

CUA guideline on the management of cystic renal lesions

Patrick O. Richard, MD;¹ Philippe D. Violette, MD;² Michael A.S. Jewett, MD;³ Frederic Pouliot, MD;⁴ Michael Leveridge, MD;⁵ Alan So, MD;⁶ Thomas F. Whelan, MD;⁷ Ricardo Rendon, MD;⁸ Antonio Finelli, MD³

¹Division of Urology, Department of Surgery, Centre Hospitalier Universitaire de Sherbrooke and Centre de recherche du CHUS, Université de Sherbrooke, Sherbrooke, QC, Canada; ²Division of Urology, Woodstock General Hospital, Woodstock, ON, Canada; ³Division of Urology, Departments of Surgery and Surgical Oncology, Princess Margaret Cancer Centre, University Health Network and the University of Toronto, Toronto, ON, Canada; ⁴Division of Urology, Department of Surgery, Université Laval, Centre de Recherche du Centre Hospitalier Universitaire de Québec, Québec City, QC, Canada; ⁵Department of Urology, Queen's University, Kingston General Hospital, Kingston, ON, Canada; ⁶Division of Urology, Department of Surgery, University of British Columbia, Vancouver, BC, Canada; ⁷Division of Urology, Department of Surgery, Saint John Regional Hospital, Dalhousie University, Saint John, NB; ⁸Department of Urology, QEII Health Sciences Centre, Dalhousie University, Halifax, NS

Cite as: *Can Urol Assoc J* 2017;11(3-4):E66-73. <http://dx.doi.org/10.5489/auaj.4484>
Published online March 16, 2017

Introduction

Cystic renal lesions are usually diagnosed incidentally on routine imaging. With the increased use of abdominal imaging, there is a growing number of individuals being diagnosed with renal cystic disease.¹ It is estimated that up to one-third of individuals over 60 years of age will be diagnosed with at least one simple renal cyst following abdominal imaging.² Therefore, patients are often referred to urologists for opinions about diagnosis and management of these lesions. Physicians managing these masses need to distinguish cystic lesions from solid renal masses with necrotic components, which behave more aggressively.³ Hence, the characterization of these cystic renal masses is crucial to determine the best clinical approach to be adopted. We reviewed the literature with the aim to offer guidance to physicians managing cystic renal lesions and to standardize their management across Canada.

Methods

A comprehensive search of the literature was done using MEDLINE and Pubmed. A keyword and MeSH search were used to identify English and French publications from January 1, 1980 to June 30, 2016 relevant to the topic of interest. The search terms were: Bosniak, Bosniak classification, renal cysts, renal cell carcinomas, renal and kidney cancers. Prospective or retrospective studies, as well as review studies providing data on the classification, management, and outcomes of complex cystic renal masses were included. Reports limited to children or animal and basic science studies were excluded. Similarly, reports limited to congenital

or acquired renal cystic diseases and case reports of five or fewer cases were also excluded (Supplementary Fig. 1).

The International Consultation of Urologic Disease (ICUD)/World Health Organization (WHO) modified Oxford Centre for Evidence-Based Medicine grading system was used to grade the quality of evidence for each topic assessed. The level of evidence was summarized according to the following: Level 1: meta-analysis of randomized, controlled trials (RCTs) or a good-quality RCT; Level 2: low-quality RCT or meta-analysis of good-quality prospective cohort studies; Level 3: Good-quality retrospective case-control studies or case series; Level 4: Expert opinion. Based on these levels of evidence, we have graded recommendations as follows: Grade A: consistent with Level 1 evidence; Grade B: Consistent with Level 2 or 3 evidence; Grade C: "majority" evidence from Level 2 or 3 studies or level 4 evidence; Grade D: no recommendation possible or expert opinion without a formal analytic process. Importantly, all recommendations were based on expert review of the literature and represent the consensus of all coauthors of these guidelines.

The objectives of these guidelines were to systematically review the literature and to make recommendations on the characterization, management, and followup of incidentally discovered cystic lesions. The panel proceeded with full awareness of the limitations of the cystic renal lesions literature. The low-quality evidence made it difficult to make strong recommendations for the optimal treatment and followup of cystic renal lesions. Furthermore, as the majority of Bosniak category II and IIF cystic lesions were managed conservatively, the literature tends to overestimate the true malignancy risk of these lesions, as only the most complex ones undergo surgery. Nevertheless, while taking these limitations into account, the panel did its best to summarize the current literature and to provide some guidance of the management of cystic lesions.

Evidence synthesis

Bosniak classification – Introduction

Renal cysts can be easily identified using standard medical imaging and, in most cases, a histological diagnosis is not required. However, lesions that are more complex may require a more detailed characterization to allow for determination of differential diagnoses and subsequent management approach.

The Bosniak renal cyst classification was initially described in 1986⁴ and was later updated to add a new category called category IIF.⁵ It was originally described using computed tomography (CT) imaging, but other modalities, such as magnetic resonance imaging (MRI), ultrasound (US), or contrast-enhancement ultrasound (CEUS), are now being used to help better delineate these lesions.⁶⁻¹⁰ The panel believes that if a complex cyst is first identified on US, contrast-enhanced axial imaging should be performed to better characterize the cyst. (**Level of evidence: 4; Recommendation: D**)

Although the Bosniak classification remains the most commonly used classification to characterize renal cysts, it has traditionally been subject to poor interobserver agreement.^{5, 11-17} Nevertheless, a recent report by Graumann et al has validated the reproducibility of the updated classification in a large

cohort.¹⁴ The authors demonstrated very good interobserver and intraobserver variation among uro-radiologists. Most of the observed variation was seen among cysts categorized as Bosniak II, IIF, and III. It is the panel's opinion that when there is disagreement or doubt regarding the classification of a renal cyst, such case should be presented at a multidisciplinary meeting. (**Level of evidence: 4; Recommendation: D**)

Description of Bosniak classification

By means of the Bosniak classification, renal cystic lesions can be categorized in increasing order according to risk of malignancy as follows (Table 1):

Bosniak category I

Lesions classified as category I are simple renal cysts and represent the majority of renal lesions detected by abdominal imaging.² These lesions are characterized by their regular contour and a clear interface with the renal parenchyma. They do not contain any septa, or calcifications, nor do they demonstrate enhancement following intravenous contrast agent injection. They are homogeneous, with fluid attenuation varying from 0–20 HU on CT scan. These lesions are also easily identifiable by US and appear as thin-walled, anechoic lesions with posterior enhancement and sharply margined smooth walls.^{5,8}

Table 1. The Bosniak classification and management recommendations

Bosniak classification – key findings	Recommendations
Bosniak category I (simple renal cyst) <ul style="list-style-type: none"> • Usually round or oval shape • Anechoic with posterior enhancement on US • Regular contour with clear interface with renal parenchyma • No septa, calcification or enhancement 	<ul style="list-style-type: none"> • No followup required
Bosniak category II <ul style="list-style-type: none"> • Thin septum (<1 mm) • Fine calcification (often small, linear, parietal, or septal) • Small hyperdense cyst (<3 cm; >20 HU) • No perceived contrast enhancement 	<ul style="list-style-type: none"> • No followup required
Bosniak category IIF <ul style="list-style-type: none"> • Cyst unequivocally categorized as category II or III cysts • Multiple thin septa or a slightly thickened, but smooth septa • Calcifications – thick or nodular • No perceived contrast enhancement • Large hyperdense cysts (≥3 cm) 	<ul style="list-style-type: none"> • Followup recommended • Imaging at 6 months and 12 months after diagnosis and then annually for at least 5 years if no progression.
Bosniak category III <ul style="list-style-type: none"> • Uniform wall thickening and/or nodularity • Irregular, thickened, and/or calcified septa • Contrast-enhancing sept 	<ul style="list-style-type: none"> • Surgical excision is suggested • Conservative management and RFA in select cases
Bosniak category IV <ul style="list-style-type: none"> • Wall-thickening • Gross, irregular, and nodular septal thickening • Solid contrast-enhancing component, independent of septa 	<ul style="list-style-type: none"> • Malignant until proven otherwise • Surgical excision is suggested • Potential role for pretreatment RTB (of solid component) to confirm malignancy • RFA and conservative management in select cases

US: ultrasound; RFA: radiofrequency ablation; RTB: renal tumour biopsy.

Bosniak category II

These cysts are slightly more complex than category I cysts.⁵ They may present with a few hairline-thin septa (<1 mm) and may have some calcifications (usually small [1–2 mm], linear, parietal, or septal).¹⁸ Small hyperdense cysts (<3 cm in diameter and >20 HU) are also classified in this category. These cysts also do not typically show contrast enhancement on imaging.¹⁹

The majority of category II cysts are considered benign. Although the review of the literature has demonstrated that approximately 11% of the operated category II cysts are malignant, this is thought to be an overestimation of the true malignancy risk, as a significant proportion of these studies were published before the addition of the Bosniak IIF category and many of these cysts were managed conservatively without pathological confirmation (Table 2). If we exclude the earlier studies and believe that most of the conservatively managed cysts were benign, the risk of malignancy for these lesions would be less than 5%. This rate is still believed to be a gross overestimation of the true risk, as most of the malignant category II lesions had features that made them too complex to be considered a true category II cyst.

Bosniak category IIF

This newest category was added by Dr. Bosniak to decrease the rates of malignancy in category II and to decrease the rate of benign disease in category III.⁵ This category represents moderately complex cystic lesions that cannot be unequivocally classified as category II or III cysts. They may contain an increased number of thin septa or slightly thickened, but smooth septa. Thick or nodular calcification may also be present, but without contrast-enhancing features. Large hyperdense cysts (≥ 3 cm and >20 HU) also belong to this group.^{20–22} Any lesions not fulfilling the criteria for category II, but not as complex as category III should be classified in this category.

Similar to the previous two categories, most of the cysts classified in this category are benign. According to our review of the literature, approximately 27% of surgically treated lesions are malignant. However, because of the aforementioned limitations, this is likely an overestimation of the true malignancy risk. If all conservatively managed Bosniak IIF cysts were benign, the risk of malignancy would approach 8%; therefore, the true malignancy rate of Bosniak category IIF cysts likely falls somewhere between 8 and 27% (Table 2).

Bosniak category III

This category encompasses a variety of cystic lesions whose differentiation between malignant and benign cannot be reliably made by imaging.⁵ They present with wall irregularity and thickening, as well as wall nodularity. They may also demonstrate contrast-enhanced septa (usually multiple) that

are usually irregular, thickened, and/or calcified. A significant proportion of these cysts are thought to be malignant (mean of 54%; Table 2),^{6,11–13,15,20–48} with larger lesions being more likely to be malignant than smaller ones.^{47,49}

Bosniak category IV

Category IV cysts may have similar characteristics to those classified as category III. They usually demonstrate wall thickening and/or gross and nodular thickened septa, but a solid contrast-enhancing component is also observed adjacent to the cyst wall or septa.^{5,13,18,19,22,50} Lesions in this category should be considered malignant until proven otherwise (mean of 88%; Table 2).^{5,22,51}

Intervention and followup

Bosniak category I

This category is composed of simple cysts that are considered benign. One should remember that the natural history of these cysts is that the majority will grow over time and thus, growth should not necessarily be considered a sign of malignancy.^{52,53} Transformation into a more complex cyst is rare and has been reported in only a handful of cases.^{52–57} As this is rare in occurrence, these cysts do not require followup. (**Level of evidence: 3; Recommendation: B**) Intervention is only warranted if the cyst becomes symptomatic (i.e., bleeding, recurrent infection or pain), in which case treatment options include: percutaneous management (aspiration +/- sclerotherapy) or surgery.⁵⁸ (**Level of evidence: 3; Recommendation: B**) Percutaneous cyst decompression may also be considered prior to offering definitive treatment as a means to confirm that the source of symptoms are cyst-related. (**Level of evidence: 4; Recommendation: D**)

Bosniak category II

These minimally complex cysts are also generally considered benign, but there are reports in the literature of category II lesions being malignant (Table 2).^{11,12,15,23–27,31,33,34,39,40,42,43,47,51,59} However, the literature is thought to overestimate the true risk of malignancy among category II cysts, as the majority were managed conservatively or had features that made them too complex to be categorized as a Bosniak II cyst.^{6,12,26,29,31,32,35,38,59} Importantly, even if malignant, most behave in a relatively benign fashion. Consequently, similar to category I cysts, a followup for properly classified Bosniak II cysts is not warranted (**Level of evidence: 3; Recommendation: C**) and intervention is not recommended unless the patient is symptomatic. (**Level of evidence: 3; Recommendation: B**) When there is doubt as to their categorization based on imaging characteristics, these

Table 2. Studies and risk of malignancy for complex cystic lesions (pathologically confirmed)

Authors (year of publication)	Cohort size n (path. confirmed)	Bosniak category I* n (%)	Bosniak category II n (%)	Bosniak category IIF n (%)	Bosniak category III n (%)	Bosniak category IV n (%)
Brown (1989) ²⁵	24 (24)	0/2 (0)	0/4 (0)	-	3/12 (25)	4/6 (67)
Aronson (1991) ²³	16 (16)	-	0/4 (0)	-	5/9 (56)	7/7 (100)
Wilson (1995) ¹⁵	24 (24)	0/7 (0)	4/5 (80)	-	4/4 (100)	6/6 (100)
Cloix (1996) ¹¹	32 (32)	1/2 (50)	1/7 (14)	-	4/13 (31)	5/10 (50)
Siegel (1997) ⁴⁰	70 (70)	0/22 (0)	1/8 (13)	-	5/11 (46)	26/29 (90)
Bielsa (1999) ²⁴	20 (20)	-	1/8 (13)	-	7/9 (78)	3/3 (100)
Curry (2000) ¹²	116 (82)	0/4 (0)	0/11 (0)	-	29/49 (59)	18/18 (100)
Koga (2000) ³³	35 (35)	0/11 (0)	1/2 (50)	-	10/10 (100)	12/12 (100)
Limb (2002) ³⁴	57 (57)	-	3/28 (11)	-	8/29 (28)	-
Harisinghani (2003) ²⁸	28 (28)	-	-	17/28 (61)	-	-
Israel (2003) ²⁹	81 (40)	-	-	0/3 (0)	9/21 (43)	16/16 (100)
Israel (2003) ³⁰	42 (3)	-	-	2/3 (67)	-	-
Israel (2004) ³¹	69 (25)	0/1 (0)	-	0/1 (0)	12/15 (80)	8/8 (100)
Spaliviero (2005) ⁴³	47 (47)	1/1 (100)	2/9 (22)	1/4 (25)	6/12 (50)	19/21 (91)
Loock (2006) ³⁵	53 (17)	-	-	2/2 (100)	4/8 (50)	6/7 (86)
Quaia (2007) ³⁸	40 (30)	-	-	-	3/12 (25)	18/18 (100)
Clevert (2008) ⁶	37 (14)	-	-	1/1 (100)	3/6 (50)	7/7 (100)
Song (2008) ⁴²	104 (104)	-	3/26 (12)	0/3 (0)	21/38 (55)	32/37 (86)
Gabr (2009) ²⁶	50 (7)	-	1/3 (33)	4/4 (100)	-	-
O'Malley (2009) ³⁶	112 (34)	-	-	0/1 (0)	27/33 (82)	-
Kim (2010) ⁴⁶	125 (125)	0/34 (0)	3/23 (13)	1/10 (10)	21/25 (84)	28/33 (85)
Pinheiro (2011) ³⁷	37 (37)	-	-	-	5/15 (33)	19/22 (86)
Weibl (2011) ⁵⁹	113 (69)	-	0/2 (0)	1/1 (100)	15/27 (56)	30/39 (77)
You (2011) ⁴⁵	75 (75)	-	-	-	22/39 (56)	31/36 (86)
Smith AD (2012) ⁴¹	213 (123)	-	-	4/16 (25)	58/107 (54)	-
Han (2012) ²⁷	98 (98)	-	0/9 (0)	3/18 (17)	21/39 (54)	29/32 (91)
Graumann (2013) ²⁰	32 (3)	-	-	2/3 (67)	-	-
El-Mokadem (2014) ¹³	154 (39)	-	-	8/9 (89)	10/16 (63)	12/14 (86)
Kim (2014) ³²	164 (85)	-	-	6/21 (29)	26/38 (68)	26/26 (100)
Hindman (2014) ²¹	156 (19)	-	-	17/19 (90)	-	-
Reese (2014) ³⁹	113 (113)	-	2/16 (13)	2/6 (33)	21/32 (66)	50/59 (85)
Xu (2014) ⁴⁴	87 (87)	-	-	0/10 (0)	14/26 (54)	47/51 (92)
Smith (2015) ⁴⁸	286 (100)	-	-	3/8 (38)	29/72 (40)	18/20 (90)
Oh (2016) ⁴⁷	324 (324)	1/103 (1)	2/53 (4)	7/41 (17)	27/71 (38)	46/56 (82)
Total	3032 (2106)[†]	3/187 (2)	23/218 (11)[†]	81/300 (27)[†]	402/727 (54)	477/537 (88)

*Studies limited to the ones where complex lesions were also evaluated; †overall, 142 Bosniak category II, 668 Bosniak category IIF, 115 Bosniak category III, and 21 Bosniak category IV were managed by surveillance; ‡represent an overestimation of the true malignancy risk given the fact that the majority of lesions were managed with surveillance.

lesions should be considered as being Bosniak category IIF lesions and followed accordingly.

Bosniak category IIF

Given the relatively high risk of malignancy among these cysts (Table 2), as the “F” in category IIF stipulates, these lesions require followup. (**Level of evidence: 3; Recommendation: B**) Approximately 15% of these category IIF cysts will progress in complexity (to Bosniak category III or IV) over time.^{7,13,20,21,36} Progression is more likely to occur within the first two years and rarely occurs after five

years.³⁶ Unfortunately, a clear progression pattern is yet to be identified and as a result, there is no evidence-based time limit for followup imaging. In view of the low metastatic potential of these lesions (if malignant), it seems reasonable to follow these lesions with a contrast-enhanced CT scan or MRI every six months for the first year. (**Level of evidence: 4; Recommendation: D**) Closer monitoring may be performed, but may potentially reduce the detection of a progression if the changes in the cysts from imaging to imaging are very small. CEUS may also be used to better delineate the septa number, septa and/or wall thickness, solid component, and the enhancement.^{8,10,60} Ultrasound in combination with CT

or MRI may be used if the lesion is stable on followup. Cases without progression should be followed annually for at least five years. **(Level of evidence: 4; Recommendation: D)**

Bosniak category III

Studies of resected Bosniak III lesions have found approximately 54% (interquartile range [IQR] 44–67%) of these cysts to be malignant (Table 2). Based on current evidence, surgical excision of Bosniak III cysts is generally suggested. **(Level of evidence: 3; Recommendation: B)** Extrapolating from small renal mass (SRM) data, partial nephrectomy (PN) is considered the treatment of choice when feasible, if surgery is planned.⁶¹ **(Level of evidence: 2; Recommendation: B)** Given the low metastatic potential of cystic renal cell carcinoma (RCC), the panel feels that reduced surgical margins and controlled cyst decompression (if required) can be performed with low risk of tumour recurrence. **(Level of evidence: 4; Recommendation: D)** Likewise, due to the same reason, active surveillance and thermal-ablation therapies may also be considered as appropriate treatment alternatives in select cases (further discussed below). **(Level of evidence: 4; Recommendation: D)**

Bosniak category IV

The majority of the lesions included in this category are malignant (Table 2), with over 80–90% of Bosniak category IV lesions being cystic RCCs.^{6,11-13,15,23,25,29,31-35,38-40,42-44,48} Surgical excision is generally suggested **(Level of evidence: 3; Recommendation: B)** with PN being the surgery of choice, when feasible. **(Level of evidence: 2; Recommendation: B)** Nevertheless, most of these malignant cysts are thought to have low metastatic potential and thus, more conservative management may be safely considered in select cases. **(Level of evidence: 4; Recommendation: D)**

Role of active surveillance for suspected cystic RCC

Physicians managing cystic RCCs need to distinguish them from solid renal masses with necrotic components, which behave more aggressively.³ Cystic RCCs are part of a spectrum of complex cystic renal masses that are known to have an increased risk of malignancy with increasing complexity (i.e., Bosniak classification III and IV cysts). The vast majority of cystic RCCs are multilocular cystic RCCs (mcRCC),⁶² but all RCC subtypes may present in a predominantly cystic form.⁶³ Although the suggested treatment of choice for these lesions remains surgical excision, there is increasing evidence that they have relatively low metastatic potential and carry an excellent prognosis.⁶³⁻⁶⁷ To the best of our knowledge, there is yet to be a report demonstrating metastases or recurrence of these lesions. To reflect this indolent behaviour, the International Society of Urological Pathology (ISUP) has recently modified its terminol-

ogy and now recommends calling these lesions multilocular cystic renal neoplasm with low malignant potential.⁶²

Several studies have compared the prognosis of mcRCCs to that of solid RCCs. mcRCCs have consistently fared better than their counterparts on both cancer-specific and overall survival.^{24,66-73} One potential explanation for this better prognosis is that the majority of mcRCCs tumour volume is fluid and thus, the actual tumour burden is much lower when compared to similar sized solid tumours.⁶⁷ As the outcomes of these tumours do not seem to be influenced by the overall lesion size, some experts have even suggested to abandon the current pathological T staging for mcRCC and to reassign them a new stage called pT1c (c for cystic).⁶⁷

Given their relatively indolent nature, there is emerging evidence suggesting that these lesions (especially Bosniak classification III) can be safely managed by active surveillance.^{6,12,13,29,31,32,35,38,41,48,59} Extrapolating from data on SRMs, Bhatt et al have suggested that Bosniak III and perhaps even Bosniak IV cysts with a solid component measuring less than 3 cm could be managed with initial surveillance.⁶⁷ Nevertheless, given the paucity of data, this management strategy should be reserved for well-informed patients and generally for patients at high surgical risk due to comorbidities or limited life expectancy. **(Level of evidence: 4; Recommendation: D)** There is currently no evidence to dictate any specific followup scheme. However, if active surveillance is considered, it seems reasonable to follow these lesions with abdominal imaging every six months for the first two years, followed by yearly imaging thereafter, if the lesion is stable. **(Level of evidence: 4; Recommendation: D)** Likewise, triggers for interventions are yet to be clearly defined and validated, but may include progression from Bosniak III to IV, growth of solid nodule over 3 cm, and fast-growing nodule. **(Level of evidence: 4; Recommendation: D)**

Thermal-ablation therapies

The current standard of care for the management of Bosniak category III and IV cysts remains surgical excision, but thermal-ablation therapies may be considered an alternative in select cases. Data supporting this approach is mostly extrapolated from the management of solid SRMs.⁶¹ Nevertheless, there is some evidence from small case series supporting radiofrequency ablation (RFA) as a treatment alternative.⁷⁴⁻⁷⁸ Overall, given the limited data, RFA should be limited to patients with small Bosniak category III and IV cysts who are poor operative candidates and in whom active surveillance is not being considered. **(Level of evidence: 3; Recommendation: C)** To the best of our knowledge, the role of cryotherapy in the management of Bosniak III or IV cysts is not well-defined, with only a handful of cases reported to have been treated by the approach in the literature.³⁶ Patients opting for the treatment alternative should be made aware of the sparse lit-

erature on the management of cystic renal lesions using these approaches. The role of renal tumour biopsy (RTB) should also be discussed with these patients prior to treatment. (**Level of evidence: 3; Recommendation: C**)

Role of renal tumour biopsy in the management of cystic lesions

There is now substantial evidence supporting the role of RTB for the pretreatment identification of the histology of solid renal masses.^{79,80} RTB is safe, accurate, and reliable. Additionally, needle core biopsy has been shown to decrease overtreatment rates when used in the management of solid small renal masses.^{80,81} However, its role in the management of cystic renal masses is not clearly defined.

There is evidence that RTBs are significantly less informative for the diagnosis of cystic lesions than for solid ones.^{79,82-84} Therefore, the utility of RTB in cystic lesions is less than that observed with solid SRMs. Nevertheless, there is literature supporting the role of RTB for histology identification of Bosniak III and IV cysts.^{28,74,75,82} It is generally felt that RTB is not diagnostic for most Bosniak III cysts, as there is minimal targetable solid component. (**Level of evidence: 3; Recommendation: D**) For Bosniak IV cysts, a biopsy of the solid component may be considered to confirm the presence of a malignant tumour and to help with decision-making in select cases (elderly, multiple comorbidities, unfit for treatment, etc).^{5,28,74,75,82,83} (**Level of evidence: 3; Recommendation: C**) Of interest, some reports have suggested that the combination of fine needle aspiration (FNA) and core biopsy may lead to a slightly higher diagnostic yield than core biopsy alone.⁸⁵ Nevertheless, in most centres of experience, RTBs are performed using core biopsy alone, as the combination is thought to add minimal value. Experts have also reported a higher diagnostic rate in Bosniak IV cyst when the solid component was greater than 1 cm.⁸³

Conclusion

The evidence for optimal management of cystic RCC, including followup, is low-quality and based on case series and indirectly from the management of solid SRMs. Nevertheless, these guidelines provide some guidance to urologists on how to best manage and follow these cystic lesions. In summary, Bosniak category I and II cysts do not routinely require followup, whereas Bosniak category IIF cysts should be followed with routine imaging. Although surgical excision is still recommended for Bosniak category III and IV cysts, there is growing evidence suggesting that alternate management can be safely considered in select cases.

Competing interests: Dr. Jewett has served as an advisor for and received honoraria from Pfizer; and holds shares in Theralase Therapeutics. Dr. Pauliot has served as an advisor for Amgen, Astellas, and Pfizer; has been a speaker for Sanofi; and has received payment and/or honoraria from Amgen, AstraZeneca, Janssen, Pfizer, and Sanofi. Dr. So has been a speaker for Amgen, Astellas,

and Janssen. Dr. Whelan has participated in clinical trials for AbbVie. Dr. Rendon has been an advisor and speaker for Amgen, Astellas, Ferring, and Janssen. The remaining authors report no competing personal or financial interests.

Tribute: These guidelines are largely based on the work of a giant in the field of uro-radiology, Dr. Morton A. Bosniak, who passed away on September 7, 2016. Dr. Bosniak was a pioneer in the field of renal mass evaluation. His work significantly impacted the management of both solid and cystic kidney masses. Dr. Bosniak was the first to recognize the need for structured categorization of cystic renal masses and his seminal classification of the malignant potential of cystic renal masses remains his signature work. The Bosniak classification is applied worldwide and is known to every urologist and radiologist, as well as to any clinicians who care for patients with renal disease. As a commemoration of his life and work, the authors would like to dedicate these guidelines to his memory.

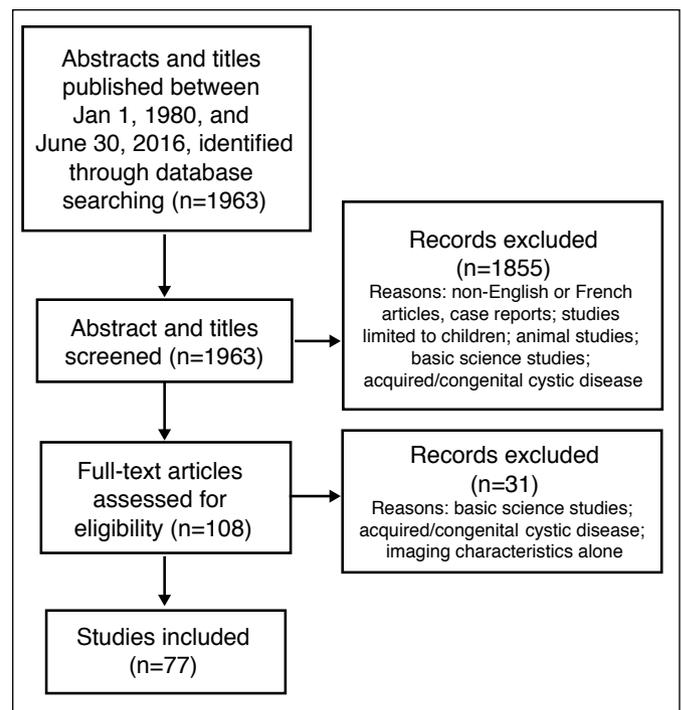
This paper has been peer-reviewed.

References

- Volpe A, Panzarella T, Rendon R, et al. The natural history of incidentally detected small renal masses. *Cancer* 2004;100:738-45. <https://doi.org/10.1002/cncr.20025>
- Marumo K, Horiguchi Y, Nakagawa K, et al. Incidence and growth pattern of simple cysts of the kidney in patients with asymptomatic microscopic hematuria. *Int J Urol* 2003;10:63-7. <https://doi.org/10.1046/j.1442-2042.2003.00577.x>
- Pichler M, Hutterer GC, Chromecki TF, et al. Histologic tumour necrosis is an independent prognostic indicator for clear cell and papillary renal cell carcinoma. *Am J Clin Pathol* 2012;137:283-9. <https://doi.org/10.1309/AJCLPBK9L9KDYQZP>
- Bosniak M. The current radiological approach to renal cysts. *Radiology* 1986;158:1-10. <https://doi.org/10.1148/radiology.158.1.3510019>
- Bosniak M. Diagnosis and management of patients with complicated cystic lesions of the kidney. *AJR* 1997;169:819-21. <https://doi.org/10.2214/ajr.169.3.9275903>
- Clevert DA, Minaifar N, Weckbach S, et al. Multislice computed tomography vs. contrast-enhanced ultrasound in evaluation of complex cystic renal masses using the Bosniak classification system. *Clin Hematol Microcirc* 2008;39:171-8.
- Ellimoottil C, Greco KA, Hart S, et al. New modalities for evaluation and surveillance of complex renal cysts. *J Urol* 2014;192:1604-11. <https://doi.org/10.1016/j.juro.2014.07.099>
- Nicolau C, Bunesch L, Sebastia C. Renal complex cysts in adults: Contrast-enhanced ultrasound. *Abdom Imaging* 2011;36:742-52. <https://doi.org/10.1007/s00261-011-9727-8>
- Graumann O, Osther SS, Osther PJ. Characterization of complex renal cysts: A critical evaluation of the Bosniak classification. *Scand J Urol* 2011;45:84-90. <https://doi.org/10.3109/00365599.2010.533695>
- Park BK, Kim B, Kim SH, et al. Assessment of cystic renal masses based on Bosniak classification: Comparison of CT and contrast-enhanced US. *Eur J Radiol* 2007;61:310-4. <https://doi.org/10.1016/j.ejrad.2006.10.004>
- Cloix P, Martin X, Pangaud C, et al. Surgical management of complex renal cysts: A series of 32 cases. *J Urol* 1996;156:28-30. [https://doi.org/10.1016/S0022-5347\(01\)65928-7](https://doi.org/10.1016/S0022-5347(01)65928-7)
- Curry NS, Cochran ST, Bissada NK. Cystic renal masses: Accurate Bosniak classification requires adequate renal CT. *AJR* 2000;175:339-42. <https://doi.org/10.2214/ajr.175.2.1750339>
- El-Mokadem I, Budak M, Pillai S, et al. Progression, interobserver agreement, and malignancy rate in complex renal cysts (> Bosniak category IIF). *Urol Oncol* 2014;32:e21-7. <https://doi.org/10.1016/j.urolonc.2012.08.018>
- Graumann O, Osther SS, Karstoft J, et al. Bosniak classification system: Interobserver and intraobserver agreement among experienced uro-radiologists. *Acta Radiol* 2015;56:374-83. <https://doi.org/10.1177/0284185114529562>
- Wilson TE, Doelle EA, Cohan RH, et al. Cystic renal masses: A re-evaluation of the usefulness of the Bosniak classification system. *Acad Radiol* 1996;3:564-70. [https://doi.org/10.1016/S1076-6332\(96\)80221-2](https://doi.org/10.1016/S1076-6332(96)80221-2)
- Benjaminov O, Atri M, O'Malley M, et al. Enhancing component on CT to predict malignancy in cystic renal masses and interobserver agreement of different CT features. *AJR* 2006;186:665-72. <https://doi.org/10.2214/AJR.04.0372>
- Bertolotto M, Zappetti R, Cavallaro M, et al. Characterization of atypical cystic renal masses with MDCT: Comparison of 5-mm axial images and thin multiplanar reconstructed images. *AJR* 2010;195:693-700. <https://doi.org/10.2214/AJR.09.3113>

18. Israel GM, Bosniak MA. An update on the Bosniak renal cyst classification system. *Urology* 2005;66:484-9. <https://doi.org/10.1016/j.urol.2005.04.003>
19. Warren KS, McFarlane J. The Bosniak classification of renal cystic masses. *BJU Int* 2005;95:939-42. <https://doi.org/10.1111/j.1464-410X.2005.05442.x>
20. Graumann O, Osther SS, Karstoft J, et al. Evaluation of Bosniak category IIF complex renal cysts. *Insights Imaging* 2013;4:471-80. <https://doi.org/10.1007/s13244-013-0251-y>
21. Hindman NM, Hecht EM, Bosniak MA. Followup for Bosniak category 2F cystic renal lesions. *Radiology* 2014;272:757-66. <https://doi.org/10.1148/radiol.14122908>
22. Weibl P, Klatter T, Waldert M, et al. Complex renal cystic masses: Current standard and controversies. *Int Urol Nephrol* 2012;44:13-8. <https://doi.org/10.1007/s12555-010-9864-y>
23. Aronson S, Frazier HA, Baluch JD, et al. Cystic renal masses: Usefulness of the Bosniak classification. *Urol Radiol* 1991;13:83-90. <https://doi.org/10.1007/BF02924596>
24. Bielsa O, Lloreta J, Gelabert-Mas A. Cystic renal cell carcinoma: Pathological features, survival and implications for treatment. *Br J Urol* 1998;82:16-20. <https://doi.org/10.1046/j.1464-410x.1998.00689.x>
25. Brown WC, Amis ES Jr, Kaplan SA, et al. Renal cystic lesions: Predictive value of preoperative computerized tomography. *J Urol* 1989;141:426A.
26. Gabr AH, Gidor Y, Roberts WW, et al. Radiographic surveillance of minimally and moderately complex renal cysts. *BJU Int* 2009;103:1116-9. <https://doi.org/10.1111/j.1464-410x.2008.08171.x>
27. Han HH, Choi KH, Oh YT, et al. Differential diagnosis of complex renal cysts based on lesion size along with the Bosniak renal cyst classification. *Yonsei Med J* 2012;53:729-33. <https://doi.org/10.3349/ymj.2012.53.4.729>
28. Harisinghani MG, Maher MM, Gervais DA, et al. Incidence of malignancy in complex cystic renal masses (Bosniak category III): Should imaging-guided biopsy precede surgery? *AJR* 2003;180:755-8. <https://doi.org/10.2214/ajr.180.3.1800755>
29. Israel GM, Bosniak MA. Calcification in cystic renal masses: Is it important in diagnosis? *Radiology* 2003;226:47-52. <https://doi.org/10.1148/radiol.226101704>
30. Israel GM, Bosniak MA. Followup CT of moderately complex cystic lesions of the kidney (Bosniak category IIF). *AJR Am J Roentgenol* 2003;181:627-33. <https://doi.org/10.2214/ajr.181.3.1810627>
31. Israel GM, Hindman N, Bosniak MA. Evaluation of cystic renal masses: Comparison of CT and MR imaging by using the Bosniak classification system. *Radiology* 2004;231:365-71. <https://doi.org/10.1148/radiol.2312031025>
32. Kim MH, Yi R, Cho KS, et al. Three-phase, contrast-enhanced, multidetector CT in the evaluation of complicated renal cysts: Comparison of the postcontrast phase combination. *Acta Radiol* 2014;55:372-7. <https://doi.org/10.1177/0284185113495837>
33. Koga S, Nishikido M, Inuzuka S, et al. An evaluation of Bosniak's radiological classification of cystic renal masses. *BJU Int* 2000;86:607-9. <https://doi.org/10.1046/j.1464-410x.2000.00882.x>
34. Limb J, Santiago L, Kaswick J, et al. Laparoscopic evaluation of indeterminate renal cysts: Long-term followup. *J Endourol* 2002;16:79-82. <https://doi.org/10.1089/089277902753619555>
35. Loock PY, Debierre F, Wallerand H, et al. Kystes atypiques et risque de cancer du rein. Interet et «danger» de la classification de Bosniak. *Prog Urol* 2006;16:292-6.
36. O'Malley RL, Goday G, Hecht EM, et al. Bosniak category IIF designation and surgery for complex renal cysts. *J Urol* 2009;182:1091-5. <https://doi.org/10.1016/j.juro.2009.05.046>
37. Pinheiro T, Sepulveda F, Natalin RH, et al. Is it safe and effective to treat complex renal cysts by the laparoscopic approach? *J Endourol* 2011;25:471-6. <https://doi.org/10.1089/end.2010.0254>
38. Quaia E, Bertolotto M, Ciuffi V, et al. Comparison of contrast-enhanced sonography with unenhanced sonography and contrast-enhanced CT in the diagnosis of malignancy in complex cystic renal masses. *AJR* 2008;191:1239-49. <https://doi.org/10.2214/AJR.07.3546>
39. Reese AC, Johnson PT, Gorin MA, et al. Pathological characteristics and radiographic correlates of complex renal cysts. *Urol Oncol* 2014;32:1010-6. <https://doi.org/10.1016/j.urolonc.2014.02.022>
40. Siegel CL, McFarland EG, Brink JA, et al. CT of cystic renal masses: Analysis of diagnostic performance and interobserver variation. *AJR* 1997;169:813-8. <https://doi.org/10.2214/ajr.169.3.9275902>
41. Smith AD, Remer EM, Cox KL, et al. Bosniak Category IIF and III cystic renal lesions: Outcomes and associations. *Radiology* 2012;262:152-60. <https://doi.org/10.1148/radiol.11110888>
42. Song C, Min GE, Song K, et al. Differential diagnosis of complex cystic renal mass using multiphase computerized tomography. *J Urol* 2009;181:2446-50. <https://doi.org/10.1016/j.juro.2009.01.111>
43. Spaliviero M, Herts BR, Magi-Galluzzi C, et al. Laparoscopic partial nephrectomy for cystic masses. *J Urol* 2005;174:614-9. <https://doi.org/10.1097/01.ju.0000165162.21997.11>
44. Xu Y, Zhang S, Wei X, et al. Contrast enhanced ultrasonography prediction of cystic renal mass in comparison to histopathology. *Clin Hemorheol Microcirc* 2014;58:429-38.
45. You D, Shim M, Jeong IG, et al. Multilocular cystic renal cell carcinoma: Clinicopathological features and preoperative prediction using multiphase computed tomography. *BJU Int* 2011;108:1444-9. <https://doi.org/10.1111/j.1464-410x.2011.10247.x>
46. Kim DY, Kim JK, GE M, et al. Malignant renal cysts: Diagnostic performance and strong predictors at MDCT. *Acata Radiol* 2010;51:590-8. <https://doi.org/10.3109/02841851003641826>
47. Oh YT, IY S. The role of Bosniak classification in malignant tumour diagnosis: A single-institution experience. *Investig Clin Urol* 2016;57:100-5. <https://doi.org/10.4111/icu.2016.57.2.100>
48. Smith AD, Allen BC, Sanyal R, et al. Outcomes and complications related to the management of Bosniak cystic renal lesions. *AJR* 2015;204:550-6. <https://doi.org/10.2214/AJR.14.13149>
49. Goenka AH, Remer EM, Smith AD, et al. Development of a clinical prediction model for assessment of malignancy risk in Bosniak III renal lesions. *Urology* 2013;82:630-5. <https://doi.org/10.1016/j.urol.2013.05.016>
50. Israel GM, Bosniak MA. How I do it: Evaluating renal masses. *Radiology* 2005;236:441-50. <https://doi.org/10.1148/radiol.2362040218>
51. Silverman SG, Israel GM, Herts BR, et al. Management of the incidental renal mass. *Radiology* 2008;249:16-31. <https://doi.org/10.1148/radiol.2491070783>
52. Park H, Kim CS. Natural 10-year history of simple renal cysts. *Korean J Urol* 2015;56:351-6. <https://doi.org/10.4111/kju.2015.56.5.351>
53. Terada N, Ichioka K, Matsuta Y, et al. The natural history of simple renal cysts. *J Urol* 2002;167:21-3. [https://doi.org/10.1016/S0022-5347\(05\)65373-6](https://doi.org/10.1016/S0022-5347(05)65373-6)
54. Bowers DL, Ikeguchi EF, Is S. Transition from renal cyst to a renal carcinoma detected by ultrasonography. *Br J Urol* 1997;80:495-6. <https://doi.org/10.1046/j.1464-410x.1997.00295.x>
55. Nishibuchi S, Suzuki Y, Okada K. [A case report of renal cell carcinoma in a renal cyst]. *Hinyokika Kiyo*. 1992;38:181-4.
56. Sakai N, Kanda F, Kondo K, et al. Sonographically detected malignant transformation of a simple renal cyst. *Int J Urol* 2001;8:23-5. <https://doi.org/10.1046/j.1442-2042.2001.00239.x>
57. Qin X, Ye L, Zhang H, et al. Complicated variation of simple renal cyst usually means malignancy—results from a cohort study. *World J Surg Oncol* 2014;12:316-9. <https://doi.org/10.1186/1477-7819-12-316>
58. Agarwal MM, Hermal AK. Surgical management of renal cystic disease. *Curr Urol Rep* 2011;12:3-10. <https://doi.org/10.1007/s11934-010-0152-2>
59. Weibl P, Klatter T, Kollarik B, et al. Interpersonal variability and present diagnostic dilemmas in Bosniak classification system. *Scand J Urol* 2011;45:239-44. <https://doi.org/10.3109/00365599.2011.562233>
60. Ragel M, Nedumaran A, Makowska-Webb J. Prospective comparison of use of contrast-enhanced ultrasound and contrast-enhanced computed tomography in the Bosniak classification of complex renal cysts. *Ultrasound* 2016;24:6-16. <https://doi.org/10.1177/1742271X15626959>
61. Jewett MA, Rendon RA, Lacombe L, et al. Canadian guidelines for the management of small renal masses (SRM). *Can Urol Assoc J* 2015;9:160-3. <https://doi.org/10.5489/auaj.2969>
62. Srigley JR, Delahunt B, Eble JN, et al. The International Society of Urological Pathology (ISUP) Vancouver classification of renal neoplasia. *Am J Surg Pathol* 2013;37:1469-89. <https://doi.org/10.1097/PAS.0b013e318299f2d1>
63. Donin NM, Mohan S, Pham H, et al. Clinicopathologic outcomes of cystic renal cell carcinoma. *Clin Genitourin Cancer* 2015;13:67-70. <https://doi.org/10.1016/j.clgc.2014.06.018>
64. Corica FA, Iczkowski KA, Cheng L, et al. Cystic renal cell carcinoma is cured by resection: A study of 24 cases with long-term followup. *J Urol* 1999;161:408-11. [https://doi.org/10.1016/S0022-5347\(01\)61903-7](https://doi.org/10.1016/S0022-5347(01)61903-7)
65. Murad T, Komaiko W, Oyasu R, et al. Multilocular cystic renal cell carcinoma. *Am J Clin Pathol* 1991;95:633-7. <https://doi.org/10.1093/ajcp/95.5.633>
66. Nassir A, Jollimore J, Gupta R, et al. Multilocular cystic renal cell carcinoma: A series of 12 cases and review of the literature. *Urology* 2002;60:421-7. [https://doi.org/10.1016/S0090-4295\(02\)01742-9](https://doi.org/10.1016/S0090-4295(02)01742-9)
67. Bhatt JR, Jewett M, Richard PO, et al. Multilocular cystic renal cell carcinoma: Pathological T staging makes no difference to favourable outcomes and should be reclassified. *J Urol* 2016;196:1350-5. <https://doi.org/10.1016/j.juro.2016.05.118>
68. Aubert S, Zini L, Delomez J, et al. Cystic renal cell carcinomas in adults. Is preoperative recognition of multilocular cystic renal cell carcinoma possible? *J Urol* 2005;174:2115-9. <https://doi.org/10.1097/01.ju.0000181210.72528.ab>
69. Gong K, Zhang N, He Z, et al. Multilocular cystic renal cell carcinoma: An experience of clinical management for 31 cases. *J Cancer Res Clin Oncol* 2008;134:433-7. <https://doi.org/10.1007/s00432-007-0302-1>
70. Koga S, Nishikido M, Hayashi T, et al. Outcome of surgery in cystic renal cell carcinoma. *Urology* 2000;56:67-70. [https://doi.org/10.1016/S0090-4295\(00\)00540-9](https://doi.org/10.1016/S0090-4295(00)00540-9)
71. Webster WS, Thompson RH, Chevile JC, et al. Surgical resection provides excellent outcomes for patients with cystic clear cell renal cell carcinoma. *Urology* 2007;70:900-4. <https://doi.org/10.1016/j.urol.2007.05.029>
72. Suzigan S, López-Beltrán A, Montironi R, et al. Multilocular cystic renal cell carcinoma: A report of 45 cases of a kidney tumour of low malignant potential. *Am J Clin Pathol* 2006;125:217-22. <https://doi.org/10.1309/AH6FC77PYR2V6YAY>
73. Winters BR, Gore JL, Holt SK, et al. Cystic renal cell carcinoma carries an excellent prognosis regardless of tumour size. *Urol Oncol* 2015;33:e9-13. <https://doi.org/10.1016/j.urolonc.2015.07.017>
74. Allen BC, Chen MY, Childs DD, et al. Imaging-guided radiofrequency ablation of cystic renal neoplasms. *AJRT* 2013;200:1365-89. <https://doi.org/10.2214/AJR.12.9336>
75. Felker ER, Lee-Felker SA, Alpern L, et al. Efficacy of imaging-guided percutaneous radiofrequency ablation for the treatment of biopsy-proven malignant cystic renal masses. *AJR* 2013;201:1029-35. <https://doi.org/10.2214/AJR.12.10210>

76. Park BK, Kim CK, Lee HM. Image-guided radiofrequency ablation of Bosniak III or IV cystic renal tumours: Initial clinical experience. *Eur Radiol* 2008;18:1519-25. <https://doi.org/10.1007/s00330-008-0891-3>
77. Park JJ, Park BK, Park SY, et al. Percutaneous radiofrequency ablation of sporadic Bosniak III or IV lesions: Treatment techniques and short-term outcomes. *J Vasc Interv Radiol* 2015;26:46-54. <https://doi.org/10.1016/j.jvir.2014.09.014>
78. Menezes MR, Viano PC, Yamanari TR, et al. Safety and feasibility of radiofrequency ablation for treatment of Bosniak IV renal cysts. *Int Braz J Urol* 2016;42:456-63. <https://doi.org/10.1590/S1677-5538.IBJU.2015.0444>
79. Marconi L, Dabestani S, Lam TB, et al. Systematic review and meta-analysis of diagnostic accuracy of percutaneous renal tumour biopsy. *Eur Urol* 2016;69:660-73. <https://doi.org/10.1016/j.eururo.2015.07.072>
80. Richard PO, Jewett MA, Bhatt JR, et al. Renal tumour biopsy for small renal masses: A single-centre, 13-year experience. *Eur Urol* 2015;68:1007-13. <https://doi.org/10.1016/j.eururo.2015.04.004>
81. Halverson SJ, Kunju LP, Bhalla R, et al. Accuracy of determining small renal mass management with risk-stratified biopsies: Confirmation by final pathology. *J Urol* 2013;189:441-6. <https://doi.org/10.1016/j.juro.2012.09.032>
82. Lang EK, Macchia RJ, Gayle B, et al. CT-guided biopsy of indeterminate renal cystic masses (Bosniak 3 and 2F): Accuracy and impact on clinical management. *Eur Radiol* 2002;12:2518-424. <https://doi.org/10.1007/s00330-001-1292-z>
83. Leveridge MJ, Finelli A, Kachura JR, et al. Outcomes of small renal mass needle core biopsy, non-diagnostic percutaneous biopsy, and the role of repeat biopsy. *Eur Urol* 2011;60:578-84. <https://doi.org/10.1016/j.eururo.2011.06.021>
84. Volpe A, Matta A, Finelli A, et al. Contemporary results of percutaneous biopsy of 100 small renal masses: A single-centre experience. *J Urol* 2008;180:2333-7. <https://doi.org/10.1016/j.juro.2008.08.014>
85. Parks GE, Perkins LA, Zagoria RJ, et al. Benefits of a combined approach to sampling of renal neoplasms as demonstrated in a series of 351 cases. *Am J Surg Pathol* 2011;35:827-35. <https://doi.org/10.1097/PAS.0b013e31821920c8>



Supplementary Fig. 1. Flow diagram: Search and study selection process.

Correspondence: Dr. Patrick O. Richard, Division of Urology, Department of Surgery, Centre Hospitalier Universitaire de Sherbrooke, Université de Sherbrooke, Sherbrooke, QC, Canada; patrick.richard@usherbrooke.ca