

# The Predictive Power of Intraoperative Surgical Apgar Scores in Foreseeing Renal Function after Radical Nephrectomy

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**Keywords.** Glomerular filtration rate; Radical nephrectomy; Renal cell carcinoma; Surgical Apgar score

**Introduction.** This study was conducted to evaluate the predictive power of the Surgical Apgar Score (SAS) based on surgical blood loss, the lowest intraoperative heart rate and mean arterial pressure in foreseeing short- and long-term effects of radical nephrectomy (RN) on renal function.

**Methods.** A prospective investigation was conducted on 111 patients who underwent RN for kidney tumors at a tertiary hospital between 2016 and 2019. The SAS and age-adjusted Charlson Comorbidity Index (CCI) scores were calculated in relation to glomerular filtration rates (GFR) changes on postoperative 1<sup>st</sup> day, 3<sup>rd</sup> and 12<sup>th</sup> months.

**Results.** Patients in higher risk groups, stratified on the basis of SAS, had longer operation times, extended hospital stays, increased bleeding, and higher blood transfusion rates ( $P < .001$ ). No significant difference existed between preoperative and early postoperative GFR values in SAS-stratified risk groups ( $P = .802$ ,  $P = .342$ , respectively). However, a significant GFR decrease occurred in the high-risk group compared to the moderate and low risk groups at postoperative 3<sup>rd</sup> ( $60.79 \pm 16.86$ ,  $76.22 \pm 24.20$ ,  $69.80 \pm 18.92$ , respectively) and 12<sup>th</sup> months ( $53.57 \pm 12.74$ ,  $71.61 \pm 17.52$ ,  $71.86 \pm 19.33$ , respectively) ( $P = .034$ ,  $P < .001$ ). CCI scores predicted preoperative GFR in low, moderate, and high-risk groups ( $111.58 \pm 30.91$  ml/min,  $94.81 \pm 22.55$  ml/min, and  $85.43 \pm 32.69$  ml/min, respectively) ( $P = .001$ ), but GFR changes between CCI-defined risk groups were not significant at postoperative 3<sup>rd</sup> and 12<sup>th</sup> months ( $P = .546$ ,  $P = .481$ ).

**Conclusion.** A significant correlation was found between SAS estimated during the RN procedure and GFR changes at three and twelve months after surgery. Based on SAS, early kidney-preserving therapies like diet, and avoidance of nephrotoxic agents may be recommended for high-risk patients to prevent prolonged GFR alterations.

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## INTRODUCTION

Renal cell carcinoma (RCC) is the most commonly detected solid tumor among renal tumors, accounting for approximately 85–90% of all renal

masses and approximately 3% of all tumors detected in adults, and constitutes the most aggressive tumor group among urological organ tumors.<sup>1</sup> Primary treatment of RCC is partial nephrectomy

in T1-2 tumors when technically feasible, while radical nephrectomy (RN) is recommended in the remaining cases of localized RCC.<sup>2</sup>

Compensatory hypertrophy of the intact kidney after RN maintains glomerular filtration rate (GFR).<sup>3</sup> Despite adaptive compensatory hypertrophy, acute kidney injury (an increase in plasma creatinine > 0.3 mg/dL within 48 hours or an increase in plasma creatinine > 1.5 fold of baseline was reported in up to 33% of patients. RN, age, comorbidities such as diabetes mellitus (DM), preoperative GFR values and RENAL nephrometry scores, which grades renal masses by complexity for surgical decision-making, are among the factors that are shown to adversely affect renal function, leading to chronic kidney disease.<sup>5,6</sup>

Retrospective evaluation of 303 cases undergoing colectomy procedures using Surgical Apgar Scores (SAS) was described for the first time by Gawande *et al.* in 2007. In this ten-point scoring system, SAS scores are calculated based on the lowest mean arterial blood pressure, lowest heart rate, and blood loss observed during surgery so as to classify patients into low-, moderate-, and high-risk groups. In addition, this calculation predicts the complications in the early postoperative period, i.e., within 30 days after surgery.<sup>7</sup> Subsequent studies have demonstrated the efficacy of this scoring system in vascular, urological, orthopedic, gynecologic, and neurosurgical procedures.<sup>8-12</sup>

The present study aims to investigate the performance of SAS estimated on the basis of specified intraoperative parameters in predicting the status of renal function in the early postoperative period and in the long term in patients undergoing RN.

## MATERIALS AND METHODS

After obtaining the approval for the conduction of the study from the Clinical Trials Ethics Committee (NO: 2019/266, June 19, 2019), the Surgical Apgar Scores of 114 patients undergoing open or laparoscopic RN at a tertiary hospital (Gaziantep University Medical Faculty, Department of Urology) were calculated. Additionally, the relationship between SAS and GFR in the early postoperative period and in the long term was evaluated by using the Modification of Diet in Renal Disease (MDRD) formula.

### Study Participants

The 114 participants were included to current

study between January 2016 and June 2018 due to a renal mass and underwent open or laparoscopic RN. Demographic characteristics of participants including age, weight, height, body mass index, sex, presence of chronic disease, smoking status, American Society of Anesthesiologists (ASA) scores, laboratory findings (complete blood count (CBC), creatinine levels before and at the first day, third month and first year after surgery) were recorded. Preoperative imaging studies included computed tomography (CT) or magnetic resonance imaging (MRI) with contrast enhancement to investigate renal masses. During this assessment procedures, RENAL nephrometry score was estimated on the basis of Radius of the tumor size indicating the maximal tumor diameter, exophytic/endophytic properties of the tumor, nearness of the deepest part of the tumor to the collecting system or sinus, anterior or posterior location of the mass, and its location relative to the polar line.<sup>13</sup>

Patients with maximal tumor diameters less than 10 cm and those with low RENAL scores (< 7) were excluded from the study because they had undergone partial nephrectomy. Patients with missing data, polycystic kidney disease, preoperative GFR < 15 ml/min/1.73 m<sup>2</sup>, metastatic disease and those under the age of 18, patients with non-tumor pathology, and those who did not attend postoperative control visits or died within one year after surgery were not included in the analyses.

### Pathological Examinations

Pathological characteristics of the renal masses were retrieved from the pathological reports issued by the Gaziantep University Medical Faculty, department of Pathology. These characteristics encompassed the histological subtype, tumor stage and size, status of surgical margin, and variant histopathology. The tumors were staged according to the tumor, lymph node, metastasis (TNM) 2017 classification system.<sup>14</sup> The pathology reports also provided data on tumor volume, which was calculated by multiplication of three dimensions of the tumor mass.

### Calculation of the Surgical Apgar and Other Scores

The surgical Apgar scoring system, consisting of ten points (Table 1), is calculated using the

**Table 1.** Calculation of the surgical Apgar score

	0	1	2	3	4
Estimated blood loss (ml)	> 1000	601-1000	101-600	≤ 100	-
The Lowest MABP (mm Hg)	< 40	40-54	55-69	≥ 70	-
The Lowest Heart rate/min	> 85	76-85	66-75	56-65	≤ 55

MABP: Mean arterial blood pressure HR: Heart Rate ,min: Minute, ml: milliliters, mm Hg: millimetres of mercury

lowest mean arterial blood pressure, lowest heart rate, and blood loss observed during surgery categorise patients into high ( $\leq 4$ ) moderate (5-7), and low ( $\geq 8$ ) risk groups. The changes in GFR were evaluated within and between groups. The *P1* value indicated the level of statistical significance of intergroup percentage changes in GFR values between the postoperative 3<sup>rd</sup> and 12<sup>th</sup> months, the *P2* value referred to statistical significance of intergroup percentage changes in GFR values, and the *P3* value represented the level of statistical significance of the changes in GFR values within the individual risk groups.

All perioperative and all monitored intraoperative data (including arterial blood pressure [ABP] and heart rate [HR]) were recorded. Furthermore, the estimated blood loss was calculated and recorded, considering the blood loss observed during surgery, the amount of bloody fluid aspirated from the surgical field, the irrigation solution administered to the surgical field, and weights of all swabs, intra-abdominal sponges etc. used during surgery.

Also, the number of blood products (erythrocyte suspension, pooled platelet suspension, apheresis platelet concentrates, fresh frozen plasma) administered to the patient during surgery was recorded. At the end of the surgery, the operation time was calculated as the time from the first incision to the end of the operation.

Using the age-adjusted Charlson Comorbidity Index (CCI), the patients were grouped according to the presence or absence of at least one condition considered to have contributed to kidney injury by reducing GFR.<sup>15</sup> Patients were evaluated according to comorbid conditions in 19 different categories. Patients with CCI scores of  $\leq 3$ , 4-5, and  $\geq 6$  were classified in low-, moderate, and high-risk groups, respectively.

GFR values calculated according to the MDRD formula using urea and creatinine values measured at the initial diagnosis, in the early postoperative period, and at the last control visit were evaluated.<sup>16</sup> The GFR values were measured at 3<sup>rd</sup> and 12<sup>th</sup>

months after RN, to allow the time for adequate compensation of renal functions of the contralateral kidney<sup>17</sup>. GFR was calculated according to the MDRD formula as follows:

$$\text{GFR (mL/min/1.73 m}^2\text{)} = 175 \times (\text{serum creatinine})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female})$$

### Statistical Analysis

Descriptive data was expressed as mean, standard deviations, percentages, and numbers in statistical analyses. The nonparametric Mann-Whitney U test was used in the paired comparisons of continuous variables without normal distribution. The Kruskal-Wallis test was used in the comparison of GFR changes between preoperative period and the third and twelfth months postoperatively. The Friedman test was used to compare the dependent variables. The level of statistical significance was established at a p-value of 0.05, and values below this threshold were considered statistically significant.

### RESULTS

Three patients who met the prespecified exclusion criteria were excluded from the study. The study sample of 111 cases consisted of 70 (63.1%) male, and 41(36.9%) female patients with an overall mean age of  $57.1 \pm 13.4$  years, and BMI of  $28.2 \pm 5.2$  kg/m<sup>2</sup>.

The respective number of patients with different stages of the disease were as follows: pT1b (n: 17; 15.33%), pT2a (n:44: 39.63%), pT2b (n:39;35.13%), pT3a (n.5; 4.5%), pT3b (n:1; 0.9%), and pT4 (n.5; 4.5%) disease. Furthermore, histopathological examination revealed clear cell RCC in 50.4% (56/111), papillary RCC in 19.8% (22/111), chromophobe RCC in 14.41% (16/111), collecting duct carcinoma (CDC) in 3.6% (4/111), sarcomatoid differentiation in 3.6% (4/111), oncocytoma in 6.3% (7/111), and malignant epithelial tumor in 1.8% (2/111) of patients.

Demographic and intraoperative data of the patients in the high, moderate, and low-risk groups are summarized in Table 2 according to the SAS. The operation time and the length of hospital stay were

**Table 2.** Demographic and operative data of patient according to SAS risk groups

	SAS GROUPS						P
	HIGH RISK		MEDIAN RISK		LOW RISK		
	Mean	SD ( ± )	Mean	SD ( ± )	Mean	SD ( ± )	
Age (year)	57	13	57	12	57	15	.976
Weight (kg)	81	18	77	13	78	13	.346
Length (cm)	167	9	166	11	168	11	.438
BMI (kg/m <sup>2</sup> )	29.11	6.51	28.03	4.02	27.83	5.83	.451
Bleeding (ml)	715	694	315	199	235	155	.001
Hospitalization (day)	5.8	1.9	4.6	1.3	4.1	1.0	< .001
Eritrosit Suspension (Unit)	1.60	2.01	0.36	0.71	0.29	0.61	.001
FFP (Unit)	0.80	1.54	0.17	0.55	0.16	0.37	.068
ASA	2	1	2	1	2	1	.861
Preoperative Hemoglobine (g/dl)	12.8	1.7	13.1	1.6	13.4	2.0	.355
Postoperative Hemoglobine (g/dl)	11.3	1.7	12.1	1.7	12.4	1.8	.092
Tumor length (cm)	10.13	4.26	7.85	3.96	6.84	2.28	.009
Operation Duration (min)	152	39	129	22	132	29	.012

FFP: Fresh Frozen Plasm, ASA: American Society of Anesthesiologists, g/dl: Grams per decilite, min: Minute, cm: Centimeter, ml: Milliliter, kg/m<sup>2</sup>: Kilogram per meter squared

longer, and the amount of blood transfusion was higher in the high-risk group than in the moderate and low-risk groups ( $P < .001$ ). In addition, the operation time was longer ( $P = .012$ ) and tumor size ( $P = .013$ ) was larger in the high-risk group.

Preoperative GFR values were not different between the groups ( $P1 = .802$ ). There was also no significant intergroup difference in terms of postoperative GFR values ( $P1 = .342$ ). However, there were significant differences between GFR values measured at the 3rd-month and 12th-month follow up visits ( $P1 = .034$  and  $P1 < .001$ ) (Table 3).

In the analysis of the percentage changes in GFR values between the groups ( $P2$ ), the decreases in GFR values immediately after surgery ( $P2 = .193$ ) and at the postoperative 3rd months ( $P2 = .072$ ) were not statistically significant. On the contrary, the decrease in GFR values in the high-risk group

in the 12th month was significant compared to moderate and low-risk groups ( $P2 < .001$ ) (Table 3).

In the analysis of individual groups ( $P3$ ), there was a significant decrease in the postoperative GFR values on the first day, 3rd and 12th months in the three groups ( $P3 < .001$ ). This was an anticipated decrease considering that the kidney undergoing RN due to a tumor was not a nonfunctioning but a functioning kidney in general (Table 3).

The analysis of comorbidities showed that 65 of 111 patients (58.6%) had at least one comorbid condition. The patients were classified on the basis of their estimated CCI scores independently of their surgical Apgar scores in terms of their comorbid conditions. Accordingly, the indicated numbers of patients had CCI scores of  $\leq 3$  (n: 35; 31.5%); 4–5 (n: 47; 42.3%),  $\geq 6$  (n: 29; 26.12%) and they were included in, low-, moderate, and high-risk groups,

**Table 3.** GFR values changes according to SAS risk groups

	HIGH RISK		MODERATE RISK		LOW RISK		P1	P2
	Median ± SD	Changes (%)	Median ± SD	Changes (%)	Median ± SD	Changes (%)		
Number (n)	20		58		33			
Preoperative GFR (ml/min)	95.77 ± 26.98		99.05 ± 30.10		94.44 ± 24.89		.802	
Postoperative 1st day GFR (ml/min)	71.26 ± 23.73	25.5 ± 21.9	79.92 ± 22.80	19.3 ± 17	76.47 ± 19.54	19 ± 40.8	.342	.193
Postoperative 3rd month GFR (ml/min)	60.79 ± 16.86	36.5 ± 20.3	76.22 ± 24.20	23 ± 19.1	69.80 ± 18.92	26 ± 24.8	.034	.072
Postoperative 12th month GFR (ml/min)	53.57 ± 12.74	44 ± 19.2	71.61 ± 17.52	27.7 ± 18.3	71.86 ± 19.33	23.9 ± 19.8	.001	.001
P3	.001		.001		.001			

n: Number GFR: Glomerular Filtration Rate, ml: milliliters, min: minute, SD: standard deviation

**Table 4.** GFR changes according to Age Adjusted Charlson Co-morbidity Index Score

	Age adjusted Charlson Co-morbidity Index score						P	
	≤3 (low risk)		4-5 (moderate risk)		≥6 (High risk)		P1	P2
	Mean ± SD	Changes (% ± SD)	Mean ± SD	Changes (% ± SD)	Mean ± SD	Changes (% ± SD)		
n (%)	35 (31.5)		47 (42.34)		29 (26.12)			
preoperative GFR (ml/min)	111.58 ± 30.91		94.81 ± 22.55		85.43 ± 32.69		.001	
postoperative GFR (ml/min)	87.35 ± 21.43	19.06 ± 17.97	75.99 ± 23.29	19.17 ± 15.77	68.04 ± 24.93	19.11 ± 16.31	.005	1
postoperative 3rd month GFR (ml/min)	81.06 ± 26.07	25.73 ± 18.77	68.75 ± 17.73	25.98 ± 16.29	57.60 ± 24.82	30 ± 22.66	< .001	.601
postoperative 12th. month GFR (ml/min)	77.37 ± 18.2	28.13 ± 16.9	67.93 ± 15.16	26.17 ± 16.45	57.61 ± 22.41	31.02 ± 17.73	< .001	.481

n: numerous GFR: Glomerular filtration rate, ml: milliliters, min: minute, SD: standard deviation

respectively. Preoperative GFR values differed between the groups ( $P = .001$ ), and the analysis to find out the group that caused the intergroup difference showed that preoperative GFR values according to the CCI classification system were higher in the low-risk group than in the moderate and high-risk groups ( $P = .001$ ). No significant differences were observed between the moderate and high-risk groups regarding preoperative GFR values ( $P = .546$ ). However, the intergroup comparisons of percent changes in GFR values ( $P2$ ) showed that GFR significantly decreased in both groups. However, GFR values estimated at the 3<sup>rd</sup> and 12<sup>th</sup> month control visits did not significantly differ between groups ( $P2 = .601$ ,  $P = .481$ ) (Table 4).

## DISCUSSION

Many studies have investigated changes in GFR in patients who have undergone RN due to renal cancer.<sup>18-20</sup> Palacios *et al.* determined that young patients with a low preoperative eGFR level had a greater propensity for functional compensation of the contralateral kidney following RN, especially when the removed kidney had a more functional capability.<sup>18</sup> Zabor *et al.* conducted a multicenter study that investigated improvements in eGFR values in patients who underwent RN for renal cancer. They demonstrated that those patients who had preoperative eGFR < 60 ml/min/1.73 m<sup>2</sup> and a larger tumor volume experienced greater improvements in postoperative GFR values.<sup>19</sup> In the new baseline glomerular filtration rate (NBGFR) formula, which is used to predict postoperative GFR levels after RN, the lower preoperative GFR value and larger (> 7 cm) tumor size have a

favorable effect while advanced age and a history of diabetes mellitus have an unfavorable effect on GFR.<sup>21</sup> Rathi *et al.* emphasized that when calculating NBGFR after RN, the split renal function of the contralateral kidney has an impact on postoperative GFR values, so the selection of the surgical option (nephron sparing nephrectomy or RN) should be determined accordingly.<sup>17</sup>

Further studies are necessary to evaluate the effects of intraoperative variables during RN on renal functions in the long term. In a recently published prospective Japanese research study on 422 patients, a new equation involving preoperative markers and gender was described to predict GFR outcomes at postoperative first year in patients undergoing RN due to RCC. Tumor size and BMI were not independent factors in this equation based on age, tumor size, and BMI. Accordingly, the equation that was modified to include gender allowed better prediction of GFR (eGFR) at one year after RN, and it was suggested that this prediction would be of benefit for preoperative patient counseling and the selection of surgery type in patients undergoing elective partial or RN.<sup>22</sup> Analysis of changes in GFR values according to BMI showed a significant decrease in GFR at the first postoperative year in obese patients. In the present study, we evaluated comorbidities that may adversely affect GFR, using age-adjusted CCI and observed that the decrease in GFR values was more serious in patients in the high-risk group.

SAS is based on a scoring system that shows preoperative hemodynamic instability. In various studies, the efficacy of SAS has been demonstrated in vascular, urological, orthopedic, gynecological, and neurosurgical procedures.<sup>23-26</sup> The common feature

of these studies was that the rate of transfusions, length of hospital stays, and the amount of blood loss were higher in patients with low SAS in high-risk category.

At a center specialized in emergency abdominal and cranial surgeries, the effects of systemic inflammatory response syndrome (SIRS) and SAS on acute kidney injury were evaluated postoperatively. The patients were classified into two groups with respect to the presence of SIRS: SAS < 5 and SAS > 5. The study mentioned that presence of SIRS and SAS < 5 was an independent risk factor.<sup>27</sup> Lone *et al.* demonstrated that SAS is an independent factor in the prediction of the development of acute renal failure after radical cystectomy that should be considered after preoperative GFR values, operation time, and neoadjuvant chemotherapy.<sup>28</sup> According to SAS, longer surgery time of the patients in the high-risk group increases renal hypoperfusion with longer-term exposure to vasopressors and hemodynamic instability.<sup>28</sup> The non-adherence to the enhanced recovery after surgery (ERAS) protocol was associated with a greater likelihood of acute kidney failure due to renal hypoperfusion. SAS has been suggested to be used to identify patients in need of a more individualized liquid management plan.<sup>28,29</sup> Unlike other studies, the present study evaluated the relationship between the changes in GFR and SAS after RN and found that the decreases in GFR at three months and one year after surgery were significant in the high-risk (SAS < 4) patient group.

The relationship between SAS and GFR after RN has not been evaluated so far. The present study examined the effects of the Surgical Apgar Scores calculated on the basis of intraoperative data recorded during RN effective on GFR values in the early postoperative period and the long term after surgery. The results of the statistical analysis showed a more remarkable decrease in GFR in the high-risk group compared to the low-risk group defined according to the SAS. In the same way, this patient group experienced longer hospital stays, more blood transfusions, larger tumors, and longer operation times. The authors believe that the findings of the present study contributes to the literature by demonstrating the prediction of a decrease in GFR in high-risk groups defined by the SAS and by inspiring future studies designed to prevent or delay renal failure

using nephroprotective agents and diet after RN in this high-risk group.

### LIMITATIONS

We thought that the risk groups based on surgical Apgar scores and the negative effects of comorbid conditions may not have become evident in a one-year long postoperative follow-up period, and a comparison with a larger number of patients followed up for a longer period of time could capture a significant difference. Additionally, the fact that the split renal function of both kidneys was not calculated before RN can be considered as a limitation of the study.

### CONCLUSION

The study found a significant correlation between the SAS during the RN procedure and the changes in GFR values within three months and one year after surgery. During surgical procedures which are associated with a high risk of hemodynamic instability, close monitoring and reducing the period of hemodynamic instability can help protect against renal hypoperfusion by taking preventive measures to control bleeding, which can contribute to the preservation of early- and late-term renal function. For patients deemed to be in the high-risk group, according to the SAS, early kidney-preserving therapies, diet, and avoidance of nephrotoxic agent to prevent changes in GFR in the long term can be recommended. Due to the single-center design of the present study, prospective multicenter studies are needed to be performed in a larger number of patients to support the findings of the present study.

### DECLARATION

#### Ethical Considerations

This study was approved by the ethics committee of Gaziantep University (NO: 2019/266) and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

#### Competing Interests

The authors declare no competing interests.

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**Data availability**

The data are freely available upon reasonable request from the corresponding authors.

**Author Contributions**

Concept – S.E., H.N. ; Design – S.E.,H.N., M.B.; Supervision – S.E., Ö.B.; Resources – M.Ö., M.B.; Materials-H.N., M.Ö., İ.S. ; Data Collection and/or Processing – İ.S., M.Ö., H.N.; Analysis and/or Interpretation – H.Ş., M.B., İ.S. ; Literature Search S.E.,H.Ş., Ö.B., M.B.; Writing Manuscript – M.B., S.E., H.N.; Critical Review – S.E., Ö.B., M.B.

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