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Original Article

Impact of Serum Albumin Levels on Arterio-Venous Fistula Maturation in End-Stage Renal Disease Patients with Diabetes Mellitus

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ABSTRACT

Background: Diabetes mellitus (DM) is a well-known risk factor for the prolongation of arterio-venous fistula (AVF) maturation and hypoalbuminemia. In this study, we studied the impact of the serum albumin levels during AVF creation on AVF maturation duration in diabetic patients.

Material and Methods: This single-center observational study was carried out using the data of 131 hemodialysis patients. Sixty-seven individuals with AVF were included in the study and were divided into two groups; diabetics and non-diabetics. Serum albumin levels during AVF creation were noted. The maturation period was described as the interval between the creation and cannulation time of AVF providing a minimum of 250 ml/min blood flow during the hemodialysis session (week). The demographic and clinical features of the individuals were noted and compared.

Results: Twenty-five individuals were in the diabetic and 42 were in the non-diabetic group. Serum albumin level was lower (3.50±0.44 vs 3.84±0.32) during AVF creation in the diabetic group; $p<0.001$. A negative correlation was observed between preoperative serum albumin level and AVF maturation time; $p=0.003$ and $r=0,132$. Additionally, maturation duration was significantly higher among diabetics (6.6 vs 5.1 weeks). Serum CRP levels were similar between the two groups ($p=0.057$).

Conclusion: Longer AVF maturation time in diabetic patients is closely related to low serum albumin levels. Low serum levels of albumin should be considered when evaluating ESRD patients with DM for AVF creation.

Keywords: Arteriovenous fistula, diabetes mellitus, hypoalbuminemia, hemodialy-

INTRODUCTION

Diabetes mellitus (DM) is the leading cause of the end-stage renal disease (ESRD) in the whole World (1,2). A timely created arteriovenous fistula (AVF) is crucial in chronic kidney disease (CKD) patients when the disease is progressing to ESRD. However, the exact time to create AVF in ESRD patients with DM has not been described.

Hypoalbuminemia is a common clinical finding in the course of diabetic nephropathy (DNP) and correlates closely with mortality and poor renal outcome (3,4). Hypoalbuminemia occurs either due to severe proteinuria (especially, when clinical features of the nephrotic syndrome are apparent) or to chronic inflammation in DM (3). Hypoalbuminemia, proteinuria, and vascular endothelial injury are closely associated with each other, and the majority of cardiovascular events are explained by those factors and their interactions (5). Regardless of the pathogenesis of hypoalbuminemia (inflammation, protein malnutrition, protein loss), hypoalbuminemia is associated with worse outcomes (5-8).

Hypoalbuminemia and diabetes both have adverse impacts on all types of surgical operations (9-12). DM has a negative impact on AVF remodelling and AVF maturation duration (12-14). DM and hypoalbuminemia both might have a worse impact on AVF maturation time. In this study, we investigate the impact of serum albumin levels on AVF maturation duration in diabetic

patients with ESRD.

MATERIALS AND METHODS

Study Design and Participants

This single-center retrospective case-control study was conducted in 2021 in a university-affiliated private hospital. A total of 131 hemodialysis patients were evaluated and 67 of those whose first vascular access route was an AVF were included in the study (64 of 131 patients had started chronic hemodialysis therapy with a temporary or permanent catheter). The patients were divided into two groups; patients with DM and non-DM. The clinical and laboratory of the individuals were noted from the local computer software of the hospital.

Laboratory examinations and clinical measurements

Serum albumin, C-reactive protein (CRP), and hemoglobin levels of the individuals on the operation day of AVF were noted. An AVF that provided a 250 ml/min blood flow rate, was considered a maturated AVF. The duration from the operation day to the maturation day was considered the maturation duration. If an additional AVF creation operation or AVF-related reintervention was necessitated the first operation was considered as AV fistula dysfunction. The second operation was considered a different case. Serum albumin, CRP, and hemoglobin levels on the maturation day/week were also compared between the two groups.

Thirty-two patients were detected to have residual urine from the registries of the hemodialysis center and hospital, however, the 24-h urine analysis revealing proteinuria amount in the AVF maturation periods was not available.

Exclusion criteria

The patients with chronic liver disease, congestive heart failure, malabsorption syndromes, and >1 gr/day proteinuria also were excluded.

Ethical approval

This study was carried out in accordance with the ethical principles for medical research of Declaration of Helsinki. The consent form is not available since the study is in a retrospective design. The study was approved by the ethics committee of scientific research of Medicana International Ankara Hospital (Date: 28.01.2022, Approval number: BSH-2022/01-B).

STATISTICAL ANALYSIS

Statistical analysis was conducted using SPSS (version 13.0). In the first step, all data were tested for normality by using the Kolmogorov-Smirnov and Shapiro-Wilk tests. The normally distributed (parametric) data are presented as the mean±standard deviation and the non-normally distributed (nonparametric) data are presented as the median (minimum-maximum). The independent samples t-test was used to compare continuous parametric variables between the groups. Mann-Whitney U test was utilized to compare non-parametric variables. Pearson's or Fisher's exact test was used to compare the categorical variables. A Paired test was used to compare preoperative and postoperative serum albumin and CRP levels. Univariate and multivariate Cox regression analyses were performed to identify the impact of the laboratory data and clinical features of the individuals on the maturation duration. P-value <0.05 was considered statistically significant.

RESULTS

A total of 67 hemodialysis patients were evaluated. Forty-six of those were male and 21 were female individuals. DM and hypertension were ESRD's most common etiological factors (36.7% and 29.9%, respectively) (**Table 1**). The diabetic and non-diabetic groups were of similar age and gender (p=0.175 and p=0.142, respectively). The mean canulation duration of a maturated AVF (time period from the creation time to first canulation time in which AVF provided a > 250 ml/min blood flow) in the diabetic group was 6.6 weeks while in the nondiabetic group was 5.1 weeks (p=0.036) (**Table 2**). Preoperative serum albumine (PSA) levels were lower in the diabetic group at the

Table 1. The clinical and laboratory features of the participants

Age, year	49.92±17.62
Gender, male/female, n=	46/21
***Preoperative serum albumin, gr/dl**	3.71 gr/dl
****Postoperative serum albumin, gr/dl**	3.74 gr/dl
Hemoglobin, gr/dl	10.4 mg/dl
Serum creatinine, mg/dl	6.34 mg/dl
CRP, mg/dl	2.12 (0,01-22)
CKD, etiology	DM (37.3%), HT (29.9%), PCKD; 4.5%, GN; 7.5%, Unknown; %20.9

CRP, c-reactive protein, CKD; chronic kidney disease, DM; diabetes mellitus, HT; hypertension, PCKD; polycystic kidney disease, GN; glomerulonephritis. *serum albumin at the time of AVF creation, ** serum albumin at the time of AVF canulation

Table 2. The comparison of the diabetic and non-diabetic patients at the time of arteriovenous fistula creation

	Diabetic, N=25	Non-diabetic, N=42	P value
Age, year	54.04±15.72	47.47±18.39	0.142
Gender, male/female, n=	20/5	26/16	0.175
***Preoperative serum albumin, gr/dl**	3.50±0.44	3.84±0.32	**<0.001**
****Postoperative serum albumin, gr/dl**	3.72±0.46	3.76±0.57	0.766
Hemoglobin	10.52±	10.39±1.51	0.740
Serum creatinine, mg/dl	5.98±1.23	6.35±2.12	0.125
CRP, mg/dl	3.80(0.02-22)	1.70(0.01-12)	0.057
AVF maturation duration, week	6.60±2.73	5.09±2.80	**0.036**

CRP; c-reactive protein. *serum albumin at the time of AVF creation, ** serum albumin at the time of AVF cannulation, AVF; arteriovenous fistula

time of AVF creation (3.5±0.44 gr/dl vs 3.84±0.32 gr/dl and p<0.001) and were negatively correlated with AVF maturation duration r=0.132 and p=0.003) (**Figure 1**). C-reactive protein level was higher in the diabetic group however the distinction was not statistically significant (3.80[0.02-22] mg/dl vs 1.70[0.01-12] mg/dl and p=0.077). CRP levels positively correlated with AVF maturation duration (r=0.149 and p=0.011) (**Figure 2**). However, serum albumin and CRP levels did not reveal a correlation with each other (p=0.150). Older age also correlated with the prolongation of AVF maturation duration (r=0.096 and p=0.011) (**Figure 3**). Univariate regression analysis indicated that age, lower serum albumin levels, HD duration, CRP, and DM had an impact on AVF maturation duration (p<0.05) (**Table 3**). Multivariate analysis

Figure 1. Lower preoperative serum albumin level is negatively correlated with the maturation duration of AVF fistula

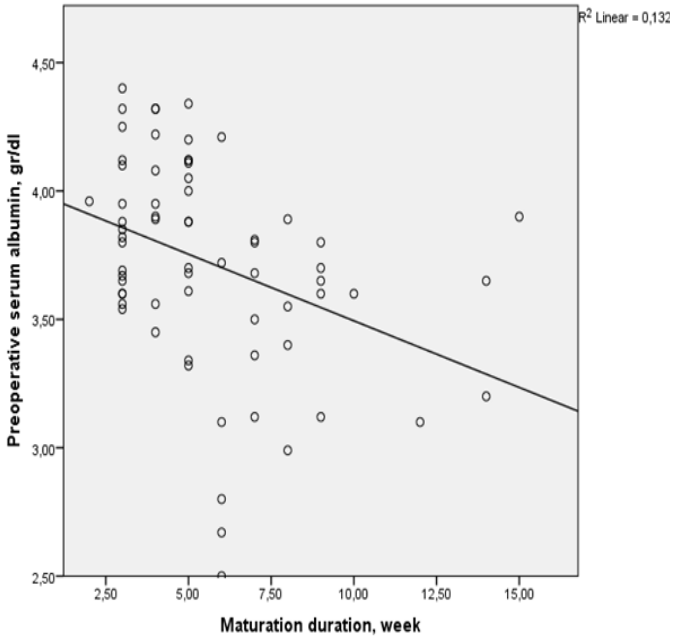


Figure 2. Higher CRP levels correlated with prolongation of AVF maturation duration

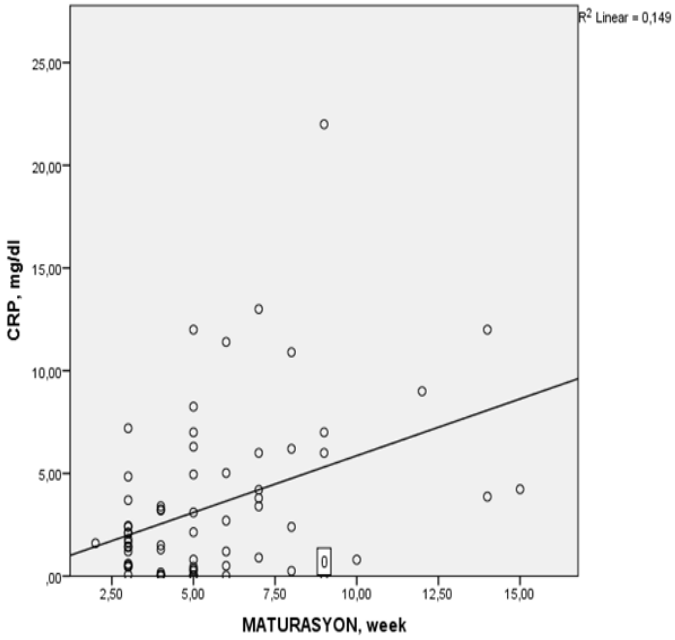
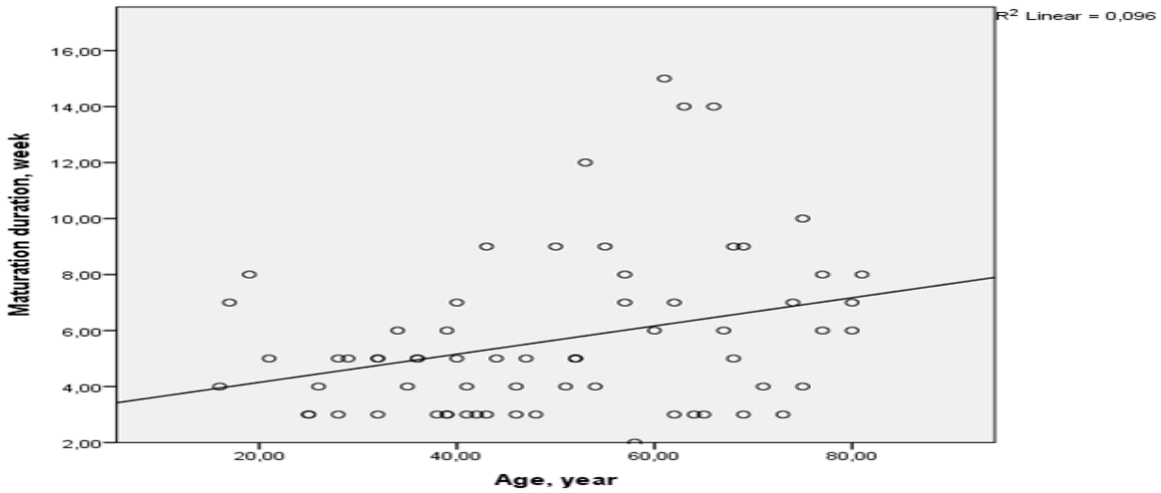


Table 3. The clinical and laboratory features of the participants

	Univariate		Multivariate	
	P value and 95% CI		P value and 95% CI	
Age, years	**0.011**	0.012 – 0.089	**0.048**	0.000 – 0.075
Hgb, g/dl	0.217	-0.722 – 0.167	-	-
CRP, mg/dl	**<0.001**	0.111 – 0.430	**0.004**	0.078 – 0.393
Preoperative serum albumin, g/dl	**0.003**	-4.150 - -0.923	0.122	-3.129 - -0.380
DM	**0.036**	-2.909 - -0.101	0.748	-1.647 – 1.192

Hgb; hemoglobin, CRP; c-reactive protein

Figure 3. Age positively correlates with maturation duration



demonstrated that preoperative CRP and age are the only factors that determine maturation duration ($p<0.05$) (Table 3). Postoperative serum albumin and CRP levels were found to be partially improved during the time of AVF cannulation compared to the preoperative levels in the diabetic group.

DISCUSSION

Arteriovenous fistula creation is the preferred vascular access route in diabetic hemodialysis patients, however, maturation duration is longer compared to nondiabetic ESRD patients. Determining factors that might have an impact on AVF maturation duration will provide benefits in evaluating diabetic patients before AVF creation. This small cohort demonstrates that age and preoperative CRP are the main factors that impact AVF maturation duration.

Strong evidence suggests that DM is more likely to cause AVF dysmaturation or failure. The pathophysiological mechanisms of DM that negatively impacts vascular endothelium are the focus of interest. The increased release of inflammation biomarkers such as interleukin-6, vascular cellular adhesion molecule-1, and monocyte chemoattractant protein-1, and thromboaggregation (increased von Willebrand factor release and platelet aggregation) lead to thrombosis based on vascular intimal injury (15,16). In this study, DM had an impact on AVF maturation duration, however, in multivariate regression analysis, this impact disappeared probably due to the low sample size of the cohort.

Small increases in CRP which is an indirect sign of low-level inflammation predict the likelihood of cardiovascular injury both in diabetic and nondiabetic populations (17). Further, local CRP increase suggests diabetic atherosclerosis plaques in diabetic individuals (17). Zadeh et al. suggested that CRP before AVF surgery is an indicator of fistula function (18). In our study, preoperative CRP level was higher among diabetic patients compared to nondiabetic ESRD patients and positively correlated with the prolongation of AVF maturation duration.

Reduced serum albumin is associated with increased adipose tissue inflammation, adiposity, and dysglycemia in type 2 DM. Hypoalbuminemia may be a consequence of a decreased act of insulin on protein synthesis or chronic inflammation involving infiltration of macrophage into adipose tissue (19). Additionally, at the time of AVF creation, ESRD patients may have malnutrition. Whether the cause of hypoalbuminemia is inflammation or malnutrition, it has a clear association with AVF failure (20,21). In our study, ESRD patients with DM were hypoalbuminemic and hypoalbuminemia negatively correlated with AVF maturation duration. However, surprisingly CRP and hypoalbuminemia did not exhibit a significant relation, and in multivariate regression analysis, CRP was a stronger predictor for AVF maturation duration than presurgical albumin levels. We think in this cohort hypoalbuminemia is further related to malnutrition rather than inflammation. The anabolic activity of the body likely improved due to alleviation in the uremic state, the patients gained appetite, and serum albumin levels significantly increased following initiating hemodialysis. Although serum CRP levels decreased following initiating hemodialysis, a correlation between improvement in CRP and postoperative serum albumin levels was not available.

Low hemoglobin level is associated with worse AVF survival, especially when hemoglobin level < 8 gr/dl (22). In this study, hemoglobin levels were > 10 gr/dl, and probably this level of hemoglobin is beneficial for AVF maturation as reported by Gheith et al (23).

Advanced age is another risk factor for worse AVF survival, or failure (23,24). In our cohort, older age was found to correlate with AVF maturation duration.

Predicting worse outcomes by using useful tools can provide better healthcare for ESRD patients. Since a

prolonged AVF maturation duration can be expected in ESRD patients with a higher level of CRP, older age, and hypoalbuminemia, avoiding to use of a temporary central catheter, struggling with malnutrition as a cause of hypoalbuminemia, and evaluating the older ESRD patients carefully before AVF creation, are essential.

This study has some limitations; including low-sample size, not taking into account the site of AVF, the presence of catheter simultaneously, comorbidities, and medicine use such as angiotensin-converting enzyme inhibitors. However, the content will provide some data to physicians in considering an AVF creation.

CONCLUSION

AVF creation in diabetic ESRD patients is a challenge and requires a complete evaluation that involves inflammation, malnutrition, and anemia correction.

DECLARATIONS

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