

MORPHOLOGIC FEATURES OF INCIDENTALLY IDENTIFIED RENAL TUMORS

MARCOS F. DALL'OGGIO, MIGUEL SROUGI, PIERRE D. GONÇALVES, KÁTIA M. LEITE,
FLÁVIO HERING

Division of Urology, Paulista School of Medicine, Federal University of São Paulo (UNIFESP), São Paulo,
SP, Brazil

ABSTRACT

Objective: To compare the pathological features and the evolution of incidental renal cell carcinoma (RCC) in patients submitted to surgical treatment, and correlate nuclear grade, tumor size and pathological staging of these tumors with the same parameters in patients with symptomatic disease.

Materials and Methods: From 1988 to 1999, 115 patients (86 males and 29 females) were analyzed. The patients were divided into two groups, according to the diagnosis of the primary tumor, incidental or symptomatic. Tumor nuclear grade, tumor and pathological stage were analyzed retrospectively. The t-student and chi-square tests were used for the statistical analysis.

Results: When the two groups were compared, it was observed that the incidental tumors had a lower nuclear grade ($p < 0.001$), smaller size ($p = 0.001$) and low stage in 47 incidental tumors PT1 ($p < 0.001$).

Conclusion: In this series, the incidental tumors had more indolent features than the symptomatic, with more aggressive features when larger than 4 cm in diameter.

Key words: kidney; renal cell, carcinoma; incidental; nephrectomy; treatment outcome

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INTRODUCTION

Renal cell carcinoma (RCC), described for the first time in 1826 by Grawitz, corresponds to 2 - 3% of solid tumors in adults. In 1998, it was estimated that 29,900 new cases of RCC would be diagnosed in The United States and there would be 11,600 deaths (1). Surgical treatment presents the best results when the tumor is limited to the kidney, and there is no effective systemic therapy in metastatic RCC (2).

Tumor growth speed is from zero to 1.6 cm per year (3), yet there are some cases of tumors smaller than 3 cm that produce early metastasis (4). The biological behavior cannot be forecasted. Tumors can be seen in autopsies either as aggressive or as senescent (5). More rarely, the spontaneous regression of metastatic tumors can be seen (6), suggesting an immunological influence.

Thanks to the new radiological techniques such as ultrasonography and computed tomography (CT) scan there has been an increase above 30% in early diagnosis, enabling the discovery of small lesions, with favorable prognosis and low incidence of metastasis (7).

Survival depends on the extension of the disease at diagnosis (8), but within well-defined prognosis factors such as tumor nuclear grade (9), size (10) and pathological stage (8,11-13).

With the objective of studying the behavior of incidental and symptomatic RCC, tumor nuclear grade, size and disease stage were evaluated in these two groups of patients.

MATERIALS AND METHODS

This is a retrospective non-controlled study of 128 patients submitted to renal surgery due to RCC

operated by the same group of surgeons from 1988 to 1999.

One hundred and fifteen patients were evaluated. The mean age was 59.1 years (9 - 87) and the median was 60 years; there were 86 males (75%), and 29 females (25%). They underwent complementary diagnostic exams to confirm the expansive renal lesion: ultrasonography, excretory urography, CT scan, magnetic nuclear resonance and arteriography.

Criteria for inclusion and exclusion: All 128 patients operated due to RCC had a complete file, and surgical pathological material and slides for revision were included. Thirteen patients were excluded and a total of 115 patients were enrolled. A single pathologist evaluated all specimens of nephrectomies.

Pathological analysis: Tumors were evaluated according to the following morphological and histological parameters: 1)- Tumor size: divided into 4 groups, according to sizes: 0.5 - 4 cm, 4.1 - 7 cm, 7.1 - 10 cm, and greater than 10 cm; 2)- Nuclear grade; 3)- TNM Stage (11).

Follow-up was carried out in the office, and 3 months after the last appointment, a telephone call was made to ask about the current status of the patient. In the postoperative follow-up, patients were seen every 3 months in the first year, twice a year

from the second to the fifth year and yearly after this period. Follow-up lasted 2 - 138 months (median: 30 months).

Patients were divided into 2 groups, incidental and symptomatic, according to the detection of the tumors (RCC).

Incidental group - Incidental finding: expansive renal lesion identified after radiological exams in routine health check-ups or complaints non-related to RCC.

Symptomatic group - Patients who had symptoms related to RCC.

The t-student test, chi-square test and confidence interval of 95% ($p \leq 0.05$) were used in the statistical analysis.

RESULTS

Among the 115 patients, 56 were symptomatic (49%) and 59 had an incidental diagnosis (51%). One hundred and fifteen renal surgeries were performed with 96 radical nephrectomies (84%) and 19 conservative renal surgeries (16%).

Among the symptomatic renal tumors, 55% were in the right side and 41% in the left side. There

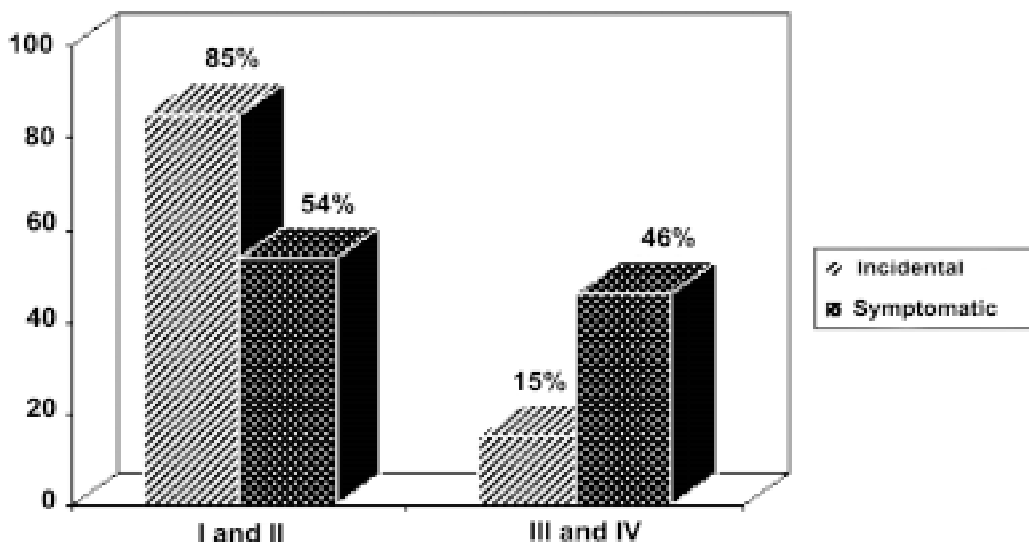


Figure 1 - Type of detection and nuclear grade jointly, $p < 0.001$

MORPHOLOGIC FEATURES OF INCIDENTAL RCC

Table 1- Type of detection and size of the tumor

Type of Detection	Tumor Size (cm)				Total
	0.5 - 4	4.1 - 7	7.1 - 10	> 10	
Incidental (%)	30 (51)	21 (36)	5 (8)	3 (5)	59 (100)
Symptomatic (%)	11 (20)	22 (39)	14 (25)	9 (16)	56 (100)
Total (%)	41 (36)	43 (37)	19 (17)	12 (10)	115 (100)

$\chi^2_{3df} = 16.02, p = 0.001$

were 2 patients with bilateral tumors (4%). Among the incidental renal tumors, 48% were in the right side, 50% in the left, and there was one patient with bilateral tumor (2%).

The predominant histological type was clear cells in 37 (63%) and 31 patients (55%), followed by papillary in 15 (25%) and 11 (20%), chromophobe in 6 (10%) and 6 (11%), and sarcomatous in 1 (2%) and 8 (14%) for the incidental and symptomatic groups, respectively (non significant).

As to the nuclear grade, there was predominance of low grade tumors in the incidental, and of

high grade in the symptomatic group, as shown in Figure-1 ($p < 0.001$).

As to the tumor size, they were divided into 4 groups (0.5 - 4 cm, 4.1 - 7 cm, 7.1 -10 cm, and > 10 cm) and in correlation to the detection mode (Table-1) ($p = 0.001$). Later they were divided into 2 groups: smaller and larger than 4 cm (Figure-2) ($p < 0.001$). The mean size (diameter) of the incidental tumors was 4.6 ± 2.3 cm (0.5 - 13), and of the symptomatic was 7.3 ± 3.6 cm (1.5 - 19.5) ($p = 0.001$).

The division by stage is shown in Table-2, with most of the incidental as PT1 (Figure-3) ($p < 0.001$).

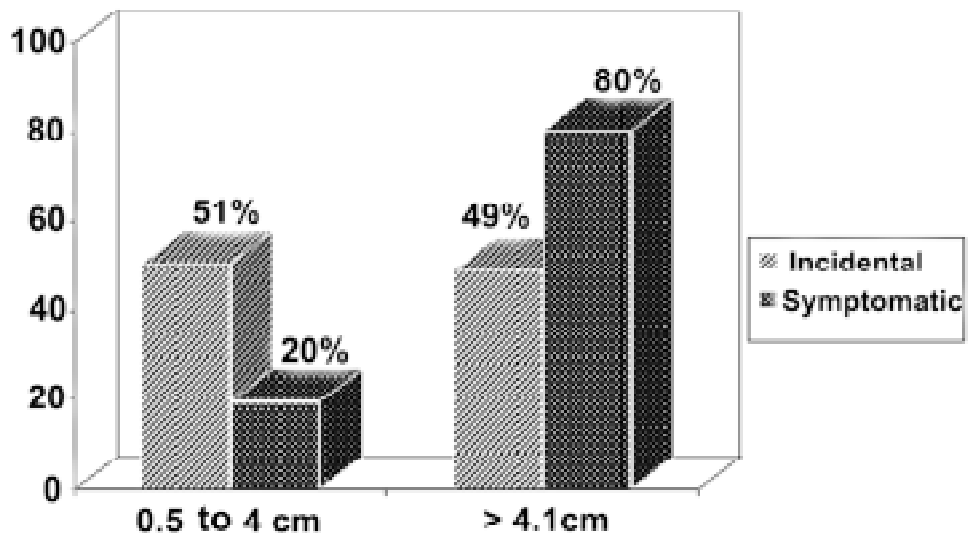


Figure 2 - Type of detection and tumor size

Table 2 - Type of detection and stage

Stage	Type of Detection		
	Incidental	Symptomatic	Total
T1 N0 M0	47	27	74
T2 N0 M0	5	11	16
T1 N1 M0	-	1	1
T3a N0 M0	7	2	9
T3b N0 M0	-	3	3
T3b N1 M0	-	1	1
T3a N2 M0	-	2	2
T3b N2 M0	-	1	1
T4 N0 M1	-	4	4
T4 N1 M1	-	1	1
T4 N2 M1	-	3	3
Total	59	56	115

DISCUSSION

The results of this study show that the incidental tumors have a better prognosis because they are smaller in size, have lower nuclear grade, and are in the initial stages of the disease. With the modern imaging exams, 9 - 38% of RCC is diagnosed when smaller than 3 cm (7).

The incidental group underwent conservative surgery in 24% of the cases, and the symptomatic in 9%. Obviously, this difference is justified by the smaller size of the incidental tumors. Conservative surgical techniques for RCC management became popular, with partial nephrectomies, enucleations, and even laparoscopic surgery.

It is believed that the nuclear grade is related to survival, independently from the pathological stage and it is a good prognosis indicator (8,9). This is true mainly in the case of clear and papillary cells, as the relationship is not the same in the case of chromophobe subtype (14). According to Fuhrman (9), the nuclear grade reflects the biological potential of the tumor before its clinical expression. In this series the incidental detection is associated to low nuclear grade tumors (I e II) in 50 patients (85%). Symptomatic tumors of high nuclear grade (III e IV) were seen in 26 patients (46%). These results show that the in-

cidental tumors had a low nuclear grade ($p < 0.001$) (Figure-1), as seen in the results of several other series (15-17). These data are very important, as they show clearly that incidental diagnosis and low grade tumors are directly associated.

In the symptomatic patients, larger tumors are found and with a worse prognosis, while the incidental detection offers a better prognosis because normally these are smaller tumors, easier to remove and thus the surgery has a greater potential of cure (7). Yet, the behavior of these lesions will depend on the histology and stage at the diagnosis (7,18).

On dividing the detection in incidental and symptomatic (Table-1), more than a half of the incidental tumors is less than 4 cm of diameter. On the other hand, about 80% of the symptomatic tumors have more than 4.1 cm.

In the present series, the mean tumor size in the incidental group was 4.6 ± 2.3 cm (0.5 - 13), and in the symptomatic group was 7.3 ± 3.6 cm (1.5 - 19.5) ($p = 0.001$). Several authors have shown that the incidental tumors are smaller than the symptomatic ones (16,19).

Herr (20) has shown that the mean size of incidental tumors before 1985 was 6.9 cm, and later was reduced to 3.5 cm thanks to the early detection provided by better imaging techniques. At the end of

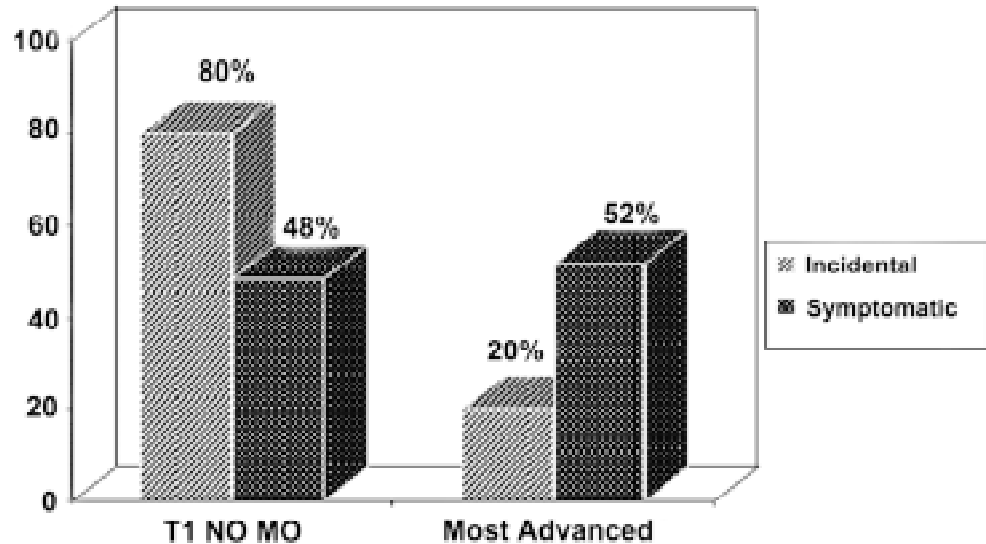


Figure 3 - Type of detection and stage.

this study none of the 33 patients with tumors equal or smaller than 4 cm had signs of recurrence of the disease, while from the 82 patients with tumors larger than 4 cm, 10 died (12%) and 6 (7%) had progression of the disease.

Bosniak et al. (15) defend observation management in selected cases of aged patients where the surgery is of high risk, without affecting the longevity. Due to the increase in life expectancy and to the low morbidity currently related to the surgery, this study suggests that the conservative management be employed only in selected cases. Also, although there are still doubts about the real malignancy potential of small renal tumors bellow 3 cm (21), there is a definite association of small tumors to metastasis (4,5,7). The disease progression is unusual when the tumor is limited to the kidney, with a 5-year survival of 82 - 95% (12,22).

The tumor stage is the most important prognostic factor of RCC (12). In this study, there are 80% tumors in stage T1 in the incidental group (Table-2). In the symptomatic group there were T2-4, 29 (52%), as shown in Figure-3 ($p < 0.001$). Several studies could show that the incidental tumors are detected in early stages (8,18,23).

Many authors have proposed changes in the TNM staging with cuts for T1 of 5 cm (24) and 5.5 cm (10), justifying the subdivision in T1 for a better selection of candidates to a conservative renal surgery. Javidan (13) believes that the TNM staging (1997) will allow a better classification of cases according to survival. Hafez et al. (25) suggest T1a for tumors smaller than 4 cm and T1b for those larger than 4 cm. This study considers that the ideal cut would be at 4 cm, as patients with tumors smaller than 4 cm might be dismissed from post-operative follow-up, if the criteria of good prognosis are confirmed. In this study the current TNM (1997) was used with 100% survival for the T1 during the period. For Javidan et al. (13), stage 1 had a 10-year survival in 95% of the incidental and 81% of the symptomatic patients. In the present study, the majority of incidental tumors are PT1, similar to the results of previous series (17,19). An important perspective is that the incidental diagnosis of RCC will provide greater chances of cure because the disease is localized.

The future proposals are new prospective and randomized studies to show the behavior of small incidental tumors and research of specific markers for RCC, both for screening and surveillance.

CONCLUSION

The incidental RCC have lower nuclear grade, smaller size and are in the initial stages of the disease, suggesting that only after reaching 4 cm in size do they start to show more aggressive pathological features.

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Correspondence address:

Dr. Marcos Francisco Dall'Oglio
 Rua Manoel da Nóbrega, 853 casa 22
 São Paulo, SP, 04001-084, Brazil
 E-mail: marcosdalloglio@uol.com.br

EDITORIAL COMMENT

It is evident that the 1997 version of TNM system is used for the classification of the tumors in this study. This version (1997) is so far the latest, but presumably not the last, as said by the authors.

This topic of morphologic features in RCC

is not very original, but still of importance and worth taking up. Renal cell cancer, even not being very frequent, is the most mortal of the urinary tract tumors, and modern imaging technology has enabled early detection, essential for therapeutic efficacy.

Dr. Lennart Andersson

*Division of Urology, Karolinska Institute
 Stockholm, Sweden*