THE FOLLOW-UP OF PATIENTS WITH SURGICAL SOLITARY KIDNEY - THE UNDER-ESTIMATED ROLE OF COMORBIDITIES

C. Pricop¹, D. Puia¹*, I. Chiriac², Adelina Miron¹

“Grigore T. Popa” University of Medicine and Pharmacy Iasi Faculty of Medicine
1. Department of Surgery (II)
“Dr. C. I. Parhon” Clinical Hospital, Iasi, Romania
2. Clinic of Urology and Kidney Transplantation,
*Corresponding author. E-mail: drdragos83@yahoo.com

THE FOLLOW-UP OF PATIENTS WITH SURGICAL SOLITARY KIDNEY - THE UNDER-ESTIMATED ROLE OF COMORBIDITIES (Abstract): In order to customize the follow-up plan and lower the risks of end-stage renal disease progression (ESRD), we set out to create a monitoring program for patients with surgical solitary kidneys. Additionally, by determining the underlying etiology and comorbidities (such as pre-existing CKD or Diabetes).

91 patients have been found who satisfy the inclusion requirements. Material and methods: There were 51 ladies and 40 guys among them. They ranged in age from 20 to 90. The average age was 60.69 years (SD +/- 15.87). There was no difference in the mean age between the genders (63.22 vs. 58.71, p=0.08). Kidney cancer (50.54%), upper urothelial tract carcinoma (25.27%), pyonephrosis (17.58%), and kidney trauma (6.59%) were the primary pathologies for which surgery was performed. The patients were also arbitrarily separated into three age groups: Group A, 20-40 years old; Group B, 41-60 years old; and Group C, over 60 years old.

Results: One month after discharge, C-reactive protein increased (p=0.05), and eGFR decreased significantly (p=0.003). The most common comorbidity (74.72%; n=68) was arterial hypertension. Of these, 51.47% (n=35) have diabetes mellitus concurrently. Diabetes was the second-highest occurrence, with 49.45% (n=45) of patients receiving therapy for it. Also, at the time of surgery, 12.08 % (n=11) had CKD, according to KDIGO definition. Since acquired solitary kidney patients are more likely to experience rapidly declining renal function, they require continuous monitoring. Conclusions: Younger individuals are more prone to develop CKD slowly. Therefore, the clinician has to monitor issues like kidney stones or urinary tract infections. Keywords: SURGICAL SOLITARY KIDNEY, COMORBIDITIES, CHRONIC KIDNEY DISEASE.

In patients with acquired solitary kidneys, reduced renal mass causes higher intraglomerular pressure and glomerular hyperfiltration, including individuals who have undergone unilateral nephrectomy for living kidney donation, renal cancers, or trauma. These physiological modifications to the single kidney may aggravate other inherited and pre-existing diseases that might increase glomerular disorders or establish susceptibility to them, leading to adverse renal outcomes. According to Brenner et al.’s hypothesis from the 1980s, a patient is more likely to develop hyper-
tension, proteinuria, and a long-term reduction in glomerular filtration rate (GFR) if they have fewer nephrons (1). A growing body of research indicates that a congenital or acquired decrease in renal mass is associated with a higher risk of renal impairment. Nephrosclerosis and nephron hypertrophy might have a significant role in CKD and mortality. However, studies on the effects of these microstructural traits have only been conducted on tiny tissue specimens from people chosen for either having healthy kidneys or renal disease. To investigate kidney structure-outcome relationships, patients with radical nephrectomy (often renal cancer) represent a special cohort. These people are chosen neither for the lack of nephropathy (such as live kidney donors) nor for the presence of nephropathy (such as those who have had a nephrologist perform a biopsy), despite the fact that they frequently have major comorbidities. We aimed to develop a monitoring program for patients with solitary kidneys in order to personalize the follow-up scheme, thus minimizing the risks of end-stage renal disease progression (ESRD) based on comorbidities at the moment of nephrectomy and after. (e.g., Diabetes Mellitus-DM, pre-existing chronic kidney disease-CKD)

MATERIAL AND METHODS

Even if, at first glance, the patient with a solitary kidney, especially those who do not have surgical history, should be monitored by a nephrologist, we believe that multidisciplinary management is needed. We initiated a prospective follow-up program for this group of patients in our hospital. We enrolled patients with surgically single kidneys (after high urothelial tumors, parenchymal tumors, pyonephrosis, renal trauma, etc.) who underwent nephrectomy between February 2022 and February 2023. Exclusion criteria have been represented by: pregnancy, age under 18 years, and lack of compliance. We collected demographic data, personal history, chronic medication, and biochemical parameters. The last item was evaluated in patients who underwent nephrectomy before the surgery, after one week, and after one month. We realized the statistical analysis using the ANOVA, chi-square, and t-Student tests. A p-value of < 0.05 was considered statistically significant. We have also used IBM SPSS Statistics version 27.0.1.0 for our statistical analysis.

RESULTS

We have identified 91 patients who meet the inclusion criteria. Of these, 40 were males, and 51 were females. They were aged between 20 and 90 years. The mean age was 60.69 (SD+/- 15.87) years. The mean age was not different between the genders (63.22 vs. 58.71, p=0.08). The evolution of the biochemical parameters preoperatively, before discharge, and one month after discharge is represented in first table.

The main pathology for which surgery was performed was kidney cancer (50.54%), upper urothelial tract carcinoma (25.27%), pyonephrosis (17.58%), and kidney trauma (6.59%). We also arbitrarily divided the patients into three age groups: Group A, 20-40 years; Group B, 41-60 years; and Group C >60 years old.

We compared the values of serum hemoglobin, creatinine, C-reactive protein, and eGFR between groups, as shown in Table II.

We have identified the several comorbidities. Arterial hypertension was the most frequent encountered, 74.72% (n=68) patients were diagnosed. Of which 51.47%
(n=35) simultaneously having diabetes mellitus. This condition was the second most frequent encounter, 49.45% (n=45) of patients receiving treatment for it. Both are well known kidney injury elements even in patients without a history of nephrectomy. Before surgery, 12.08% (n=11) had CKD, according to KDIGO definition (<60 mL/min/1.73 m² in the last three months). As shown in Table II, most patients diagnosed with this conditions had over 60 years of age (group C).

### TABLE I.
Evolution of biochemical parameters

<table>
<thead>
<tr>
<th></th>
<th>Preoperatively</th>
<th>Before discharge</th>
<th>One month after discharge</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11.96 (+/-2.51)</td>
<td>10.85 (+/-2.18)</td>
<td>11.76 (+/-1.65)</td>
<td>0.005</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>1.78 (+/-2.04)</td>
<td>1.67 (+/-1.58)</td>
<td>1.46 (+/-0.71)</td>
<td>0.600</td>
</tr>
<tr>
<td>Serum urea (mg/dL)</td>
<td>45.38 (+/-25.09)</td>
<td>44.10 (+/-24.82)</td>
<td>41.39 (+/-19.59)</td>
<td>0.680</td>
</tr>
<tr>
<td>C-reactive protein (mg/dL)</td>
<td>40.59 (+/-64.13)</td>
<td>75.45 (+/-76.46)</td>
<td>18.58 (+/-26.86)</td>
<td>0.001</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73m²)</td>
<td>65.54 (+/-32.34)</td>
<td>56.70 (+/-22.40)</td>
<td>59.25 (+/-26.24)</td>
<td>0.130</td>
</tr>
</tbody>
</table>

### TABLE II.
Biochemical parameters one month after discharge according to the age-group

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients</td>
<td>11</td>
<td>28</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11.95(+/-1.72)</td>
<td>12.07(+/-1.84)</td>
<td>11.55(+/-4.5)</td>
<td>0.640</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>1.02(+/-0.2)</td>
<td>1.41(+/-0.71)</td>
<td>1.58(+/-0.76)</td>
<td>0.270</td>
</tr>
<tr>
<td>C-reactive protein (mg/dL)</td>
<td>12.58(+/-8.76)</td>
<td>12.16(+/-9.65)</td>
<td>22.19 (+/-33.52)</td>
<td>0.050</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73m²)</td>
<td>95.67(+/-7.94)</td>
<td>63.89(+/-31.82)</td>
<td>46.41(+/-21.6)</td>
<td>0.003</td>
</tr>
<tr>
<td>Arterial hypertension (n)</td>
<td>2</td>
<td>16</td>
<td>50</td>
<td>0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus (n)</td>
<td>2</td>
<td>11</td>
<td>32</td>
<td>0.034</td>
</tr>
<tr>
<td>CKD</td>
<td>1</td>
<td>3</td>
<td>7</td>
<td>0.280</td>
</tr>
</tbody>
</table>

### DISCUSSION
In the past decades, much research has been done on the possibility of reduced renal function in solitary kidneys. Numerous clinical studies, mostly on people with congenital renal illness, have been undertaken to validate physiopathological results in animal models. Congenital solitary kidney patients had a considerably increased probability of needing dialysis, according to a retrospective assessment by Sanna-Cherchi et al. (2). This finding raises the possibility that subclinical solitary kidney anomalies are to blame for the worsened renal outcome. Previous observational studies have looked at the short- and long-term renal outcomes of living kidney donors. According to certain longitudinal investigations of living kidney donors, renal function had been well-maintained following unilateral nephrectomy, with a mean follow-up duration of 10.7 years to 25 years (3). Studies have shown that individuals with solitary kidneys have an in-
increased risk of developing kidney stones compared to those with two functioning kidneys. The exact incidence can vary widely, but research suggests the risk is significantly higher in this population.

CKD progression in patients with solitary kidneys has been studied, especially in children. Groen In’t Woud S et al. evaluated 944 patients (children) diagnosed with a single functional kidney (congenital and acquired) (4). At the end of the study, 553 (59%) patients presented at least one indicator for renal failure (≥1 indicator of kidney injury), and 255 (27%) presented at least one indicator for severe renal failure. Akyol et al. in a cohort of 101 children, 71 with congenital single kidney (of which 55 with unilateral renal agenesis and 16 with polycystic dysplastic kidney) and 30 with acquired single kidney (17 with unilateral nephrectomy for renal tumor and 13 urological structural anomalies) highlighted renal injury in 9 (9%) of the patients and a positive correlation between uric acid concentration and renal injury. In adults, Argueso et al. performed a study on 157 patients with unilateral renal agenesis (5). The authors showed that 7 (19%) of 37 tested patients developed proteinuria (>150 mg/24h), 22 (47%) of 47 tested patients developed hypertension, and in 4 (13%) of 32 tested patients, renal function (creatinine) it degraded. At the end of the study, 43 (27%) patients died, 6 (4%) were due to renal failure. Xu et al. studied 118 patients with unilateral renal agenesis. At the initial evaluation, 14 (11.9%) had additional abnormalities, 15 (12.7%) had a heredocolateral history, and 30 (25.4%) presented with renal failure. They concluded that renal failure is common in patients with unilateral renal agenesis and that family history is a risk factor for severe renal failure (6).

Although, according to Worcester et al., nephrectomy does not negatively impact stone disease, it may decrease renal function among younger males(7). In our study, patients over 60 years had more often comorbidities that could lead to kidney stones (8). Some of these conditions are known to worsen CKD. Kiberd et al. evaluated 381 transplant patients, in which they diagnosed 111 (29%) cases of diabetes, of which 17 were considered to have pre-existing diabetes, and 94 were new cases (31 transient, 63 fixed) (9). Alfandary et al. evaluated 353 patients with solitary functional kidneys (10). Compared to the control group, the prevalence of renal injury is higher at 42.2% vs. 23.5%, hypertension at 31.7% vs. 23.1%, proteinuria at 18.2% vs. 0.4%, and eGFR at 12.0% vs. 0.1 %. They concluded that a solitary kidney is associated with a significant risk of renal injury. Obesity is also a major modifiable factor for kidney injury.

According to Ellis et al., nephrectomy can have unfavorable effects and induce progressive eGFR drop in individuals with preoperative CKD and in patients without preoperative CKD who later develop postoperative CKD. This is due to poor nephron mass reduction adaption or underlying kidney injury. This damage has been recognized in patients with clinically-evident CKD prior to nephrectomy. This damage may not be present, may only be modest, and may never have become symptomatic in individuals who did not have clinically obvious CKD prior to nephrectomy. This damage may be present, may only be modest, and may never have become symptomatic in individuals who did not have clinically obvious CKD prior to nephrectomy. Nephrectomy alters this, and individuals are then categorized as having CKD. The difference in overall survival between the two groups (patients with CKD before surgery and patients with incident CKD after nephrectomy) could be attributed to lead-time
bias if patients who develop CKD after nephrectomy are thought to have had subclinical CKD before surgery. The sole difference between subclinical and clinically-evident CKD, assuming the underlying pathogenic mechanisms are thought to be fundamentally comparable, is the timing of the first occurrence. Individuals with CKD that is clinically obvious before nephrectomy are more likely to have an earlier start of the underlying disease that causes CKD, making them more likely to die as a result of CKD than individuals who do not have CKD that is clinically evident until after nephrectomy (11).

The third underlying disease that led to nephrectomy was lithiasic pyonephrosis. Considering that kidney stones have a complex etiology and often we encounter a so-called “metabolically active lithiasis,” the follow-up of the patients is even more justified (12). A screening of lithiasic patients could prevent hydronephrosis episodes, which, over time, have a negative impact on kidney parenchyma. Often hydronephrosis is accompanied by urinary tract infection, especially in high-volume stones (13,14). According to Naqvi et al., infection outcomes in CKD patients are 3 to 4 times worse than in healthy subjects (15). Also, according to Shang et al., patients with kidney have a 1.47 relative risk of developing CKD (16).

In light of this, the following pertinent query is: How does the mortality risk for patients with new-onset CKD following surgery compared to that of individuals with medical causes of CKD who do not have nephrectomy? Demirjian et al. partially addressed this using the Cleveland Clinic Surgical Registry dataset, comparing all-cause mortality and non-renal cancer mortality in patients with “medical/surgical” and “surgical” CKD (n=1,097 and 1,053, respectively), as well as a cohort of 42,658 patients with CKD that wasn’t brought on by nephrectomy and were treated by nephrologists at the Cleveland Clinic (17). The claim that CKD brought on by surgical nephron reduction has less clinical importance than CKD brought on by other sources has a problem. Clinical recommendations’ thresholds for CKD stages are based on the facts that 60 mL/min per 1.73 m² is almost half of the average person’s maximal physiological eGFR, can be correctly discriminated against using estimating equations, and is linked to a higher risk of adverse outcomes (18).

In our opinion, patients who are more likely to develop lithiasis should be evaluated at 3 months. For those with urinary tract infections, monthly after administration of the treatment according to urine culture and antibiogram, while for those with associated pathologies (hypertension, diabetes etc.), six months evaluation is the most cost-efficient, with subsequent monitoring depending on the clinical manifestations.

**CONCLUSIONS**

Patients with acquired solitary kidneys need close follow-up because they are prone to rapidly decreasing renal function. Although, according to our data, serum creatinine and eGFR do not have a significant modification, one month after patients discharge, degradation will likely occur over time. In younger patients, CKD is likely to develop slower; the clinician needs to follow up on the conditions like kidney stones or urinary tract. We suggest that patients who are more likely to develop lithiasis should be evaluated at three months. In our opinion, the most important comorbidity that should be followed is
The follow-up of patients with surgical solitary kidney - the under-estimated role of comorbidities

urinary tract infection, the doses and duration of the treatment being adapted for eGFR, but the others should not be neglected. Patient education to avoid as much as possible any trauma to the single kidney must be included in the therapeutic plan.

CONFLICT OF INTEREST AND FUNDING
The authors declare that there is no conflict of interest, and they received no specific funding regarding this scientific research.

REFERENCES