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Correlation between CRP and early failure of arteriovenous fistula (AVF)

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Abstract

Background: Arteriovenous Fistula (AVF) is the ideal method of vascular access for patients on maintenance hemodialysis (HD). Therefore it is an important part of treatment in HD. There are several observations that indicate the role of inflammation in failure of AVF. The aim of this study was to evaluate the hematologic and inflammatory biomarkers in early AVF failure.

Methods: This case-control study included 110 ESRD patients, whom were undergone AVF creation, divided in two groups. About 700 radius-cephalic AVF were created during these two years. We found 55 cases with AVF failure. In this study, we compared those 55 failures with 55 functional AVF which were selected using randomized sampling from the rest of patients according to age, gender, and AVF location. Levels of serum C-reactive protein (CRP) were checked in both groups to evaluate the relation between AVF failure and CRP level before surgery.

Results: The mean±SD age of the patients was 49.7±17.28 years. CRP was positive in 34 patients (61.8%) with unsuccessful fistula function, while only 4 (7.3%) of those with successful AVF had positive CRP and the rest had negative CRP. The difference between the two groups of patients was strongly significant ($p<0.001$). Statistically, there was not any significant difference between the average of age (p: 0.580) of patients in the control and experimental groups. However, the gender (p: 0.832) discrepancies was not meaningful between the groups.

Conclusion: AVF thrombosis is one of the main complications after AVF creation. Therefore, it is recommended to check CRP before AVF surgery to prevent possible failure of the fistula function.

Keywords: Vascular Access, Arteriovenous Fistula, CRP, Failure.

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Introduction

With large advances during recent years in medicine and general heath, the life span of ESRD patients has been increased (1). New studies show that the prevalence of ESRD patients is increasing 7-9% each year (2, 3)

Hemodialysis (HD) is the most common renal replacement procedure performed for end stage renal disease (ESRD) patients (4). Vascular Access is the most important medical procedure in these cases.

Nowadays, AVF is one of the most common Vascular Access for HD (5). Vascular access failure and its complications are the most frequent hospital admission cause in these patients. In overall, dialysis grafts, that are not frequent in Iran, last shorter than AVF and are more prone to infection and thrombosis (6).

At clinical level, early failure has been defined as an AVF that never develops adequately for dialysis (failure to mature), or which fails within one month of starting dialysis. As identified, increased age, female gender, high blood pressure, presence of diabetes, Caucasian race, vasculature diseases and hemodynamic profile may

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complicate the prognosis of AVF (7). Technical errors in AVF creation are the main causes of early AVF failure (8). Factors such as low hemoglobin levels and high calcium and phosphorous concentrations have been demonstrated as other causes of early AVF failure. Likewise heart failure, distal ischemia, aneurysm formation, median nerve injury, local bleeding, venous hypertension and Steal's syndrome can be some other probable sources of the complications (9-10).

Thrombosis in the arteriovenous anastomosis is a common complication. (11-12) In addition, there are some other risk factors that can influence physiopathology of vascular access destruction (13). So far, there are not many studies relating clinical factors and biomarkers to AVF failure, and furthermore, there are many controversies in these studies. A study in the UK had concluded that low Albumin levels could be a risk factor for AVF failure (14). Another study demonstrated low hemoglobin levels as a destructive factor (9). However, all studies have suspected the importance of inflammatory process. Furthermore, there are not many studies regarding inflammatory biomarkers and AVF failure. The relation between hemoglobin, Albumin, inflammation and other biomarkers are still unclear (9, 11-13). Thus, finding clinical and para clinical factors that can indicate early and late failure of the fistula is essential (14-16). In our study, we evaluated the relationship between inflammation biomarker (CRP) and early rejection of AVF in ESRD patients.

Methods

Subjects

This is a case-control study of patients who were all candidates of fistula creation and hospitalized at Hasheminejad Kidney Center as a referral kidney hospital between December 2010 and October 2012. About 700 radius-cephalic AVF were done during these two years and we had 55 failure. In this study we compared those 55 failures to another 55 functional AVF which were selected using randomized sampling from the rest of patients according to their age, gender, and AVF site.

The study and analysis included 55 ESRD patients with functional AVF and 55 others who experienced failure due to AVF thrombosis during one month after surgery. Therefore, we classified the 55 patients with AVF dysfunction as 'Failure' and those 55 with successful AVF creation as 'Survived' groups. Data related to age, gender and AVF complication was also analyzed.

The demographic data and other related information were recorded on a checklist paper. CRP levels were recorded as well. Other complications related to the AVF were also assessed in the study.

Blood sample assays

Blood samples were obtained before the AVF surgery from antecubital vein of the opposite hand. All Biochemical assays were carried out in the Hasheminejad Kidney Center laboratory. CRP levels were measured with high sensitive CRP (hs-CRP) assay based on the principle of a solid phase Enzyme-linked immunosorbent assay (ELISA) using goat anti Human CRP antibody (hs-CRP ELISA kit, DRG Instrument GmbH, Germany). The intra- and inter-assay coefficients of variation (CV) are both under 5%. All CRP levels higher than 200 nm/L were considered as positive values.

Statistical analysis

Descriptive statistics such as mean and standard deviation were used. Independent T-test was used to analyze quantitative data. Chi-square test was used for qualitative data.

Ethical issues

Patients were given information on the goal and subject of the study; oral approval for their participation as a subject of study were also gained. The participants' information kept confidential. The protocol of the study gained the approval of the Tehran

Table 1. Comparison of different variables between survived and control groups

Variable	Case N(%)	Control N(%)	p
Gender (male)	39/55(70.9%)	40/55(72.7%)	0.832
DM positive	27/55(49.1%)	27/55(49.1%)	1.000
Hypertension	30/55(54.5%)	30/55(54.5%)	1.000
CRP +	34/55(61.8%)	4/55(7.3%)	0.000

Table 2. Frequency distribution of CRP status in survived and failure group

Failure	Category	N	%
No (survived Group)	no	51	92.7
	yes	4	7.3
	Total	55	100.0
Yes (Failure Group)	no	21	38.2
	yes	34	61.8
	Total	55	100.0

University of Medical Sciences Institutional board review.

Results

In this study, 110 ESRD patients underwent AVF creation surgery. The mean±SD age of the patients was 50.62 ±16.7 years. The case group included 55 patients who experienced AVF failure because of thrombosis. The control (survived) group included 55 patients, whose AVF installations were successful. Variables such as age, gender and CRP levels were also studied in both groups.

Thirty one cases (28.2%) were female and 79 (71.8%) were male. Among all the patients, 54 (49.1%) had diabetes and 60 patients (54.5%) had hypertension. Of all cases, 38 (34.5%) were CRP positive and 72 (65.5%) were CRP negative.

Surgery was performed at the radius-cephalic area, including 11.5% side to side and 88.5% end to side anastomosis. 93% of the AVFs were created in the left hand. None of the patients showed infection, hemorrhage or pseudo aneurysm. Site of AVF (left or right hand) also had no difference in both groups (p: 1.000).

Mean±SD of age and hemoglobin level (Hb) were 49.75±17.28 and 8.7 ±1.33, respectively. According to the t-test analysis, Hb level and age had no statistical difference between the failure and survived groups (p: 1.000 &0.549 respectively). Thirty nine cases (70.1%) of thefailure group were male and 29.1% were female. However, the gender of participants showed no meaningful difference in the success or failure of their AVFs (p: 0.832). Diabetes and hypertension had no statistical difference between the failure and survived groups (p: 1.000 in both groups) (Table 1).

Chi Square analysis showed meaningful relation between failure of AVF and CRP status of the patients (sig: 0.000) in the failure group (55 patients).

Within the 55 patients who experienced failure in the AVF function, 34 (61.8%) were CRP positive; Only 4 (7.3%) with positive CRP had successful AVF creation (p<0.001) (Table 2).

In the logistic regression analysis, age, sex, diabetes, Hb level, hypertension and CRP status effects on failure of AVF were evaluated; CRP (+/-) had statistical significance (p<0.001) in this analysis (Table 3).

Table 3. Results from logistic regression

Variable	B	SE	p	OR	95% CI for OR	
					Lower	Upper
Age	-0.003	0.015	0.818	0.997	0.968	1.026
Sex	-0.358	0.522	0.493	0.699	0.251	1.947
diabetes	0.220	0.493	0.656	1.246	0.474	3.277
hb	-0.163	0.184	0.377	0.850	0.592	1.219
htn	-0.110	0.480	0.818	0.896	0.349	2.295
CRP	3.174	0.615	<0.001	23.896	7.161	79.735

Discussion

General findings: In our study, the mean age of our subjects was 53.27±17.47 years, generally lower than other studies in western countries (17-18).

In a study in the 90s, 11% of patients had suffered from AVF thrombosis (19). Another study in 2011 showed that 23% of thrombosis was occurred in malnutrition patients, which points to the probability of lower albumin level association with higher AVF loss in that study. There has been some higher rates of unsuccessful AVFs in some other studies, in which they have reported much larger rates of other complications, such as infection and psuedoaneurysm (7-9, 13, 20). Another study in Croatia demonstrated that high blood pressure, history of diabetes and HD duration is related to long term AVF inefficiency (17). The difference between those results and our finding is probably due to shorter duration of follow-up and smaller sample size in our study. However, in most of previous studies (7-9), no significant difference was seen within age, gender and history of diabetes groups, under the condition of early AVF failure.

Inflammatory biomarker: In our study, patients with AVF failure showed significantly higher CRP levels. Roy-Chaudhury was the first who found the role of inflammation, following an invasive procedure such as angiography, in AVF failure. The study demonstrated the aggressive intimal hyperplasia in anastomotic vessels is associated with thrombotic closure of AVF, resulting in AVF failure (21).

Another study showed an association between fibrinolytic/ endothelial cell function and increased inflammatory biomarkers (fibrinogen and CRP) in ESRD patients (22).

There are some other studies with consistent results, which can work as positive proof to our study. In a study, catheter insertion and AV graft creation resulted in a transient state of high CRP within first postoperative week, while this was not observed after AVF surgery (23, 24). In another study, significantly lower hemoglobin levels related to AVF failure in patients was identified as a prognostic factor (25). Furthermore, there are some studies demonstrating association between low hemoglobin levels and AVF failure (26, 27). Based on these evidences, it is very likely that in ESRD patients low hemoglobin levels induce local low grade inflammation, which can accelerate the thrombosis formation in AVF site. Thus, seems likely that patient with anemia to be more prone to AVF thrombosis with high CRP as a predictor biomarker, than other non-anemic ones.

Conclusion

Our study suggests that inflammatory factors inducing thrombosis might be important causes of early AVF failure in ESRD patients. CRP level is high in failed AVF cases. Probably larger sample size would further clarify the role of inflammatory biomarkers in prognosis of AVF failure.

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