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REVIEW

Diagnostic value of percutaneous sampling in Bosniak III–IV renal cysts: a systematic review and meta-analysis

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Objectives: *Complex cystic renal lesions pose a significant diagnostic challenge in the preoperative assessment of malignancy. Although percutaneous renal mass biopsy is well established for solid tumours diagnosis, its role in cystic lesions remains controversial. This systematic review aims to evaluate the diagnostic performance, safety, and clinical impact of percutaneous sampling—fine-needle aspiration (FNA) and core needle biopsy (CNB)—in Bosniak III–IV renal cysts.*

Methods: *A systematic review and meta-analysis were conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [International Prospective Register of Systematic Reviews (PROSPERO) ID CRD420251124563]. PubMed/MEDLINE (Medical Literature Analysis and Retrieval System Online), Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, and Web of Science were searched (1980–May 2025). Eligible studies included adult patients with Bosniak III–IV cysts undergoing FNA or CNB. Pooled diagnostic estimates were calculated using a bivariate random-effects model.*

Results: *Seven studies, including 954 patients, met the inclusion criteria. Three studies evaluated FNA, yielding a pooled sensitivity of 59% [95% Confidence Interval (CI): 14–93], specificity of 84% (95% CI: 62–94), and an overall diagnostic performance of 0.84 [Area under the curve (AUC)]. Sensitivity estimates varied widely, whereas specificity was consistently high. Four studies assessed CNB, reporting diagnostic yields between 75% and 81%. Cystic morphology was identified as the strongest independent predictor of non-diagnostic sampling, with odds ratios (OR) up to 13.9. No major complications or cases of tumour seeding were reported across the included studies. Reporting of minor complications was limited and heterogeneous, precluding a pooled analysis.*

Conclusions: *Percutaneous sampling of Bosniak III–IV cystic renal masses is feasible but diagnostically challenging. FNA provides limited value due to high rates of non-diagnostic and false-negative results. CNB achieves higher accuracy, particularly when a solid component is present, and may be considered within a multidisciplinary setting when histological confirmation is likely to influence treatment decisions.*

Key Words: Bosniak classification, complex renal cyst, percutaneous renal sampling, fine-needle aspiration, core needle biopsy, renal mass biopsy

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Introduction

Complex cystic renal lesions classified as Bosniak III and IV represent a challenging clinical entity due to the difficulty in distinguishing benign from malignant cysts preoperatively.[1–3] Despite major advances in cross-sectional imaging, accurately distinguishing benign from malignant cystic lesions before treatment remains difficult, with important implications for patient counselling and therapeutic decision-making.[4–6] While Bosniak IV cysts are associated with a high likelihood of malignancy, Bosniak III lesions display substantial histological heterogeneity, with reported malignancy rates ranging from 40% to 60%, exposing a relevant proportion of patients to potential overtreatment.[7–9]

This diagnostic uncertainty is particularly relevant in clinical scenarios where treatment decisions must balance oncological risk against patient-specific factors, including comorbidities, life expectancy, and competing causes of morbidity.[10,11]

In the current era of nephron-sparing surgery and active surveillance, the ability to refine preoperative risk stratification in cystic renal masses has become increasingly relevant, particularly for lesions with indeterminate malignant potential.[12–14]

While percutaneous renal mass biopsy (RMB) has become an established diagnostic tool for solid renal tumours, its application in complex cystic lesions remains controversial.[15,16] Technical limitations in sampling thin septa or small solid nodules, along with a higher risk of non-diagnostic results due to the paucity of specimen retrieved, have hindered the widespread use of RMB in this context.[17] These challenges are fundamentally different from those encountered in solid renal masses and reflect both biological and procedural constraints inherent to cystic tumours.[18]

As a result, the role of percutaneous sampling in cystic renal lesions remains incompletely defined, and its use in clinical practice is characterised by substantial heterogeneity. Clarifying the diagnostic performance and limitations of biopsy techniques in this specific setting is therefore essential to inform appropriate patient selection and avoid misinterpretation of biopsy results.

Fine-needle aspiration (FNA) and core needle biopsy (CNB) represent the two main percutaneous techniques explored in this setting. FNA is a minimally invasive approach aimed at collecting cellular material for cytological evaluation, typically under ultrasound or computed tomography (CT) guidance, using a thin hollow needle (≤21 gauge) to aspirate cystic fluid or cells.[19] CNB, conversely, enables histological characterization by obtaining tissue cores through the percutaneous insertion of a larger bore needle (typically 18 gauge) via a coaxial cannula, under real-time imaging guidance.[20–23] Samples are then fixed in formalin, allowing architectural evaluation and immunohistochemistry when required.[19]

Beyond tissue sampling, FNA of cyst fluid has been explored as a minimally invasive approach for the preoperative evaluation of complex renal cysts.[24] In addition to cytological analysis, the assessment of aspirated fluid for potential molecular biomarkers—such as carbonic anhydrase IX (CAIX)—has also been investigated in selected studies.[25]

These approaches aim to enhance diagnostic yield and guide clinical management, especially in patients for whom surgical risk or comorbidities favour a conservative strategy.[26,27]

Despite these efforts, the evidence base supporting percutaneous sampling of complex renal cysts remains limited, heterogeneous, and largely composed of small retrospective series. Therefore, international guidelines continue to recommend a cautious and selective use of biopsy in cystic renal masses, generally discouraging its application in lesions lacking a solid, targetable component.[28]

A clearer understanding of the diagnostic yield, limitations, and potential clinical implications of percutaneous sampling in this specific setting is therefore needed to inform contemporary practice.

The objective of this systematic review and meta-analysis was to evaluate the diagnostic performance, safety, and potential clinical impact of percutaneous sampling, including fine-needle aspiration (FNA) and core needle biopsy (CNB), in patients with Bosniak III–IV cystic renal lesions.

Evidence Acquisition

Protocol

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[29] The study protocol was registered a priori on the International Prospective Register of Systematic Reviews (PROSPERO; registration ID CRD420251124563). The review question, eligibility criteria, outcomes, and analytical plan were prespecified within the PROSPERO registration. The review was conducted and reported in line with PRISMA 2020 principles, with the aim of maximising transparency and reproducibility of study selection, data extraction, and synthesis.

Literature search

A comprehensive literature search was performed in PubMed/MEDLINE, Embase, Cochrane CENTRAL, Scopus, and Web of Science from January 1980 to May 2025. Search terms included combinations of the following keywords and MeSH terms: *"Bosniak III"*, *"Bosniak IV"*, *"complex renal cyst"*, *"cystic renal mass"*, *"renal mass biopsy"*, *"percutaneous sampling"*, *"fine-needle aspiration"*, and *"core needle biopsy"*. Reference lists of all eligible studies and relevant reviews were screened for additional records. In addition, we screened reference lists of key methodological papers and relevant narrative reviews to maximise capture of older series and non-standard terminology. No restrictions were applied based on country of origin or clinical setting. The search was conducted independently by two investigators, and discrepancies were resolved by consensus.

Search terms were combined using Boolean operators and adapted to the syntax of each database to optimise sensitivity for both cystic renal lesions and percutaneous diagnostic procedures (FNA/CNB). The strategy was intentionally broad to capture older series performed before contemporary terminology and reporting standards were established.

In addition to electronic database searches, backward citation tracking (screening reference lists of included studies and relevant reviews) was performed to identify potentially eligible records not retrieved through the primary search strategy. All retrieved records were exported to a reference manager (Zotero, version 7.0.23) for merging and de-duplication prior to screening.

Inclusion and exclusion criteria

Eligible studies were defined a priori according to pre-specified PICO criteria.

Inclusion criteria were defined as follows: studies enrolling adult patients (≥18 years) with radiologically defined complex renal cysts classified as Bosniak III or IV and evaluating percutaneous sampling using FNA and/or CNB performed under imaging guidance, including ultrasound and/or computed tomography. Eligible studies were required to report diagnostic performance outcomes for malignancy, such as sensitivity, specificity, predictive values, diagnostic yield, or sufficient data to derive these measures, using surgical pathology as the reference standard when available, or clinical and/or radiological follow-up in conservatively managed cases. Both prospective and retrospective cohort studies, as well as case series including at least ten patients, were considered eligible. Studies enrolling mixed populations of cystic and solid renal masses were included only if data specific to Bosniak III–IV cystic lesions could be extracted separately or clearly identified.

Exclusion criteria were defined as follows: studies focusing exclusively on solid renal tumours or simple renal cysts (Bosniak I–II), enrolling paediatric populations (<18 years), or not reporting extractable diagnostic performance data for Bosniak III–IV lesions. Case reports, conference abstracts, editorials, letters, and expert opinions were also excluded due to insufficient methodological detail or incomplete reporting of diagnostic outcomes and reference standards.

Following de-duplication, study selection was conducted through independent screening of titles and abstracts, followed by full-text assessment of potentially eligible records. The overall study selection process is summarised in the PRISMA flow diagram (Figure 1).

Data extraction

Two reviewers (AB, AM) independently extracted data in duplicate using a piloted form. Extracted variables included: study characteristics, patient demographics, lesion features, biopsy technique, pathological outcomes, diagnostic performance, complications, and clinical impact. Any discrepancies were resolved by discussion or adjudication by a third reviewer (NC). The extraction form was piloted on a subset of studies and refined to ensure consistent capture of diagnostic accuracy and procedural variables. In addition to core study descriptors (design, setting, enrolment period, sample size), we extracted imaging modality used for lesion characterisation and biopsy guidance (CT vs. ultrasound), Bosniak category (III vs. IV when available), presence of a targetable solid component when reported, and biopsy technique details (FNA vs. CNB; needle gauge and coaxial use when specified), together with the reference standard applied (surgical histopathology vs. follow-up).

For diagnostic outcomes, we extracted sensitivity, specificity, predictive values, diagnostic yield, and non-diagnostic rates as reported by each study. Where sufficiently reported, we attempted to reconstruct 2×2 tables to support quantitative synthesis; when this was not feasible due to incomplete reporting or heterogeneous outcome definitions, data were summarised narratively. We also recorded study-specific definitions of non-diagnostic and indeterminate results to facilitate consistent interpretation across cohorts.

For safety outcomes, we extracted complications and grading systems when provided. When complication reporting was absent, not stratified, or not

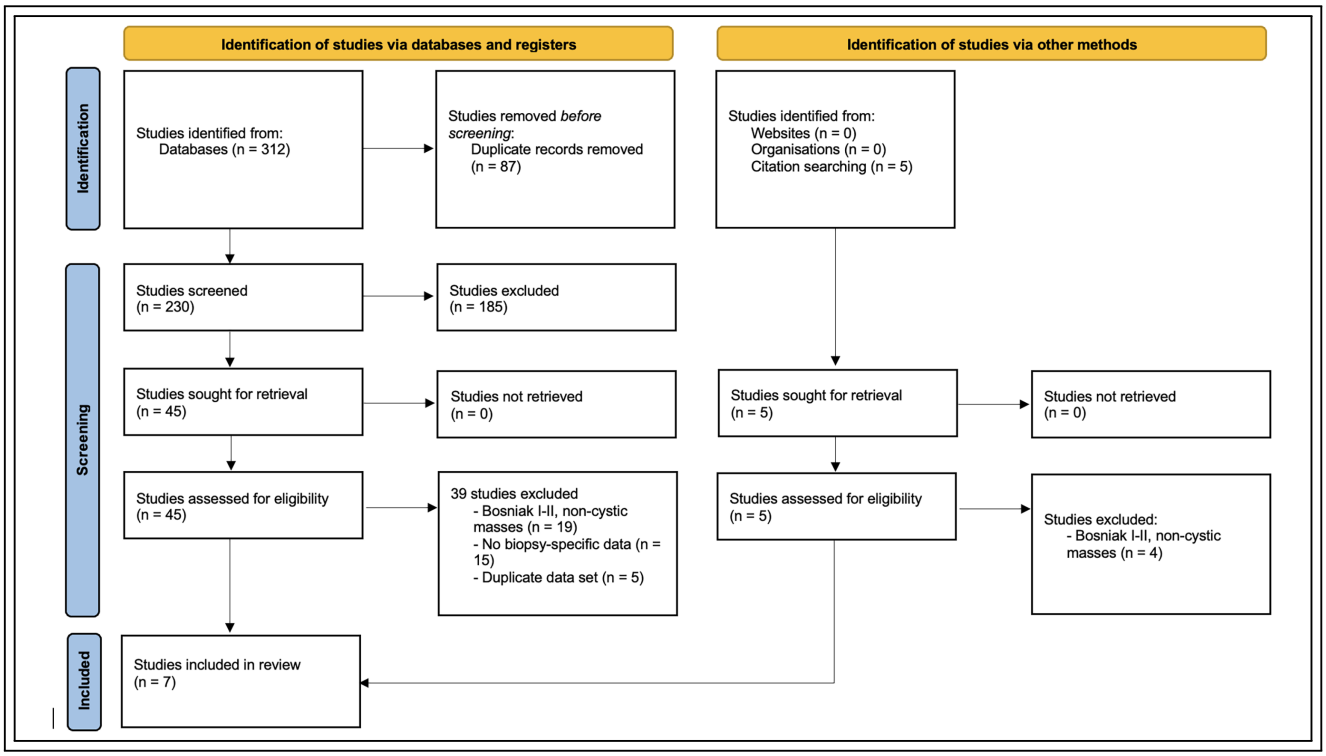

FIGURE 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram

clearly defined, this was recorded as "not reported" rather than inferred.

Risk of bias assessment

The methodological quality of included studies was assessed using the QUADAS-2 tool across four domains: patient selection, index test, reference standard, and flow/timing.[30] Applicability concerns were evaluated for patient selection, index test, and reference standard. Two reviewers (AB, AM) independently performed the assessment. In case of disagreement, consensus was achieved through discussion or adjudication by a third reviewer (NC).

The results of the risk of bias assessment are summarised in Figure 2, using the *traffic-light plot* generated with the Robvis web application.[31]

Risk-of-bias judgements were made using domain-level signalling questions, with a conservative approach adopted when reporting was insufficient to support a "low risk" judgement. Applicability concerns were considered particularly relevant in this topic given variations in case-mix (Bosniak III vs. IV proportions), biopsy indications, and reference standards across centres.

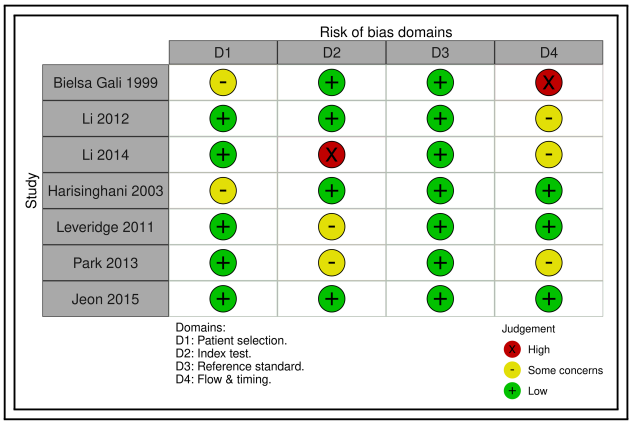

FIGURE 2. Risk of bias assessment across included studies according to quality assessment of diagnostic accuracy studies 2 (QUADAS-2) domains

The QUADAS-2 assessment informed interpretation of the evidence base and guided sensitivity analyses where feasible.

Statistical analyses

Pooled sensitivity, specificity, diagnostic odds ratios (OR), and corresponding 95% confidence intervals

(CI) were calculated using a bivariate random-effects model. Summary receiver operating characteristic (SROC) curves and area under the curve (AUC) values were generated. Heterogeneity was assessed using Cochrane's Q test and the I^2 statistic, with $I^2 > 50\%$ considered substantial. When <3 studies with comparable data were available, results were synthesised narratively. Sensitivity analyses were performed by excluding studies judged to be at high risk of bias in ≥2 QUADAS-2 domains and by restricting to cohorts explicitly reporting Bosniak III–IV subgroups. The bivariate random-effects model was selected a priori because it jointly models sensitivity and specificity while accounting for their correlation across studies and for between-study heterogeneity, which is expected in diagnostic accuracy research. SROC/HSROC-based visualisation was used to summarise diagnostic performance across studies when pooling was appropriate, whereas narrative synthesis was prioritised for outcomes with heterogeneous definitions (e.g., non-diagnostic results and minor complications) or insufficient study numbers. Given the limited number of eligible FNA studies and the absence of sufficient homogeneous datasets for CNB, additional subgroup analyses (e.g., by guidance modality, Bosniak subgroup, or needle gauge) were not prespecified beyond the reported sensitivity analyses, as such comparisons would be underpowered and potentially misleading. Publication bias assessment was not undertaken because established methods are unreliable in diagnostic test accuracy meta-analyses when few studies are available and heterogeneity is substantial. All analyses were conducted using R statistical software (version 4.2.0; R Foundation for Statistical Computing, Vienna, Austria) with the Metafor package (Viechtbauer, 2010)[32] and Review Manager (RevMan, version 5.4; Cochrane Collaboration, Oxford, UK).

Results

Fine-needle aspiration

Three studies encompassing 80 patients evaluated FNA in Bosniak III–IV cystic renal lesions (Table 1).[24,25,33] Diagnostic performance was highly variable, with reported sensitivity ranging from 22% to 95.2% and negative predictive values between 31% and 47%.[24,25,33] In the CT-guided series, adequate cyst fluid was obtained in all cases, with cytology reported as positive or suspicious in 34% of samples and negative or non-diagnostic in 66%.[24] Among resected lesions, more than half of malignant cysts had false-negative cytology, whereas the accuracy of a positive cytological diagnosis exceeded 90%.[24] In a complementary study, carbonic anhydrase IX (CAIX) concentrations in cyst fluid were markedly higher in malignant compared with benign cysts (mean 2043 ± 62 pg/mL vs. 162 ± 133 pg/mL; $p < 0.001$).[25] In another series, sensitivity and negative predictive value for malignancy were 22% and 47%, respectively.[33] No procedure-related complications were reported across any of the studies.[24,25,33]

Core needle biopsy

Four studies comprising 874 patients evaluated CNB in complex cystic renal masses (Table 1).[34–37] Diagnostic yield ranged from 75% to 81%, while cystic morphology consistently emerged as the strongest independent predictor of non-diagnostic sampling.[34–37] In the Bosniak III cohort, malignant biopsy findings were confirmed in all surgical specimens, with complete biopsy–surgery concordance; benign biopsies remained stable during a median 18-month follow-up, allowing avoidance of surgery in nearly 40% of patients.[34] In the ultrasound-guided series, the diagnostic rate was 81%; cystic lesions accounted for 4% of diagnostic versus 37% of non-diagnostic samples ($p = 0.009$), and cystic morphology was the strongest predictor of non-diagnostic outcome (OR 13.1; 95% CI 2.02–85.7).[35] In the multicentre cohort, the non-diagnostic rate was 25% in cystic versus 10% in solid lesions ($p = 0.043$), with cystic architecture confirmed as an independent predictor (OR 3.28; 95% CI 1.07–10.08).[36] Repeat biopsy after a non-diagnostic result was diagnostic in 100% of cases.[36] In the large RMB programme, cystic components accounted for 12% of cases and were a strong predictor of biopsy failure (OR 13.9; 95% CI 3.78–50.7); 73% of initially non-diagnostic lesions were subsequently confirmed malignant.[37] Complication rates were low across series: in the largest cohort, complications occurred in 10% of procedures with only one Clavien-Dindo (CD) 3a event (0.3%);[37] in the multicentre study, transfusion was required in <1% of patients and embolization in 0.5%;[36] and in the ultrasound-guided series, minor perirenal haematoma or pain occurred in 20%, all CD 1.[35]

Meta-analysis

In the meta-analysis of three studies evaluating FNA in Bosniak III–IV cystic renal masses, the pooled sensitivity was 0.59 (95% CI: 0.14–0.93) and the pooled specificity was 0.84 (95% CI: 0.62–0.94). The overall diagnostic performance was 0.84 (AUC, HSROC model), with heterogeneity (I^2) ranging from 0% to 59% (Table 2). Sensitivity estimates across individual studies varied substantially, whereas specificity

TABLE 1. **Summary of studies evaluating fine-needle aspiration (FNA) and core needle biopsy (CNB) in Bosniak III–IV cystic renal masses**

Study	Patients (n)	Key findings
FNA studies		
Bielsa Galí et al., 1999[33]	13	Sensitivity: 22% NPV[1]: 46.7%
Li et al., 2014[24]	32	Sensitivity: 47.6% PPV[2]: 90.9% NPV: 31.3%
Li et al., 2012[25]	35	Sensitivity: 95.2% CAIX[3] level: malignant 2043 pg/mL vs. benign 162 pg/mL
CNB studies		
Harisinghani et al., 2003[34]	28	100% biopsy-surgery concordance (17/17 surgically resected); No progression in benign biopsies at ≥12-month follow-up; Surgery avoided in 39%
Leveridge et al., 2011[37]	345	Cystic nature strong predictor of biopsy failure (OR[4] 13.9); 73.3% malignancy among nondiagnostic cases
Park et al., 2013[35]	59	Diagnostic rate: 81%; Cystic morphology strongest predictor of nondiagnostic result (OR[4] 13.1)
Jeon et al., 2015[36]	442	Nondiagnostic rate: 25% (cystic) vs. 10.4% (solid); Cystic architecture independent predictor of nondiagnostic result (OR[4] 3.28)

Note. [1]NPV: Negative Predictive Value; [2]PPV: Positive Predictive Value; [3]CAIX: Carbonic Anhydrase IX; [4]OR: Odds Ratio.

TABLE 2. **Pooled diagnostic performance of fine-needle aspiration (FNA) for Bosniak III/IV cystic renal masses based on bivariate random-effects meta-analysis**

Metric	Estimate	95% CI
Pooled sensitivity	0.59	0.14–0.93
Pooled specificity	0.84	0.62–0.94
AUC (HSROC)	0.84	–
I^2 (heterogeneity)	0–59%	–

Note. CI: confidence interval; AUC: area under the curve; HSROC: hierarchical summary receiver operating characteristic.

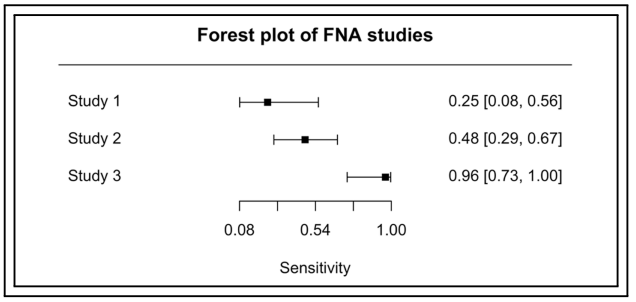

FIGURE 3. Forest plot of individual studies evaluating fine-needle aspiration (FNA) in complex renal cysts, showing study-level sensitivity and specificity with 95% confidence intervals

was more consistent. Study-level diagnostic estimates with 95% CI are shown in the forest plot (Figure 3). For CNB, quantitative synthesis was not feasible due to heterogeneity in study design and incomplete reporting of diagnostic accuracy data across the included studies.

Discussion

Complex cystic renal lesions continue to represent a major diagnostic challenge, as imaging alone often fails to reliably distinguish between benign and malignant cysts, raising uncertainty in preoperative decision-making.[38,39] This limitation is particularly relevant in contemporary clinical practice, where increasing emphasis is placed on nephron-sparing

strategies, individualised risk assessment, and avoidance of unnecessary surgery.[40–42] In patients with complex renal cysts, the inability to confidently characterise malignant potential preoperatively may directly influence counselling, treatment selection, and the balance between oncological safety and functional preservation.[43]

In this context, percutaneous sampling has been investigated as a potential adjunct to improve diagnostic accuracy and to guide management strategies.[44,45] This systematic review and meta-analysis provides an updated synthesis of the available evidence, underscoring both the strengths and limitations of FNA and CNB in Bosniak III–IV clinical settings.

FNA demonstrated low sensitivity (22–48%) and high false-negative rates, primarily due to acellular or paucicellular aspirates.[24,33] While positive cytology showed a high positive predictive value (up to 90.9%), negative results were frequently non-diagnostic and unreliable in ruling out malignancy.[24]

These findings reinforce the concept that the diagnostic performance of FNA in cystic renal masses is intrinsically limited by lesion biology rather than technical execution. Cyst fluid often lacks sufficient cellular material, and malignant cells may be unevenly distributed along septa or focal mural nodules, resulting in a high probability of sampling error.[46] Consequently, the absence of malignant cells on cytology should not be interpreted as evidence of benign disease, and negative FNA findings provide limited reassurance in clinical decision-making.[47]

Early exploratory data on CAIX concentrations in cyst fluid suggested a potential role as a molecular adjunct for the differentiation of benign and malignant cystic renal lesions.[25] In particular, the study by Li et al. demonstrated markedly higher CAIX levels in the fluid of malignant cystic renal tumours compared with benign cysts, with a high concordance between tissue expression and cyst fluid measurements.[25] However, this evidence derives from small, single-centre experiences, lacks external validation and standardized analytical thresholds, and has not been incorporated into routine clinical practice.[48] Although molecular analysis of cyst fluid is conceptually appealing, particularly given the biological heterogeneity of renal cancers presenting as complex cystic lesions, available evidence remains preliminary.[49,50] Importantly, other molecular biomarkers, including miRNAs and omics-based approaches, have been extensively investigated in renal cancer in different biological settings, but have not been systematically evaluated in cyst fluid and have never been applied in a diagnostic sense within percutaneous biopsy or fine-needle aspiration of complex renal cysts.[51,52] Variability in sampling techniques, analytical methods, and reporting standards currently limits the generalisability of molecular findings and precludes routine clinical adoption.

On the other hand, CNB achieved higher diagnostic performance, with overall diagnostic rates ranging from 75% to 81% in the included studies.[34,37] However, cystic morphology was consistently associated with a significantly increased risk of non-diagnostic sampling compared with solid lesions (OR up to 13.9).[35,37]

This observation highlights that histological sampling is subject to substantial limitations in cystic lesions, where the presence of thin septa, small solid components, or complex internal architecture reduces the likelihood of obtaining representative tissue cores.[15] As a result, diagnostic failure in this setting should be regarded as an expected limitation rather than an indicator of procedural inadequacy.[53]

Importantly, a non-diagnostic CNB result should not be interpreted as reassuring, as up to 73% of such lesions were subsequently found to be malignant in large contemporary series.[37] This finding highlights the potential oncologic risk associated with indeterminate biopsy results.

Our quantitative synthesis of three studies evaluating FNA in Bosniak III–IV cystic renal masses demonstrated a pooled sensitivity of 59% and a pooled specificity of 84%, with an overall diagnostic accuracy of 0.84 (AUC, HSROC model). Considerable variability was observed in sensitivity across studies, whereas specificity was consistently high.

This imbalance between sensitivity and specificity has important practical implications. While a positive biopsy result reliably confirms malignancy and may meaningfully inform treatment planning, the converse does not hold true. The limited negative predictive value of percutaneous sampling remains a major barrier to its broader clinical application in cystic renal masses.

This heterogeneity in sensitivity may be explained by differences in patient selection, lesion characteristics (size, cystic vs. solid component predominance), biopsy technique and operator expertise. Moreover, variability in lesion selection criteria and biopsy indications across centres likely contributed to the observed differences in diagnostic performance, further limiting direct comparability between studies. Such heterogeneity reflects real-world practice but complicates interpretation of pooled estimates. In

contrast, specificity is less affected by these factors, as false positives are rare when malignancy is cytologically or histologically demonstrated.

Previous broader meta-analyses, such as that by Marconi et al., which included >5000 renal mass biopsies—mostly for solid tumours—reported excellent diagnostic accuracy for CNB (sensitivity 99.1%, specificity 99.7%) and lower performance for FNA. In the cystic subgroup, however, CNB sensitivity dropped to 83.6%, reflecting the technical and biological challenges inherent to these tumours, including paucicellularity and difficulty in targeting.[15]

These findings place the results of the present review into appropriate context, underscoring that diagnostic paradigms established for solid renal masses cannot be directly extrapolated to cystic lesions without acknowledging their distinct biological behaviour.

Concerns regarding tumour seeding with percutaneous biopsy, although historically considered relevant, now appear negligible with modern coaxial techniques. Marconi et al. documented an extremely low incidence of tumour seeding, with no cases involving cystic lesions.[15] Similarly, a systematic review by Renshaw et al. identified only 16 cases of tumour seeding reported in the literature, none of which involved cystic renal masses.[54]

Beyond oncological safety, procedure-related complications represent an additional consideration when evaluating percutaneous sampling in complex cystic renal lesions. Across the studies included in this review, reported complication rates were low and predominantly minor. Most adverse events consisted of transient haematuria, self-limiting perirenal haematoma, or mild post-procedural pain, with major complications being rare. Importantly, no signal of increased morbidity specific to cystic lesion sampling emerged when contemporary image-guided techniques and coaxial systems were used.

However, interpretation of safety outcomes is limited by heterogeneous and frequently incomplete reporting. Definitions of complications varied across studies, grading systems were inconsistently applied, and minor adverse events were often underreported. This variability precluded quantitative synthesis of complication rates and limits direct comparison between cohorts, highlighting the need for standardised reporting of safety outcomes in future studies focused on cystic renal lesions.

From a clinical standpoint, the role of percutaneous sampling in complex cystic renal lesions should be driven by its potential to provide clinically meaningful diagnostic information rather than by procedural safety alone. Although the risk of complications appears low, safety considerations must be weighed alongside the recognised diagnostic limitations imposed by cystic architecture, reinforcing the importance of careful patient selection and multidisciplinary discussion.

Current international guidelines remain cautious and selective regarding biopsy of complex cystic renal masses. The European Association of Urology (EAU) recommends renal mass biopsy only when results are likely to alter management and discourages its use in cystic lesions lacking a solid, targetable component.[28] Similarly, the American Urological Association (AUA) highlights the limited role of biopsy in complex cystic masses and emphasises the primacy of imaging-based Bosniak classification in clinical decision-making.[55]

The findings of the present review are largely concordant with these recommendations and support a selective, case-by-case approach to percutaneous sampling in Bosniak III–IV cystic renal lesions.

A principal strength of this review is its focused design, representing the first systematic synthesis dedicated exclusively to percutaneous sampling in Bosniak III–IV cystic renal lesions. Additional strengths include rigorous adherence to PRISMA methodology and comprehensive extraction of both diagnostic and safety outcomes. Several limitations, however, deserve careful consideration. First, the overall evidence base remains limited, with a small number of eligible studies and a predominance of retrospective designs, which increases the risk of selection bias and limits causal inference. Second, substantial methodological heterogeneity was observed across studies, including differences in imaging guidance (ultrasound versus CT), needle calibre, biopsy technique, operator experience, and definitions of non-diagnostic sampling. As a result, the pooled estimates should be interpreted as exploratory rather than definitive, particularly with respect to sensitivity, where confidence intervals were wide and between-study heterogeneity was substantial. Third, the reference standard was not uniform across studies, as surgical pathology was unavailable for all lesions and some benign diagnoses relied on clinical or radiological follow-up, potentially leading to misclassification bias. This heterogeneity in reference standards may have led to an underestimation of false-negative results, particularly if slow-growing malignancies remained stable during follow-up. Fourth, formal assessment of publication bias was not feasible due to the small number of pooled studies, and selective reporting cannot be excluded. Finally, because only a single study met

inclusion criteria for quantitative synthesis of CNB outcomes, pooled estimates for this technique could not be generated, limiting direct comparison between FNA and CNB.

These limitations highlight the need for future prospective studies with standardised biopsy protocols and uniform reporting of outcomes to better define the role of percutaneous sampling in this challenging clinical setting.

In conclusion, percutaneous sampling of Bosniak III–IV renal cysts appears technically safe but diagnostically inconsistent. CNB should be selectively considered when a solid, targetable component is present and results are likely to influence management, whereas FNA provides limited diagnostic reliability in this setting.

Until higher-quality evidence becomes available, careful patient selection and multidisciplinary discussion remain essential when considering biopsy in complex cystic renal masses.

Conclusion

Percutaneous sampling of Bosniak III–IV renal cysts is technically feasible but intrinsically constrained by the architectural complexity of cystic lesions. FNA demonstrates low diagnostic reliability, whereas CNB achieves a higher diagnostic yield when a solid, targetable component is present, although non-diagnostic sampling remains frequent.

The available evidence indicates that non-diagnostic biopsy results are common in complex cystic renal lesions and occur in a substantial proportion of cases ultimately found to be malignant. This finding underscores the inherent limitations of tissue acquisition in cystic lesions rather than procedural inadequacy. Consequently, percutaneous sampling provides incomplete risk stratification in this setting and should be applied selectively, with careful consideration of lesion characteristics, the specific clinical question being addressed, and full awareness of its diagnostic constraints.

In contemporary clinical practice, interpretation of biopsy results—when available—should be integrated within a multidisciplinary discussion involving urologists, radiologists, pathologists, and oncologists, to ensure balanced incorporation of imaging findings, procedural limitations, and patient-specific factors into management decisions.

Future prospective studies focusing specifically on cystic renal lesions, supported by standardised biopsy protocols and uniform reporting of non-diagnostic outcomes, are required to better define the clinical utility of percutaneous sampling within modern nephron-sparing strategies.

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Author Contributions

The authors confirm contribution to the paper as follows: study conception and design: Attilio Barretta, Angelo Mottaran; methodology: Attilio Barretta, Nicolas Carl; software: Attilio Barretta, Angelo Mottaran, Nicolas Carl; formal analysis and interpretation of results: Attilio Barretta, Nicolas Carl; investigation: Attilio Barretta, Angelo Mottaran; data curation: Sara Tamburini, Edoardo Beatrici, Mario De Angelis, Francesco Cei, Natali Rodriguez Peñaranda, Francesco Pepillo, Alessio Guidotti, Vincenzo Cavarra, Claudio Brancelli, Pietro Pasquini; draft manuscript preparation: Attilio Barretta, Angelo Mottaran, Nicolas Carl, Francesco Prata; manuscript review and editing: Francesco Prata, Pietro Piazza, Cristian Vincenzo Pultrone, Hussam Dababneh; visualization: Attilio Barretta; supervision: Alessandro Larcher, Lorenzo Bianchi, Francesco Prata, Alexandre Mottrie, Rocco Papalia, Riccardo Schiavina; project administration: Attilio Barretta. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials

No new data were generated or analysed in this study. All data supporting the findings of this systematic review are derived from previously published studies and are available in the public domain. Therefore, data sharing is not applicable.

Ethics Approval

Not applicable. This study is a systematic review and meta-analysis of previously published literature and

did not involve human participants or animal subjects. As such, ethical approval and informed consent were not required.

Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Materials

The supplementary material is available online at https://www.techscience.com/doi/10.32604/cju.2026.078354/s1.

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