

An anatomopathological profile of 324 nephrectomies performed on renal tumours: a cross-sectional study

Perfil anatomopatológico de 324 nefrectomias realizadas por tumores renais: um estudo transversal

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ABSTRACT

Introduction: Although kidney cancer is a relevant and relatively frequent pathology there is shortage of literature based on Brazilian data. **Objective:** To analyze a group of patients who had been submitted to nephrectomy by renal mass, taking into consideration the histopathological profile and the surgical approach used. **Methods:** Undertaken in a hospital in the Metropolitan Region of Belo Horizonte, Minas Gerais, Brazil, this cross-sectional, observational study utilises data taken from anatomopathological reports and analysis of surgery description of nephrectomies carried out on primary renal tumours between 2007 and 2018. **Results:** We analyzed 324 cases, 65.1% of male with an average age of 60.5±14.1 years. Partial nephrectomies (PN) were performed in 61.1% of the cases and there was a tendency to increase the incidence of this type of surgery over time ($p = 0.024$), in addition to an increase in PN laparoscopies ($p < 0.001$). The most frequent histological diagnoses were clear cell carcinomas (64.5%), followed by papillary renal cell carcinomas (11.8%) and chromophobic renal cell carcinomas (10.9%). Benign lesions were evident in 9.6% of cases, with an equal proportion of angiomyolipomas and oncocytomas. **Conclusion:** The findings of this study corroborate the data found in the international literature, whilst the increase in the number of PN and laparoscopic procedures follows a trend towards more conservative surgery and the use of minimally invasive techniques.

Keywords: Kidney neoplasms; Renal cell carcinoma; Nephrectomy; Laparoscopy.

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RESUMO

Introdução: O câncer renal, patologia relevante e relativamente frequente, tem pouca literatura baseada em dados brasileiros. **Objetivo:** Analisar um grupo de pacientes submetidos à nefrectomia por massas renais, quanto ao perfil histopatológico e a abordagem cirúrgica utilizada. **Métodos:** Trata-se de um estudo observacional transversal realizado em um hospital da Região Metropolitana de Belo Horizonte/MG, Brasil, utilizando dados de laudos anatomopatológicos e análise da descrição cirúrgica de nefrectomias por tumor primário renal, no período de 2007 a 2018. **Resultados:** Foram analisados 324 casos, sendo 65,1% de pacientes do sexo masculino, com idade média de 60,5±14,1 anos. As nefrectomias parciais (NP) foram realizadas em 61,1% dos casos e foi observada tendência de aumento da realização deste tipo de cirurgia ao longo do tempo ($p = 0,024$), além do aumento das NP laparoscópicas ($p < 0,001$). Os diagnósticos histológicos mais frequentes foram os carcinomas de células claras (64,5%), seguidos dos carcinomas de células renais (CCR) papilares (11,8%) e CCR cromóforos (10,9%). Achados de lesões benignas ocorreram em 9,6% dos casos, com proporção igual entre angiomiolipomas e oncocitomas. **Conclusão:** Os achados deste estudo corroboram os dados da literatura internacional. O aumento no número de NP e cirurgias laparoscópicas seguem uma tendência de realização de cirurgias mais conservadoras e utilização de técnicas minimamente invasivas.

Palavras-chave: Neoplasias renais; Carcinoma de células renais; Nefrectomias; Laparoscopia.

Ethics Committee:

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INTRODUCTION

Globally, renal cancer (RC) accounts for 5% of the cancers diagnosed in men and 3% of those diagnosed in women, with peak incidence occurring in patients between 60 and 70 years old¹. Nearly 15,000 deaths are forecast in the United States from renal cell carcinoma (RCC) in 2020². RC is more prevalent in western countries probably due to higher rates of obesity, smoking, high blood pressure and diabetes mellitus³.

Although a portion of the global epidemiological data does not differentiate between RCC and urothelial carcinoma, it is estimated that the latter represents only 10% of cases and manifests distinct characteristics^{2,4}. RCC is a complex entity that involves a heterogeneous group of tumours that emerge from the epithelial cells of the renal tubules⁵. This type of condition is classified according to histological, cytogenetic and histochemical findings and is associated with different patterns of prognosis, biological behaviour and therapeutic particularities⁶. According to the World Health Organization (WHO), clear renal cell carcinoma (CCCR), papillary renal cell carcinoma (PRCC) and chromophobic cell carcinoma (CRCC) are the most

frequent subtypes⁶. In addition to the histological type, other factors interfere with the prognosis and treatment of RCC, such as lesion size, nuclear grade, the presence of necrosis, angiolymphatic invasion, sarcomatoid differentiation and lymph node involvement⁷.

The gold standard and reference treatment for RCC is surgical removal by radical nephrectomy (RN) as described by Robson in 1969⁸. However, guidelines for the treatment of RCC have recommended the use of partial nephrectomy (PN) for kidney tumours less than 4cm⁹. Minimally invasive approaches such as laparoscopy and more recently robotic surgery have been gaining space, with a large number of publications showing greater benefits to patients than PN and RN^{10,11}.

The Brazilian literature lacks epidemiological data on RCC and studies that describe the national epidemiological profile are thus essential. The National Cancer Institute presents annual data on only the 10 most prevalent types of malignant tumours¹¹. The aim of this study is to describe the anatomopathological findings and the surgical techniques used to treat primary renal tumours performed in a private Brazilian hospital.

METHODS

Undertaken in a private hospital in the Metropolitan Region of Belo Horizonte, MG, Brazil, between January 2007 and December 2018, this is an observational cross-sectional study of nephrectomy involving primary renal tumours. All surgical parts were analyzed by the hospital's pathology service. Data was collected from anatomopathological reports and descriptions of the partial or total nephrectomy surgery performed.

All cases of nephrectomy recorded during the study period were initially included. Exclusion criteria were applied to cases manifesting inflammation, terminal hydronephrosis, urothelial tumours and those whose data on the type of surgery or age was incomplete, in addition to patients under 18 years of age.

The variables analyzed comprised gender, age, histological subtype, degree of tumour differentiation (when applicable) and stage of the lesion according to the classification of the American Joint Committee on Cancer¹². The findings of necrosis, peritumoral angiolymphatic invasion, invasion of Gerota's fascia and sarcomatoid differentiation were evaluated. The access routes (open or laparoscopic) and the surgical techniques employed - partial or total (PN or RN), were also analyzed according to the period.

This study project was approved by the Ethics Committee at *Faculdade Ciências Médicas de Minas Gerais* under the number 3.857.538, CAAE 91793618.5.0000.5134.

SAMPLE SIZE

The sample size was calculated to test the prevalence of partial nephrectomy during the study period. At a 5% significance level and minimum power of 80% and in order to test a minimum difference of 10% in relation to the prevalence of 50%, at least 197 individuals in the sample were needed.

DATA ANALYSIS

Qualitative variables were presented as absolute and relative frequencies. Quantitative variables were submitted to the Shapiro-Wilk normality test and presented as mean \pm standard deviation (median). To assess the association between qualitative variables, the chi-square test, Fisher's exact test and a binary logistic model were used. An analysis of variance yielded a comparison of the quantitative variables between three groups, whilst the Wilcoxon Mann-Whitney test was applied to two groups and the Mann Kendall test was used to assess the tendency. Analysis was performed using the free program R version 4.0.0 and $p < 0.05$ was considered statistically significant.

RESULTS

From January 2007 to December 2018, 452 nephrectomies were performed. Of this number, 26 were excluded due to urothelial tumours and 99 due to inflammatory processes or terminal hydronephrosis, as these

phenomena were not the focus of this study. One patient was underage and two possessed incomplete data.

The analysis was performed in 324 cases. There was a predominance of males (65.1%) and the average age of all sample was 60.5 ± 14.1 years. No significant difference was noted between genders in relation to the average age. The nuclear grade (Fuhrman) was assessed only for CCCR with grade III being the most prevalent (46.3%), followed by grade II (42.9%). Necrosis was observed in 56.9% of the cases, peritumoral angiolymphatic invasion in 8.5% and invasion of Gerota's fascia in 12.4%. Most tumours had a diameter of less than 7 cm, with 53.9% exhibiting a size smaller than 4cm (pT1a) (Table 1).

It was found 198 (61.1%) PN and 126 (38.9%) RN performed. The average annual number of PN was 16.5 ± 8.2 and RN 10.5 ± 1.8 ($p = 0.028$). Over the years covered there was a tendency to increase the realization of PN ($p = 0.024$) (Figure 1). An increase in laparoscopic surgery was also observed, with a significant increasing trend in PN ($p < 0.001$) to the detriment of open RN ($p < 0.001$) (Figure 2).

Comparing the findings between PN and RN, it was observed that patients undergoing RN were older ($p = 0.037$) and had higher percentages of nuclear grade 4 ($p = 0.017$), necrosis ($p < 0.001$), peritumoral angiolymphatic invasion ($p < 0.001$), invasion of Gerota's fascia ($p < 0.001$) and a pT2 diameter classification or greater ($p < 0.001$) (Table 1).

In the evaluation of histological types, the most common were CCCR (64.5%), PRCC (11.8%) and CRCC (10.9%) (Table 2). Benign tumours were found in 9.6% of cases. When comparing histological types, the patients with benign tumours (angiomyolipomas or oncocytomas) included a lower proportion of men ($p < 0.001$) and a higher proportion of laparoscopic surgery ($p = 0.013$). The distribution of age, type of surgery and diameter classification was similar between histological types (Table 3).

DISCUSSION

Globally, RCC is considered a serious condition and associated with a significant mortality rate and increasing incidence¹. The references to the biological and epidemiological behaviour of this tumour in Brazil have been based on studies characterised by low representativeness, but which allow comparison with the international literature. This cross-sectional study was conducted with data from 324 nephrectomies performed between 2007 and 2018 in a private hospital in Brazil.

From the epidemiological findings, it is known that the greatest risk factor for RCC is age, especially in the over fifties¹. In the present series, the average age was 60.6 ± 13.3 years for men and 60.3 ± 15.6 years for women, with no significant difference between genders. The highest prevalence of RCC was found in men, in the proportion of 1.86:1, a finding compatible with the literature¹³. The lower concentration of visceral fat and the adoption of better lifestyle habits are some of the explanations for the lower occurrence of RCC in women, which may suggest a

Table 1. Sample characterization of the nephrectomy reports associated with primary renal tumors collected from a private hospital in the Metropolitan Region of Belo Horizonte, MG-Brazil, between 2007 and 2018, and comparison according to the type of surgery performed (PN - partial nephrectomy, RN - radical nephrectomy).

Variables	Total (n=324)	PN (n=198)	RN (n=126)	p-value
Gender				0.113 ^C
Female	113 (34.9%)	63 (31.8%)	50 (39.7%)	
Male	211 (65.1%)	135 (68.2%)	76 (60.3%)	
Age (years)	60.5±14.1 (61)	59.1±13.9 (60)	62.6±14.3 (64)	0.037 ^W
18 to 44 years	45 (13.9%)	29 (14.6%)	16 (12.7%)	
45 to 64 years	150 (46.3%)	101 (51%)	49 (38.9%)	
65 years or more	129 (39.8%)	68 (34.3%)	61 (48.4%)	
Nuclear degree (only CCCR)*				0.017 ^L
1	5 (2.5%)	4 (3.3%)	1 (1.2%)	
2	87 (42.9%)	59 (48.8%)	28 (34.1%)	
3	94 (46.3%)	53 (43.8%)	41 (50%)	
4	17 (8.4%)	5 (4.1%)	12 (14.6%)	
Necrosis* (n=290)	165 (56.9%)	80 (46.5%)	85 (72%)	<0.001 ^C
Peritumoral angiolymphatic invasion *	25 (8.5%)	6 (3.5%)	19 (15.8%)	<0.001 ^C
Invasion of Gerota's fascia (n=291)	36 (12.4%)	6 (3.5%)	30 (25.4%)	<0.001 ^C
Sarcomatoid Differentiation	3 (0.9%)	2 (1%)	1 (0.8%)	1.000 ^F
Classification diameter* (n=321)				<0.001 ^C
pT1	17 (5.3%)	6 (3.1%)	11 (8.8%)	
pT1a	173 (53.9%)	143 (73%)	30 (24%)	
pT1b	62 (19.3%)	34 (17.3%)	28 (22.4%)	
≥pT2	69 (21.5%)	13 (6.6%)	56 (44.8%)	

CCCR = Carcinoma in clear renal cells; * Missing Data; ^C Chi-Square test; ^W Wilcoxon Mann-Whitney test; ^L Binary logistic model; ^F Fisher's exact test. Source: Research database.

promising field for the possible development of stratified therapeutic strategies between the genders¹⁴⁻¹⁶.

It is known that the clinical stage is the most important factor in the prognosis of RCC¹⁷. The universalizing of abdominal imaging exams has increased the diagnosis of renal mass each year¹⁸, thus allowing early tumour diagnosis. The findings of this study corroborate the tendency as the majority of the samples consisted of tumours at the pT1 stage which may permit the option of more conservative surgery.

Improved knowledge of tumour biology has started to allow PN to be performed with oncological results similar to radical surgery¹⁹. Such modalities have as their pillars the prevention of renal failure²⁰ and improvement in survival rates independent of the RCC²¹. The series presented shows an increasing trend in partial surgery, totalling 61.1% of the PN undertaken as a treatment option for RCC (Figure 1). Although its growing advocacy is widely corroborated in the literature, controversies still exist about the advantages attributed to PN in comparison to RN^{7,22}.

Minimally invasive surgical technologies such as laparoscopy and, more recently, robotic surgery have gradually become more accessible, allowing for shorter hospital stays and faster patient recovery²³. First noted in 1992, laparoscopic partial nephrectomy has today conquered a definitive space in surgery carried out on kidney tumours of up to 4cm²². In the present study, 2015 was a milestone in terms of the rise in nephrectomies performed laparoscopically (Figure 2). Thus, in providing guaranteed accessibility to these surgical modalities, the National Supplementary Health Agency has come to offer renal oncological surgery utilizing laparoscopic approaches²³.

Despite the limitations of the study, formatted from retrospective data in a single hospital using only report data and without access to medical record data, the histopathological findings are compatible with national and international publications. The most prevalent malignant histological subtype in this series was the CCCR (64.5%), which was comparable to another national study which produced a finding of 73.6%²⁴.

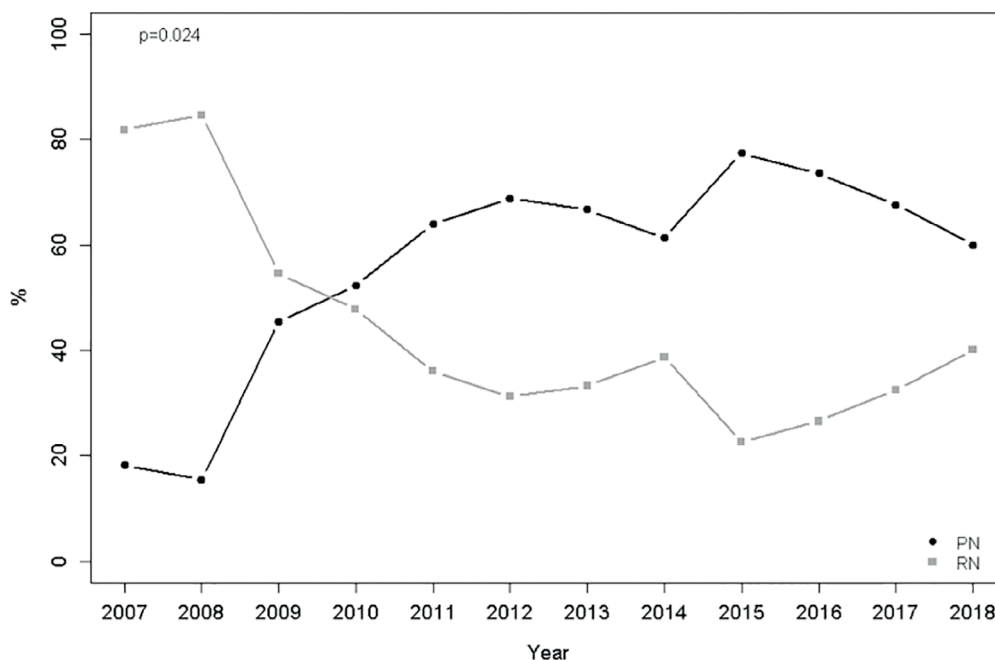


Figure 1. Distribution of the type of nephrectomy (RN - radical nephrectomy, PN - partial nephrectomy) by year. Sample data taken from nephrectomy reports of primary renal tumours, observed in a private hospital in the Metropolitan Region of Belo Horizonte, MG, Brazil, between 2007 and 2018. The p-value refers to the Mann Kendall test for trend ($\tau = 0.515$ for PN and $\tau = -0.515$ for RN). Source: Research database.

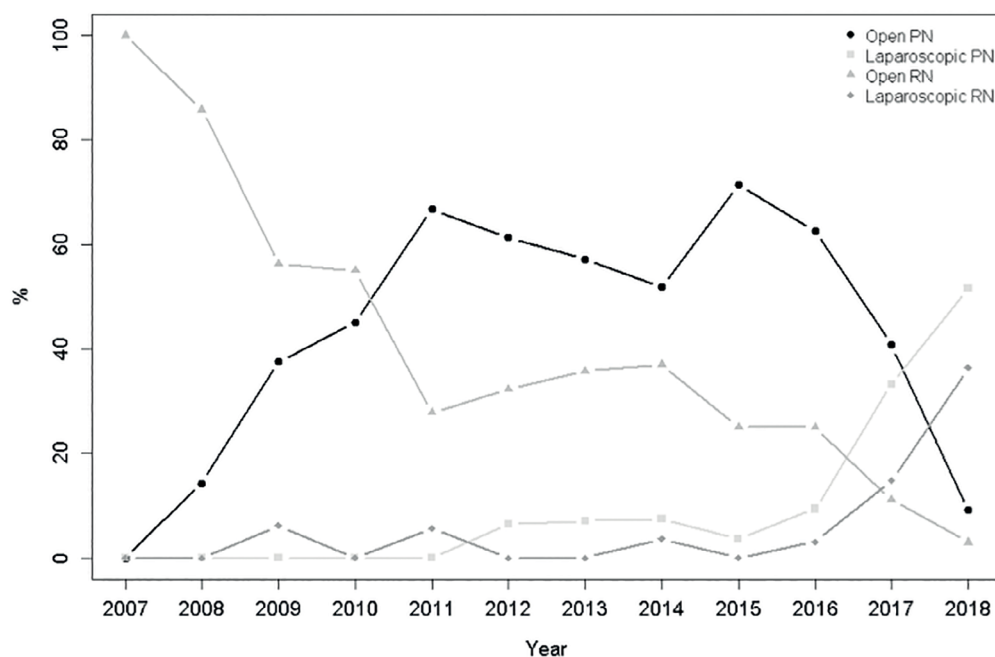


Figure 2. Distribution of types of nephrectomy and surgery format by year (n=269). Sample data taken from nephrectomy reports associated with primary renal tumours, observed in a private hospital in the Metropolitan Region of Belo Horizonte, MG, Brazil, between 2007 and 2018. The tendencies showing a significant Mann-Kendall test result were from the partial laparoscopic nephrectomies ($\tau = 0.822$, $p < 0.001$) and from the open radicals ($\tau = -0.809$, $p < 0.001$). Source: Research database.

Table 2. Description of the histological types of the sample taken from nephrectomy reports associated with primary renal tumours, observed in a private hospital in the Metropolitan Region of Belo Horizonte, MG-Brazil, between 2007 and 2018 (n=313).

Histological type	Statistics
Carcinoma in clear renal cells	202 (64.5%)
Type 1 papillary renal cell carcinoma	13 (4.1%)
Type 2 papillary renal cell carcinoma	24 (7.7%)
Chromophobic cell type renal cell carcinoma	34 (10.9%)
Oncocytoma	15 (4.8%)
Angiomyolipom	15 (4.8%)
Others	10 (3.2%)

Source: Research database.

Table 3. Description of the histological types of the sample in found nephrectomy reports associated with primary renal tumours, observed in a private hospital in the Metropolitan Region of Belo Horizonte, MG-Brazil, between 2007 and 2018 (n=303).

Characteristics	CCCR (n=202)	RCC cromophobic (n=34)	RCC papillary (n=37)	Benign* (n=30)	p-value
Gender					<0.001 ^C
Female	69 (34.2%)	8 (23.5%)	9 (24.3%)	20 (66.7%)	
Male	133 (65.8%)	26 (76.5%)	28 (75.7%)	10 (33.3%)	
Age (years)	61.51±13.68 (62)	60.56±13.72 (60.5)	58.65±14.86 (61)	58.30±15.98 (59)	0.508 ^A
18 to 44 years	24 (11.9%)	5 (14.7%)	5 (13.5%)	7 (23.3%)	
45 to 64 years	95 (47%)	14 (41.2%)	18 (48.6%)	13 (43.3%)	
≥ 65 years	83 (41.1%)	15 (44.1%)	14 (37.8%)	10 (33.3%)	
Surgery					0.552 ^C
PN	121 (59.9%)	20 (58.8%)	23 (62.2%)	22 (73.3%)	
RN	81 (40.1%)	14 (41.2%)	14 (37.8%)	8 (26.7%)	
Surgical approach**					0.013 ^C
Open	139 (82.2%)	22 (75.9%)	27 (84.4%)	13 (54.2%)	
Laparoscopic	30 (17.8%)	7 (24.1%)	5 (15.6%)	11 (45.8%)	
Diameter classification**					0.882 ^C
pT1	12 (5.9%)	3 (8.8%)	1 (2.7%)	-	
pT1a	108 (53.5%)	17 (50%)	19 (51.4%)	16 (59.3%)	
pT1b	41 (20.3%)	7 (20.6%)	7 (18.9%)	4 (14.8%)	
≥ pT2	41 (20.3%)	7 (20.6%)	10 (27%)	7 (25.9%)	

CCCR = Clear renal cell carcinoma; RCC = Renal cell carcinoma; PN = Partial nephrectomy; RN = Radical nephrectomy; *Benign: Angiomyolipomas and oncocytomas; **Variable processing missing data; C Chi-square test; A Variance analysis. Source: Research database.

In relation to this survey's most frequent histological subtypes and in agreement with the literature, the PRCC (11.8%) and CRCC (10.9%) percentages are presented. In a national series, Nardi et al. (2010)²⁴ found 6.5% and 9.1%, whilst Chow et al. (2010)⁴, in a review of databases taken from several countries, reported figures of 10.7% and 4.9% for PRCC and CRCC respectively. In general, these tumours have a better prognosis than CCCR, at least in non-metastatic diseases^{25,26}. In this series, there was no relevant difference between malignant histological subtypes in relation to the patient's age or gender. There was also no

significance in the association of these subtypes with the size of the lesions, in contrast to the literature that shows that the CRCC tend to be larger²⁷.

In 1992, Fuhrman et al.²⁷ proposed tumour classification based simultaneously on the analysis of shape, nuclear size and nucleolar prominence, correlating these findings to the outcome of the pathology. In the present study, there was a predominance of grade III in almost half of the cases. The identification of grade IV, more prevalent in radical surgery, suggests the presence of larger and more complex tumours. Currently, the classification of RCC is experiencing a

transition period, in which a more objective methodology, proposed by the International Society of Urologic Pathology (ISUP) and endorsed by the WHO, may gradually become adopted⁶. The presence of tumour necrosis, peritumoral angiolytic invasion and invasion of Gerota's fascia - all factors associated with a worse prognosis - were also more prevalent in RN⁷.

A further relevant factor is the discovery of angiomyolipomas and oncocytomas present in 9.6% of cases - with a higher prevalence in females - many of whom had their diagnosis confirmed only after surgery. Although there are recent questions in the literature about the need for prior renal biopsy²⁷, the surgical recommendation is still based on the radiological findings of the renal mass⁹.

CONCLUSION

The findings show that the anatomopathological profile of kidney tumours, identified in a Brazilian hospital, is compatible with international results. The PN performed using minimally invasive techniques seems to be gaining space in Brazil. However, the literature still lacks further studies conducted in national centres, mainly in relation to cohort and clinical trials. Enhanced knowledge about the national epidemiological situation may serve as a basis for the development of policies for the screening and treatment of RCC.

AUTHORS' CONTRIBUTION

Renato T. P. Mascarenhas – Conceptualization; Data curation; Investigation; Methodology; Original manuscript writing.

Daniel X. Lima – Conceptualization; Data curation; Investigation; Methodology; Original manuscript writing (edition and review).

Guilherme C. B. Oréfica – Data curation; Methodology.

Alberto J. A. Wainstein – Conceptualization; Investigation; Data curation; Methodology; Original manuscript writing (edition and review).

Isabel C.G. Moura – Conceptualization; Data curation; Formal analysis; Project administration; Supervision; Investigation; Methodology; Original manuscript writing (edition and review).

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