

ARTICLE

Multi-disciplinary team conference clarifies bosniak classification of complex renal cysts

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ABSTRACT

Objectives: The aims of this study are to determine the progression rate of Bosniak IIF cysts, the malignancy rates of complex renal cysts in patients undergoing surgery and explore the influence of multi-disciplinary team conference (MDT) on re-classification of Bosniak cysts.

Materials and Methods: All CT scans from January 2010 to 2017 were pooled into a database. Initially, 167 patients were identified with possible Bosniak IIF, III or IV cysts. Patients with follow up of less than 24 months, without progression or regression were excluded.

Results: Thirty-one (18.6%) cysts of the initial 167 cysts were either up or downgraded at a MDT. Twenty-six of the 31 cysts were up or downgraded at the primary MDT, 13 cysts (50%) were downgraded, five cysts (19.2%) were upgraded and eight cysts (30.8%) were re-classified as solid tumors. Of those 19/26 (73.1%) were primary interpreted by a periphery radiologist and re-classified centrally. The last five patients 5/120 cysts (4.2%) were re-classified during follow up.

Results: 116 patients with a total of 120 cysts met the inclusion criteria, 79 (65.8%) Bosniak IIF, 28 (23.3%) Bosniak III and 13 (10.8%) Bosniak IV cysts represented.

Results: Median follow up of Bosniak IIF cysts were 46 months. One Bosniak IIF cyst progressed to a solid tumor at 15 months from diagnosis, progression rate 1.3%. Histopathology was papillary renal cell carcinoma. Malignancy rates of Bosniak III and IV cysts were 50% and 78%, respectively.

Conclusion: Multi-disciplinary team conference may have an important role in correct classification of Bosniak cysts.

Trial registration: None

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Introduction

The widespread use of CT scans in the daily clinical practice has increased the number of identified cystic renal lesions. In 1986, the Bosniak classification was introduced, categorizing cystic renal lesions into four categories. Bosniak I and II renal cysts show low malignant potential and do not require further follow-up. Bosniak III and IV cysts are considered malignant, thus requiring surgical treatment [1]. In 1993, Bosniak et al. introduced the Bosniak IIF category, making active surveillance possible for lesions that are not complex enough to be classified as a Bosniak III lesion, nor benign enough to be classified as a Bosniak II lesion. Stable Bosniak IIF cystic lesions are considered benign but have the potential to progress to malignant lesions, therefore follow-up is recommended [2,3]. If a Bosniak IIF cyst progresses to a Bosniak III or IV cyst, malignancy rates are high among resected lesions of the progressed Bosniak IIF cysts [3].

The general recommendation for Bosniak category IIF lesions is a 5-years follow-up with computed tomography (CT) urography every 6–12 months to ensure the stability of the cysts [4].

Most studies have focused on the malignancy rates of Bosniak lesions, but only a few have focused on the time to progression [2,4,5]. The sample sizes have been rather small, but lately, larger cohorts have been reported [6–8].

The aims of this study are to describe the progression and regression rates of Bosniak lesions at our institution, determine the time to progression and malignancy rates of cysts in patients treated surgically and to explore the influences of a multi-disciplinary team conference (MDT) on the re-classification of Bosniak cysts.

Materials and methods

Access to patients' charts and scans was approved by the Danish Patient Safety Authority, reference number 3-3013-2902/1.

The study was conducted as a retrospective, single-center study at the Department of Urology, Zealand University Hospital, Roskilde.

Our institution's follow-up guidelines for Bosniak IIF cysts includes CT urography after six months of diagnosis, and then annually for five years. Our region consists of seven

radiological centers where CT scans are performed and interpreted by local radiologists. All patients with complex renal cysts are referred to our department and presented at a MDT conference consisting of one or two radiologists with 20 years of experience, oncologists and four urologists with 10 years of experience in management of renal tumors.

A database with all the CT scan reports, both contrast-enhanced and non-contrast-enhanced, required from our department was retrieved through the IMPAX software system. Data was retrieved from January 1st, 2010 to January 1st, 2017. During this period, 25,192 CT reports were identified; 1,621 scans were identified through a search of the CT reports using the keywords 'cyst,' 'Bosniak,' 'complex cyst,' 'complex,' 'I,' 'II,' 'IIF,' 'III' and 'IV.' Inclusion criteria was adults > 18 years, diagnosed with Bosniak IIF, III or IV cysts in the CT reports. The selection of the patients was conducted as illustrated in [Figure 1](#), resulting in 167 patients with potential Bosniak IIF, III and IV cysts qualifying for patient chart review.

Patients with Bosniak IIF cysts were excluded if they had a follow-up of less than 24 months without progression or regression on a CT urography. Patients without CT urography, patients who were only diagnosed with ultrasound examination, patients with Bosniak I or Bosniak II cysts and patients with solid renal tumors on the ipsilateral side were also excluded from the analysis.

Patient charts were reviewed for updates until April 2020. The following data was extrapolated from the patients' charts: Age, gender and cyst characteristics (size, Bosniak status, time of follow-up, progression/regression in Bosniak classification, upgrade or downgrade at an MDT, death and cancer-specific death). Surgically removed cysts were characterized using histopathology. Active surveillance of Bosniak III and IV cysts and the time of follow-up were reported. The time of follow-up was defined as the date of the first scan until the date the last scan was performed.

The terms 'upgrading' and 'downgrading' were used if there was re-classification at an MDT conference of the

original CT report, regardless of the center that the report was made at (either peripheral or central center). The terms 'progression' and 'regression' were used if there was a change in the classification of the Bosniak cysts during the follow-up time. Any uncertainties when reviewing the patients' charts were discussed with a senior consultant specialized in renal surgery.

Non-parametric data were described by median and inter-quartile ranges. A *p*-value less than 0.05 were considered statistically significant. IBM SPSS statistic program version 26 was used for analysis.

Results

We identified 167 patients with potential Bosniak cysts through a key word search ([Figure 1](#)). After read through of the patients charts patients were excluded according to [Figure 2](#). Twenty-two patients were excluded due to invalidation of Bosniak cysts $\geq$ Bosniak IIF. Ten cysts were downgraded at a MDT to Bosniak I-II ([Table 1](#)). Of the other 12 patients, five patients appeared with benign cysts after CT urography was performed. Four patients had non-contrast CTs and additional ultrasounds performed classifying the cysts as Bosniak I-II. Two patients had an additional ultrasound to a CT urography that confirmed a benign cyst. The last patient had a cystic/solid tumor and had biopsies performed.

Thus a total of 116 patients with 120 cysts met the inclusion criteria; 77 patients with 79 Bosniak IIF cysts (65.8%), 27 patients with 28 Bosniak III cysts (23.3%) and 13 patients with Bosniak IV cysts (10.8%) ([Figure 2](#)). One of these patients had a Bosniak IIF cyst and a contralateral resected Bosniak IV cyst, thus represented in two Bosniak categories.

The demographic data, follow up and treatment of patients are described in [Table 2](#). None of the patients had a positive von Hippel-Lindau status. Cancer specific death was reported in one patient with a Bosniak III cyst in active surveillance that developed bilateral renal tumors within a follow up of 25 months.

Re-classification at first MDT

Thirty-one cysts of the 167 (18.6%) patients were either upgraded or downgraded at a MDT. Of those 26 cysts (15.6%) were up or downgraded at the first MDT ([Table 1](#)). Eight cysts were upgraded to solid tumors, of them six tumors were primary classified as Bosniak IIF cysts and the other two cysts were Bosniak III and IV cysts. Six of the patients with solid tumors had a renal surgery performed (partial or total nephrectomy), five of the resected cysts presented with histopathology of papillary renal cell carcinoma (papRCC) and one benign tumor. One patient chose active surveillance, without biopsy a biopsy of the tumor. The last cyst was interpreted as an onchocytoma by ultra sound and patient follow up was terminated.

The patients whose scans were re-classified at the first MDT had their primary CT performed and described in

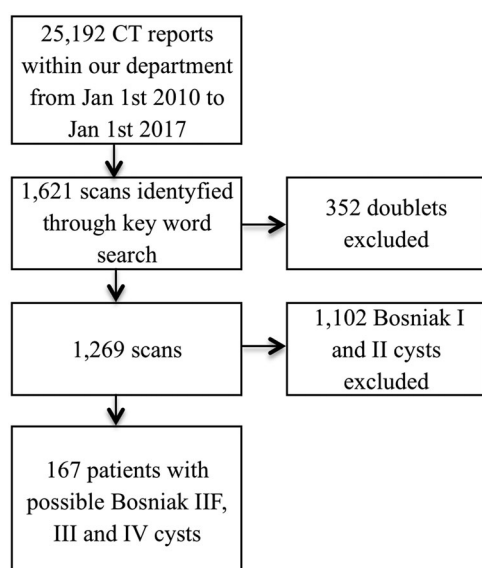
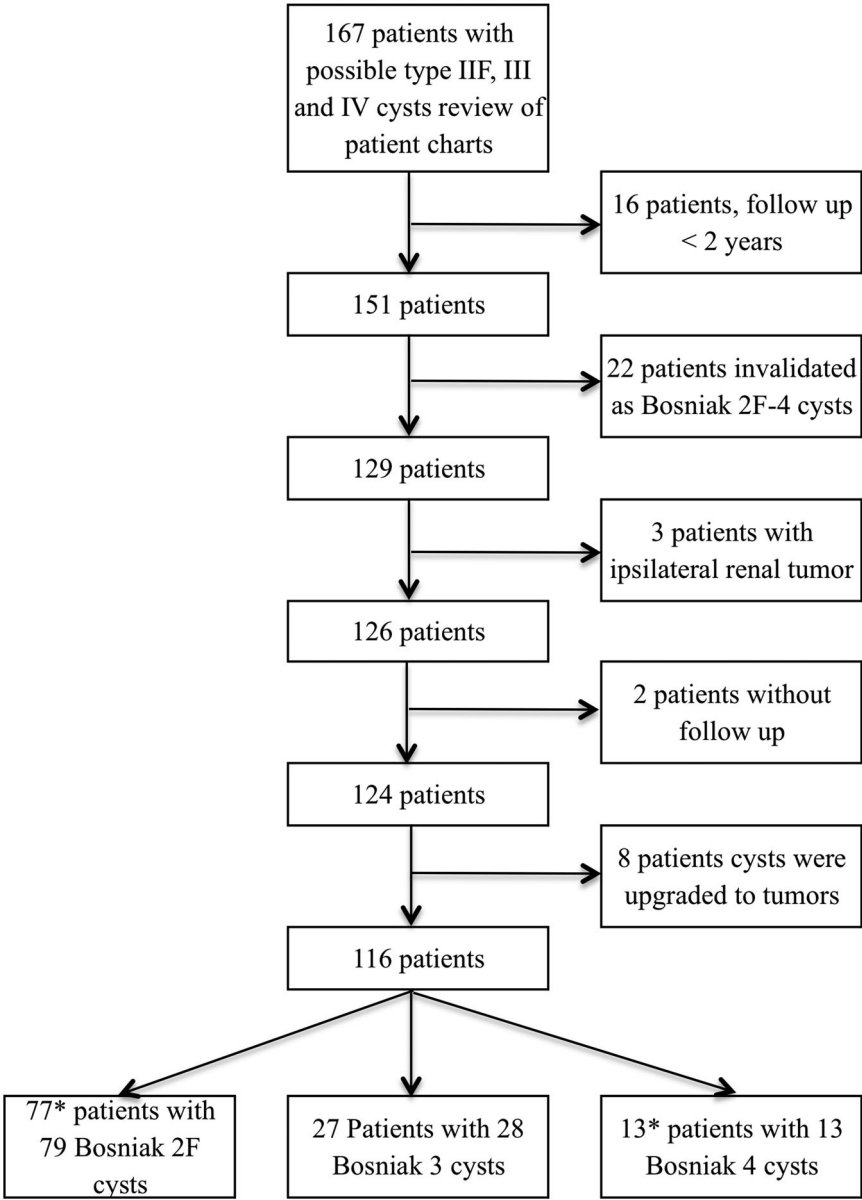


Figure 1. The primary selection and exclusion of patients according to selection criteria.



*One patient represented in two categories with a Bosniak IIF cyst and a Bosniak IV cyst

Figure 2. Flow chart of the final inclusion of patients within Bosniak classified groups.

Table 1. The reclassification of Bosniak cysts at the primary multi-disciplinary team conference.

Change	No.
Total	26 (15.6%)
Upgraded from II to IIF	2 (7.7%)
Upgraded from IIF to III	3 (11.5%)
Downgraded from III to II/I	2 (7.7%)
Downgraded from IIF to II/I	8 (30.8%)
Downgraded from III to IIF	1 (3.8%)
Downgraded from IV to IIF	1 (3.8%)
Downgraded tumor to III	1 (3.8%)
Reevaluated as solid tumors	8 (30.8%)

peripheral centers in 19/26 (73.1%) patients. The other seven were performed centrally and re-classified centrally. Ten patients (Table 1) were downgraded to benign cysts, four patients had a follow up with contrast-enhanced CT

performed due to other indications and the entire downgraded cysts remained stable. Median follow up time for four of the cysts were 49.5 months. Two of the other six patients had non-contrast CTs performed due to urolithiasis, the cysts were not mentioned in the CT reports. The rest of the patients had no further radiological follow up. Biopsies for diagnostics were only performed in one patient, who had a solitary kidney and was followed with CT scans due to renal stones, and not as a follow up for simple renal cysts. This patient had a Bosniak I cyst that progressed to a Bosniak III cyst. Two consecutive sets of biopsies were performed without malignancy. The patient was offered active surveillance. Otherwise biopsies of cystic renal masses are not routinely performed in our department based on the current evidence [9].

Table 2. The demographic data of 116 patients Bosniak classified cysts.

	Bosniak IIF	Bosniak III	Bosniak IV
No. Male / female (ratio)	54/23 (2.3 : 1)	20/7 (2.9 : 1)	10/3 (3.3 : 1)
Age, median (IQR)	67 (59 : 73)	66 (62 : 70)	64 (51 : 78)
Number of scans, median (IQR)	5 (4 : 6)	3 (1 : 5)	1 (1 : 3)
Size of cyst, mm median (IQR)	30 (19 : 52)	36 (17 : 58)	40 (23 : 60)
Follow up and treatment			
Follow up time in months, median (IQR)	46 (36 : 59)	37 (20 : 54)	32 (24 : 38.5)
Deaths (%)	5 (6.5%)	4 (14.8%)	1 (7.7%)
Cancer specific deaths (%)	0 (0%)	1 (3.7%)	0 (0%)
Surgery (%)	0 (0%)	14 (50%)	9 (69.2%)
Active surveillance	79 (100%)	14 (50%)	4 (30.8%)

Re-classification at follow-up MDT

Five cysts were re-classified during follow up 5/120 (4.2%). Four of them were classified primarily as Bosniak IIF cysts, then downgraded to Bosniak II cysts but re-classified to the original Bosniak grade at the MDT. The time to re-classification was after six months regarding two of the cysts and the other two at 36 months and 45 months.

The last patient was diagnosed with a Bosniak III cyst and offered active surveillance (AS). The cyst was downgraded to a Bosniak IIF cyst after six months but reclassified as a Bosniak III cyst and the patient remained in AS. The cyst proved stable after 15 months of follow up.

Regression and progression during follow-up

Only one Bosniak IIF cyst progressed on a CT urography upon 15 months of follow up and was classified as a solid tumor. Radical nephrectomy was performed with a final histopathology of papillary renal cell carcinoma, type 2, pT3a and pN1. This patient had no sign of recurrence during a follow-up period of 76 months. The progression rate of the Bosniak IIF cyst was 1.3% (1/79). Eleven (13.9%) Bosniak IIF cysts regressed during follow up. Median time to regression were 28 months, IQR (18: 34.5).

One Bosniak III cyst regressed during AS with a follow up of 36 months. Two Bosniak III cysts progressed, one to a Bosniak IV cyst after 43 months but still remained in AS, the other one progressed to a solid tumor after 24 months representing the one cancer specific death. None of the Bosniak IV cyst in AS (four cysts) regressed or progressed during follow up.

The malignancy rates of patients that underwent surgery were 7/14 (50%) for Bosniak III and 7/9 (78%) for Bosniak IV. Histopathology of the resected cysts is described in Table 3.

In a multivariable regression with an adjustment for tumor size, the patients' ages were a significant predictor to choose AS for patients with Bosniak IV with an OR of 18.3 ($p=0.0003$), but this was not the case for Bosniak III ($p=0.4$).

Discussion

MDT conference

Our study supports the importance of MDT conferences in interpreting and accurately classifying Bosniak cysts, allowing

Table 3. The histopathology of resected cysts in patients who underwent surgery.

Histopathology	Bosniak III	Bosniak IV
ccRCC	5	5
Papillary RCC	1	2
Multilocular RCC	1	–
Benign	6	2
Angiomyolipoma	1	–
Malignancy rate	7/14 (50%)	7/9 (78%)

urologist to offer the most suitable management to these patients. We observed the re-evaluation of the Bosniak classification at the first MDT in 15.6% of the patients. Of those, 10 cysts were downgraded to Bosniak I/II cysts, thus discontinuing further follow up. Correct classification in these circumstances prevents unnecessary CT scans and potential surgical procedures.

We reported that 73.1% of the Bosniak cysts, that were re-classified at the first MDT, were interpreted primarily by a radiologist from a peripheral center. This supports the importance of having routinized experienced radiologists within the MDT conference which leads to high quality classification of Bosniak cysts [9].

Shoots et al. [3] identified an inter-observer variability of up to 75% in Bosniak II, IIF and III cysts, while Hindman et al. [10] evaluated 225 cysts with overall quadratic-weighted κ -statistic values mean 0.943 (0.856 – 1.0) between two very experienced genitourinary radiologists, which is a very good to excellent agreement between the two readers. A study by Lucocq et al. [12] had a setup with a primary interpretation of the CT scans with a subsequent referral to an MDT. They reported a 70% agreement between one radiologist and an experienced genitourinary radiologist. Surprisingly the lowest disagreement in their study was regarding the Bosniak IIF cysts (20%) and the highest disagreement was seen in Bosniak II (47%) cysts. The re-classification of five cysts during follow up, which then was re-classified back to their original Bosniak grade, also reflects on an inter-observer variability.

We found a slightly lower malignancy rate of Bosniak IV cysts compared to the literature, which may be related to the sample size.

Bosniak IIF progression rate

This study features the lowest progression rate of Bosniak IIF cysts to date, with only one patient (1.3%) progressing from

Bosniak IIF to a solid tumor in our cohort compared to other studies and systematic reviews in which the progression rate ranged from 4% to 17% [3].

The time median to progression in our study was 15 months compared to other studies, which have reported the median time to progression as a range between 11 and 24 months [8,10–12].

In this study, the median follow-up time was 46 months. We excluded patients with a follow-up time of less than 24 months if there were no sign of progression or regression, compared to a median time of follow-up in other studies, which was as low as 20 months [5,10,11].

Malignancy rates

The malignancy rates of Bosniak III and Bosniak IV cysts in patients who underwent surgery in were 50% and 78%, respectively. The malignancy rates of Bosniak III in our study were comparable to other studies, reporting malignancy rates ranging between 51% and 55%. However, the malignancy rates of Bosniak IV cysts in our study were slightly lower than the literature, which ranged between 86% and 91% [3,13]. The number of patients with Bosniak III and Bosniak IV cysts in our study cohort was rather small, which can influence this difference.

We observed that elderly patients with Bosniak IV were more frequently offered an AS management (OR 18.3), which is supported by other studies as well [7]. In contrast, age did not influence the type of treatment for patients with Bosniak III, which may reflect the bias in patient selection [3]. In addition, the preference of the surgeon, patient co-morbidities and decision-making on an MDT conference can influence the choice of management.

Our study has several limitations. This study is a single-center, retrospective study with smaller sample sizes, especially of patients with Bosniak III and IV cysts, which can result in selection bias of patients also noting that 16 patients (9.6%) (Figure 2) were excluded due to follow up less than two years.

The classification of Bosniak renal cysts has been updated since its debut in 1986. A new recommendation has recently been published to address the shortcomings of the current inter-observer variabilities [14]. Follow-up studies after this adjustment are needed to validate the classification system.

This study has, to our knowledge, the lowest rate of progression of Bosniak IIF cysts within a median follow-up period of 46 months. The MDT conference may play an important role in correct classification of complex renal cysts especially at the primary scan.

We recommend that all complex renal cysts are evaluated in an MDT conference.

Disclosure statement

The authors have nothing to declare, nor any potential conflicts of interest.

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