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Renal Function in Patients Undergoing Nephrectomies for Benign and Malignant Causes: An Expected Outcome

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Abstract

Objective: to assess the evolution of serum creatinine in patients undergoing radical nephrectomy (malignant) or total (benign), to identify risk factors connected with an unfavorable renal function outcome. **Material and Methods:** observational, transversal and retrospective study, through analysis of records and lab exams of 146 patients undergoing nephrectomy from January 2015 to December 2018. **Results:** Statistically significant difference was found between etiology and patients' age (p-value < 0.001). Mean age of patients with malignant etiology (59.4 years) was significantly higher than the mean age of patients with benign etiology (47.3 years). As for the surgical technique, 49 had video-laparoscopic (VLP) nephrectomy. The main causes of nephrectomy were renal cancer (52%) and lithiasis (35.6%). Most patients had a fairly uneventful postoperative course (65%). There was a statistically significant difference between etiology and creatinine levels, with a significantly lower creatinine median in the patients with malignant etiology as compared to benign etiology in the preoperative period. **Conclusion:** This study shows that a large number of young patients undergo nephrectomy, many times avoidable; within a benign disease context with an increased risk of developing renal failure. Greater attention from the public service is required to tackle such chronic condition and its complications.

Keywords

Nephrectomy, Kidney Function, Chronic Kidney Disease, Health Plans and Programs

1. Introduction

Nephrectomy is indicated, mainly, within the benign diseases context, such as

non-functional kidney, urinary stones, infection and trauma (total or simple nephrectomy) [1] and malignant ones, in the cases of large tumors (radical nephrectomy) [1] [2]. The procedure, regardless of etiology, is associated with adverse perioperative and long term events.

Acute renal injury is a frequent complication following nephrectomy that may lead to the development of chronic renal disease (CRD) and further comorbidities [3] [4]. Strict follow-up of such patients is strongly recommended [5] [6].

In the literature, it is quite clear that preoperative renal dysfunction, old age, male gender and associated morbidities (DM, SAH, obesity) are a few of the risk factors connected with the occurrence of CRD following nephrectomy [1] [3] [7]. However, scarce is the data comparing whether the type of nephrectomy (radical vs. total) is associated with the development of CRD and related morbidity.

The total nephrectomy has been performed in younger patients within a chronic disease context and it may be considered a public health issue [8]. Formation of lithiasis occurs through a multifactorial and complex process, often leading to higher kidney function rates and comorbidities as compared to patients with renal tumors.

Based on analysis of patient records in a public service in the state of São Paulo, the aim of this paper was to assess the evolution of serum creatinine in patients undergoing radical or total nephrectomy, also identifying the factors connected with an unfavorable kidney function outcome.

2. Material and Methods

This is an observational, transversal and retrospective study that analyses the records and lab tests of patients undergoing radical or total unilateral nephrectomy from January 2015 through December 2018 approved by Institutional Review Board of the Santa Marcelina Hospital under number 1.014.385. The study included patients aged over 14 years, regardless of gender or ethnic, undergoing total or radical nephrectomy by an open or video-laparoscopic surgical approach.

The study data were captured through the electronic surgical records system, starting from the surgery name "nephrectomy—total and radical", thus informing the date of the procedure and the name of all patients who had had the surgery for later analysis of the entire record, collecting: age, cause of surgery, comorbidities and vices. Also analyzed were urea and creatinine serum lab tests: preoperative, immediate surgical postoperative, recent (3 months following surgery) and late (1 year after surgery). Information on the tumor size, surgical technique (video-laparoscopic or open) and postoperative complications (Clavien-Dindo) was also collected.

Patients with previous terminal renal failure, patients undergoing a living donor procedure for transplantation or partial nephrectomy were excluded. Those who missed outpatient follow-up during the first year after surgery were ex-

cluded as well.

The data analysis process began with a descriptive exploration of databases, including the distribution of variables frequencies and calculation of parameters as mean, standard deviation, median and interquartile range.

For comparison of etiology groups (benign and malignant), the Qui-square test or Fisher's exact test was used for qualitative variables; and T tests or Mann-Whitney test for quantitative variables. For comparison between the levels of urea and creatinine measured at different moments, within each group, Friedman's test was used, having Wilcoxon's test with Bonferroni's correction as *post hoc*.

As computer support we used IBM SPSS 26 (IBM corp., 2019) and Microsoft Excel 365® Software. All tests carried out took into consideration a two-tailed 0.05 α significance and a 95% confidence interval (CI).

3. Results

One hundred and forty-six (146) patients were assessed, irrespective of gender or ethnics, with average age of 59.4 ± 11.5 years for patients with a malignant disease and of 47.3 ± 14.1 for those with a benign disease (Table 1). Among the patients, approximately 51% were hypertensive, 25% diabetic, 10% had some degree of chronic renal failure, 21% smokers and 2% with a previous AMI (Table 2).

Table 1. Presentation of the study variables comprising the quantitative descriptive analysis of patients and nephrectomy surgeries performed.

Variables		Etiology			
		Benign		Malignant	
		Mean (±DP)	Median (P25 - P75)	Mean (±DP)	Median (P25 - P75)
Patient age* (years)		47.3 (±14)	48 (36 - 53)	59.4 (±11)	61 (53 - 67)
Urea	**Pre**	45 (±33)	31 (26 - 56)	37 (±17)	32 (26 - 42)
	POI	51 (±39)	36 (26 - 53)	47(±23)	45 (33 - 54)
	POT	54 (±40)	37 (30 - 57)	49.6 (±23)	44 (33 - 61)
	1 year	54 (±41)	41 (31 - 62)	49.7 (±26)	42 (35 - 56)
Creatinine	**Pre****	2.2 (±3.2)	1.07 (0.9 - 2)	1.15 (±0.9)	0.98 (0.7 - 1.3)
	POI	2.5 (±3.2)	1.2 (0.98 - 2)	1.6 (±0.94)	1.45 (1 - 1.9)
	POT	2.4 (±3.2)	1.16 (0.9 - 1.8)	1.5 (±0.9)	1.35 (1.07 - 1.6)
	1 year	2.3 (±2.8)	1.2 (0.9 - 1.9)	1.5 (±1.4)	1.22 (1 - 1.6)
Hospitalization (days)		4.8 (±6.7)	3 (3 - 4)	4 (±1.9)	3 (3 - 4)
Cancer Size		-	-	7.54 (±4)	7 (4.7 - 1)

*p-value < 0.001; **p-value = 0.1.

Table 2. Distribution of the study variables frequency, comprising qualitative descriptive analysis of patients and nephrectomy surgeries performed.

Variables	Etiology				Total (n = 146)	
	Benign (n = 69)		Malignant (n = 77)			
	N	%	n	%	n	%
Surgery						
Open	40	66.7	34	44.2	74	50.7
VLP	29	33.3	43	55.8	72	49.3
Laterality						
Right	27	39.13	38	49.35	65	44.52
Left	42	60.87	39	50.65	81	55.48
VLP Approach						
Retro	3	10.34	3	6.98	6	8.33
Trans	26	89.66	40	93.02	66	91.67
Cause						
Angiomyolipoma	1	1.45	-	-	1	0.68
Endometrioma	1	1.45	-	-	1	0.68
UPJ Stenosis	6	8.70	-	-	6	4.11
Lithiasis	52	75.36	-	-	52	35.62
Pyelonephritis	1	1.45	-	-	1	0.68
Vesicoureteral Reflux	1	1.45	-	-	1	0.68
Polycystic Kidney	4	5.80	-	-	4	2.74
Tuberculosis	1	1.45	-	-	1	0.68
Other	2	2.90	-	-	2	1.37
Renal cancer	-	-	76	98.70	76	52.05
Retroperitoneal Tumor	-	-	1	1.30	1	0.68
Age (years)						
20 - 30	8	11.59	1	1.30	9	6.16
31 - 40	17	24.64	5	6.49	22	15.07
41 - 50	19	27.54	10	12.99	29	19.86
51 - 60	11	15.94	22	28.57	33	22.60
61 - 70	10	14.49	28	36.36	38	26.03
71 - 80	3	4.35	10	12.99	13	8.90
>80	1	1.45	1	1.30	2	1.37
Comorbidities						
SAH	29	42.03	45	58.44	74	50.68
	40	57.97	32	41.56	72	49.32

Continued

DM	11	15.94	26	33.77	37	25.34
	58	84.06	51	66.23	109	74.66
CRD	11	15.94	4	5.19	15	10.27
	58	84.06	73	94.81	131	89.73
Smoking	9	13.04	22	28.57	31	21.23
	60	86.96	55	71.43	115	78.77
AMI	1	1.45	2	2.60	3	2.05
	68	98.55	75	97.40	143	97.95
Clavien-Dindo						
0	46	66.67	49	63.64	95	65.07
I	10	14.49	18	23.38	28	19.18
II	4	5.80	6	7.79	10	6.85
IIIa	1	1.45	0	0.00	1	0.68
IIIb	4	5.80	2	2.60	6	4.11
IVa	2	2.90	2	2.60	4	2.74
IVb	1	1.45	0	0.00	1	0.68
V	1	1.45	0	0.00	1	0.68

In regard to the surgical technique, about 49% had undergone video-laparoscopic nephrectomy, mostly through a transabdominal approach (91.7%), and 50.7% through an open approach. The left side was the main side approached in 44.5% of the patients. When analyzing the main etiologies, the main causes of nephrectomy were renal cancer (52%) and lithiasis (35.6%), the latter being the principal cause among the benign diseases (Table 2).

Most patients had no complications that would change the normal postoperative course (65%), and as few as 13 patients (8.9%) had severe complications (Clavien-Dindo III-IV), with death as adverse outcome for just one patient who underwent total open nephrectomy for a benign disease (Table 2).

A statistically significant difference was found between etiology and patient's age (p-value < 0.001). Mean age of patients with a malignant etiology (59.4 years and 95% CI [56.79 - 62.02]) is significantly higher than the mean age of patients with benign etiology (47.3 years and 95% CI [43.93 - 50.71]) (Table 1).

There was no statistically significant difference between etiology and urea levels, at any of the moments measured (Pre: p-value = 0.508; POI: p-value = 0.111; POT: p-value = 0.198; 1 year: p-value = 0.616). However, when each group was separately compared, in the benign etiology group, the median for urea levels at pre moment was significantly lower than at the "1 year" moment. Whereas in the malignant etiology group, the median for urea levels at pre moment was significantly lower as compared to POI, POT and 1 year (Table 3).

A statistically significant difference was found between etiology and creatinine

Table 3. Statistical analysis by groups separately, to verify the difference between urea and creatinine levels among the moments measured.

		Etiology	
		Benign	**Malignant**
		p-value	**p-value**
Urea	Pre × POI	0.187	<0.001*
	Pre × POT	0.010	<0.001*
	Pre × 1 year	0.001*	<0.001*
	POI × POT	0.073	0.039
	POI × 1 year	0.066	0.753
	POT × 1 year	0.474	0.502
Creatinine	Pre × POI	**0.002***	<0.001*
	Pre × POT	**0.172**	<0.001*
	Pre × 1 year	**0.031**	<0.001*
	POI × POT	**0.165**	0.032
	POI × 1 year	**0.300**	<0.001*
	POT × 1 year	**0.287**	0.013

*p-value considered significant by Bonferroni's correction (<0.008).

Table 4. Distribution of comorbidities according to the etiologic group (benign vs. malignant).

		Etiology – n (%)		Total (100%)
		Benign	**Malignant**	
SAH	**No**	40 (55.6)	32 (44.4)	72
	Yes	29 (39.2)	45 (60.8)	74
DM*	**No**	58 (53.2)	51 (46.8)	109
	Yes	11 (29.7)	26 (70.3)	37
CRD	**No**	58 (44.3)	73 (55.7)	131
	Yes	11 (73.3)	4 (26.7)	15
Smoking**	**No**	60 (52.2)	55 (47.8)	115
	Yes	9 (29)	22 (71)	31
AMI	**No**	68 (47.6)	75 (52.4)	143
	Yes	1 (33.3)	2 (66.7)	3

*p-value = 0.021. **p-value = 0.026.

levels at Pre moment; *i.e.*, at Pre moment, the median for the creatinine levels in the patients with a malignant etiology is significantly lower than creatinine levels median in the patients of benign etiology (Table 1).

In the analysis of groups individually, we noticed that in the benign etiology

group, the median for creatinine levels at Pre moment was significantly lower as compared to POI moment. Whereas in the malignant etiology group, the median for creatinine levels at Pre moment was significantly lower as compared to moments POI, POT and 1 year (Table 3).

When combining the etiologic groups (benign vs. malignant) and the comorbidities, a statistically significant difference was found only in regard to Diabetes Mellitus and smoking. The proportion of patients with DM of malignant etiology (70%) is significantly higher than the proportion of patients with DM of benign etiology (29.7%). And the proportion of smoking patients with malignant etiology (71%) is significantly higher than the proportion of smoking patients with benign etiology (29%) (Table 4).

4. Discussion

Our study showed mean age of patients with malignant etiology (59.4 years) and benign etiology (47.3 years) patients with a malignant etiology is significantly lower than creatinine levels median in the patients of benign etiology.

Most studies compare nephrectomy for renal tumor (radical) and nephrectomy in renal donors. However, this study carries an analysis between nephrectomies for malignant and benign causes, assessing evolution of the renal function and associated factors.

In this study, it is noticed that patients undergoing unilateral nephrectomy, irrespective of etiology, present higher levels of serum creatinine in the immediate postoperative period as compared to preoperative values. Such information, matches Garofalo *et al*. [4] findings, showing almost 50% of patients developing to acute renal injury in the immediate postoperative period, usually associated with aggravation of progressive renal function.

Development of CRD following a curative renal surgery is known to be associated with an increased risk of cardiovascular events, hospitalization and death [3] [4]. Regardless of the etiology, any loss of nephrons involves a risk of renal dysfunction [9]. In the literature, it is pointed that about 40% of patients undergoing unilateral nephrectomy will develop a progressive chronic renal disease, the main reason being adaptation of the contralateral kidney with hyperfiltration and hyperplasia of the nephrons, known as compensatory renal hypertrophy. At first and to a certain extension, this process keeps the glomerular filtration rate (GFR) stable, however causing structural changes such as glomerulosclerosis and tubular atrophy, evolving to an increased loss of nephrons and permanent renal injury [1] [4].

Lithiasis disease is the most common cause among the benign diseases that require nephrectomy secondary to the development of complications, 75% of cases as shown in our study. Chronic pain, recurrent urinary infections and hypertension are counted among indications for nephrectomy in such patients [10] [11] [12] [13].

Despite the benign character, nephrectomy for urolithiasis, especially through

the laparoscopic approach, is most likely said to be more challenging than radical nephrectomies, on account of intense inflammatory reaction, demanding procedures that are time consuming, complex, and of greater surgical trauma. Many times, the need for conversion to an open surgery is unavoidable [11]. In this study, we demonstrate the viability of a laparoscopic procedure in approximately half the cases connected with benign diseases, with a favorable outcome in all cases through such technique. We had but one death, precisely of a patient who underwent total open nephrectomy, within a benign disease context, evidencing all the technical difficulty in such cases.

The paper has a few limitations, such as retrospective analysis based on patients treated in a single referential center, and a small sample size. A further limitation is connected with underestimation of the glomerular filtration rate as mathematical formulae are not used to better assess the renal function, taking into account other parameters, besides serum creatinine.

In this series, the mean age was significantly smaller in the patients undergoing nephrectomy for benign disease (47.3 ± 14), as compared to a malignant one (59.4 ± 11), with an increased risk, along the time, of developing to a chronic renal disease, even requiring a renal substitution therapy (dialysis or renal transplantation). Such condition can be considered a public health issue to be tackled, due to the significantly higher government costs for patients with a chronic renal disease. Implementation of policies focusing on health promotion is important, as well as tracking risk factors at the primary care level, emphasizing prevention and early treatment.

5. Conclusion

This study shows that a large number of young patients undergo nephrectomy within a benign disease context, many times avoidable, with an increased risk of evolving to renal failure. More attention to the public service is important to tackle this chronic condition and its complications.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

DM = Diabetes mellitus
SAH = systemic arterial hypertension
AMI = acute myocardium infarct
Pre = preoperative
POI = immediate postoperative
POD = delayed
VLP = video-laparoscopic
UPJ = ureteropelvic junction
GFR = glomerular filtration rate