

# Factors responsible for fistula failure in hemodialysis patients

*Ahmed Saif Al-Islam Abd Elfattah, MD*

*Department of Vascular Surgery, Sohag University, Sohag, Egypt.*

## Abstract

*Background: Autogenous arteriovenous fistula (AVF) is regarded as the first and perhaps the best choice of vascular access in hemodialysis patients. Vascular access procedures and their subsequent complications represent major causes of morbidity, hospitalization, and cost for chronic hemodialysis patients.*

*Aim of the study: The main objective of this study is to identify risk factors for failure of autogenous arteriovenous fistulae which had successfully matured and were used for dialysis in hemodialysis patients.*

*Patients and methods: Sixty selected cases of chronic renal failure patients who were referred for AVF during March 2006 to April 2008 were operated on to create AVF and followed up for two years.*

*Results: There were a total of 76 autogenous AVF performed for 60 patients. 32 (53.3%) of the procedures were distal fistulae, followed by 25 (41.7%) cubital fossa fistulae (proximal fistulae) and other sites fistulae were only 3 (5%). Hypertension was present in 24 (40%) of the patients, and diabetes was present in 11 (18.3%). 12 (20%) of the studied cases were overweight. HCV was found in 28 (46.7%) of the patients. 21 (35%) of patients had past history of fistula failure during their course of renal dialysis. Patients who developed AVF failure had significantly lower hemoglobin levels and were more likely to have previous fistula failure.*

*Conclusion: Predictors of AV-fistula malfunction in our dialysis population were lower hemoglobin levels and previous fistula failure.*

*Key words: Arteriovenous fistula, hemodialysis, vascular access, fistula failure, fistula thrombosis.*

## Introduction:

End-stage renal disease (ESRD) is a major public health problem, the incidence of which is increasing every year. It is associated with significant morbidity and mortality, and incurs a huge financial cost, of which a significant portion is directly related to vascular access, not only related to complications of the procedures themselves, but also for management of thrombotic events or infections of different blood accesses.<sup>1</sup>

The most frequently used fistula and the standard one, by which all other fistulae are compared is the Brescia- Cimino fistula.<sup>2,3</sup> Fistula procedure requires well experienced surgeons and ensuring of adequate collateral flow from the ulnar artery by performing Allen test before surgery, in order to minimize the

problem of hand ischemia. In addition, evaluating superficial veins and distal arteries must be achieved for selecting the best site for fistula.<sup>4</sup>

Autogenous arteriovenous fistula (AVF) is regarded as the first and perhaps the best choice of vascular access in hemodialysis patients. Among the various sites, fistula placed at the wrist is the first choice of access because of its simplicity and fewer complications.<sup>5,6</sup>

Arteriovenous fistula transforms a vein into a high-flow vessel. It is obvious that obstacles to flow must be avoided, e.g., kinking, acute angles, torque etc. They create turbulence, damage endothelial cells, and increase the risk of stenosis formation. Transverse cutaneous incisions should be avoided, and we recommend longitudinal incisions if possible.

It has been recommended that veins should be mobilized so that they can be more easily adapted to the artery.<sup>7</sup>

Most AVFs require a maturation period of 4 to 6 weeks before they can be used for hemodialysis; however, some do not mature in this period. These AVFs, which experience nonmaturation, are left to mature longer but often without success and are frequently eventually abandoned altogether.<sup>8</sup>

Anemia is a characteristic and an important clinical manifestation of progressive kidney diseases. It usually worsens with the development of kidney failure. Severe anemia (Hb level lower than 10 g/dL), age (older than 60 years), diabetes mellitus, and smoking were risk factors for access failure.<sup>9</sup>

### **Aim of the work:**

The main objective of this study is to identify risk factors for failure of autogenous arteriovenous fistulae which had successfully matured and were used for dialysis in hemodialysis patients.

### **Patients and methods:**

A prospective clinical study of selected 60 patients (50 men and 10 women) on regular renal hemodialysis were included in our study to whom 76 autologous fistulae were created.

Data of all AVFs created between March 2006 and April 2008 in Vascular Surgery Department Sohag University Hospital were prospectively collected. Data collected included gender, age at the creation of AVF, history of renal disease, presence of diabetes, hypertension, obesity, haemoglobin level, and characteristics of AVF (date of creation, site of creation; distal radiocephalic or proximal brachio-cephalic or brachio-basilic). Study included all chronic hemodialysis patients who met the following inclusion criteria:

- (1) On renal hemodialysis at the time of the first access cannulation.
- (2) Had a mature AVF.
- (3) Had a successful first cannulation of the access with adequate dialysis achieved.

### **Statistical analysis:**

The statistical analysis was performed using the SPSS software version 10. Demographic, clinical variables and initial laboratory data

were compared between patients with and without fistula failure using a two-sample t test for continuous variables and Pearson's Chi-square test for discrete variables. The survival functions of the AVF were studied using the Kaplan-Meier method. The AVF creation date was considered as the starting point, while the first AVF failure as the event. Covariates for fistula survival were analyzed using the Cox regression model.

### **Results:**

There were a total of 76 autogenous AVF performed for 60 patients. There were 50 males (83.3%) and 10 females (16.7%). The mean  $\pm$  SD for age and dialysis duration were  $46 \pm 18.5$  years and  $25.24 \pm 21.04$  months, respectively. Hypertension was present in 24 (40%) of the patients, and diabetes was present in 11 (18.3%). 12 (20%) of the studied cases were overweight. HCV was found in 28 (46.7%) of the patients. 21 (35%) of patients had past history of fistula failure during their course of renal dialysis.

Baseline clinical, comorbidity variables and initial laboratory data in patients who developed AVF failure were compared to those without AVF failure **Table(1)**: Patients who developed AVF failure were significantly more likely to have lower hemoglobin levels and history of previous fistula failure. While hypertension was significantly reported more in patients without fistula failure, this may pay the attention to the role of hypotension as a risk factor for fistula failure.

Sites of AV fistulae created in hemodialysis patients **Figure(1)**: More than half of the procedures were by distal fistulae 32 (53.3%), followed by 25 (41.7%) cubital fossa fistulae (proximal fistulae) and other sites fistulae were only 3 (5%).

Frequency of different causes of AVF failure **Figure(2)**: Showed that thrombosis was the commonest complication in fistulae failure (55%), followed by bleeding and infection (25%, 20% respectively).

The Kaplan-Meier analysis for fistula survival **Figure(3)**: The Kaplan-Meier analysis revealed the 12 and 24 months cumulative fistula survivals were 83% and 73% respectively.

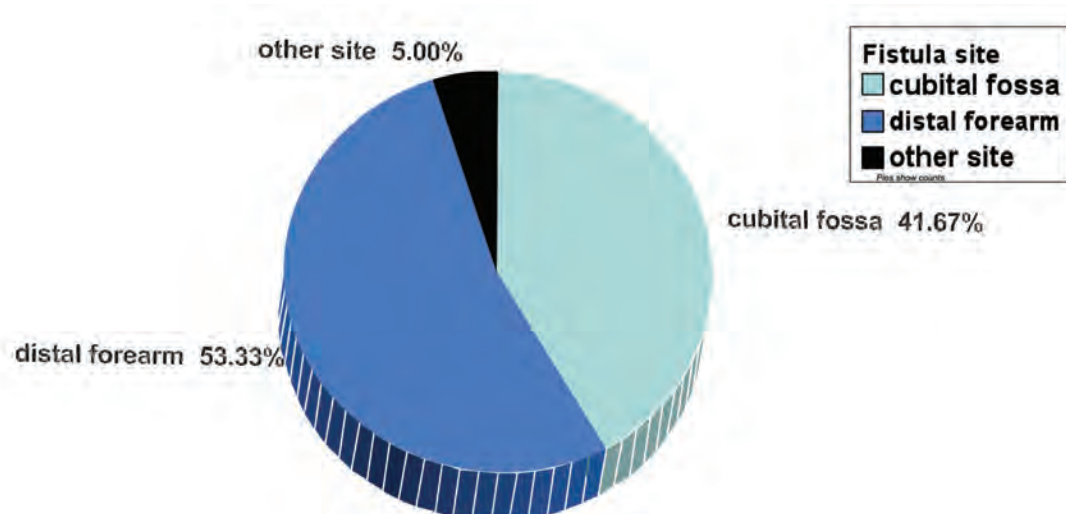
Effect of hemoglobin on fistula survival **Figure(4):** In patients with haemoglobin level less than 9 gm/dl, cumulative fistula survivals were 77% and 61% after 12 and 24 months respectively. While in patients with hemoglobin level more than 9 gm/dl was 86% both after 12 and 24 months. AVF survived significantly longer among patients with hemoglobin greater than 9 g/dL than in those with lower

hemoglobin levels ( $P = 0.030$ ).

Cox regression multivariate analysis for risk factors in fistula failure **Table(2):** The only factors that significantly influenced fistula patency, were previous fistula failure ( $P = 0.023$ ,  $RR = 5.140$ ,  $CI = 1.265 - 25.443$ ) and hemoglobin level ( $P = 0.030$ ,  $RR = 4.705$ ,  $CI = 0.076 - 0.878$ ).

**Table (1): Baseline clinical, comorbidity variables, and initial laboratory data in patients who developed AVF failure were compared to those without AVF failure.**

|                            | Patients with AVF failure<br>16 (26.7%) | Patients without AVF failure<br>44 (73.3%) | P value |
|----------------------------|---|--|---------|
| Age, mean $\pm$ SD         | 43.4 $\pm$ 13.7                         | 46.9 $\pm$ 13.5                            | 0.375   |
| Male/female, (%)           | 14(87.5%) / 2(12.5%)                    | 36(81.8%) / 8(18.2%)                       | 0.593   |
| Anatomical location, n(%)  |   |  | 0.480   |
| Distal forearm AVF         | 10 (62.5%)                              | 22 (50%)                                   |         |
| Cubital fossa AVF          | 6 (37.5%)                               | 19 (43.2%)                                 |         |
| Previous fistula failure   | 9 (56.3%)                               | 12 (27.3%)                                 | 0.037   |
| Comorbidities, (%)         |   |  |         |
| Hypertension               | 3 (18.8%)                               | 21 (47.7%)                                 | 0.043   |
| Diabetes                   | 2 (12.5%)                               | 9 (20.5%)                                  | 0.467   |
| Obesity                    | 1 (6.3%)                                | 11 (25%)                                   | 0.070   |
| Hemoglobin (mean $\pm$ SD) | 8.44 $\pm$ 1.06                         | 9.28 $\pm$ 1.63                            | 0.028   |
| < 9gm/dl                   | 12 (38.7%)                              | 19 (61.3%)                                 |         |
| > 9gm/dl                   | 4 (13.8%)                               | 25 (86.2%)                                 |         |
| HCV+ve                     | 8 (50%)                                 | 20 (45.5%)                                 | 0.755   |



**Figure (1): Sites of AV fistulae created in hemodialysis patients.**

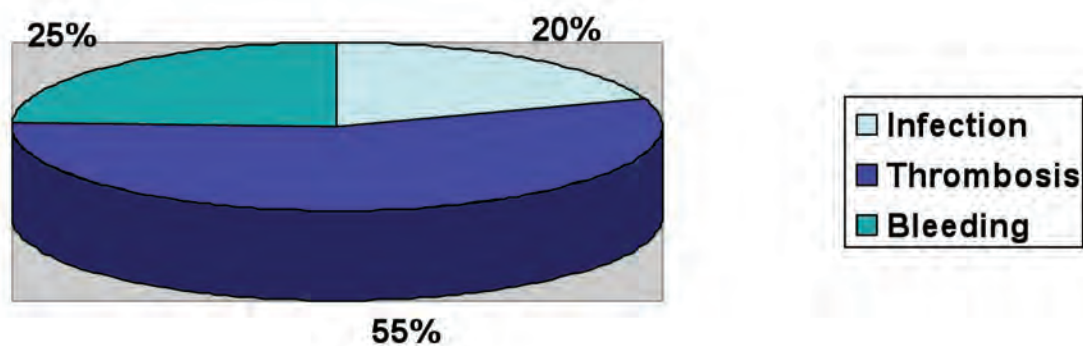


Figure (2): Frequency of different causes of AV fistulae failure.

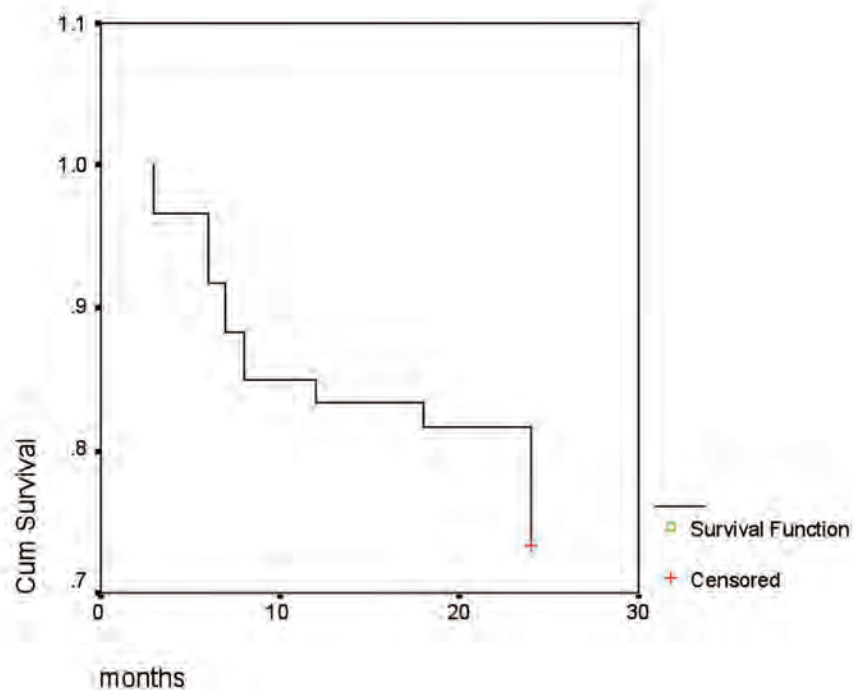


Figure (3): The Kaplan-Meier analysis for fistula survival.

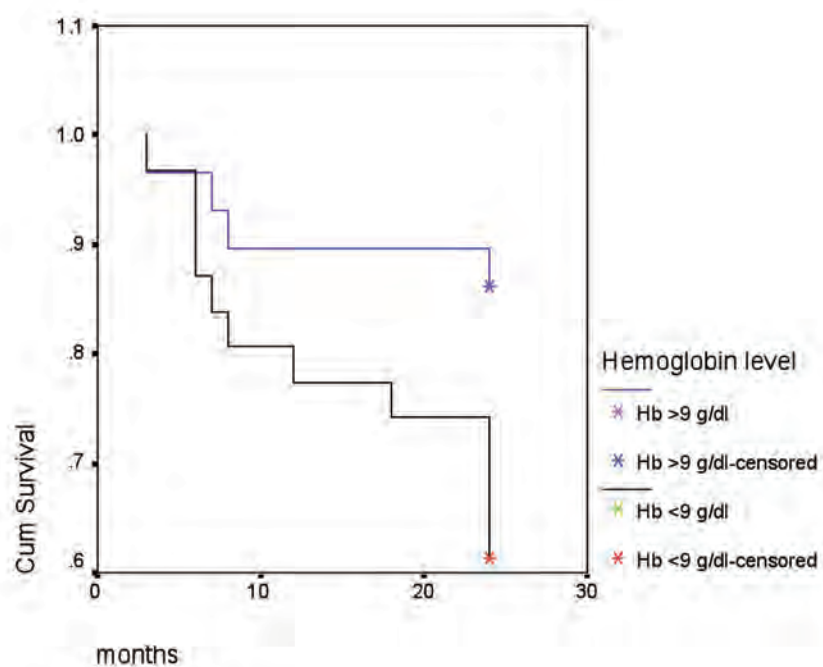


Figure (4): The Kaplan-Meier analysis of the effect of hemoglobin level on fistula survival ( $P = 0.030$ ).



**Table (2): Cox regression multivariate analysis for risk factors in fistula failure.**

| Covariates               | RR    | 95% CI         | P value |
|--------------------------|-------|----------------|---------|
| Previous fistula failure | 5.140 | 1.265 - 25.443 | 0.023   |
| Hemoglobin level         | 4.705 | 0.076 - 0.878  | 0.030   |
| Age                      | 3.089 | 0.929 - 1.004  | 0.076   |
| Sex                      | 0.876 | 0.411 - 12.362 | 0.349   |
| Hypertension             | 2.291 | 0.95 - 1.354   | 0.130   |
| Diabetes                 | 0.150 | 0.126 - 4.002  | 0.698   |
| Obesity                  | 0.027 | 0.082 - 8.259  | 0.869   |
| Fistula site             | 0.007 | 0.339 - 2.70   | 0.934   |
| Serology                 | 0.487 | 0.622 - 2.716  | 0.485   |

*RR = relative risk.*

### Discussion:

The autogenous arteriovenous fistula is the access of choice in hemodialysis patients. It produces the highest survival compared to grafts and catheters, is less thrombotic and results in fewer infectious complications.<sup>7</sup>

In our study, fistula failure occurred in 26.7% of the created AV fistulae and this incidence of fistula failure is similar to the 23-53% observed by previous studies.<sup>10-13,5</sup>

Our results showed no significant difference in the age between patients with and without fistula failure. This is in agreement with many studies.<sup>14-16</sup> But in contrast to Lok, 2007 and Gheith and Kamal, 2008, who reported that old age was a risk factor for the vascular access failure.<sup>17, 9</sup>

In our study we found no significant difference in gender distribution between patients with and without fistulae failure ( $P = 0.593$ ). This is in agreement with Gheith and Kamal, 2008, who found insignificant impact of sex on the mean duration of fistula survival.<sup>9</sup> However, in other research, being female has been associated with a higher incidence of loss of primary functional patency, hypothesized to be due to smaller vascular structures in women.<sup>13</sup> Also, Sajgure et al., 2007 found fistula patency was affected by gender, with longer patency noted in males.<sup>18</sup>

Gheith and Kamal., 2008 found diabetes mellitus associated with a higher frequency of fistula failure.<sup>9</sup> This is in contrast to our results

as we found insignificant difference in the frequency of diabetes mellitus between patients with and without fistulae failure also we noticed hypertension was significantly more in patients without fistula failure, this may pay the attention to the role of hypotension as a risk factor for fistula failure in this field, further studies are needed. But our results were in agreement with Gheith and Kamal., 2008 as regards the higher frequency of fistula failure in severely anemic patients than among less anemic patients.<sup>9</sup>

In our study, we found hypertension and diabetes mellitus in 40% and 18.3% in patients on renal dialysis respectively. While Qasaimeh et al., 2008 reported that diabetes mellitus was the most common etiology of renal failure, followed by hypertension.<sup>19</sup>

In our study, we found significant differences in fistula survival in patients with Hb levels below 9 g/dL and above 9 g/dL ( $P = 0.028$ ). This is in agreement with Gheith and Kamal, 2008 who reported that vascular access survived longer in less anemic patients than among severely anemic patients.<sup>9</sup>

Thrombosis of arteriovenous fistula used for chronic hemodialysis remains a major cause of morbidity in hemodialysis patients.<sup>20</sup> Intimal fibromuscular hyperplasia at the venous anastomosis may be an important factor associated with thrombosis.<sup>21</sup>

In our study, we found that thrombosis was the commonest complication in fistulae failure where it was present in 55% of patients with

fistula failure. Also, Hodges et al., 1997 reported that the most common reason for access failure in AVF was thrombosis.<sup>15</sup>

We found no significant difference in the frequency of fistula failure between patients with distal forearm and cubital fossa AVF ( $P = 0.480$ ). On the contrary Dixon et al, 2002, and Roozbeh et al., 2006 found forearm fistulae were at greater risk of loss of patency compared with those located in the upper arm ( $P = 0.014$ ).<sup>5,20</sup>

Hayakawa and colleagues 2008 reported that the older age, female sex, and diabetes mellitus were risk factors for fistula failure. In our study, predictors of AVF failure were previous fistula failure and low hemoglobin level, while the other clinical and demographical factors did not influence AV-fistula patency.<sup>22</sup>

### Conclusion:

Predictors of AVF failure in our dialysis population were lower hemoglobin levels and previous fistula failure. These risk factors can be used as a guide for intensive management protocol after fistula operation to maintain its patency. We recommend further multicenter studies on other risk factors which may have a role in fistula failure like hypotension and hypercoagulability.

### References:

- 1- Feldman HI, Kobrin S, Wasserstein A: Hemodialysis vascular access morbidity. *J Am Soc Nephrol* 1996; 7(4): 523-535.
- 2- Veith FJ, Hobson RW: Vascular surgery: Principles and practice. McGraw-Hill (Publisher); 2<sup>nd</sup> edn. 1994; p.1025-1038.
- 3- Townsend CM, Beauchamp RD, Evers BM, Mattox KL: Sabiston textbook of surgery. Philadelphia: Saunders Company (Publisher); 16<sup>th</sup> edn. 2001; p.1450-1462.
- 4 - Hirth RA, Turenne MN, Woods JD, Young EW, Port FK, Pualy MV, et al: Predictors of type of vascular access in hemodialysis patients. *JAMA* 1996; 276(16): 1303-1308.
- 5- Dixon BS, Novak L, Fangman J: Hemodialysis vascular access survival: Upper-arm native arteriovenous fistula. *Am J Kidney Dis* 2002; 39(1): 92-101.
- 6- Keuter XH, De Smet AA, Kessels AG, van der Sande FM, Welten RJ, Tordoir JHA: Randomized multicenter study of the outcome of brachial-basilic arteriovenous fistula and prosthetic brachial-antecubital forearm loop as vascular access for hemodialysis. *J Vasc Surg* 2008; 47(2): 395-401.
- 7- Konner K, Nonnast-Daniel B, Ritz E: The arteriovenous fistula. *J Am Soc Nephrol* 2003; 14: 1669-1680.
- 8- Voormolen E H, Jahrome A K, Bartels L W, Moll F L, Mali W P, Blankestijn P J: Nonmaturation of arm arteriovenous fistulas for hemodialysis access: A systematic review of risk factors and results of early treatment. *Journal of Vascular Surgery* 2009; 49(5): 1325-1336.
- 9- Gheith OA, Kamal MM: Risk factors of vascular access failure in patients on hemodialysis. *IJKD* 2008; 2(4): 201-207.
- 10-Miller A, Hölzenbein TJ, Gottlieb MN, et al: Strategies to increase the use of autogenous arteriovenous fistula in end-stage renal disease. *Ann Vasc Surg* 1997; 11(4): 397-405.
- 11-Miller PE, Tolwani A, Luscly CP, et al: Predictors of adequacy of arteriovenous fistulas in hemodialysis patients. *Kidney Int* 1999; 56(1): 275-280.
- 12-Allon M, Lockhart ME, Lilly RZ, et al: Effect of preoperative sonographic mapping on vascular access outcomes in hemodialysis patients. *Kidney Int* 2001; 60(5): 2013-2020.
- 13-Miller CD, Robbin ML, Allon M: Gender differences in outcomes of arteriovenous fistulas in hemodialysis patients. *Kidney Int* 2003; 63: 346-352.
- 14-Windus DW, Jendrisak MD, Delmez JA: Prosthetic fistula survival and complications in hemodialysis patients: Effects of diabetes and age. *Am J Kidney Dis* 1992; 19: 448-452.
- 15-Hodges TC, Fillinger MF, Zwolak RM, Walsh DB, Bech F, Cronenwett JL: Longitudinal comparison of dialysis access methods: Risk factors for failure. *J Vasc Surg* 1997; 26: 1009-1019.
- 16-Miller PE, Carlton D, Deierhoi MH, Redden DT, Allon M: Natural history of arteriovenous grafts in hemodialysis patients. *Am J Kidney Dis* 2000; 36: 68-74.

- 17-Lok CE: Fistula first initiative: Advantages and pitfalls. *Clin J Am Soc Nephrol* 2007; 2: 1043-1053.
- 18-Sajgure A, Choudhury A, Ahmed Z, Choudhury D: Angiotensin converting enzyme inhibitors maintain polytetrafluoroethylene graft patency. *Nephrol Dial Transplant* 2007; 22: 1390-1398.
- 19-Qasaimeh G R, El Qaderi S, Al Omari G, Al Badadweh M: Vascular access infection among hemodialysis patients in Northern Jordan: Incidence and risk factors. *The Southern medical journal* 2008; (101)5: 508-512.
- 20-Roozbeh J, Serati AR, Malekhoseini SA: Arteriovenous fistula thrombosis in patients on regular hemodialysis: A report of 171 patients. *Arch Iranian Med* 2006; 9 (1): 26-32.
- 21-Swedberg SH, Brown BG, Sigley R, Wight TN, Gordon D, Nicholls SC: Intimal fibromuscular hyperplasia at the venous anastomosis of PTFE grafts in hemodialysis patients. *Circulation* 1989; 80: 1726-1736.
- 22-Hayakawa K, Miyakawa S, Hoshinaga K, Hata K, Marumo K, Hata M: The effect of patient age and other factors on the maintenance of permanent hemodialysis vascular access. *Ther Apher Dial* 2007; 11: 36-41.