



# Active surveillance for complex renal cysts: is it time for III-F and IV-F?

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Renal cysts are highly common and estimated to be present in at least one-third of all individuals over the age of 60 (1). In 1986, Dr. Bosniak introduced a radiographic classification for renal cysts to guide the management of renal cyst according to the underlying risk of malignancy (2). Bosniak I renal cysts are simple renal cyst while Bosniak II are mildly complex; both of these classes of renal cysts are categorized as benign renal cysts and do not require intervention or surveillance imaging. In contrast, Bosniak III and IV are complex renal cysts with a considerable risk of harboring malignancy (3). The typical initial management for Bosniak III and IV is partial or radical nephrectomy surgery. In 1993, a modification to the classification system was made by creating the Bosniak IIF category, which refers to moderately complex cysts not obviously falling into the Bosniak II or Bosniak III categories; the “F” nomenclature represents the general recommendation for “follow-up” with radiographic studies rather than deferring imaging, as in the case for Bosniak II renal cysts, or surgery, as in the case for Bosniak III renal cysts (4). This new category was introduced to avoid underestimating the malignant potential of certain renal cysts while simultaneously avoiding unnecessary upfront surgery for others.

Over the last several decades, the detection of renal masses, both cystic and solid, has increased dramatically due to the widespread use of cross-sectional imaging (5). The incidence of kidney cancer has doubled in the US; however,

mortality rates remain the same, suggesting overdiagnosis of clinically insignificant kidney cancers (6). As a result, the treatment of solid small renal masses (SRM) has shifted dramatically. The recognition that the majority of SRM represent either indolent malignancies or benign tumors led clinical management away from immediate radical nephrectomy and towards a focus on avoiding overtreatment and surgical morbidity through the use of nephron-sparing approaches such as partial nephrectomy, thermal ablation, as well as an emphasis on active surveillance (AS) (7) with possible delay intervention for those who show signs of clinical progression (8,9). During this same period, there have been updates to the Bosniak classification system, in 1993, 1997, 2005, and most recently in 2019. Recent updates to the Bosniak classification of cystic renal masses, such as the version published in 2019, have incorporated magnetic resonance imaging and other advances in imaging modalities (10,11). These updates improve clarity on the classification scheme, facilitating clinical management decisions for renal cysts. However, no significant changes in treatment recommendations occurred; thus, overall clinical management remains largely unchanged compared to previous versions of this classification system. Thus, while the medical community has embraced a conservative approach for the management of solid SRM, there has been minimal enthusiasm for a similar approach for complex cystic lesions concerning for malignancy. If AS is an

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**Table 1** Current guidelines recommendations

Bosniak	Guidelines recommendations		
	EAU	AUA	Canadian
III	Manage Bosniak type III cysts the same as localized RCC or offer AS	AS when the risk of intervention or competing risks of death outweighs the potential oncologic benefits of active treatment. In case AS is offered:	AS or thermal ablation
IV	Manage Bosniak type IV cysts the same as localized RCC	<ul style="list-style-type: none"> <li>• Repeated cross-sectional images to assess growth rate</li> <li>• Consider renal mass biopsy</li> <li>• Shared decision-making</li> </ul>	Surgical excision is suggested, with partial nephrectomy as the surgery of choice; however, more conservative management may be safely considered in selected cases

Guidelines adopted AS as an alternative for managing renal complex cysts Bosniak III and IV. EAU, European Association of Urology; AUA, American Urological Association; RCC, renal cell carcinoma; AS, active surveillance.

appropriate, and arguably favored, option for SRM, should the same strategy not be applied to Bosniak III and IV renal cysts?

There is a limited but growing body of literature showing that cystic renal cell carcinoma (RCC) is associated with the less aggressive compared to solid RCC of similar size with a better overall (12). A plausible explanation for more indolent natural history of cystic RCC may be that it is only the solid component of the cystic lesion that is harboring the malignant cells, which typically represents a small minority of the total volume of the complex renal cyst. Thus, in comparison to a solid malignant RCC, there is simply less malignant mass present in a similarly sized cystic RCC. For instance, the prognosis for a 3.5 cm malignant Bosniak IV renal cyst with a focal 1 cm mural nodule may be far more similar to a 1 cm malignant SRM rather than a 3.5 cm malignant SRM. Perhaps the optimal treatment for Bosniak III and IV renal cysts should be determined solely by its solid component and not by its total diameter or change in size?

Given the typically indolent nature of cystic RCC, the conventional treatment paradigm for expeditious extirpative surgery is arguably overly aggressive for Bosniak III and IV renal cysts. Schoots *et al.* published a systematic review and meta-analysis, including 39 studies. They found that the number necessary to treat (NNT) to prevent the metastatic spread was 1 in 140 for Bosniak III and 1 in 40 in patients with Bosniak IV (13). Not surprisingly, recent studies focused on longitudinal assessment of renal cysts conclude that the majority of surgeries for a Bosniak III will result in over-treatment because treatment does not confer a true benefit (14,15). Moreover, these kidney surgeries are associated with potential surgical morbidity. In a cohort of

286 patients with renal cysts managed with surgery, Smith *et al.* reported that 19% experienced moderate to severe complications, of which 7% suffered severe complications, including multiorgan failure, acute myocardial infarction, acute ischemic stroke, conversion to hemodialysis-dependent kidney disease, and severe postoperative bleeding (16).

Fortunately, recent guideline updates from various medical organizations suggest a shift in management in renal cysts towards more conservative management (*Table 1*). The European Association of Urology (EAU) guidelines now recommend managing Bosniak III and IV cysts the same as localized RCC and even incorporating AS as an option for Bosniak III renal cysts (17). The American Urological Association (AUA) recommends prioritizing AS when the competing risks of death outweigh the potential benefits of active treatment, without a distinction between Bosniak III and IV complex cystic renal masses, with repeat imaging at 3–6 months to assess growth kinetics (8,18). This AUA recommendation also highlights shared decision-making with an understanding from the patient about the risk and benefits of delayed intervention including but not limited to exposure to ionizing radiation, psychological stress, and potential for non-compliance. When the benefit is uncertain, the AUA guideline recommends considering a renal mass biopsy if the renal cyst has a solid component to improve risk stratification. Finally, the Canadian guideline on managing renal cysts also recommends offering AS for Bosniak III as an appropriate alternative for managing these lesions. Due to the low metastatic potential, thermal ablation therapies may also be considered. For Bosniak IV, surgical excision remains the recommended treatment strategy, with partial nephrectomy as the surgery of choice; however, more conservative management may be safely

considered in selected cases (19).

The improving clinical management of SRM and improved understanding of the natural history of renal cysts have increased the confidence in a more conservative approach characterized by AS in the management of Bosniak III and IV. Proper patient select, weighing the potential oncological benefit and the competing risks of death, is the key to ensuring adequate treatment for Bosniak III and IV renal cysts. It is time to shift from the classic “one size fits all” to a more personalized approach offering AS with possible delayed intervention limited to patients with Bosniak III and IV renal cysts. Historically, AS was limited to Bosniak IIF solely; moving forward, it is time to view more complex renal cysts as “Bosniak IIIF” and “Bosniak IVF” thus emphasizing the practical role of initial management with AS, and thus reserving surgery only for a few patients who would benefit from intervention.

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