RESEARCH ARTICLE / *Araştırma Makalesi*

Factors Affecting Mortality and Morbidity After Endovascular Aortic Repair for Abdominal Aortic Aneurysms

Abdominal Aort Anevrizmalarına Yönelik Uygulanan Endovasküler Aort Tamiri Sonrası Mortalite ve Morbiditeye Etki Eden Faktörler

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Geliş Tarihi / Received : **11.11.2019** Kabul Tarihi / Accepted : **06.02.2020**

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(Sakarya Med J / ***Sakarya Tıp Dergisi*** **2020, 10(1):65-73) Doi: Doi: 10.31832/smj.645571**

Öz

Amaç — Endovasküler aort tamiri (EVAT) abdominal aort anevrizmalarında artan bir oranda cerrahi seçenek olarak uygulanmaktadır. Minimal invazif bir prosedür olan EVAT işlemi sonrası mortalite ve morbiditeye etki eden faktörleri araştırdık.

Gereç ve Yöntemler — Eylül 2014 ile Ocak 2019 yılları arasında toplam 96 (91 erkek, 5 kadın) elektif EVAT uygulanmış hastalar çalışmaya dahil edildi. Ameliyat öncesi ve sonrası bilgisayarlı tomografi görüntüleri incelendi ve rutin kontroller ile takip edildi. Demografik faktörler, anevrizmanın anatomik özellikleri ve diğer risk faktörleri incelendi. Kaplan-Meier sağkalım analizi yapıldı. Cox regresyon analizi ile risk faktörlerinin mortalite ve morbiditedeki artış riski hesaplandı ve HR (hazard ratio) olarak değer belirtildi.

Bulgular — Ortalama takip süresi 27,45 ± 12,99 aydı. Aort boyun morfolojisin istatistiksel anlamlı olarak mortalite üzerine etkili olduğu görüldü (p değeri:0.046). Aort boyun açısı, sigara, perifer arter hastalığı (PAH), koroner arter hastalığı, kronik obstrüktif akciğer hastalığının bulunmasıyla mortalite üzerinde zarar görme riskinin yükseldiği görüldü (HR sırasıyla: 1,39; 1,45; 3,33; 1,84; 1,87; 3,60). Artmış kreatinin seviyesi (p değeri:0.003), kronik böbrek yetmezliği (p değeri:0.013), şeker hastalığı (p değeri: 0.038)'nın morbidite üzerinde istatistiksel olarak anlamlı olumsuz etkisi olduğu görüldü. Obezite ve PAH'nın morbidite üzerine zarar verme riskinin arttığı görüldü (HR sırasıyla: 4,58; 1,61).

Sonuç — Bu çalışma bize hayatta kalımın ve morbiditenin EVAT sonrası, ameliyat öncesi ve sonrası faktörlerden etkilendiğini gösterdi. EVAT işlemi öncesi anevrizmanın anatomik özelliklerinin ayrıntılı değerlendirilmesi, işlemden en iyi oranda fayda görülmesi açısından önemlidir.

Anahtar Kelimeler — endovasküler prosedürler; aort anevrizması, abdominal; ölüm oranı; morbidite

Abstract

Objective — *Endovascular aortic repair (EVAR) has been preferred increasingly surgical repair for abdominal aortic aneurysms (AAAs). This minimally invasive procedure has favorable effects in the early period but our purpose is to reveal the anatomical and non-anatomical risk factors affecting mortality and morbidity after EVAR in the prolonged period.*

Materials and Methods — *A total of 96 patients (91 male, 5 female) electively EVAR operated for infrarenal AAAs between September 2014 to January 2019 is included to the study. Preoperative and postoperative computed tomography (CT) scans is controlled periodically and determined individually. Demographic factors, anatomical properties of the AAAs and non-anatomical risk factors are assessed. Kaplan-Meier survival analysis was used to determine survival rates. Cox regression and hazard ratio (HR) was used to assess the relation of these determined factors on mortality and morbidity.*

Results — *Mean follow up time was 27,45 ± 12,99 months. We found that aortic neck morphology has an statistically significant effect on mortality (p value: 0.046 and HR: 1,73 [1,01-2,96]). Aortic neck angle, cigarette smoking, obesity, peripheral artery disease (PAD), coronary artery disease, chronic obstructive pulmonary disease have an increased hazard ratio on mortality (HR in order; 1,39; 1,45; 3,33; 1,84; 1,87; 3,60). Increased creatinine level (p value: 0.003), presence of chronic renal failure (p value: 0.013) and diabetes mellitus (p value: 0.038) have an statistically significant negative effect on morbidity. Obesity and PAD have an increased hazard ratio on morbidity (HR in order; 4,58; 1,61).*

Conclusion — *This study showed us survival after EVAR procedure is connected with several pre and postoperative factors. Preoperative detailed evaluation for the anatomical properties of aneurysm is important to achieve prolonged benefit and postoperative follow up is crucial.*

Keywords — *endovascular procedures; endovascular repair; aortic aneurysm, abdominal; mortality; morbidity*

Introduction

Abdominal aortic aneurysm (AAA) is defined as 50 % enlargement of the maximum normal diameter of the infrarenal abdominal aorta and predominantly seen in males to females.[1] There are several risk factors associated with AAAs; such as increased age, cigarette smoking, male sex, atherosclerosis, hypertension (HT) and family history. For all that, some studies showed the risk correlation of chronic obstructive pulmonary disease (COPD) and obesity with AAAs.[2] Different population follow-up series vary by countries and age, a mean 5,70 % prevalence is detected and this range from 1,00-12,70 %.[3,4]

Most of the AAA cases are asymptomatic. Due to this asymtomatic nature of the disease it refers as a silent killer. Autopsy series showed a 0,50 – 3,20 % prevalence of AAAs.[1] Rupture is the mortal result of the AAAs and this is a real emergency of cardiovascular surgery. It is the 13th leading cause of death in the USA and 15 000 people dies per year because of this.[5] The goal of AAAs detection is to identify asymptomatic AAAs, and secondly an elective surgical repair of aortic aneurysms aims to prevent death from rupture.

The disease is seen commonly in the aged population. The incidence of the disease increases with the advancing age. Percentage of the elderly population (>65 age) in Turkey is 8,74 % to the Turkish Statistical Institute (TUIK). TUIK's population projections showed that the estimated elderly population will increase than currently in developed countries of the world.[6]

The only surgical method was open repair for AAAs before 1991. Parodi et al. described endovascular treatement of abdominal aortic aneurysm (EVAR) by the year 1991.[7] EVAR is reported a minimally invasive procedure and reduce intensive care unit stay (ICU), hospital stay, perioperative mortality and patients quality of life is not affected in the early period. But new studies showed that more frequent reinterventions is seen.[8] In the elderly and high-risk population EVAR is recommended for AAAs.

We evaluate retrospectively EVAR performed AAA patients in our clinic. AAA is a silent disease and is a real cause of mortality in the elderly population. We know the risk factors of AAAs and related risk factors in open repair. But our aim is to reveal the factors affecting mortality and morbidity in the endovascular aortic repaired AAA patient population.

Materials and Methods

Our study is designed as a retrospective cohort study in single center. A total of 96 patients (91 male, 5 female) who underwent endovascular aortic repair (EVAR) for infrarenal abdominal aort aneurysm between September 2014 – January 2019 in Sakarya University Research and Education Hospital is included to the study. Data of the patients were observed retrospectively from the patients files.

Our center has got some routine preperations before major endovascular surgical procedures. Contrast thoracoabdominal CT (computed tomography), coronary angiography (via radial artery), carotid and peripheral arterial doppler ultrasound was done before surgery. Routine Chest disease clinic consultation was done to all elective patients. Mean follow up time was 27,45 ± 12,99 months. Primary endpoint was 30-day mortality, aneurysm and non-aneurysm related mortality.

Patients who had got infrarenal fusiform abdominal aortic aneurysm upper than 55 mm diameter, saccular aneurysm regardless of diameter, aneurysms with ulcerated plaque, symptomatic and rapidly growing cases were included to the study. Urgent and other procedures combined cases were excluded. All patients had got a major risk factor for open repair.

All EVAR procedures were performed in the angiography unit with one surgical team. AnacondaTM AAA stant graft system-Vascutek (84 patients) and MedtronicTM En-

durant II stent graft systems (12 patients) were used as endovascular stent grafts for the procedures. All operations were performed under general anesthesia. Femoral arteries were used for vascular access. Femoral longitudinal and minimally invasive oblique bikini incisions were used. A purse suture on the femoral artery was used to control the arterial bleeding during the procedure. Postoperative routine follow-up procedure is as follows; tenth day, 3rd month, 6th month, in the first year and than every year after the discharge. If there isn't a complaint or a positive physical examination we are scanning with CT in the 3rd month and in the first year after discharge.

As mentioned before, data were collected from intensive care unit (ICU) and day care unit patient file. Forward clinic and policlinic examination reports and CT images of the patients were analyzed from the hospital online database. Demographic data, risk factors concomitant to AAAs, comorbidities, laboratory findings such as renal functions, aneurysm diameter, aneurysm type, aneurysm neck properties, aneurysm morphology, mortality information and complications were analyzed for study.

Peri-operative mortality is defined as death within 30 days of the procedure. Morbidity is defined as the presence of aneurysm rupture, graft migration, endoleak, graft thrombosis, peripheral vascular complications, new-onset renal failure and femoral wound healing problems after procedure.

Statistical Analysis: IBM SPSS Statistics version 23.0 was used. Demographic, clinical and contunious numerical variables were summarized with mean, median and standart deviation. Nominal data were summarized with percentage and quantities. Cox regression analyze was used to assess the relation of mortality and morbidity with preoperative and postoperative variables. Independent risk factors were evaluated by Cox regression analysis. Hazard ratios (HR) %95 confidence interval was presented as (%95 CI). Kaplan Meier analysis was used for survival and graft complication distribution statistics. Statistically significance was accepted as P <0,05.

Ethics Committee Approval

Sakarya University Ethics Committee was confirmed to our study with the approval number 71522473/050.01.04/281.

Results

A total of 96 patients were admitted for elective repair of an AAA between September 2014 – January 2019. Only 5 of the patients were women. Emergent cases such as ruptured and dissected aortic aneurysms were excluded. All patients had an indication for surgical intervention and all patients had a minimum one risk factor for open surgical repair. Mean follow up time was 27,45 ± 12,99 months. Mean preoperative aneurysm diameter was 59,70 ± 12,09 mm. All EVAR operated patients aneurysms diameter was upper than 50 mm except 6 patients. 4 of them have ulcerated plaque, 2 of them were symptomatic saccular aneurysms. All preoperative and demographic details are showed in table 1.

Technical details of the aneurysms are showed in table 2. This data give us information about identifying the hostile status of aortic neck and grading the aortic aneurysm to modify the outcomes of EVAR procedure.[9]

Postoperative data and complication development information investigated. Risk factors affecting mortality and morbidity was assessed with Cox regression analysis. Results are shown in table 3 and 4.

The Cox regression model confirmed that worse morbidity was associated with diabetes mellitus, obesity, peripheral artery disease, the presence of chronic renal failure and significant increase in creatinine postoperatively after EVAR.

Adverse anatomy, aortic neck morphology was also a common feature in patients experiencing mortality and this

was statistically significant with the Cox regression model. There wasn't a statistically significance by the Cox regression analysis but patients with male sex, obesity, chronic obstructive pulmonary disease, cigarette smoking, peripheral artery disease, aortic neck upper than 60 degree have an increased hazard ratio on mortality after EVAR.

Table 1. Preoperative demographic values and data of the patients.

Variables	Total n=96
Sex	91 male, 5 female
Age (year)	67,51±8,88
HT	87 (90,60 %)
DM	15 (15,60%)
HL	27 (28,12 %)
COPD	46 (47,90 %)
Previous Abdominal Surgery	21 (21,80 %)
Previous Cardiac surgery	19 (19,70 %)
PAD	35 (36,40 %)
CAD	61 (63,50 %)
Cigarette Smoking	52 (54,10 %)
Obesity	10 (10,40 %)
CRF	16 (16,60 %)
Preoperative Ure (mg/dl)	44,99±24,70
Preoperative Creatinine (mg/dl)	1,17±1,11
HD	2 (2,08 %)
LV EF (%)	56,72±7,93

HT: Hypertension, DM: Diabetes mellitus, HL: Hyperlipidemia, COPD: Chronic obstructive pulmonary disease, PAD: Peripheral artery disease, CAD: Coronary artery disease, CRF: Chronic renal failure, HD: Hemodialysis, LV EF: Left ventricular ejection fraction.

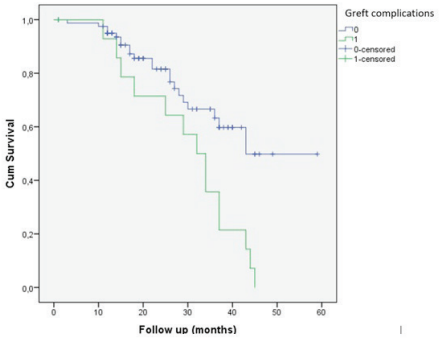
Table 2. Descriptive data of aneurysm

Variables	Frequency (n)	Percent (%)
Aneurysm Type		
Fusiform	86	89,60
Saccular	10	10,40
Aortic Neck Length		
< 15 mm	15	15,60
> 15 mm	81	84,40
Aortic Neck Angle		
<30	56	58,30
30-45	12	12,50
45-60	16	16,70
>60	12	12,50
Aortic Neck Morphology		
Straight	41	42,70
Tapered	14	14,60
Reserve tapered	6	6,25
Angulated	28	29,16
Bulge	7	7,29
Aneurysm Calcification		
Mild (<%25)	42	43,80
Moderate (25-50%)	30	31,30
Severe (>%50)	24	25,00

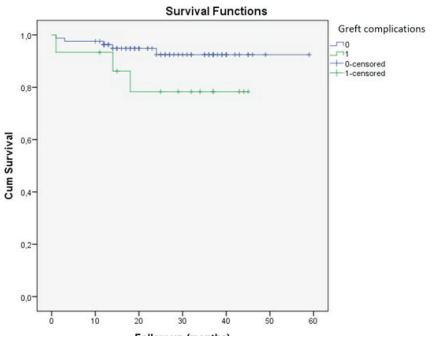
Table 3. Risk factors affecting morbidity by Cox regression analysis.		
Variables	HR (%95 CI)	p value
Age	1,042 (0,949 - 1,144)	0.389
Sex	0,377 (0,011 - 13,21)	0.591
HT	0,646 (0,13 - 3,207)	0.593
DM	0,107 (0,013 - 0,888)	0.038
HL	0,97 (0,21 - 4,469)	0.969
COPD	0,688 (0,141 - 3,361)	0.644
CAD	0,685 (0,282 – 1,665)	0.404
PAD	1,612 (0,529 - 4,909)	0.401
Obesity	4,581 (0,702 - 29,896)	0.112
Cigarette smoking	0,611 (0,164 - 2,285)	0.465
CRF	0,022 (0,001 - 0,448)	0.013
Preop Ure	0,978 (0,912 - 1,05)	0.544
Preop Creatinine	0,313 (0,027 - 3,662)	0.355
Postop Ure	1,012 (0,972 - 1,054)	0.552
Postop Creatinine	31,182 (3,138 - 309,827)	0.003
Saccular aneurysm	23,94 (0,046 – 1278,96)	0.319
Fusiform aneurysm	0,042 (0 – 27,264)	0.338
Aneurysm diameter (mm)	1,01 (0,955 - 1,068)	0.729
Aortic neck length(mm)	0,723 (0,159 - 3,277)	0.674
Aortic neck angulation	0,922 (0,386 - 2,203)	0.855
Aortic neck morphology	0,868 (0,466 - 1,617)	0.656
Aneurysm calcifiaction/Thrombi	0,963 (0,417 - 2,222)	0.929
HR: Hazard ratio, HT: Hypertension, DM: Diabetes mellitus, HL: Hyperlipidemia, COPD: Chronic obstructive pulmonary disease, CAD: Coronary artery disease, PAD: Peripheral artery disease, CRF: Chronic renal failure		

Table 4. Risk factors affecting mortality by Cox regression analysis		
Variables	HR (%95 CI)	p value
Age	1,06 (0,965 - 1,166)	0.225
Sex	3 (0,294 - 30,619)	0.354
HT	0,7 (0,076 - 6,431)	0.753
DM	0,755 (0,086 - 6,625)	0.800
HL	0,341 (0,04 - 2,909)	0.325
COPD	3,6 (0,688 - 18,828)	0.129
CAD	1,877 (0,36 – 9,794)	0.455
PAD	1,839 (0,43 - 7,864)	0.411
Obesity	3,333 (0,575 - 19,328)	0.179
Cigarette smoking	1,454 (0,327 - 6,46)	0.623
CRF	0,695 (0,08 - 6,075)	0.742
HD	0 (0 - 0)	0.999
Preop Ure	0,992 (0,954 - 1,03)	0.665
Preop Creatinine	0,809 (0,249 - 2,635)	0.725
Postop Ure	0,987 (0,951 - 1,024)	0.485
Postop Creatinine	0,522 (0,102 - 2,673)	0.435
Saccular aneurysm	0 (0 - 0)	0.999
Fusiform aneurysm	0 (0 - 0)	0.999
Aneurysm diameter (mm)	1,043 (0,989 - 1,101)	0.123
Aortic neck length(mm)	0,52 (0,095 - 2,861)	0.452
Aortic neck angle	1,398 (0,766 - 2,551)	0.275
Aortic neck morphology	1,73 (1,011 - 2,96)	0.046
Aneurysm calcification/ Thrombi	0,899 (0,362 - 2,234)	0.819
HR: Hazard ratio, HT: Hypertension, DM: Diabetes mellitus, HL: Hyperlipidemia, COPD: Chronic obstructive pulmonary disease CAD: Coronary artery disease, PAD: Peripheral artery disease, CRF: Chronic renal failure, HD: Hemodialysis.		

By Kaplan-Meier analysis, morbidity and mortality analysis to the graft complication status are shown on graphic 1 and 2.



Graphic 1: Morbidity analysis graphic for graft complication status. (p value: 0.138)



Graphic 2: Mortality analysis graphic for graft complication status. (p value 0.105)

Discussion

AAAs are typically asymptomatic disorder until the catastrophic event of rupture. The nature of this silent disease can change the aortic shape to huge diameters leading to dissection of the aorta or the unwanted mortal ending aortic rupture. Despite these frightening endings, endovascular treatment is a less invasive procedure which can reduce risks, allow much quicker patient recovery and can be applicable with good clinical results for high risk patients compared to open surgery. Previous studies showed early-mid and long term results of both techniques in the literature.[10] Our aim is to reveal the factors affecting survival and morbiditiy after endovascular aneurysm repair.
Most of the literature studies have good clinical outcomes with early detected, not complicated suitable infrarenal AAAs.[10] This is what all the surgeons wanted to experience. In the other hand, the dark side of the moon is not as clear as the patient type of less suitable and complicated infrarenal AAAs.

As we know that with the advancing age, the risk of the procedures is increasing proportionally. As one of a result of our study there was a light increase in the risk of mortality and morbidity compared with advancing age. The probability of the light increase of hazard ratio is because the mean age is 67,51 years in our study and this value is under 70 and our number of study population is an another limitation. Previous studies showed the association between long-term survival with age.[11,12] De Bruin et al. showed age >70 is associated with reduced survival.[13] With the advancing age, the exposure time of the patient with aneurysm is longened, and this cause an increase in diameter and a complicated morphology.

The other demographic factor is gender. Different studies showed unlike results. Some of them showed a significance with long-term survival with gender, some of them showed no relation with gender.[14] There was no statistically significance on morbidity in our study with gender, but there was an increase in the hazard ratio of mortality in male sex in our study (HR:3,0 [0,294-30,619]). The reason for this may be that there are only 5 females in our study.
Peripheral artery disease (PAD), ischemic coronary artery disease (CAD) and aortic aneurysms has a common side in pathophysiology; atherosclerosis. PAD can cause femoral arterial access problems during endovascular surgical procedure. Our results showed no statistically significance on mortality and morbidity in the precence of PAD. But occurence risk of morbidity is increased in the presence of PAD (HR: 1,612 [0,529 – 4,909]) and similarly mortality is increased in the presence of PAD too (HR: 1,839, [0,43 - 7,864]). Previous studies showed the relation of all-cause mortality with PAD following EVAR.[11] On the other hand ischemic heart disease have conflicting results. Some studies showed as and independent predictor for long-time mortality and some of them found no association.[14] Our results showed no association between morbidity after EVAR but there is an increased hazard risk in the precence of CAD after EVAR (HR: 1,87 [0,36-9,79]).

Previous studies reported the association of obesity and abdominal aortic aneurysms. These studies enounced the increased body mass index or increased waist circumference has an association with the presence of AAAs.[15,16] Our results showed no statistically significance on mortality and morbidity in the precence of obesity. On the other hand risk increase on mortality and morbidity there is an association with the presence of obesity. In order odds ratio of mortality and morbidity is (HR: 3,333 [0,575 – 19,328]), (HR: 4,581 [0,702-29,896]).

One of the risk factors of abdominal aortic aneurysms is COPD. Meijer et al. in their cohort study, Xiong J in their meta-analyze showed the increased prevelance of AAAs with the presence of COPD.[17,18] COPD presence with AAAs had a higher risk of all-cause death and morbidity than lack of COPD.[11,18,19] With the importance of COPD, we assess the pulmonary functions before surgery in our clinic. We perform to the patients spirometry before surgery and make a Chest Diseases clinic consultation

before EVAR. Our study results showed no statistically significance on mortality and morbidity in the precence of COPD. But there is an increase in the hazard ratio on mortality with the presence of COPD and AAAs (HR: 3,6 [0,688 – 18,828]). Closely related case to COPD is an habit; smoking behaviour. As we know that smoking is the major risk factors of atherosclerosis and the result of this pathophsiology. And in addition that atherosclerosis in the abdominal aortic wall lead to AAAs. Takagi et al. reported that smokers have got 9 times greater risk to develop AAAs than to nonsmokers and smoking increases the rupture risk of AAAs.[20, 21] Koole et al. showed that increased growth with cigarette smoking preoperatively can cause an enlargement after EVAR and this can cause increased risk of graft migration.[22] By the way the importance of cigarette smoking is as clear as in the literature the presence of cigarette smoking increased the hazard ratio of mortality after EVAR procedure in our study (HR: 1,454 [0,327-6,46]).

Presence of diabetes mellitus had significant effect on morbidity in our study (p value: 0.038). Previous studies similarly to De Rango's meta-analyze, with the presence of DM survival was affected unfavorably after EVAR.[23] This is mostly result of the effect of DM leading to the cardiovascular events. Another independent factor is chronic renal failure (CRF) and related creatinine level. Several studies showed the poor outcomes and increased mortality after EVAR with the presence of CRF patients.[12,24,25] We can be count this as; end stage renal disease, hemodialysis requiring CRF, increased creatinine level. Our results showed that CRF and increased creatinin level have a statistically significant effect on morbidity (in order p values are: 0.013, 0.003). On the other hand we couldn't show an effect on mortality with the presence of CRF or increased creatinine level.

Leaving behind the non-aneurysm related factors evaluation, we made an assessment of the the anatomical properties of aneurysm. Most obvious view in the literature is that the diameter of the aneurysm have a strong relation with the survival.[12,14,26,27] To sum up of these studies; large aneurysms the outcomes after EVAR procedure was associated with increased rates of mortality (both aneurysm related and unrelated deaths), rupture and surgical conversion. But the large aneurysm definition varies in these studies. In order physicians accept larger aneurysm diameter; 60-64-65-70 mm. Only 34 patients aneurysm diameter was more than 60 mm in our study. The diameter of aneurysm in our patients was upper than 50 mm except 6 patients. Four of these smaller aneurysms have ulcerated plaque and 2 of them were symptomatic saccular aneurysm. Because of this smaller size of large aneurysm population in our study we couldn't achive statistically significant results. Hazard ratio was slightly increased effect on mortality and morbidity (HR in order: 1,043 [0,989-1,101], 1,01[0,955-1,068]). However Jim et al. showed there is no differences between small (<54 mm, 48,5 mm [38-54]) and large aneurysms (>55 mm, 62,8 mm[55-88]) over 30 days, 1 and 5 years result.[28] Saccular aneurysm morphlogy is an another type of AAAs and if detected endovascular surgical intervention is required independent of diameter. As a result of our study hazard ratio is prominently increased after EVAR with the presence of saccular type (HR: 23,94). Hostile neck consept was defined as the presence of one or all of five important subtitles; aortic neck length, aortic neck diameter, aortic neck angle, Aortic neck morphology and aneurysm calcification.[28] The more small neck lengt, increased angulation, increased diameter and calcification means severe and hostile neck. Here is the landing zone of the graft and the importance of the neck anatomy had shown in a meta-analyze before.[29] More angulated upper than 45˚-60˚ , reverse tapered and bulge morphology have the risk of migration, type 1a endoleak and aneurysm related mortality.[30,31] Boult et al. showed that upper than 45˚ angle and short neck (<15 mm) aneurysms had increased type 1 endoleak. And also larger aneurysms and more than 45˚ angle are poor prognostic criterias.[26] Similar to this study Albertini et al reported necks with more angulation and increased in diameter have an increase in endoleak and migration.[32] We found that aortic neck morphology

has an statistically significant effect on mortality (p value: 0.046 and HR: 1,73 [1,011-2,96]). Increased aortic neck angle has an increased hazard ratio (HR: 1,398 [0,766 – 2,551]). In our study, because the number of patients with severe calcification and short neck length was small, we couldn't achieve statistically significant values.

Limitations of the study: Our most prominent limitation was the small number of the patients. Although there were 96 patients in our study, the results were not enough to show significance in some cases. We can report more powerful statistics with wider and more patient including population.

In conclusion; endovascular repair is feasible for abdominal aortic aneurysms. However, aortic neck morphology was correlated with a significant increase in mortality. Diabetes, chronic renal failure and increased creatinine level were significanlty associated with increased morbidity.

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