, and the incidence of complications is low with each modality.[12,17] Therefore, many options for imaging modalities for renal biopsy are available, and the physician should select an imaging modality based on the facility's equipment and the concurrent treatment, such as image-guided cryoablation.

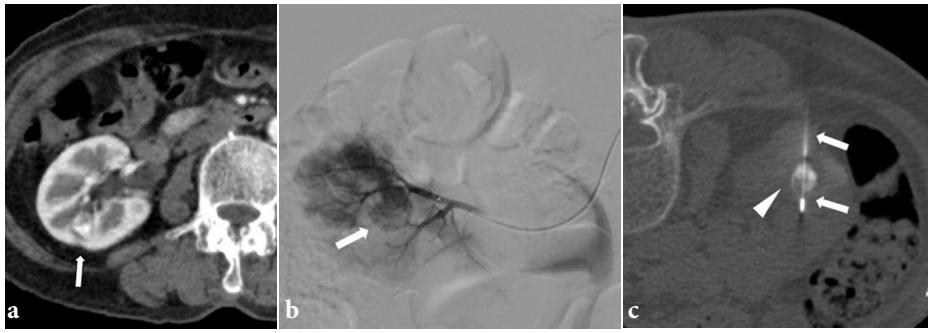

Figure 3. Simultaneous computed tomography (CT)-guided biopsy and cryoablation of renal cell carcinoma in a 76-year-old woman in the presence of lipiodol deposition. (a) Contrast-enhanced CT showed an endophytic lesion with an 11 mm diameter in the central part of the right kidney (arrow). (b) Lipiodol was deposited into the lesion (arrow) using a transarterial approach the day before to improve the visibility of the lesion. (c) Biopsy and cryoablation using a cryoprobe (arrow) were performed on the lipiodol-deposited tumor (arrowhead) in the same session the next day. The histological diagnosis was clear cell carcinoma with no severe complications during or after the procedure.

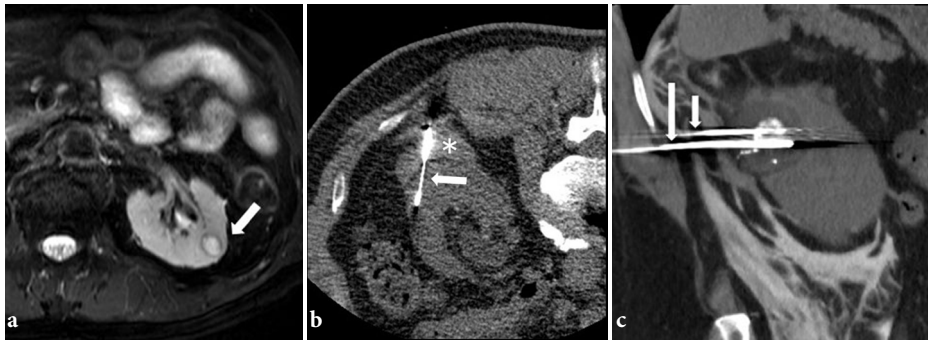

Figure 4. Computed tomography-guided biopsy separated from cryoablation of renal cell carcinoma in a 76-year-old man. (a) T2-weighted magnetic resonance image revealed an endophytic lesion with a diameter of 15 mm in the left central kidney that was suspected to be renal cell carcinoma (arrow). **(b)** A biopsy was performed using a biopsy needle (arrow), followed by lipiodol marking using a transarterial approach the day before cryoablation. (c) Cryoablation was performed using cryoprobes (arrow) the next day. The histological diagnosis was clear cell carcinoma. A perirenal hematoma (grade 1) was observed (b, asterisk), but no severe complications were detected during or after the procedures.

Limitations include the fact that the study was not randomized, that some complications were not strictly distinguishable in biopsy or cryoablation, and that non-neoplastic lesions may be considered undiagnosed. For tumors <15 mm, the histological diagnostic rate was higher in patients with separate sessions or pre-lipiodol marking. A future study is needed because both separate sessions and pre-lipiodol marking may increase the success rate of histological diagnosis.

In conclusion, for renal lesions with small tumor diameters, a biopsy performed in a separate session from cryoablation and using pre-lipiodol marking may improve the histological diagnostic rate.

Conflict of interest

The authors declare that they have no conflicts of interest.

References

1. Thompson RH, Atwell T, Schmit G, et al. Comparison of partial nephrectomy and percutaneous ablation for cT1 renal masses. *Eur Urol.* 2015;67(2):252-259. [CrossRef]
2. Uhlig J, Strauss A, Rücker G, et al. Partial nephrectomy versus ablative techniques for small renal masses: a systematic review and network meta-analysis. *Eur Radiol.* 2019;29(3):1293-1307. [CrossRef]
3. Yoshimatsu R, Yamagami T, Nishimori M, et al. Time-Dependent Effects of Cryoablation for Renal Tumor on Overall and Split Renal Function. *J Vasc Interv Radiol.* 2019;30(3):460-465. [CrossRef]
4. Kane CJ, Mallin K, Ritchey J, Cooperberg MR, Carroll PR. Renal cell cancer stage migration: analysis of the National Cancer Data Base. *Cancer.* 2008;113(1):78-83. [CrossRef]
5. Gill IS, Aron M, Gervais DA, Jewett MA. Clinical practice. Small renal mass. *N Engl J Med.* 2010;362(7):624-634. [CrossRef]
6. Rioux-Leclercq N, Karakiewicz PI, Trinh QD, et al. Prognostic ability of simplified nuclear grading of renal cell carcinoma. *Cancer.* 2007;109(5):868-874. [CrossRef]
7. Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H. Solid renal tumors: an analysis of pathological features related to tumor size. *J Urol.* 2003;170(6 Pt 1):2217-2220. [CrossRef]
8. Beland MD, Mayo-Smith WW, Dupuy DE, Cronan JJ, DeLellis RA. Diagnostic yield of 58 consecutive imaging-guided biopsies of solid renal masses: should we biopsy all that are indeterminate? *AJR Am J Roentgenol.* 2007;188(3):792-797. [CrossRef]
9. Marconi L, Dabestani S, Lam TB, et al. Systematic review and meta-analysis of diagnostic accuracy of percutaneous renal tumour biopsy. *Eur Urol.* 2016;69(4):660-673. [CrossRef]
10. Kajiwara K, Yoshimatsu R, Nishimori M, et al. Efficacy of arterial infusion of iodized oil on CT-guided cryoablation for renal cell carcinoma. *Minim Invasive Ther Allied Technol.* 2021;30(6):327-333. [CrossRef]
11. Hongo F, Yamada Y, Ueda T, et al. Preoperative lipiodol marking and its role on survival and complication rates of CT-guided cryoablation for small renal masses. *BMC Urol.* 2017;17(1):10. [CrossRef]
12. Cazzato RL, De Marini P, Auloge P, et al. Diagnostic accuracy and safety of percutaneous MRI-guided biopsy of solid renal masses: single-center results after 4.5 years. *Eur Radiol.* 2021;31(2):580-590. [CrossRef]
13. Jeon HG, Seo SI, Jeong BC, et al. Percutaneous kidney biopsy for a small renal mass: a critical appraisal of results. *J Urol.* 2016;195(3):568-573. [CrossRef]
14. Iguchi T, Hiraki T, Tomita K, et al. Simultaneous biopsy and radiofrequency ablation of T1a renal cell carcinoma. *Diagn Interv Imaging.* 2016;97(11):1159-1164. [CrossRef]
15. Richard PO, Jewett MA, Bhatt JR, et al. Renal tumor biopsy for small renal masses: a single-center 13-year experience. *Eur Urol.* 2015;68(6):1007-1013. [CrossRef]
16. Cooper S, Flood TA, Khodary ME, et al. Diagnostic yield and complication rate in percutaneous needle biopsy of renal hilar masses with comparison with renal cortical mass biopsies in a cohort of 195 patients. *AJR Am J Roentgenol.* 2019;212(3):570-575. [CrossRef]
17. Park SY, Park BK, Kim CK, Kwon GY. Ultrasound-guided core biopsy of small renal masses: diagnostic rate and limitations. *J Vasc Interv Radiol.* 2013;24(1):90-96. [CrossRef]