

Risk Factors for Complications in Simple Nephrectomy: 17-Year Results from Single Institution

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What's known on the subject? and What does the study add?

Simple nephrectomy is a common but potentially risky surgery for benign kidney diseases. This study aims to enhance the quality of care for these patients by identifying the preoperative factors that influence the surgical outcomes. We found that American Society of Anesthesiologists score, preoperative hemoglobin level and male gender were associated with higher complication rates and longer hospital stays. We suggest that patients with these risk factors should receive individualized treatment and that elective laparoscopic surgery should be preferred whenever possible.

Abstract

Objective: To determine which preoperative patient characteristics are predictive of intraoperative complications (IOC) and postoperative complications (POC) in patients undergoing nephrectomy for non-oncological diseases.

Materials and Methods: Demographics, pre-operative characteristics, the surgical technique and perioperative outcomes of 295 adult patients who had undergone simple nephrectomy between 2002 and 2019 in a single reference institution were analyzed retrospectively. Univariate and multivariable statistical analyses were performed to determine the factors affecting POC (Clavien-Dindo score ≥ 1) and IOC. All statistical analyses were performed using the Statistical Package for the Social Sciences v. 24.0 (SPSS Inc., Chicago, IL, USA) software for Windows.

Results: The mean age of the patients was 44.84 ± 15.51 years, with a female-to-male ratio of 154/141. The statistically significant factors associated with IOC in the multivariable analysis were male gender, higher American Society of Anesthesiologists (ASA) score and urgent surgical intervention ($p=0.002$, $p=0.001$, $p=0.021$, respectively). In multivariable analysis, preoperative anemia, emergency surgery and open surgery were found to be statistically significant and associated with POC ($p<0.001$, $p=0.004$, and $p=0.049$, respectively).

Conclusion: Improved surgical outcomes can be achieved through treatment adapted to individual preoperative characteristics such as ASA score, pre-operative hemoglobin level and male gender. An elective laparoscopic approach should be used whenever possible.

Keywords: Nephrectomy, laparoscopic nephrectomy, intraoperative complications, postoperative complications

Introduction

Nephrectomy for benign disease is a surgical technique that involves the removal of a non-functional kidney. The loss of kidney renal function may be caused by a variety of benign conditions (1). Some of these causes are of preventable nature. Patients undergoing simple nephrectomy represent a very diverse group that require thorough pre-operative planning.

Some individual cases present major challenges for physicians at every step of the process.

Currently, nephrectomy for benign disease remains a major standard surgical procedure with a risk of severe complications, including death. The term "simple" has been criticized in the relevant literature as potentially misleading. "Non-radical" or "benign" nephrectomy terms are more precise given

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that complication rates are not lower than their "radical" counterparts (1,2).

The objective of this study was to determine which pre-operative patient characteristics are predictive of intraoperative complications (IOC) and postoperative complications (POC) complications in patients undergoing nephrectomy for non-oncological diseases.

Materials and Methods

This retrospective study was approved by the Institutional Ethics Committee (approval number: 2020/03-28) and conducted in accordance with the principles of the World Medical Association Declaration of Helsinki's Ethical Principles for Medical Research Involving Human Subjects.

A total of 295 adult patients who underwent simple nephrectomy for benign diseases from April 2002 to December 2019 at our institution are included in this study. Nephrectomy due to renal trauma were not included. Demographic data, pre-operative health status and perioperative outcomes were analyzed retrospectively.

Complications occurred within 30 days of surgical intervention were evaluated using the Clavien-Dindo classification (3). Tools such as the American Society of Anesthesiologists (ASA) score and Charlson Comorbidity Index (CCI) were used to determine the general health status of pre-operative patients. Renal function was assessed by the estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease equation and patients were classified into three groups as eGFR >90 mL/min/1.73 m², eGFR between 60 and 90 mL/min/1.73 m² and eGFR <60 mL/min/1.73 m² (4). According to the WHO, hemoglobin levels <12 g/dL for women and <13 g/dL for men are indicators of anemia (5).

Laparoscopic cases include trans peritoneal, retroperitoneal and hand-assisted laparoscopic procedures. Simple nephrectomies performed for pyelonephritis or recurrent urinary tract infections were classified as the infectious group; whereas simple nephrectomies performed for conditions such as persistent flank pain, hematuria, dyspnea and alike were classified as the non-infectious group. Univariate and multivariable statistical analyses were performed to determine factors affecting POC (Clavien-Dindo score ≥1) and IOC.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences v. 24.0 (SPSS Inc., Chicago, IL, USA) software for Windows. Chi-square test was used for nominal data; Mann-Whitney U test was used for non-

parametric variables, while t-test was used for parametric variables in univariate analysis. Mean ± standard deviation was used for parametric variables, while the median and interquartile range were used for non-parametric variables. Binary logistic regression analysis and the backward stepwise model were used for multivariable analysis. A p-value less than 0.05 was considered statistically significant.

Results

The mean age of the patients was 44.84±15.51 years, with a female-to-male ratio of 154/141. Two female and two male patients underwent surgery twice for both sides at different times. Twenty-three patients (7.8%) required emergency surgery, whereas seven patients (2.4%) underwent bilateral nephrectomy at the same session. The median follow-up period was 61 (12.75 to 127.5) months. Patient demographics and pre-operative characteristics are shown in Table 1.

The most common indications for surgery were persistent flank pain, followed by urinary tract infection and hypertension. Most cases were performed by the open surgical approach (n=195, 66.1%). Among these minimally invasive surgical approaches, 65 (22%) were performed with a trans peritoneal approach, 20 (6.8%) were performed retroperitoneal and 15 (5.1%) were performed with hand-assisted laparoscopic approach. The median estimated blood loss was 50 (50-85) mL. Blood transfusion was required in 46 patients (15.6%). The most common pathological diagnosis was pyelonephritis (56.3%), followed by atrophic renal degeneration (36.3%). Perioperative and post-operative variables are shown in detail in Table 2.

The number of patients with Clavien-Dindo grade 1, grade 2, grade 3, grade 4 and grade 5 complications were 4 (1.4%), 63 (21.4%), 9 (3%), 1 (0.3%) and 3 (1%), respectively. The most common grade 1 complication was a fever that required antipyretics, which developed in 3 (1%) patients. Among the grade 2 complications, 27 patients (9.1%) developed postoperative UTI, which required treatment by appropriate antibiotics and 29 (9.8%) patients required blood transfusion. The incision site infection requiring revision in 5 (1.6%) patients was the most common grade 3 complication. As a grade 4 complication postoperative sepsis developed in a patient with the diaphragm injury treated with repair and thoracic tube drainage, which has recovered after intensive care treatment. Three patients were lost due to sepsis (n=1) disseminated intravascular coagulation (n=1) and duodenal injury, which was identified postoperatively (n=1) (Figure 1). Factors such as the male gender, higher CCI, high ASA score, low preoperative eGFR, preoperative anemia were significantly associated with POC in univariate analysis (p=0.042, p=0.003, p<0.001, p=0.004, p<0.001, respectively).

Parameters			
Gender; n (%)	Female	154 (52.2)	
	Male	141 (47.8)	
Age, year, mean (SD)		44.84 (15.51)	
BMI, kg/m ² , mean (SD)		25.49 (4.31)	
CCI; n (%)	0	194 (65.8)	
	1-8	101 (34.2)	
ASA score; n (%)	1	73 (24.7)	
	2	175 (59.3)	
	3	47 (15.9)	
Preoperative GFR, mL/min/1.73 m ² ; n (%)	>90	98 (33.4)	
	60-90	119 (40.3)	
	<60	78 (26.3)	
Preoperative Hb; n (%)	Normal	199 (67.5)	
	Anemic	96 (32.5)	
Surgical side; n (%)	Right	128 (43.4)	
	Left	160 (54.2)	
	Bilateral	7 (2.4)	
Preoperative hydronephrosis; n (%)	Positive	201 (68.1)	
	Negative	94 (31.9)	
Anticoagulant use; n (%)	Positive	16 (5.4)	
	Negative	279 (94.6)	
Ipsilateral stone disease; n (%)	Positive	161 (54.6)	
	Negative	134 (45.4)	
History of ipsilateral renal intervention; n (%)	Positive	100 (33.9)	
	Negative	195 (66.1)	
History of abdominal surgery; n (%)	Positive	122 (41.4)	
	Negative	173 (58.6)	
Character of surgery; n (%)	Urgent	23 (7.8)	
	Elective	272 (92.2)	
Kidney size, mm, median (IQR)		100 (85-140)	
Surgical indication; n (%)	Non-infectious presentation	Persistent flank pain	151 (51.1)
		Hematuria	3 (1)
		Dyspnea secondary to enlarged kidney	3 (1)
		Colorenal fistula	1 (0.3)
		Retroperitoneal mass invasion	2 (0.7)
	Infectious presentation	Recurrent urinary tract infection	50 (16.9)
		Recurrent pyelonephritis	22 (7.5)
		Perinephric abscess	12 (4.1)
		Xanthogranulomatous pyelonephritis	6 (2)
	Hypertension		33 (11.2)
PKD		11 (3.8)	

ASA: American Society of Anesthesiologists, CCI: Charlson comorbidity index, GFR: Glomerular filtration rate, Hb: Hemoglobin, IQR: Interquartile range, PKD: Polycystic kidney disease, SD: Standard deviation

Parameters		
Operation time; min, mean (SD)		146.9 (55)
Blood loss mL, median (IQR)		50 (50-85)
Intraoperative complications; n (%)		32 (10.8)
Length of hospital stay, day, median (IQR)		3 (2-4)
Operation technique; n (%)	Open	195 (66.1)
	Laparoscopic	100 (33.9)
Hiler lymphadenopathy; n (%)	Positive	35 (11.9)
	Negative	260 (88.1)
Specimen weight, gr, median (IQR)		210 (119-404.5)
Pathological diagnosis; n (%)	Pyelonephritis	166 (56.3)
	Atrophic kidney	107 (36.3)
	PKD	11 (3.7)
	Neoplasia	5 (1.7)
	Other	6 (2)
Postoperative complications; n (%)	Clavien 1	4 (1.4)
	Clavien 2	63 (21.4)
	Clavien 3	9 (3)
	Clavien 4	1 (0.3)
	Clavien 5	3 (1)

IQR: Interquartile range, PKD: Polycystic kidney disease, SD: Standard deviation

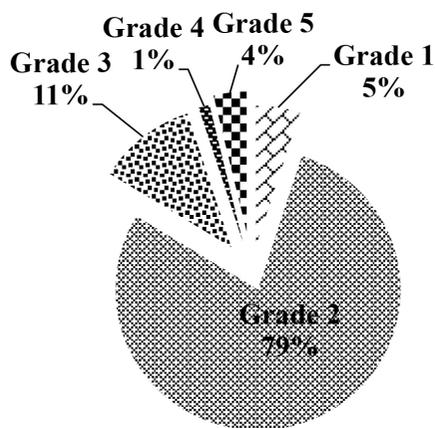


Figure 1. Post-operative complications according to Clavien-Dindo classification

Surgical factors such as simultaneous bilateral surgery, history of prior abdominal surgery, urgent character, open approach, pre-operative increased kidney size, simple nephrectomy indicated for recurrent infection and polycystic kidney disease were significantly associated with POC in univariate analysis as well ($p=0.028$, $p=0.018$, $p<0.001$, $p=0.001$, $p=0.025$, $p<0.001$, respectively) (Table 3). In multivariable analysis, pre-operative anemia, emergency surgery and open surgery were found to

be statistically significant and associated with POC ($p<0.001$, $p=0.004$, and $p=0.049$, respectively) (Table 3).

The IOC rate was 10.8% ($n=32$). The most common IOC was adrenal injury ($n=19$). Other IOCs were the spleen ($n=1$), liver ($n=1$), diaphragm ($n=3$), aorta ($n=1$), colon ($n=1$), duodenum ($n=2$) and pancreas ($n=1$) in bleeding requiring transfusion ($n=3$). Male gender, higher CCI, high ASA score, pre-operative anemia, bilateral surgery and emergency surgery were the factors associated with IOC in the univariate analysis ($p=0.001$, $p=0.002$, $p<0.001$, $p=0.009$, $p=0.021$, $p=0.006$, respectively). Male gender, higher ASA score and emergency surgery were the statistically significant factors associated with IOC in multivariable analysis ($p=0.002$, $p=0.001$, $p=0.021$, respectively) (Table 4).

The two chronologically categorized groups were compared to analyze the changes in trends in surgical techniques and the change in post-operative outcomes. The rate of laparoscopic simple nephrectomy increased significantly, while the rate of POC decreased significantly between 2011 and 2019 compared to the years 2002 to 2010 (22.7% vs. 46.1%, $p<0.001$; 32.5% vs. 21.3%, $p=0.031$; respectively) (Figure 2).

Discussion

The etiology of non-functional kidney may vary from one geographic area to another. Most causes are preventable and

fall under public health area of interest. In most series, stone disease and urinary tract infections, among the other causes, are reported as the major causes of simple nephrectomies. Previous studies have focused on the correlation between definitive

pathological findings and complication rates. The focus of our study was on the preoperative characteristics of patients that can be predictive of IOC and POC. Considering that our center provides care to a diversely represented population, findings

Table 3. Univariate and multivariable analysis of factors affecting POC

Parameters		Univariate analysis			Multivariable analysis	
		Positive	Negative	p	OR (95% CI)	p
Gender (%)	Female	22.1	77.9	0.042*	-	0.692
	Male	32.6	67.4			
Age, year, mean (SD)		47.09 (15.79)	44.01 (15.36)	0.130 [†]	-	-
BMI, kg/m ² , mean (SD)		24.48 (4.34)	25.82 (4.27)	0.081 [†]	-	-
CCI (%)	0	21.6	78.4	0.003*	-	0.320
	1-8	37.6	62.4			
ASA score (%)	1	17.8	82.2	<0.001*	-	0.375
	2	24	76			
	3	53.2	46.8			
Preoperative GFR, mL/min/1.73 m ² (%)	>90	21.4	78.6	0.004*	-	0.739
	60-90	22	78			
	<60	41.6	58.4			
Preoperative Hb (%)	Normal	15.2	84.8	<0.001*	15.344 (5.265-44.722)	<0.001
	Anemic	52.1	47.9			
Surgical side (%)	Right	25.8	74.2	0.028*	-	0.156
	Left	26.3	73.7			
	Bilateral	71.4	28.6			
Preoperative hydronephrosis (%)	Positive	26	74	0.375*	-	-
	Negative	31.1	68.9			
Anticoagulant use (%)	Positive	31.3	68.7	0.773*	-	-
	Negative	26.9	73.1			
Ipsilateral stone disease (%)	Positive	28.6	71.4	0.538*	-	-
	Negative	25.4	74.6			
Ipsilateral renal intervention (%)	Positive	34	66	0.057*	-	-
	Negative	23.6	76.4			
Previous abdominal surgery (%)	Positive	34.4	65.6	0.018*	-	0.110
	Negative	22	78			
Character of surgery (%)	Urgent	78.3	21.7	<0.001*	12.542 (2.266-69.420)	0.004
	Elective	22.8	77.2			
Operation technique (%)	Open	33.3	66.7	0.001*	3.517 (1.008-12.275)	0.049
	Laparoscopic	15	85			
Kidney size, mm, median (IQR)		110 (96-162.5)	100 (80-140)	0.025 [†]	-	0.582
Surgical indication (%)	Non-infectious Presentation	20.3	79.7	<0.001*	-	0.546
	Hypertension	6.1	93.9			
	PKD	54.5	45.5			
	Infection Presentation	43	57			

POC: Postoperative complications, ASA: American Society of Anesthesiologists, CCI: Charlson Comorbidity index, GFR: Glomerular filtration rate, Hb: Hemoglobin, IQR: Interquartile range, PKD: Polycystic kidney disease, SD: Standard deviation, OR: Odds ratio, CI: Confidence interval. Bold values indicate statistically significance, *: Chi-square test, †: Student's t-test, ‡: Mann-Whitney U test

Parameters		Univariate analysis			Multivariable analysis	
		Positive	Negative	p	OR (95% CI)	p
Gender (%)	Female	5.2	94.8	0.001*	3.917 (1.632-9.401)	0.002
	Male	17	83			
Age, year, Mean (SD)		46.69 (17.52)	44.62 (15.27)	0.477 [†]	-	-
BMI, kg/m ² , Mean (SD)		24.43 (4.03)	25.65 (4.34)	0.219 [†]	-	-
CCI (%)	0	6.7	93.3	0.002*	-	0.413
	1-8	18.8	81.2			
ASA score (%)	1	4.1	95.9	<0.001*	-	0.001
	2	9.1	90.9		2.349 (0.647-8.525)	
	3	27.7	72.3		8.755 (2.238-34.253)	
Preoperative GFR, mL/min/1.73 m ² (%)	>90	6.1	93.9	0.126 [†]	-	-
	60-90	11.9	88.1			
	<60	15.6	84.4			
Preoperative Hb (%)	Normal	7.6	92.4	0.009*	-	0.570
	Anemic	17.7	82.3			
Surgical side (%)	Right	9.4	90.6	0.021*	-	0.484
	Left	10.6	89.4			
	Bilateral	42.9	57.1			
Preoperative hydronephrosis (%)	Positive	9.9	90.1	0.390*	-	-
	Negative	13.3	86.7			
Anticoagulant use (%)	Positive	12.5	87.5	0.688*	-	-
	Negative	10.8	89.2			
Ipsilateral stone disease (%)	Positive	9.9	90.1	0.582*	-	-
	Negative	11.9	88.1			
Ipsilateral renal intervention (%)	Positive	9	91	0.465*	-	-
	Negative	11.8	88.2			
Previous abdominal surgery (%)	Positive	11.5	88.5	0.771*	-	-
	Negative	10.4	89.6			
Character of surgery (%)	Urgent	30.4	69.6	0.006*	3.518 (1.208-10.250)	0.021
	Elective	9.2	90.8			
Operation technique (%)	Open	13.3	86.7	0.055*	-	-
	Laparoscopic	6	94			
Kidney size, mm, Median (IQR)		120 (87.5-187.5)	100 (89-140)	0.525 [†]	-	-
Surgical indication (%)	Non-infectious presentation	8.9	91.1	0.512*	-	-
	Hypertension	9.1	90.9			
	PKD	18.2	81.8			
	Infection presentation	14	86			

IOC: Intraoperative complications, ASA: American Society of Anesthesiologists, CCI: Charlson Comorbidity index, GFR: Glomerular filtration rate, Hb: Hemoglobin, IQR: Interquartile range, PKD: Polycystic kidney disease, SD: Standard deviation, OR: odds ratio, CI: Confidence interval. Bold values indicate statistically significance, *: Chi-square test, †: Student's t-test, ‡: Mann-Whitney U test

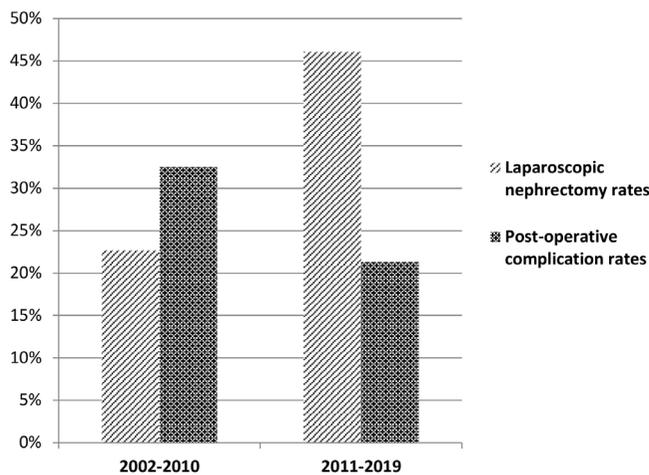


Figure 2. Changes in rates of laparoscopic approach and post-operative complications

of this study may guide health-care providers in our region. A recent article by Ames et al. (6) shows that this topic remains relevant. Their study demonstrates that causes of kidney loss may vary considerably among healthcare providers. Local patient characteristics should be considered when developing prevention and treatment strategies for a non-functional kidney.

In their series of 1039 benign nephrectomies from 112 institutions, Zelhofer et al. (2) reported IOC and POC rates of 5.2% and 11.9%, respectively. Compared with 1095 T1 radical nephrectomies in the same study, simple nephrectomies were associated with a higher risk of IOC and POC (5.2% vs. 3.7% and 11.9% vs. 10%, respectively). These complication rates were inconsistent with those reported earlier in a single centre study with a relatively high number of patients comparing simple and radical nephrectomies, in which the authors described simple nephrectomy as an easier procedure (7). Being the largest series of benign nephrectomies compared to radical procedures, Zelhofer et al. (2) provided strong data on the issue of previously inconsistent findings from mostly single center studies (7-9). It serves as a reference for the interpretation of our results. The study indicates that among the pathologies, stone disease had the highest risk of IOC and POC. The conversion rate to open surgery was found to be higher in stone and inflammatory diseases. Laparoscopy achieved better intra- and post-operative outcomes compared to open surgery. Our results show a significant association between open surgery and POC, but not with IOC. Manohar et al. (10) published similar inferior results for the open approach compared with laparoscopic surgery. As per our analysis, stone disease was not statistically associated with POC and IOC. Given that surgeries after infectious causes was significantly associated with POC in univariate analysis.

The history of inflammation and perirenal fibrosis affects the outcome more than the history of stone disease alone. This finding is supported by numerous publications in one of which routine excision outside the Gerota's fascia is recommended to minimize complications (10-12). Due to the aforementioned reasons, laparoscopic nephrectomy performed for inflammatory etiology is considered challenging (9).

Our data showed no association between POC and IOC and the history of prior ipsilateral interventions despite published articles on this topic (13,14). Male sex has been strongly associated with IOC. It appears that the much dense and firm Gerota's fascia may have contributed to the difficult dissection in some cases. The phenomenon of "toxic fat" needs to be clarified in future studies.

Anemia is strongly associated with POC. Patients probably required transfusion more often, contributing to Clavien ≥ 2 grade complications. Anemia was significantly associated with IOC only in the univariate analysis.

In a recent retrospective study of 149 Nephrectomy for stone disease, Danilovic et al. (15) identified that a higher ASA score, emergency surgery, kidney size ≥ 12 cm and preoperative abscess were associated with POC Clavien > 1 . In our results, emergency surgery was associated not only with POC but also with IOC. A higher ASA score was associated with IOC instead of POC. Such discrepancy between the mentioned study and our findings may be explained by broader inclusion criteria and a higher number of patients in our cohort.

Our data demonstrate a significant association in the multivariable analysis of IOC and POC with emergency surgery. There is a rationale to avoid surgery in an urgent setting in favor of elective surgery (15,16). It is a good strategy to stabilize the affected renal unit as well as the patient before intervention whenever emergency nephrectomy is indicated.

In a recent article by Lubennikov et al. (16) investigated 108 bilateral nephrectomy patients for autosomal dominant polycystic kidney disease (ADPKD), approximately 80% of patients required surgery for infected cysts and pyelonephritis. An overwhelming 46.2% of the 39 patients who underwent emergency bilateral nephrectomies suffered a lethal outcome. In our series, bilateral nephrectomies of the same session were performed electively in limited cases for ADPKD in end-stage kidney disease patients. Bilateral nephrectomy was significantly associated with complications only in the univariate analysis. Such a result could be due to the limited number of patients (n=7). Considering the convincing findings from other studies, the same session bilateral nephrectomy should be approached with great caution.

Study Limitations

The main limitation of our study is its retrospective and non-randomized design. Past clinical decisions may have been biased according to the preferences of the primary surgeon at the time frame of the procedure. Differences in thresholds for parenteral antibiotic treatment inception and transfusion throughout the extensive time interval of the study could have contributed to the rates of Clavien >1 POC. Nevertheless, our results provide a valuable insight into the dynamics of practice in our institution over the past 17 years. Prospective randomized trials must further investigate the variables responsible for complications in nephrectomy for benign diseases.

Conclusion

The findings of this study will be useful to improve the quality of care in simple nephrectomy patients. Treatment plan should be tailored on an individual basis, particularly in male patients and those with higher ASA scores. Treatment of pre-operative anemia would reduce the need for post-operative transfusion rates. Necessary measures must be taken to avoid an emergency nephrectomy. An elective approach combined with laparoscopic surgery promises the best outcomes.

Ethics

Ethics Committee Approval: This retrospective study was approved by the Institutional Ethics Committee (approval number: 2020/03-28).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.G., B.A., F.T.A., C.Y.B., S.Y., Concept: M.A., H.B.H., S.Y., Design: M.A., H.B.H., S.Y., Data Collection or Processing: M.A., H.B.H., Ö.F.B., Analysis or Interpretation: M.A., H.B.H., Ö.F.B., B.A., F.T.A., S.Y., Literature Search: M.A., H.B.H., Ö.F.B., A.G., C.Y.B., Writing: M.A., H.B.H., Ö.F.B., S.Y.

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