

## ORIGINAL ARTICLE

# The Effect of Newly Onset Renal Impairment on the Mortality Rates of the Patients Undergoing Endovascular Aortic Repair

## Yeni Başlayan Böbrek Yetmezliğinin Endovasküler Aort Onarımı Yapılan Hastalarda Mortalite Oranlarına Etkisi

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### ABSTRACT

**Background:** Visceral organ blood circulation is seriously impaired in aortic pathologies especially aortic dissection involving descending thoracic and abdominal aorta. Herein, we aimed to determine the effect of the newly onset renal function impairment on postoperative mortality rates of the patients undergoing EVAR and TEVAR procedures.

**Methods:** Patients who underwent an EVAR / TEVAR procedure in our clinic included in this retrospective study. Patients were divided into two groups according to the presence of renal function impairment. Mortality rates were calculated for the groups.

**Results:** A total of 60 patients who underwent an EVAR/TEVAR procedure between November 2016 and May 2021 included in this study. Group 1 included 48 (80%) patients without postoperative renal dysfunction. Group 2 included 12 (20%) patients with postoperative renal function impairment. The initial analysis of the data revealed significant differences in the age and sex variables of the groups (P=0.038 and P=0.008 respectively). Then propensity score matching was performed to avoid bias in the groups. After propensity score matching Group 1 included 12 (50%) patients without postoperative renal impairment and Group 2 included 12 (50%) patients with postoperative renal dysfunction. There were no significant differences between the groups after propensity matching. Mortality rate was significantly different between the groups which was 1 patient (8.33%) in Group 1 vs 6 (50.00%) patients in Group 2 (P=0.020).

**Conclusions:** Renal functions after EVAR/TEVAR procedures should be carefully monitored because renal impairment is closely related with postoperative mortality. We suggest that more studies with larger patient numbers should be conducted on the relation of renal functions and mortality after regularly performed EVAR/TEVAR procedures.

**Keywords:** Endovascular aortic repair, Renal impairment, Mortality

### Öz

**Amaç:** Aort patolojilerinde özellikle inen torasik ve abdominal aortayı içeren aort diseksiyonlarında visseral organ kan dolaşımı ciddi şekilde bozulur. Bu çalışmada EVAR ve TEVAR uygulanan hastalarda yeni başlayan böbrek fonksiyon bozukluğunun postoperatif mortalite oranlarına etkisini belirlemeyi amaçladık.

**Yöntemler:** Bu retrospektif çalışmaya kliniğimizde EVAR/TEVAR işlemi uygulanan hastalar dahil edildi. Hastalar böbrek fonksiyon bozukluğuna göre iki gruba ayrıldı. Gruplar için ölüm oranları hesaplandı.

**Bulgular:** Kasım 2016 ile Mayıs 2021 arasında EVAR/TEVAR prosedürü uygulanan toplam 60 hasta bu çalışmaya dahil edildi. Grup 1, postoperatif böbrek fonksiyon bozukluğu olmayan 48 (%80) hastayı içermiştir. Grup 2'de postoperatif böbrek fonksiyon bozukluğu olan toplam 12 (%20) hasta vardı. Verilerin ilk analizi, grupların yaş ve cinsiyet değişkenlerinde anlamlı farklılıklar olduğunu ortaya koydu (sırasıyla P=0.038 ve P=0.008). Daha sonra gruplarda yanlılığı önlemek için eğilim skoru eşleştirmesi yapıldı. Eğilim skoru eşleştirmesinden sonra Grup 1'e postoperatif böbrek yetmezliği olmayan 12 (%50) hasta ve Grup 2'ye postoperatif renal disfonksiyonu olan 12 (%50) hasta dahil edildi. Eğilim eşleştirmesinden sonra gruplar arasında önemli farklılıklar yoktu. Ölüm oranı gruplar arasında önemli ölçüde farklıydı.

**Sonuçlar:** EVAR/TEVAR prosedürlerinden sonra böbrek fonksiyonları dikkatle izlenmelidir çünkü böbrek yetmezliği postoperatif mortalite ile yakından ilişkilidir. Düzenli olarak uygulanan EVAR/TEVAR işlemleri sonrası böbrek fonksiyonları ve mortalite ilişkisi konusunda daha geniş hasta sayıları ile daha fazla araştırma yapılması gerektiğini düşünüyoruz.

**Anahtar Kelimeler:** endovasküler onarım, böbrek yetmezliği, mortalite

### Introduction

Endovascular aortic repair (both thoracic and abdominal aorta) (TEVAR, EVAR) is the first-line treatment modality for the pathologies of the aorta in thoracic and abdominal regions. The mortality and morbidity rates of EVAR/TEVAR are superior to open repair in midterm follow-up period (1). The causes of renal damage during or after EVAR/TEVAR procedures theoretically consist of nephropathy due to contrast medium administration, renal microembolization, ischemia-reperfusion injury or post-operative contrast medium injury due to diagnostic imaging or

reintervention (2). The incidence of acute renal injury (ARI) after elective EVAR operations are reported as 18.8% (3). The rate of ARI after TEVAR for type B aortic dissections is reported between 17 – 21% (4).

Renal function impairment is associated with poor outcomes after EVAR / TEVAR procedures. The rate of major adverse events, 30-day mortality and myocardial infarction were reported significantly higher in patients with renal insufficiency compared to the control group after TEVAR procedures (5). Also, development of ARI is associated with increased mortality and adverse

cardiovascular event rates after EVAR procedures (3).

Herein, we aimed to determine the effect of the newly onset renal function impairment on postoperative mortality rates of the patients undergoing EVAR and TEVAR procedures.

### Material and Method

Patients who underwent an EVAR / TEVAR procedure in our clinic included in this retrospective study. Patients with preoperative renal dysfunction or on hemodialysis program were excluded. Patient data were collected from hospital records retrospectively. Renal impairment was defined as acute renal failure, hematuria and contrast nephropathy which occurred in the early postoperative period. Patients were divided into two groups according to the presence of renal function impairment. Mortality rates were calculated for the groups. Local ethical committee approval was obtained for conducting the study.

A modern definition based on serum creatinine and urine was made by changing the RIFLE (Risk of renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function, and End-stage kidney disease) criteria defined in 2004 to make it a standard definition. RIFLE criteria changed with a simplified definition. Acute renal failure was accepted according to this regulation as an abrupt (48 hours) reduction in renal function with an absolute increase in SCr concentration 0.3 mg/dL (26.4  $\mu$ mol/L), a 50% increase in SCr concentration (1.5- fold from baseline), or a reduction in urine output (0.5 mL/kg/h) for 6 hours. These criteria were accepted in our study (6).

### The operative procedure

All procedures were performed under local anesthesia in angiography laboratory. After electrocardiography and blood pressure monitoring, a 5000 IU of intravenous heparin was administered at the beginning of the procedures. Activated clotting time was monitored and maintained over 150 seconds. All procedures were performed through a femoral artery access. The main body of the TEVAR graft (Valiant Captivia, Medtronic, CA, USA) was introduced through the 24F sheath (Sentrant, 24F 28 cm, Medtronic, Santa Rosa, CA, USA) in the femoral artery. If a type 1 endoleak was observed, then an extension graft (aortic cuff) was placed and balloon dilatation of the grafts was performed.

In EVAR procedures, both femoral arteries were explored with open surgical technique. Main body of the aortic stent graft was (Endurant II, Medtronic, CA, USA) introduced through the femoral sheath and placed just below the orifice of the renal arteries. The contralateral limb of the graft was placed through the contralateral femoral artery access. All procedures were completed with technical success. All patients received proper intravenous fluid support containing n-acetylcysteine (3000 ml regular saline solution containing 1500 mg n-acetylcysteine) as an infusion therapy over 24 h. Also, antiagregant and anticoagulant medication were administered in all patients in the intensive care unit. The patients with an

uneventful follow-up were discharged from hospital in the third postoperative day with a prescription of 100 mg ASA and 75 mg clopidogrel once-in-a-day orally. The operative procedure was described more detailed in our previous study (7).

### Statistical analysis

SPSS (Statistical Package for the Social Sciences) v13 software was used for statistical analysis of the data. The qualitative data are expressed as percentage (%) and quantitative data are expressed as mean  $\pm$  standard deviation (SD). The distribution of the data was tested for normality with Kolmogorov-Smirnov test. The significance of the parametric data was tested with t-test and the significance of non-parametric data was tested with chi-square and Mann-Whitney U tests. P value <0.05 was accepted as statistically significant. Propensity scores were calculated with binary logistic regression analysis. Groups were matched according to propensity scores with one-to-one matching algorithm. The Hosmer-Lemeshow goodness-of-fit test yielded a P value of 0.709 which indicated a well-fit model.

### Results

A total of 60 patients who underwent an EVAR/TEVAR procedure between November 2016 and May 2021 were included in this study. Group 1 included 48 (80%) patients without postoperative renal dysfunction. Group 2 included 12 (20%) patients with postoperative renal function impairment. The initial analysis of the data revealed significant differences in the age and sex variables of the groups (P=0.038 and P=0.008 respectively) but other comorbidities were similar. Then propensity score matching was performed to avoid bias in the groups. After propensity score matching, Group 1 included 12 (50%) patients without postoperative renal impairment and Group 2 included 12 (50%) patients with postoperative renal dysfunction. There were no significant differences between the groups after propensity matching. Preoperative data are presented in Table 1.

Abdominal EVAR was performed in 8 (66.67) patients in Group 1 and 5 (41.67%) patients in Group 2. Thoracic EVAR (TEVAR) was performed in 3 (25.00%) patients in Group 1 and 6 (50.00%) patients in Group 2. Combined EVAR and TEVAR were performed in 1 (8.33%) patient in Group 1 and 1 (8.33%) in Group 2. There were no statistically significant differences between these values (P=0.424) (Table 2). Open surgery needed only in 1 (8.33) patient in Group 2 (P=0.232). Mortality rate was significantly different between the groups which was 1 patient (8.33%, %95 Confidence Interval for mean 0.59 – 1.08) in Group 1 vs 6 (50.00%, %95 Confidence Interval for mean -0.10 – 0.27) patients in Group 2 (P=0.020). Postoperative data are presented in Table 3.

In Group 2, 10 (83.33%) patients had acute renal failure and needed hemodialysis, 1 (8.33%) patient had hematuria and 1 (8.33%) patient had contrast nephropathy which occurred with increase in blood urea and creatinine levels in the postoperative period.

**Table 1.** Preoperative data (propensity matched)

	Group1 (n=12)	Group2 (n=12)	P value	
Age mean ± SD	79 ± 8.45	78 ± 7.94	0.941	
Sex n (%)	6 (50.00)	6 (50.00)	1.000	
ASA score mean ± SD	3.83 ± 0.39	3.92 ± 0.52	0.683	
Emergency surgery n(%)	4 (33.33)	8 (66.67)	0.102	
Preoperative arrhythmia n(%)	None	8 (66.67)	9 (75.00)	0.486
	AF	3 (25.00)	3 (25.00)	
	AV block	1 (7.42)	0	
	Pacemaker	0	0	
Peripheral artery disease n(%)	1 (7.42)	2 (16.67)	0.534	
Cerebrovascular event n(%)	2 (16.67)	4 (33.33)	0.342	
Preoperative COPD n(%)	7 (58.33)	8 (66.67)	0.673	
Tobacco product consumption n(%)	6 (50.00)	7 (58.33)	0.682	
Hypertension n(%)	11 (91.67)	11 (91.67)	1.000	
Diabetes mellitus n(%)	7 (58.33)	6 (50.00)	0.682	
EF % mean ± SD	54 ± 5.06	52 ± 9.46	0.932	
Triglyceride mg/dl mean ± SD	138 ± 61.23	139 ± 85.04	0.843	
LDL mg/dl mean ± SD	125 ± 69.49	114 ± 66.16	0.514	
Preoperative eGFR ml/min/1.73 m <sup>2</sup>	54.25 ± 21.66	48.83 ± 30.41	0.620	
Preoperative creatinine mg/dl mean ± SD	1,7 ± 1.52	1,9 ± 1.27	0.514	

SD: Standard deviation; ASA: American Society of Anesthesiologists; AF: Atrial fibrillation/flutter; AV: Atrioventricular; COPD: Chronic obstructive pulmonary disease; EF: Ejection fraction; LDL: Low density lipoprotein; eGFR: Estimated glomerular filtration rate.

**Table 3.** Postoperative data

	Group 1 (n=12)	Group 2 (n=12)	P value	
Intensive care unit stay time days mean ± SD	2.83 ± 2.98	5.25 ± 4.86	0.156	
In-hospital stay time days mean ± SD	8.67 ± 4.05	7.58 ± 5.09	0.570	
ES transfusion units mean ± SD	1.08 ± 1.98	2.00 ± 2.80	0.365	
FFP transfusion units mean ± SD	0.17 ± 0.39	0	0.152	
Stent graft length mm mean ± SD	151.30 ± 30.07	158.64 ± 35.04	0.614	
Additional stent needed n(%)	3 (25.00)	5 (41.67)	0.385	
Open surgery needed n(%)	0	1 (8.33)	0.232	
Mortality n(%)	1 (8.33)	6 (50.33)	0.020	
Pulmonary complications n(%)	3 (25.00)	1 (8.33)	0.264	
Cardiac complications n(%)	1 (8.33)	3 (25.00)	0.264	
Access site complications n(%)	1 (8.33)	1 (8.33)	1.000	
GIS complications n(%)	None	10 (83.33)	10	0.236
	Abdominal compartment syndrome	1 (8.33)	0	
	Ileus	1 (8.33)	0	

SD: Standard deviation; ES: Erythrocyte suspension; FFP: Fresh frozen plasma.

**Table 2.** Aortic pathologies and interventions

	Group 1 (n=12)	Group 2 (n=12)	P value	
Aortic diameter cm mean ± SD	5.81 ± 1.10	6.44 ± 1.85	0.319	
Aortic pathologies n(%)	Abdominal			
	aorta	5 (41.67)	4 (33.33)	0.708
	aneurysm			
	Thoracic			
	aorta	2 (16.67)	3 (25.00)	
	aneurysm			
	Type 3 aortic	1 (8.33)	1 (8.33)	
	dissection			
	Abdominal			
	aorta +	2 (16.67)	1 (8.33)	
iliac artery				
aneurysm				
Ruptured				
abdominal	1 (8.33)	0		
aorta				
aneurysm				
Ruptured				
thoracic aorta	0	1 (8.33)		
aneurysm				
Thoracic +				
abdominal	1 (8.33)	2 (16.67)		
aorta				
aneurysm				
Aortic intervention				
EVAR	8 (66.67)	5 (41.67)	0.424	
TEVAR	3 (25.00)	6 (50.00)		
TEVAR + EVAR	1 (8.33)	2 (16.67)		
Type of endoleak n(%)				
None	7 (58.33)	9 (75.00)	0.397	
Type 1	3 (25.00)	1 (8.33)		
Type 2	1 (8.33)	0		
Type 3	0	1 (8.33)		
Type 1 +	1 (8.33)	1 (8.33)		
Type 3				

SD: Standard deviation; EVAR: Endovascular aortic repair; TEVAR: Thoracic endovascular aortic repair.

## Discussion

The results of this study suggested that postoperative newly onset renal dysfunction had a significant effect on the postoperative mortality rates after EVAR/TEVAR. Visceral organ blood circulation is seriously impaired in aortic pathologies especially aortic dissection involving descending thoracic and abdominal aorta. Beside this preoperative risk, toxicity of the opaque regents used in endovascular treatment procedures has an additive effect on the postoperative organ dysfunction especially on renal failure.

ARI was reported to occur in the rate ranging from 13 to 36% after the pathologies involving descending and abdominal aorta (8-11). It was also reported that mild renal dysfunction was related to increased mortality in type B aortic dissection patients (12).

There are many studies conducted on characteristics, risk factors and incidence of renal injury in the aortic pathologies involving the descending and abdominal aorta (13-15). In most of the studies, postoperative serum creatinine level increase was acknowledged as the marker of ARI and postoperative urine output was not recognized as a criterion (16,17). According to these criteria, immediate postoperative ARI has a lower incidence in EVAR patients when compared with open repair (18). Nevertheless, some studies demonstrated a similar or more remarkable changes in the incidence of ARI after EVAR procedures. A retrospective study which analyzed The National Surgical Quality Improvement Program in the USA, including 6.514 patients, showed that immediate postoperative ARI (defined as >30% increase in serum creatinine levels) had similar incidence rate in EVAR patients when compared with open repair (19). Gawenda et al. studied 485 patients undergoing EVAR or open repair in their prospective, non-randomized study. They reported a significant increase in serum creatinine levels and a drop in creatinine clearance in EVAR patients (from 1.0 [0.9 - 1.3] mg/dl to 1.08 [0.9 - 1.36] mg/dl, and from 67.6 [51.3 - 85.10] ml/min to 66.7 [49.9 - 81.4] ml/min) but not in open repair patients (20). In the Dutch Randomized Endovascular Aneurysm Management (DREAM) trial, it was reported that perioperative changes in serum creatinine levels and the need for hemodialysis were similar in EVAR and open repair patients (21). A more recent study including 11.753 patients showed that ARI incidence is lower in EVAR patients than open repair patients (0.4% vs. 2.7%,  $p < .001$ ) but the definition of renal failure is not clear in the study (21). According to these findings, the incidence of immediate postoperative ARI after EVAR procedures is unclear and also it is not as low as it is expected. We did not compare EVAR and open repair patients for the incidence of ARI. All of our patients were EVAR patients but the incidence of ARI was similar to the literature in our study.

Contrast medium injury is one of the mechanisms of renal injury in the course of aortic pathologies treated with endovascular methods (2). There are miscellaneous studies previously conducted on prevention of contrast-associated ARI which compared sodium bicarbonate, sodium chloride and acetylcysteine. However, their results were inconsistent (23-29). Also, acetylcysteine is recommended in the kidney disease: Improving Global Outcomes (KDIGO) guidelines because of its low cost and lack of side effects for the prevention of CIN (30). We administered intravenous saline and acetylcysteine solution to all of our patients in the postoperative period as soon as they were admitted to the intensive care unit. Also, we administered saline solution without acetylcysteine during the procedures in all of the cases.

The coexistence of any thoracic and abdominal aortic pathology was reported between 10% and

29% (31,32). There are few studies conducted on the endovascular repair of both aortic segments and most of them describe staged repair. Crawford et al. (33) reported 30% early postoperative mortality after isolated endovascular repair of thoracic aortic aneurysms and most of them were patients with concomitant untreated abdominal aortic aneurysm. On the contrary, there are studies with favorable results reporting 75 - 100% survival and 0 - 25% reintervention rates after simultaneous EVAR and TEVAR procedures (34,35). There were three patients (25%) with concomitant thoracic and abdominal aortic diseases, one in Group 1 (8.33%) and two (16.67%) in Group 2, and they were treated with combined EVAR and TEVAR procedures in our study.

The 30-day mortality rate after EVAR was reported as 24.2% and age, aneurysm size and hypertension were the major risk factors (36). In another study, Mathlouthi et al. (37) reported 5.9% in-hospital mortality rate after TEVAR in patients with type B aortic dissection and age, emergent repair and presence of multiple comorbidities (higher Charlson comorbidity index) were the risk factors related with mortality. We found relatively higher mortality rate in our study. The major interest point of our study is renal impairment and it is related with adverse outcomes in general knowledge. We think that our results have made a contribution to this fact. The number of emergent operations was two times higher, although not statistically significant, in Group 2 and it might have had an additive effect on mortality rate of the Group 2 patients.

#### Limitations of the study

The study was a single center retrospective study and the number of patients was low. Because endovascular treatment is expensive and most of the emergent patients could not reach a health center on time in our region. Moreover, endovascular interventions were preferred in limited number of patients with advanced age (high ASA score), and comorbidity with pararenal/juxtarenal aortic abdominal aneurysm. But the study was focused on the patients undergoing EVAR/TEVAR and had renal impairment in the postoperative period. Also, we could not have a technical opportunity to make Doppler measurements of the flow in the renal arteries pre- and postoperatively.

#### Conclusion

Renal functions after EVAR/TEVAR procedures should be carefully monitored because renal impairment is closely related with postoperative mortality. Renal protection with medical agents such as acetylcysteine is recommended but there are controversial results about it. We suggest that more studies with larger patient numbers should be conducted on the relation of renal functions and mortality after regularly performed EVAR/TEVAR procedures.

#### Author Contributions

Conception and design of the research: Coskun Sungur E. Statistical analysis: Altınay L. Acquisition of data: Tekin A., Coskun Sungur E. Analysis and interpretation of the data: Turan SA, Altınay L. Writing of the manuscript: Coskun Sungur E., Altınay L. Critical revision of the manuscript for important intellectual content: Tutun U.

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