DOI: 10.4081/aiua.2022.2.129

ORIGINAL PAPER

Outcomes of nephrectomy for renal cell carcinoma: An ecologic retrospective study in a middle-income country

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Summary *Objective: The aim of this study was to describe and compare the outcomes and indirect costs of oncological radical (RN) and partial nephrectomies (PN) in hospitals from the São Paulo public health system, Brazil.*

Materials and methods: An ecologic retrospective study was performed from 2008 to 2019, using the TabNet Platform of the Brazilian Unified Health System Department of Informatics. Hospitals were classified according to volume of surgeries (low and high-volume, and also into four quartiles according to volume of surgeries), and with or without medical residency program in urology. The results were compared between groups.

Results: In the period analyzed were performed 2.606 RN in 16 hospitals. Data available for PN ranged only from 2013-2019 and included 1.223 surgeries comprising 15 hospitals.

Overall mortality rates were 0.41% for PN and 2.87% for RN. The length of hospital stay was significantly higher in low-volume hospitals for both RN and PN (8.97 vs. 5.62 days, p = 0.001, and 7.75 vs. 4.37 days, p = 0.001, respectively), and also for the RN in hospitals without residency program in Urology (9.37 vs. 6.54 days, p = 0.03). When the volume of surgeries was divided into four quartiles, the length of hospital stay and ICU hospitalization days were significantly higher in the first quartile hospitals for RN (p = 0.016) and PN (p = 0.009), respectively. The mortality rates and indirect costs were not different considering PN and RN in the different types of hospitals.

Conclusions: The length of hospital stay was significantly lower for both PN and RN in high-volume hospitals, and also for RN in hospitals with residency program in Urology.

KEY WORDS: *Nephrectomy; Renal cell carcinoma; Mortality rates; Teaching Hospital.*

Submitted 25 March 2022; Accepted 31 May 2022

INTRODUCTION

Renal cell carcinoma (RCC) derives from the renal cortex, comprising approximately 85% of all primary renal neoplasms. It mostly affects older adults, presenting between 50 years and 70 years along with known risk factors, such as smoking, obesity and hypertension. It represents 2-3% of all cancers, its incidence has been increasing worldwide, being 5.8 per 100.000, and it is the most lethal of common urological cancers, although the five-year survival rate has doubled over the last 60 years from 34% in 1954 to 75% between 2009 and 2015 (1-5).

These better outcomes in survival rate have been achieved because of the widespread use of cross-sectional imaging in recent years, leading to an increase in incidental detection (6, 7), that contribute to better prognostic factors and TNM staging, therefore leading to the best treatment approach (8).

The gold standard treatment is surgical management: *radical nephrectomy* (RN) and *partial nephrectomy* (PN).

RN can be performed open or laparoscopically (robot-assisted or not). PN has been widely used in the last few years because of improvements in surgical techniques, surgical apparatus and increased diagnosis of small RCC, and should be prioritized in the setting of solitary kidneys, bilateral renal tumors and advanced *chronic kidney disease* (CKD) (9, 10). Due to the preservation of renal function with PN, some studies suggest better overall survival in comparison with RN (11, 12). Although a randomized controlled trial (EORTC 30904) (13) did not confirm this finding for tumors < 5 cm.

Each of these procedures has specific complications which should be considered before the surgery is indicated. In terms of hemorrhage, urine leak/fistula and reoperation for complications, RN versus PN were 1.2% *vs.* 3.1%, 0% *vs.* 4.4%, and 2.4% *vs.* 4.4%, respectively (13). RN increases the risk for CKD (11, 14, 15) and has an increased cardiovascular-specific mortality in comparison with PN (12, 16).

From the 210 million Brazilian inhabitants, about 80% of patients rely on public health services, also known as *Sistema Único de Saude* (SUS) for medical treatment. *São Paulo* city has one of the largest populations worldwide, and in 2018, it had about 34 million medical appointments relying on SUS (17, 18). Hospitals of the public health system charge the procedures according to the codes and receive a predetermined fixed amount of reimbursement for each code.

We hypothesize that high volume centers with experienced staff and standardized protocols may provide lower morbidity and costs related to RCC treatment, hence providing a higher standard of care for such patients.

The outcomes of such investigation may lead to referral recommendations to concentrate procedures in such institutions. The aim of this study was to describe and compare the outcomes and costs of oncological radical and partial nephrectomies in the *Sao Paulo Public Health System, Brazil*, from 2008 to 2019, and to compare data

No conflict of interest declared.

among hospitals volume, and with or without medical residency program in urology.

Methods

An ecologic retrospective study was performed from 2008 to 2019 using the TabNet Platform of the *Department of Information Technology of the Brazilian public health system* (DATASUS). This database consists of an open data source, containing information about procedures performed in the Brazilian public health system (*Sistema Único de Saúde - SUS*), available at *https://datasus.saude.gov.br/*. Procedure codes used for this study were total nephrectomy in Oncology (code 0416010075) and Partial Nephrectomy in Oncology (code 0416010210).

The study was approved by the Research Ethics Committee of the "*Hospital Israelita Albert Einstein*" (approve code CAAE: 17208019.0.0000.0071 and date of approval 07/10/2019) and was performed in accordance with relevant guidelines and regulations.

Participants' informed consent is not applicable.

Outcomes analyzed included number of surgeries, mortality rate during hospital stay, length of hospital stay, length of *intensive care unit* (ICU) stay, and indirect costs. Since data related to cost for each hospitalization were not available, indirect cost was calculated as the total amount paid per year for each institution according to each procedure divided by the total number of hospitalizations related to the same procedure.

Hospitals were classified as low- and high-volume surgery centers, and were divided into two groups using a cut-off of 10 surgeries per year for PN (19) from 2013 to 2019, and 20 surgeries per year for RN (20) from 2008 to 2019, to consider it as a high-volume center. We also divided the hospital volume of surgeries in four quartiles according to the caseload per year. Besides, we classified the centers with and without a medical residency program in Urology. Comparisons were then made among groups.

Statistical analysis

Statistical analysis was performed using SPSS 13.0 (*SPSS for Mac OS X, SPSS, Inc., Chicago, IL, USA*). Data normality was verified using the Shapiro-Wilk test. The Mann-Whitney and Kruskal-Wallis tests were used to compare non-normal variables and T-test or ANOVA for variables with normal distribution. Proportions were analyzed using the chi-square test (mortality rate). Statistical significance was considered when $p < 0.05$.

Results

Table 1 summarizes data for overall RN and PN. A total of 2.606 RN were performed from 2008 to 2019. The procedures were performed in 16 institutions, of which seven (43.7%) presented medical residency program in Urology. Regarding the volume of surgeries, the low volume group consisted of 12 hospitals and the high volume group consisted of four hospitals. Overall mortality rate was 2.87%. Data available for PN ranged only from 2013 to 2019 and included 1.223 surgeries. The procedures were performed in 15 institutions, of which seven (46.7%) presented medical residency program in Urology. Considering the volume of surgeries, the low volume group consisted of 11 hospitals and the high volume group consisted of four hospitals. Overall mortality rate was 0.41%.

Table 2 summarizes the length of hospital stay, ICU hospitalization days, intrahospital mortality and indirect costs for RN and PN according to the volume of surgeries. The length of hospital stay was significantly higher in low-volume than in high-volume hospitals in both types of surgeries, PN and RN (7.75 days *vs.* 4.37 days, $p = 0.001$; and 8.97 days *vs.* 5.62 days, $p = 0.001$, respectively). The average ICU hospitalization days was also higher in low-volume hospitals; however, there was no statistical significance difference for both PN and RN (1.22 days *vs.* 0.77 days, $p = 0.142$; and 2.09 days *vs.*

Table 1.
Overall mean length of hospital stay, ICU hospitalization, intrahospital mortality and indirect costs of partial nephrectomy and radical nephrectomy between 2008 and 2019 in São Paulo.

Variables	Radical nephrectomies	Partial nephrectomies
Hospitals (n)	16	15
Total of surgeries (n)	2606	1223
Hospitals with Residency in Urology [a]	7 (43.7%)	7 (46.7%)
Hospitals volume (n)		
Low-volume	12	11
High-volume	4	4
Length of hospital stay [b] (days)	8.13 (2.78)	6.85 (5.93)
ICU hospitalization [b] (days)	1.87 (2.48)	1.09 (0.50)
Intrahospital mortality [b]	75 (2.87%)	5 (0.41%)
Indirect costs [b] (R$)	2614.17 (358.89)	28782.16 (52632.61)

[a] These variables are presented as total number and percentage (%). [b] These variables are presented as mean and standard deviation (SD). ICU: Intensive care unit. R$: Brazilian Real.

Table 2.
Length of hospital stay, intensive care unit hospitalization days, intrahospital mortality and indirect costs of partial nephrectomy and radical nephrectomy analyzed according to low- and high-volume hospitals from 2008 to 2019 in São Paulo.

Variables	Radical nephrectomy			Partial nephrectomy		
	Low-volume	High-volume	p-value	Low-volume	High-volume	P-value
Length of hospital staya (days)	8.97 (2.73)	5.62 (0.41)	0.001 [c]	7.75 (6.76)	4.37 (0.63)	0.001 [d]
ICU hospitalizationa (days)	2.09 (2.87)	1.22 (0.08)	0.808 [d]	1.22 (0.52)	0.77 (0.30)	0.142 [c]
Intrahopitalar mortalityb	27/931 (2.90%)	48/1675 (2.86%)	0.959 [e]	1/323 (0.3%)	4/900 (0.44%)	0.741 [e]
Indirect costsa (R$)	2612.08 (405.18)	2620.43 (204.89)	0.969 [c]	37970.19 (59357.94)	3515.08 (4715.69)	0.151 [d]

[a] These variables are presented as mean and standard deviation (SD). [b] This variable is presented as number/total of surgeries and percentage (%).
[c] T-test. [d] Mann-Whitney test. [e] Chi-square test. ICU: Intensive care unit, R$: Brazilian Real.

Table 3.
Length of hospital stay, Intensive care unit hospitalization days, intrahospital mortality and indirect costs of partial nephrectomy and radical nephrectomy according to hospitals volume (quartiles) from 2008 to 2019 in São Paulo.

Variables	Radical nephrectomy					Partial nephrectomy				
	Quartile				p-value	Quartile				P-value
	1	2	3	4		1	2	3	4	
Number of hospitals	4	4	4	4	---	4	3	4	4	---
Range of cases	1-16	17-107	136-218	248-788	---	1-7	8-42	50-59	79-506	---
Length of hospital stay [a] (days)	11.16 (2.11)	8.50 (3.02)	7.26 (1.76)	5.62 (0.41)	0.016 [c*]	7.55 (3.35)	10.49 (11.16)	5.15 (1.19)	4.37 (0.63)	0.570 [d]
ICU hospitalization [a] (days)	3.58 (4.98)	1.49 (0.80)	1.20 (0.49)	1.22 (0.08)	0.945 [d]	1.75 (0.35)	1.43 (0.34)	0.74 (0.32)	0.77 (0.30)	0.009 [c **]
Intrahopitalar mortality [b]	1/31 (0.032%)	4/191 (0.020%)	22/709 (0.031%)	48/1675 (0.028%)	0.900 [e]	0/13 (0%)	0/85 (0%)	1/225 (0.004%)	4/900 (0.004%)	0.930 [e]
Costs [a] (R$)	2843.95 (580.88)	2501.48 (194.45)	2490.81 (345.12)	2620.43 (204.89)	0.803 [c]	86293.02 (99667.48)	25543.88 (40322.65)	14154.38 (14106.48)	4715.69 (2357.84)	0.147 [d]

[a] These variables are presented as mean and standard deviation (SD). [b] This variable is presented as number/total of surgeries and percentage (%). [c] ANOVA test. [d] Kruskal wallis test. [e] Chi-square test. ICU: Intensive care unit. R$: Brazilian Real. [*] Post hoc analysis showed difference between hospitals in the first quartile and fourth quartile (p = 0.015). [**] Post hoc analysis showed difference among hospital in the first quartile and third (p = 0.032) and fourth (p = 0.039) quartile.

1.22 days, p = 0.808, respectively). Mortality rates were similar for both low- and high-volume hospitals. When considering PN, there was one death out of 323 surgeries performed in low-volume hospitals and four deaths out of 900 surgeries performed in high-volume hospitals (0.3% mortality rate *vs.* 0.44% mortality rate, p = 0.741). This can also be observed in RN, with 27 deaths out of 931 surgeries performed in low-volume hospitals and 48 deaths out of 1675 surgeries performed in high-volume hospitals (2.9% mortality rate *vs.* 2.86% mortality rate, p = 0.959). Indirect costs were higher in low-volume hospitals when considering PN, with an average of R$ 37970.19 per patient when compared to high-volume hospitals, which had an average of R$ 3,515.08 per patient. However, this difference was not statistically significant (p = 0.151). In the RN group, average indirect costs were very similar between low- and high-volume hospitals (R$ 2,612.08 *vs.* R$ 2,620.43; p = 0.969).

Table 3 summarizes the length of hospital stay, ICU hospitalization days, intrahospital mortality and indirect costs for RN and PN according to the volume of surgeries divided into four quartiles. The length of hospital stay was also significantly different considering RN: in the first quartile hospitals was observed a higher length of hospital stay compared to fourth quartile hospitals (p = 0.015). No difference was observed regarding PN.

The ICU hospitalization days were higher in the first quartile hospitals; however, there was no statistical difference considering RN.

Regarding PN, hospitals in the first quartile presented statistically higher ICU hospitalization days when compared to hospitals in the third (p = 0.032) and fourth (p = 0.039) quartiles. Mortality rates were not different among quartiles for both PN and RN. Indirect costs were higher in first quartile hospitals for both PN and RN, however, no statistical difference was observed among the quartiles.

Table 4 summarizes the length of hospital stay, ICU hospitalization days, intrahospital mortality and indirect costs for RN and PN according to the hospitals with and without medical residency program in Urology. A total of 2.232 RN were performed in hospitals with medical residency program in Urology (85.6%) and 374 (14.4%) in hospitals without medical residency program in Urology. Regarding RN, the length of hospital stay was significantly shorter in hospitals with medical residency in Urology (6.54 days *vs.* 9.37 days; p = 0.03). Considering PN, none of the outcomes were statistically difference between hospitals with and without medical residency program in Urology, although indirect costs were 4.5 times higher in hospital without medical residency program in *Urology* (R$ 45298.93 *vs.* R$ 9905.85; p = 0.205).

Table 4.
Length of hospital stay, intensive care unit hospitalization days, intrahospital mortality and indirect costs of partial and radical nephrectomies performed in hospital with and without medical residency program in Urology from 2008 to 2019 in São Paulo.

Variables	Radical nephrectomy			Partial nephrectomy		
	With residency in Urology	Without residence in Urology	p-value	With residency in Urology	Without residence in Urology	P-value
Length of hospital stay [a] (days)	6.54 (1.56)	9.37 (2.95)	0.03 [c]	5.26 (1.08)	8.24 (8.03)	0.350 [d]
ICU hospitalization [a] (days)	1.24 (0.34)	2.36 (3.30)	0.390 [d]	0.87 (0.30)	1.31 (0.58)	0.099 [c]
Intrahopitalar mortality [b]	67/2232 (3.00%)	8/374 (2.13%)	0.357 [e]	4/979 (0.40%)	1/244 (0.40%)	1 [e]
Indirect costs [a] (R$)	2536.48 (287.62)	2674.59 (412.39)	0.464 [d]	9905.85 (11713.02)	45298.93 (68954.31)	0.205 [d]

[a] These variables are presented as mean and standard deviation (SD). [b] This variable is presented as number/total of surgeries and percentage (%). [c] T-test. [d] Mann-Whitney test. [e] Chi-square test. ICU: Intensive care unit. R$: Brazilian Real.

Discussion

In this study, we described and compared the outcomes and indirect costs of RN and PN in the *Sao Paulo Public Health System, Brazil,* from 2008 to 2019, and compared data considering the hospitals volume of surgeries, and with or without medical residency program in urology.

From the perspective of the Brazilian public healthcare system, our findings showed that, both for RN and PN, length of hospital stay was significantly lower in high-volume hospitals, while indirect costs and ICU stay also trended favorably for high-volume hospitals, although no statistical difference was found between low- and high-volume hospitals.

The volume of surgeries divided into four quartiles disclosed that for RN, in the first quartile hospi-

tals was observed a higher length of hospital stay compared to fourth quartile hospitals, whereas the mean ICU hospitalization days were higher in the first quartile hospitals when compared to hospitals in the third and fourth quartiles for PN. Mortality rates and indirect costs were not different among quartiles for both PN and RN. Regarding the hospitals with and without medical residency program in Urology, the length of hospital stay was significantly lower in hospitals with residency program in Urology for RN. These data underscore the importance of concentrating complex procedures in specialized centers, so as to pursue optimized results.

RN and, especially PN, are procedures that have a significant learning curve. The competence acquisition results in a composite outcome including a combination of operative time, complications, and surgical success. In 2004, *Gaston et al.* (21) demonstrated the learning curve of residents for hand-assisted laparoscopic nephrectomy, according to difficulty scores and procedure duration, stabilized after the 6th nephrectomy. On the other hand, *Rouach et al.* (22) demonstrated that at least 10 partial nephrectomies are necessary to gain domain regarding the steps of the surgery. When performed by more experienced doctors, the length of surgery and outcomes may be optimized. *Baez-Suarez et al.* (23) demonstrated that a cutoff of 50 nephrectomies performed by the same surgeon decreased perioperative outcomes, including hospital stay length.

This might explain why our analysis demonstrated no statistical difference in the length of stay when comparing PN in hospitals with and without medical residency program in Urology, but there was a significantly lower length of stay when comparing RN in these groups of hospitals.

Following RN and PN, specific care needs to be taken in the postoperative setting. Therefore, it is expected that hospitals with a greater volume of procedures already have postoperative protocols established with ICUs and wards, favoring a rapid discharge from hospitals.

This may also explain why the length of stay was significantly lower for both RN and PN in high-volume than in low-volume hospitals. *Gozen et al.* (24) observed that the learning curve for retroperitoneal laparoscopic radical nephrectomy was shorter for the surgeons who had no or limited experience in open surgery, and that were trained by surgeons who had previous experience in open surgery but no laparoscopic training, although these surgeons operated on a significantly higher number of patients with more advanced diseases.

Recently, *Spampinato et al.* (25) concluded that assuming an adequate case volume and a proper exposure to surgical techniques, junior surgeons can readily achieve comparable levels of expertise compared with senior practitioners, and urological surgical outcomes is not only directly influenced by the individual surgical experience but also by the experience of the surgical team.

A possible explanation for the longer hospital stay in patients undergoing RN (8.13 days) when compared to those for PN (6.85 days), found in our analysis may be that patients submitted for RN hypothetically had larger tumor volumes, were more fragile and required longer/larger surgeries, leading to an important metabolic and inflammatory response. These patients also had a longer ICU length of stay (1.87 days *vs.* 1.09 days for RN and PN, respectively) and higher intrahospital mortality rates (2.87% *vs.* 0.41% for RN and PN, respectively), probably for the same reasons as hypothesized above.

PN is known to be a more complex surgery, in most cases, when compared to RN. To perform PN, there is a need for a wide range of materials available in the operating room, especially if performed laparoscopically.

This includes, among others, disposable polymer clips, laparoscopic bulldogs, absorbable sutures and eventually hemostatic agents. For this reason, an increase in costs is expected for the health system when PNs are performed. This was visible in our analysis, where the average cost of hospitalization for PN was R$ 28,782.16 compared to R$ 2,614.17 for RN hospitalization. There was no statistical difference in costs when comparing hospital volume and with or without medical residency in Urology, but this may be explained by the fact that *Brazilian Health System* (SUS) reimburse the same value to every hospital for each procedure, and the individual cost for each patient is not accounted for. Values of total hospitalization may vary if the patient has been submitted for different procedures during the same hospitalization, and this is one of the limitations of the analysis of costs presented here.

Considering the available details, a discussion can be commenced regarding the possibility of referring patients for the treatment of RCC to high-volume centers with the objective of shortening the length of hospital stay by focusing on a higher bed turnover; a scenario in which elective surgeries are sometimes cancelled due to the lack of hospital beds. The centralization of the treatment of RCC could be made the part of a public health policy to establish RCC-treatment reference hospitals and improve RCC surgical outcomes.

Per the data, it is noted that one single institution inflated the values paid (reimbursements) for partial nephrectomies in hospital without medical residency in Urology and in low-volume hospital groups. This institution is a hospital specializing in the treatment of pediatric urological pathologies and received R$ 401,162.11 for performing two PN in the period analyzed. There is no plausible explanation for this amount due to limitations of publicly available data.

This study also has other limitations. The data available in the online health system database considers only the details of one single hospitalization per patient, so mortality data and costs involving following hospitalizations after discharges are not considered in this study. The costs are indirect costs represented by modality of reimbursement of Brazilian health system. For an appropriate comparison of costs, it should be necessary to estimate direct costs in each hospital considering cost for personnel, disposables, time of use of operatory theatre and hospitalization. What can be stated is that *National Health Service* does not reimburse higher fares to high-volume hospitals. Moreover, the data were restricted to inform only the major types of surgery performed, and details such as time of procedure, patient age, specific complications and technique (open or laparoscopic) were not available. Also, the data were collected from a secondary source that is fueled by health professionals, who often do not fill out the forms correctly, therefore interfering in statistical analysis and results. In addition, our findings may not be representative of the entire

Brazilian population, since we analyzed data only from the *São Paulo* city, although this is the most populous city in the country. A final limitation is that hospitals with residency are the hospitals with the higher number of beds, so it is difficult to establish if better outcome is related to residency program or to high-volume.

Conclusions

In summary, the length of hospital stay was significantly lower for patients who underwent PN and RN in high-volume hospitals, and also in hospitals with medical residency in Urology for RN.

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