Effect of Charlson comorbidity index on complications and outcomes following Percutaneous nephrolithotomy and Retrograde intrarenal surgery in elderly patients

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February 25, 2021

Abstract

Objectives: In this study, we aimed to compare the outcomes and complication rates of percutaneous nephrolithotomy (PCNL) and retrograde intrarenal surgery (RIRS) in geriatric patients according to Charlson comorbidity index (CCI). Materials and Methods: Between April 2011 and January 2020, patients who underwent PCNL and RIRS for renal stone between 10 and 30 mm in geriatric patients were retrospectively evaluated. All patients' Pre-surgery comorbidities were recorded and the CCI was calculated. The two groups' perioperative values, stone free rates and complication rates were compared. Postoperative complications were noted according to the Clavien scoring system. Results: There were 89 and 72 patients in the PCNL and RIRS group, respectively. The median age was 67 years in both of groups (p=0.192). The stone size were 22.2 ± 3.5 and 19.9 ± 7.1 in the PCNL and RIRS group, respec¬tively (p = 0.082). CCI scores were similar in both groups (p=0.098). Stone free and complication rates were significantly higher in PCNL group (p = 0.021, p = 0.034). Also we found that overall complication and major complication rates were statistically significant difference with especially Charlson comorbidity index score [?]2 in PCNL group (p = 0,016, p = 0,029). According to correlation analysis of intraoperative and postoperative results with Charlson comorbidity index, there was positive correlation between total complication with PCNL and RIRS group, respectively (p < 0,001, p = 0.024). In addition, there was positive correlation between lenght of hospital stay with PCNL and RIRS group, respectively (p = 0,007, p < 0,001). Also there was positive correlation between blood transfusion requirement with PCNL group (p=0,009). Conclusion: Despite there was higher stone clearence in PCNL, the complication rates were higher compared to RIRS. So RIRS might be a safe alternative treatment method to PCNL in older patients with a high CCI score.

Introduction

Currently, retrograde intrarenal surgery (RIRS) and percutaneous nephrolithotomy (PCNL) are the most favored treatment options for renal stones.[1] According to EAU guideline, PCNL is the standard treatment for renal stones > 2 cm, and RIRS and shock wave lithotripsy (SWL) for renal stones < 2cm.[2] However, despite the recommendations of the EAU guideline on management of renal stones, RIRS has been widely used to treat renal stones > 2 cm by several investigators.[3,4] So, for renal stone between 10 and 30 mm, RIRS and PCNL are both options, and the choice of treatment will depend on anatomical and stone characteristics. However, surgical complications are associated with PCNL, therefore, for elderly patients, minimally invasive procedures, especially RIRS, are preferable. On the other hand, PCNL has an excellent success rate in clearing stone burdens, at reported rates of up to 96.1%.[5] The stone-free rate (SFR) for RIRS has been

reported as 77% to 96.7 % with staged procedures for renal stones > 2 cm.[6] Therefore, urologists have to make a difficult decision regarding the technical that should be preferred in geriatric patients with low cardiopulmonary performance and kidney reserves.

There are several comorbidity indices in the medical literature but Charlson comorbidity index (CCI) is widely used.[7-9]The CCI uses 19 comorbid conditions to predict mortality. In this method, patients are given a score or weight from 1 to 6, according to comorbid condition.[7] Although CCI is designed to show mortality risk, its parameters (diabetes mellitus, cardiac disease, age, etc.) are related to surgical morbities.

In this study, we aimed to compare the outcomes of PCNL and RIRS in treating renal stones of between 10 and 30 mm in geriatric patients. To our knowledge, this is the first study of the effect of CCI on complications and outcomes in elderly patients following PCNL and RIRS.

Materials and Methods

This study is a retrospective analysis of patients over 65 years of age who undergoing PCNL or RIRS for kidney stones at the Ministry of Health University Izmir Bozyaka Training and Research Hospital between April 2011 and January 2020. The data were driven from the electronic medical records of all the patients consecutively. Patients who had history of neuromuscular disease, congenital renal anomalies, coagulopathy, morbid obesity, skeletal deformity, solitary kidney and <65 years of age were excluded from the study. A total of 161 patients, were divided into two groups according to surgical technique; PCNL Group n = 89, and RIRS Group n=72. Comparisons were made among patient demographics, and perioperative and postoperative outcomes.

The following data were recorded by the two surgeons (SY and MS) immediately postoperatively: patient demographics (age, gender, body mass index, operation side, location of the stones, stone burden, Metabolic Syndrome: there were at least two illnesses (diabetes mellitus, hypertension, hyperlipidemia and obesity) and preoperative data (table-1). Perioperative data included surgery time, fluoroscopy time, length of stay, Change in Hgb and Change in creatinine (table-2). Postoperative complications were noted according to the Clavien scoring system (table-3).[10] Complications according to Clavien scoring system were divided two groups; Minor complications = Clavien grades I-II, and Major complications = Clavien grades III-IV-V. Charlson comorbidity index was measured for all patients. Correlation analysis was used for intraoperative and postoperative results with CCI (table-4). Complications rates were compared between RIRS and PCNL according to the CCI (table-5)

Sterile urine culture was detected in all patients before operation. Ceftriaxone was given as prophylaxis before the operation and continued until the nephrostomy tube was removed. No Nephrotoxic drugs were used before, during, or after the operation for any patient.

Stone burden was calculated with square millimeters in all patients : length x width x π x 0.25, where π is a mathematical constante qualto 3.14.[11] In multiple intrarenal stones, stone burden was calculated one by one and then all of them were collected. The estimated GFR was calculated using the Cockcroft–Gaultformula (CrCl = ([140-age] $\times$ weight in kg) / (serum creatinine $\times$ 72) x 0,85 (if female).[12] All PCNL and RIRS interventions were performed by two surgeons (SY and MS).

PCNL procedure

After general anesthesia, 5 or 6 F ureter catheter was inserted to the collecting system of the patient's kidney with stones in the lithotomy position. And ureter catheter fixed to a Foley catheter. Then patient was positined to prone. Access was obtained under fluoroscopy with 18-gauge needle, and tract was dilated with Amplatz dilatators to 30 F caliber. Stone fragmentation was accomplished using a pneumatic lithotripter (Vibrolith; Elmed, Ankara, Turkey). At the end of the procedure, 14 F nephrostomy tube was inserted, and antegrade pyelography was performed. Nephrostomy tube was removed in the 1st or 2nd postoperative day in the absence of fever or significant hematuria. The fluoroscopy time was recorded for every fluoroscopy use from the access to the collecting system of the kidney to antegrade pyelography was performed. Operation time was calculated from the patient was placed in the prone position to the nephrostomy tube was placed.

RIRS procedure

After general anesthesia, Firstly semi-rigid ureteroscopy was performed to evalute and actively dilate the ureter before flexible ureteroscopy. Thereafter, a 12/14 Fr ureteral access sheath (UAS) **(** Flexor 12/14Fr, Cook Medical Bloomington, IL, USA, Navigator 11/13Fr, Boston Scientific, Natik, MA, USA) was placed over the guidewire under fluoroscopic guidance. All the RIRS were performed using Flex-X2 or Flex-XC (Karl Storz Endoscope, Germany) through the ureteral access. If UAS can not be placed, double J ureteral catheter was inserted to the kidney collecting system for passive dilatation approximately 1-2 weeks before re-surgery. The stones were fragmented using a 200/273 μm Holmium laser fiber (Dornier Med-Tech GmbH, Medilas H20, Wessling, Germany). Surgery was concluded after stone-free status (ureteroscopic inspection and fluoroscopy), or detection of bleeding which blocked the surgeon's view or decision. When the AUS was withdrawn, the ureter was examined with flexible ureteroscopy. If there were any injuries, DJ was applied at the end of the procedure, according to surgeon's judgment. DJ stent was removed 2-3 weeks after surgery in all patients.

"Stone-free" status was defined as stones of less than 2 mm or no evidence of stones on one-month postoperative CT.

Statistical Analysis

Categorical data are presented as numbers and percentages. The Shapiro-Wilk test was used to determine whether the distributions of continuous variables were normal. While normal distributed data are presented as mean and standard deviation, non-normally distributed data are given as median and 25^{th}-75^{th}percentile. Independent T-test was used to compare two independent normal distributed data, while Mann-Whitney U test was used for non-normally distributed data. The frequencies of categorical variables were compared using Pearson Chi-Square, Continuity Correctionor Fisher's exact test, when appropriate. The relation of intraoperative and postoperative findings with CCI was evaluated using Spearmen correlation analysis. A p value of <0.05 was considered statistically significant. All data were analyzed using the Statistical Package for Social Sciences, version 20.0 (SPSS, Chicago, Ill) software program.

Results

In our study, there were 89 and 72 patients in the PCNL and RIRS group, respectively. The median age of both groups was 67 years. The stone sizes were 22.2 ± 3.5 and 19.9 ± 7.1 in PCNL and RIRS group, respectively (p = 0.082). Groups were similar in terms of patient and stone characteristics (age, gender, Body Mass Index (BMI), metabolic syndrome, preoperative glomerular filtration rate (GFR), SWL history, stone location and stone density). CCI scores were similar in both groups (p=0.098). The demographic data and preoperative characteristics are summarized in Table 1.

The length of hospital stay, fluoroscopy time and change in hgb were significantly higher in PCNL group (p $<$ 0.001 for all three).

Stone free and complication rates were significantly higher in PCNL group (p = 0.021, p = 0.034). Also major complication rates were significantly higher in PCNL group (p=0.024**).** After a single procedure, the stone free rates were 89.9% and 77.8% in PCNL group and RIRS group, respectively (p = 0.021).

Regarding the subgroup rates of Clavien scoring system, there was no statistically significant difference in each subgroups between the groups. Details of omplication according to Clavien classification system are summarized in Table-3.

The correlation analysis of intraoperative and postoperative results with Charlson comorbidity index show that positive correlation between total complication with PCNL group and RIRS group, respectively (P $<$ 0,001, P = 0.024). There was positive correlation between CCI and length of hospital stay with PCNL group and RIRS group (p = 0.007, p $<$ 0.001). Also there was positive correlation between Blood transfusion requirement with PCNL group (p = 0.009). Details are shown in Table-4.

When we compared the complication rates between RIRS and PCNL according to CCI, we found that the rates of total and major complication in patients with CCI [?]2 was statistically significantly higher in the PCNL group, respectively (p=0,016, p= 0,029) (table-5).

Discussion

The increase in the average human life expectancy and aging population will result in more geriatric patients with kidney stones admitted for treatment. Developments in technology, especially in endoscopy and optic quality, have led to numerous stone treatment modalities in elderly patients.[13] PCNL and RIRS have become important management modalities in this area. PCNL is considered to be an effective and safe treatment option for large renal stones.[14] Despite proof of the effectiveness of the procedure, complications ranging from 20 - 83% were reported in the literature, including hemorrhage requiring transfusion, pleural injury and colonic injury. Technological innovations have meant that RIRS has become accepted as important treatment modality of renal stones, with higher success and lower complication rates. Previous studies clearly demonstrated that RIRS can be successfully performed for moderate size renal stones.[15] In a different study, Gupta and colleagues concluded that PCNL provides better one-time stone-free rates (>90%) compared to other procedures.[16]Knoll et al. emphasized that one in two patients receiving RIRS required two procedures for a mean stone size of 19 mm.[17] This is undesireable because multiple anesthesia exposure is problematic for elderly patients.

Although many studies have investigated outcomes of either RIRS or PCNL in elderly patients, there is lack of comparative studies. To our knowledge, the present study is the first on the effect of CCI on complications and outcomes in elderly patients. Ozgor et al. evaluated a total of 118 elderly patients, 60 of them underwent RIRS and 58, mPCNL, and reported stone-free rates of 81.7% and 77.6%, respectively.[18] Akman et al., found similar success rate between PCNL and RIRS in geriatric patients with moderate-size renal stones (92.8% and 82.1%, respectively).[15] In contrast, in the present study, the stone free rate was significantly higher in PCNL than RIRS (92% and 77.8%, respectively) (p=0.021). Similar to our results, comparing the effectiveness of RIRS and mPCNL in older patients, Hu found that the success rate was statically significantly in favor of mPCNL ($p = 0.025$).[13] The present study showed no correlation between CCI and success in either group.

In this study, the mean operative time was longer in PCNL group compared with f-URS group, but this difference was not statistically significant.In contrast, many previous studies reported longer operative times in the RIRS group.[19-21] In a study involving 56 geriatric patients comparing standard PCNL and RIRS, Akman et al. found that operative duration was longer in favour of f-URS (64.5 +- 20.9 and 40.7 +- 10.7 min).[15] Another study by Hu et al. found no significant difference in terms of operative time in older patients following mPCNL and RIRS.[13] This variability can be attributed to surgical competence and experience, positioning and patient-dependent factors during operation. There are mixed results on the correlation between operative times and CCI. A study conducted by Resorlu et al.[22] reported that CCI was not a predictive factor for operative duration of PCNL in elderly patients, however, Unsal et al.[23] noted a positive correlation. In our study, we found that CCI was not a predictor on operative times for either PCNL or RIRS group.

Previous reports emphasized that PCNL has a longer hospitalization times compared to RIRS.[13,15,18] In contrast to the high morbidity of PCNL, for patients undergoing RIRS, there are lower rates of pain, hemoglobin drop, and requirement for blood transfusion requirement, and the absence of nephrostomy tubes seem to accelerate postoperative recovery, accounting for the reduced hospital stay.The effect of age and patients' comorbidities on hospitalization stay is a controversial issue. Okeke et al. stated that, after PCNL, hospitalization time was longer in older compared to younger patients.[24] In contrast, studies conducted by Karami et al. and Sahin et al. report no significant difference between older and younger patients undergoing PCNL in terms of hospitalization time.[25,26] Ozgor et al. found a significantly longer hospitalization time following mPCNL (56.5 hours) compared to RIRS (23.1 hours) in elderly patients ($p < 0.001$).[18] In accordance with the literature, our study revealed PCNL was associated with longer hospitalization stay in older patients. Unsal et al.[22] and Resorlu et al.[23] found CCI has no effect on hospitalization times after PCNL, but the present study reported a significant positive correlation in both PCNL and RIRS.

Elderly patients are more prone to comorbid disease, making them more vulnerable to bleeding and septic complications.[15]Such complications can be fatal. The use of minimally invasive surgical techniques to achieve complete stone clearance with minimal morbidity is an important advance in the management of nephrolithiasis in older patients. de la Rosette et al. and Tefekli et al. reported that overall complication rates in PCNL were 43.8% and 29.2%, respectively.[27,28] In the present study, the overall complication rate (32.6%) was in accordance with other series on PCNL, but it was slightly higher than these afor ementioned studies. This can be explained the ages of the patients, a position supported by Okeke's series, which resulted in significantly higher complication rates in elderly patients compared with younger patients in PCNL.[24] Previous reports emphasized similar and acceptable complication rates for both PCNL and RIRS. Akman et al. reported no difference in complication rates in elderly patients following PCNL and RIRS.[15] In studies, conducted by Ozgor et al. and Hu et al., no significant difference in terms of complication rates was detected between older patients undergoing mPCNL and those undergoing RIRS.[13,18] However, in present study, overall complication rates were significantly higher in PCNL group (p=0.034), and here, the Clavien-Dindo grade >2 complications were mainly observed in PCNL group (p=0.043). Another study by Unsal et al. evaluated the efficacy of CCI on PCNL to predict of morbidity and mortality, and found the CCI to be a predictive factor.[23] Aykac et al. observed that a CCI score of 2.5 was the cut-off value for medical complications of RIRS in geriatric patients.[29] In the current study, overall complication and major complications rates were significantly higher in CCI score [?]2 patients who underwent PCNL. Furthermore, there was significant positive correlation between CCI and complication rates in both PCNL and RIRS.

The first is its retrospective design with small number of patients, which is a possible cause of bias. Second, we used CCI, an index designed to predict mortality using 19 comorbid conditions, to predict surgical complications only, and not medical complications. Another limitation is short patient follow up, with no long-term comparison of complications. There is a need for prospective studies in geriatric patients with a larger series, focusing on medical complications.

Conclusion

In conclusion, the present study is the first study the effect of CCI on complications and outcomes in elderly patients following PCNL and RIRS. Both PCNL and RIRS are equally effective and acceptable treatment modalities for elderly patients with renal stones. PCNL had significantly higher rates of stone clearance, but higher complication compared to RIRS. CCI may be considered an acceptable predictive factor for higher complication rates; therefore, RIRS might be a safer alternative treatment method in older patients with high CCI scores. Further prospective randomized studies will reveal more detailed insights with larger patient series.

Funding None.

Author Disclosure Statement:

Conflict of interest: None

Ethical Standards: Informed consent was obtained pre-operatively from all of our patients which were included in our study.

Ethical compliance: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Table 1. Demographic and preoperative characteristics of the patients

Variables	**PCNL (n=89)**	**RIRS (n=72)**	p **value**$^{\#}$
Age, years, median (25^{th}-75^{th})	67 (66-70.75)	67 (65-72)	0.192
Gender, n (%) Female Male	40 (44.9) 49 (55.1)	32 (44.4) 40 (55.6)	0.949[?]
Laterality, n (%) Right Left	44 (49.4) 45 (50.6)	25 (34.7) 47 (65.3)	0.061$^{\&}$
BMI, kg/m^2, median (25^{th}-75^{th})	26.1 (24.2-29.3)	26.7 (24.6-29.6)	0.494
Metabolic syndrome, n (%)	21 (23.6)	22 (30.6)	0.416$^{\&}$
Mean Preoperative GFR, mL/min	78.6 ± 19.1	82.1 ± 21.2	0.289ˆ
Previous history of ESWL, n (%) Ipsilateral surgery, n (%)	15 (16.9) 17 (19.1)	17 (23.6) 25 (34.7)	0.384$^{\&}$ 0.039$^{\&}$
CCI, n (%)** 0 1 [?]2	52 (58.4) 22 (24.7) 15 (16.9)	30 (41.7) 23 (31.9) 19 (26.4)	0.098[?]
Stone location, n (%) Pelvis Proximal ureter Single calyx Pelvis + one calyx Multiple calyx	35 (39.3) 2 (2.2) 19 (21.3) 21 (23.6) 12 (13.5)	19 (26.4) 5 (6.9) 22 (30.6) 12 (16.7) 14 (19.4)	0.129¥
Stone density, HU	980 ± 346	988 ± 357	0.593ˆ

Variables	**PCNL (n=89)**	**RIRS (n=72)**	p **value**[#]
Stone size, mm^2,	22.2± 3.5	19.9 ± 7.1	0.082

BMI, Body mass index, ESWL, Extracorporeal shock wave lithotripsy, ASA, The American Society of Anesthesiologists (ASA) Physical Status Classification

**Each superscript letter denotes a subset of PNL and RIRS categories whose column proportions do not differ significantly from each other at the ,05 level.

[#]Mann-Whitney U test

[?]Pearson chi-square test

[&]Yate's chi-square test

[¥]Exact test

Table 2. Comparison of intra-operative and postoperative outcomes in the PCNL and RIRS groups.

Variables	**PCNL (n=89)**	**RIRS (n=72)**	p **value**[#]
Change in Hgb, g/dL	1.10 (0.6-2.0)	-0.2 (-0.3-0.0)	**<0.001**
Change in Creatinine, mg/dL	0.10 (0.0-0.22)	0.10 (0.02-0.20)	0.402
Change in e-GFR, mL/min	-9.92 (-16.9-0)	-9.05 (-15.3 - -3.1)	0.768
Operation time, min	90 (60-101.25)	80 (60-90)	0.154
Fluoroscopy time, sec	61.5 (33.75-87.75)	11 (6-21)	**<0.001**
Length of hospital stay, days	3 (2-4)	2 (1-3)	**<0.001**
Blood transfusion requirement, n(%)	4 (4.6)	0	0.127[¥]
Stone-free rates, n (%)	80 (89.9)	56 (77.8)	**0.021**[&]
Complication rates, n (%)	29 (32.6)	12 (16.7)	**0.034**[&]
Minor Complication rates (Clavien grades I-II), n(%)	20 (22.5)	11 (15.3)	0.342[&]
Major Complication rates (Clavien grade III-IV-V), n(%)	9 (10.1)	1 (1.4)	**0.024**ˆ

[#]Mann-Whitney U test

[?]Pearson chi-square test

[&]Continuity Correction

[¥]Exact test

Table-3: Classification of complications according to Clavien scoring system

Complications	**PCNL (n=89)**	**RIRS (n=72)**	**p value***

Grade 0, n(%)	60 (67.4)	60 (83.3)	**0.032***
Grade I, n (%)	**15 (16.9)**	**6 (8.3)**	0.110^
Pain	3	1	
Fever	3	2	
Bleeding not requiring blood transfusion	4	3	
Transient elevation of SCr (> 0.5 mg/dl)	2	-	
Urine leakage managed by watchful waiting	2	-	
Intestinal obstruction managed without nasogastric decompression	1		
Grade II, n (%)	5 (5.6)	5 (6.9)	0.753
Minor pelvic/ureter perforation	2	-	
Bleeding requiring blood transfusion	3	-	
Postoperative fever (>380C) managed with antibiotics in the ward	-	5	
Non-obstructive steinstrasse	-	-	
Grade III	5 **(5.6)**	1(1,4)	0.226
Grade III A, n(%)	**5**		
Urine leakage managed by ureteric stenting without general anesthesia	4 1	- -	
Perinephric abscess managed by percutanous drainage			
Grade III B, n (%)	-	1	
Stent migration	-	1	
Grade IV, V			0.129
Grade IV B, n (%)	2 (2.2)		
Sepsis	2	-	
Grade V, n(%)	2 (2.2)		
Any complication leading to death	2	-	

*Fisher's Exact test

Table 4. Correlation analysis of intraoperative and postoperative results with CCI

Spearmen's rho	Spearmen's rho	Change in Hgb	Change in Creatinine	Change in e-GFR	Operation time	Fluoroscopy time	Length of hospital stay	Blood transfusion requirement	Stone-free status
PCNLCCI	Correlation Coefficient Sig. (2-tailed) N	-.053 0.623 88	-.072 0.506 88	.098 0.365 88	.143 0.188 87	-.019 0.861 87	.285** **0.007** 87	.277** **0.009** 87	.165 0.126 87
RIRSCCI	Correlation Coefficient Sig. (2-tailed) N	-.214 0.072 72	-.159 0.182 72	-.008 0.945 72	.053 0.659 72	-.190 0.110 72	.412** **<0.001** 72	-	-.114 0.341 72

CCI: Charlson Comorbidity Index

** Correlation is significant at the 0.01 level (2-tailed)

*Correlation is significant at the 0.05 level (2-tailed)

Table 5. The comparison of complications rates between RIRS and PCNL according to the Charlson comorbidity index (CCI)

	Total	PCNL	RIRS	p value
CCI 0				
Overall Complication rates, n (%)	13/82 (15.9)	11/52 (21.2)	2/30 (6.7)	0.119*
-Minor Complication rates (Clavien grades I-II), n(%)	10/82 (12.2)	8/52 (15.4)	2/30 (6.7)	0.312*
-Major Complication rates (Clavien grade III-IV-V), n(%)	3/82 (3.7)	3/52 (5.8)	-	0.295*
CCI I				
Overall Complication rates, n (%)	11/45 (24.4)	7/22 (31.8)	4/23 (17.4)	0.260ˆ
-Minor Complication rates (Clavien grades I-II), n(%)	8/45 (17.8)	5/22 (22.7)	3/23 (13.0)	0.459*
-Major Complication rates (Clavien grade III-IV-V), n(%)	3/45 (6.7)	2/22 (9.1)	1/23 (4.3)	0.608*
CCI [?]2				

	Total	**PCNL**	**RIRS**	**p value**
Overall Complication rates, n (%)	17/34 (50.0)	11/15 (73.3)	6/19 (31.6)	**0.016ˆ**
-Minor Complication rates (Clavien grades I-II), n(%)	13/34 (38.2)	7/15 (46.7)	6/19 (31.6)	0.587ˆ
-Major Complication rates (Clavien grade III-IV-V), n(%)	4/34 (11.8)	4/15 (26.7)	-	**0.029***

*Fisher's Exact test