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# The impact of vascular diameter ratio on hemodialysis maturation time: Evidence from data mining approaches and thermodynamics law

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## Abstract

**Background:** Vascular Access (VA) is an important aspect for blood circulatory in Hemodialysis (HD). Arteriovenous Fistula (AVF) is a suitable procedure to gain VA. Maturation of the AVF is a status of AVF, which can be cannulated for HD. This study aimed to discover the parameters that effectively reduce the duration between VA and start of HD, which symbolizes the maturation time (MT).

**Methods**: Ninety-six patients who underwent AVF creation were selected for this study. The decision tree method was used based on CART/C4.5 algorithm, which is one of the data mining approaches for data classification. Vascular diameter ratio (VDR) coefficient was obtained (VDR=Artery/Vein diameters).

**Results**: We investigated the relationship between the VDR and MT in this study and found that MT is reversely related to VDR in elderly patients, while this relation was direct in younger patients.

**Conclusion**: The analysis revealed a Spearman's correlation coefficient for Vein diameter with MT. MT decreases when diameters of vein and artery are close to one another. This study can help the surgeons to identify high- risk patients who elongate MT for HD.

**Keywords**: Data Mining; Hemodialysis; Maturation Time; Vascular Diameter Ratio; Thermodynamics.

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## Introduction

Chronic kidney disease (CKD) is a condition in which the kidneys are damaged and cannot filter blood well. In the advanced stage of CKD, known as end stage renal disease (ESRD), kidney functions are reduced very severely. Hemodialysis (HD) treatment is the most common procedure which is performed for ESRD patients, and HD requires permanent vascular access (VA) as an important aspect (1). Furthermore, three main types of VA are used in HD treatment: Arteriovenous fistula (AVF), synthetic arteriovenous graft (AVG), and central venous catheter (CVC) (2). According to the clinical practice guidelines, AVF is the first choice because of its minor complications, morbidity and mortality compared to AVG and CVC.

Also, AVF has a superior survival rate (estimated at 90% after one year) than other VA types (such as 60% of AVG) (3). AVF is less expensive and remains the gold standard access. Fistula maturation depends on several changes involving the vein such as increased blood flow, increased vein diameter, and increased visibility of the vein (4). Genetic predisposition, low shear stress, increases in transmural pressure, turbulence, differences in compliance between arteries

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and veins, and vascular injury of the mobilized segment all contribute to neointimal hyperplasia and adverse vascular remodeling (5).

Reported AVF maturation rate varies widely from 30-90% (6-8). Successful fistula creation results in easy cannulation within adequate blood flow to support dialysis. Protracted hemodialysis via percutaneous catheter may be required while awaiting fistula maturation, and this increases the risk of infection and compromise the central vein patency (9).

The prevalence of CKD is increasing around the world. In 2010, in the U.S., more than 10% of people, or more than 20 million patients had CKD (10). According to the recent statistics of National Kidney Foundation (NKF), there were 26 million CKD patients in the U.S. in 2012 (11). Also, the rate of ESRD, as a chronic illness, has grown rapidly in the recent years (12). At the end of 2004, ESRD was reported to be prevalent in the world's population of 400,000 including over 300,000 HD patients (13). At the end of 2008, 547,982 U.S. residents were under treatment of ESRD and 382,343 of them received dialysis; of whom, 354,443 were under hemodialysis (14). In the U.S., AVF use increased from 27.9% in 1998 to 55.0% in 2007 (15), showing an increase from 32.4% in 2003 to 57.9% in 2011 (16). Moreover, the durability of AVF is 90% for a year after maturation for dialysis, while this rate is only 60% for AVG (3). This method was used by 91% of the patients in Japan and by 70% and 90% of patients in most European countries (17).

In Iran, the prevalence and incidence of ESRD is 378 per million populations (PMP) and 59 PMP, respectively (18). More than 14,000 patients were treated with chronic HD therapy for ESRD in 2008 in Iran (19). AVF is used by 93.4% of Iranian HD patients (1). This finding exceeds the recommendations by guidelines, 67-91% of patients reported using AVF in many western countries in the recent years (20). We described the risk factors of early AVF failure, using a Data Mining approach in an earlier study (21).Then we studied predictive data mining techniques to identify these risk factors in the next publications (22,23). The maturation of a fistula (becoming accessible for dialysis) is described as a fistula condition which can be cannulated with two needle probes permanently or routinely and supply the adequate blood flow (min 350-450ml/min) for a successful HD session (3-4 hours) each time (24).

The complicated nature of real-world biomedical data has made it necessary to look beyond traditional biostatistics. This broader field, which includes methods for data pre-processing and visualization, and new methods from machine learning, is called data mining (25). Data mining approaches have developing implications in the health area and aided the clinical data description processing via health systems transactions (26). Data mining is a process in which specific analysis are used to reveal the novel, standard and beneficial models from a great body of data. Data mining is defined as a process of extracting interesting (non-trivial, implicit, previously unknown and potentially useful) patterns or knowledge from huge amount of data (27).

KDD is defined as the non-trivial process of identifying valid, novel, potentially useful and ultimately understandable patterns in data. Data mining is becoming increasingly popular in healthcare, if not increasingly essential, and several factors motivate the use of data mining applications in healthcare including fraud and abuse detection, the ability to transform data and benefiting healthcare providers. These approaches are boosting and their applications have become increasingly essential for healthcare organizations to make decisions based on the analyses of huge amounts of clinical data, which are generated by healthcare transactions (26). Nevertheless, running these techniques on small datasets are useful, and we recently found a study on a small dataset of patients (28) and found another one on smaller datasets, which was published in Nature journal

(29). This study aimed to discover the parameters that are effective in reducing the duration between VA and the start of HD, which symbolizes Maturation Time (MT).

## Methods

### *Data*

This study was conducted using the medical history of 96 patients who referred to the Hasheminejad Kidney Center for AVF creation during 2006-2007, using cross-sectional method and classification analysis. A checklist was used to collect data on each patient's vein and artery diameter and time of fistula maturation according to their hospital records.

Our criteria for AVF maturation were as follows: (1) Easily palpable superficial vein; (2) Vein relatively straight; (3) Adequate diameter for easy cannulating needles (4mm); (4) Adequate length (≥10cm, for adequate distance between the cannulating needles); (5) Uniform thrill to palpation and auscultation. We evaluated these criteria by the help of nurses, nephrologists or surgeons. In this study, data included demographic characteristics such as age, gender, and past medical history. Moreover, data on the arterial diameter and time course of maturation were collected from the medical records of the enrolled patients and analyzed using the Rapidminer software. Maturation time (MT) was defined as the duration after the surgery up to the time when AVF becomes accessible for HD.

### *Statistical Analysis*

Descriptive method is one of the data mining approaches, similar to the clustering method, which we used in the previous study to explore the risk factors of early AVF failure in 99 HD patients (22). However, in this study, we used the predictive approach in the processing stage.

Classification is one of the predictive approaches, which classifies data using many methods, and the other is the decision tree (DT); DT consists of three parts: Root, nodes and leafs. Any DT algorithm can produce different numbers of nodes and leafs, determining deepness and complexity of DT (30).

DT algorithms are popular because of their applications and easily understandable results; some of DT algorithms are: ID3, C4, CART, C4.5, C5, CHAID, QUEST. In 1993, Quinlan designed the C4.5 algorithm and used the information gain concept to create the tree; C4.5 is recursive and greedy (31).

In this study, we used many DT operators based on CART/C4.5 algorithm, and then selected the DT with novel and usable patterns. Prior to the processing phase, we prepared and categorized the data into four frames. Due to the age distribution of the patients, they were placed into four subgroups and labeled accordingly: "A20" for 22-37 year olds; "A40" for 41-59 year olds; "A60" for 60-79 year olds; and "A80" for 81-84 year olds. The MT was classified as follows: Class A: 21 days, class B: 23-46 days, and class C: 54-145 days. These classes consisted of 54, 22 and 20 patients, respectively. Lastly, we defined the VDR coefficient as in Equation 1:

(1) VDR= Artery Diameter/Vein Diameter

After preparing the data, we executed the decision tree algorithm over the data. The decision tree (DT) is one of the predictive data mining approaches for data classification. The related DT in this analysis is illustrated in Fig. 1.

### *Assessment using Physics*

Many studies, which were conducted based on the physics laws, examined the impacts of blood flow and vessel characteristics on the arterial diseases. In one of these studies, unsteady stenosis flow was predicted and it was showed that the wall shear stress (WSS) distribution over the time interval was comparable for both non-Newtonian models; Also, according to Laplace's law, the wall stress on an ideal cylinder is directly proportional to its radius and intraluminal pressure. Even though an abdominal aortic aneurysms (AAA) is not

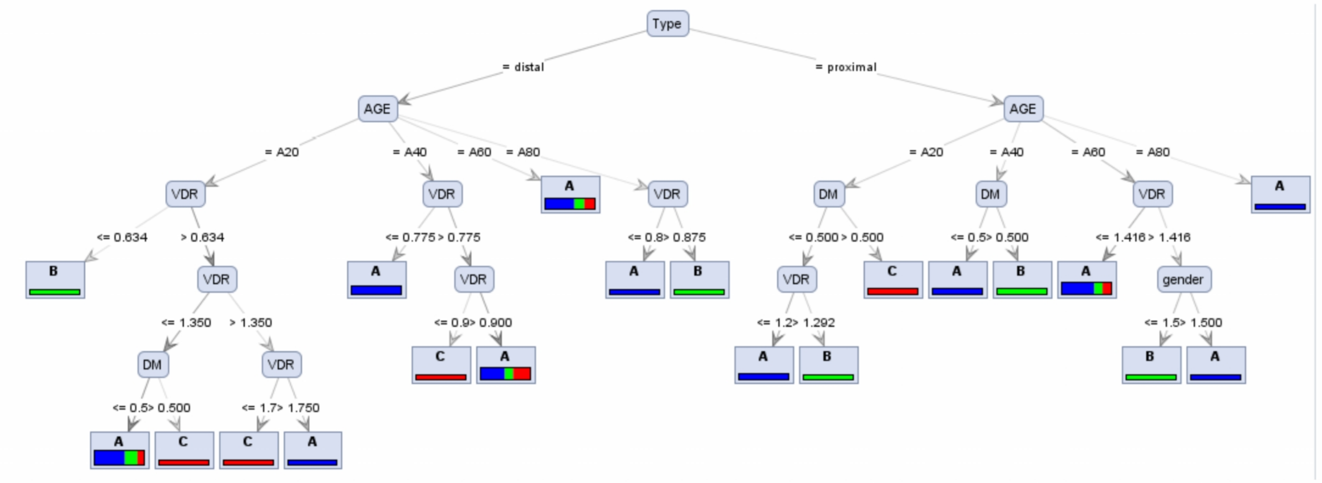


Fig. 1. The Decision Tree of the Classified MT and Its relation with VDR Ratio

an ideal cylinder, Laplace's law still applies and with an increasing aortic diameter, the internal pressure increases, and so does the risk of rupture. The increase in internal pressure against the aortic walls results in progressive growth of the AAA diameter; and eventually, this pressure may overcome the resistance of the aortic wall resulting in rupture (32). In two other studies, the computational fluid dynamics (CFD) computation was performed assuming that the arterial wall is rigid and the blood is considered a homogeneous Newtonian fluid; These researchers observed a correlation between patient-specific AAA geometric parameters, WSS and hemodynamic loads, and used it as a potential predictor of AAA arterial wall rupture and potential intra luminal thrombus (ILT) formation (33-34).

MT is low when diameters of vein and artery are close. The laws of physics confirm this fact in joining two pipes at global cases. To prove this, we considered the condition in which two pipes with different diameters joined together. For each mean velocity, $v_1$ in a smaller pipe will have a velocity of $v_2$ in a bigger pipe that is represented by cohesion equation; so far in compress flow all force on control volume horizontal side is constant. In a real situation, for severe turbulences of fluids valid in outside space of control volume, just be restored few of kinetic energy of fluids of basic flow the pressure then this kinetic energy be loss the internal energy and transition heat. In these calculations, we supposed that the restoration of pressure in this space was zero and the pressure of valid across this region is equal to $p_1$. The equation of linear momentum for control volume is obtained by (2):

$$p_1A_2 - p_2A_2 = \rho v_2^2 A_2 - \rho v_1^2 A_1 \qquad (2)$$

by replacing $v_1$ with $v_2(A_2/A_1)$ in continuity equation (3):

$$\frac{p_2 - p_1}{\rho} = v_2^2\left(1 - \frac{A_2}{A_1}\right) \qquad (3)$$

To determine the head loss, we assumed the first law of thermodynamics (FLT) for control volume and used the basic definition of the head (4):

$$\frac{V_1^2}{2} + \frac{P_1}{\rho} = \frac{V_2^2}{2} + \frac{P_2}{\rho} + h_1 \qquad (4)$$

We obtained $(P_1 - P_2)/\rho$ from the equation 4 and the sentence in the equation 3. Therefore, we obtained $h_1$ as (5):

$$h_1 = \frac{v_2^2}{2}\left(1 - \frac{A_2}{A_1}\right)^2 = \frac{v_2^2}{2}\left[1 - \left(\frac{D_1}{D_2}\right)^2\right]^2 \qquad (5)$$

We observed that (35) when pipes diameters were different, the formal friction coefficient is as (6):

$$K = \frac{[1-(D_1/D_2)^2]^2}{(D_1/D_2)^4} = \left[\left(\frac{D_2}{D_1}\right)^2 - 1\right]^2 = \left[1 - \left(\frac{D_2}{D_1}\right)^2\right]^2 \qquad (6)$$

Finally equation 6 shows that whatever the sections of the tubes (or vessels diameters) be much different, the friction force will increase, causing a rise in the temperature, and so arterial wall rupture will be followed.

## Results

Fifty-six male (58.3%) and 40 female (41.7%) patients participated in this study. The mean±SD age of all patients was 54.7±17.01 years and the mean±SD of arterial and vein diameter was 2.6±1.10 and 2.4±0.79 millimeter, respectively. The mean±SD AVF maturation time (MT) for all the patients was 36.5±35.30 days.

However, in six men (6.25% of the patients) aged over 80 years, VDR was bigger than 1 and no relation was found between vascular diameters and MT, but in the rest of the patients (90 person=93.75% of the patients) with VDR≤1, a considerable reduction was observed in MT. The average numbers of the input and output (I/O) parameters are shown in Table 1.

As demonstrated in Figure 1, we observed that "class A" is an after condition "VDR>1.5" and "VDR>1.75" in two leafs of the tree, and these leafs have only two patients, while in all other leafs with "class A" VDR was close to 1. This means that MT is low when vein's diameter is closer to diameter of (either brachial or radial) artery in AVF creation.

As illustrated in Table 2, a significant relationship was found between the MT and the vein diameter. Moreover, the vascular diameter ratio (VDR) coefficient had meaningful relations with diabetes mellitus (DM).

Table 1. The Average Numbers of the I/O Parameters

| Parameter | Number of Patients | % | Range | Mean | SD |
|---|---|---|---|---|---|
| All of patients | 96 | 100 | | | |
| Males | 56 | 58.3 | | | |
| Females | 40 | 41.7 | | | |
| VDR>1 (Artery>Vein) | 39 | 37.5 | | | |
| VDR≤1 (Artery≤Vein) | 58 | 60.41 | | | |
| MT: class A | 54 | | 21 days | | |
| MT: class B | 22 | | 23-46 days | | |
| MT: class C | 20 | | 54-145 days | | |
| Age | | | 22-84 years | 54.75 | 17.01 |
| Maturation Time | | | 21-145 days | 36.52 | 35.30 |
| Arterial Diameter | | | 1-5 millimeter | 2.56 | 1.1 |
| Vein Diameter | | | 1-4 millimeter | 2.4 | 0.79 |

Table 2. Correlations among the Associated Factors by Spearman's rho Analysis

| | | Gender | DM | arteryD | veinD | MT | VDR |
|---|---|---|---|---|---|---|---|
| Gender | Correlation Coefficient | 1.000 | | | | | |
| | Sig. (1-tailed) | . | | | | | |
| | N | 96 | | | | | |
| DM | Correlation Coefficient | .099 | 1.000 | | | | |
| | Sig. (1-tailed) | .181 | . | | | | |
| | N | 86 | 86 | | | | |
| Artery D | Correlation Coefficient | -.128 | .300** | 1.000 | | | |
| | Sig. (1-tailed) | .108 | .003 | . | | | |
| | N | 96 | 86 | 96 | | | |
| Vein D | Correlation Coefficient | -.226* | .251** | .754** | 1.000 | | |
| | Sig. (1-tailed) | .013 | .010 | .000 | . | | |
| | N | 96 | 86 | 96 | 96 | | |
| MT | Correlation Coefficient | .063 | .082 | .088 | .129 | 1.000 | |
| | Sig. (1-tailed) | .271 | .227 | .196 | .106 | . | |
| | N | 96 | 86 | 96 | 96 | 96 | |
| VDR | Correlation Coefficient | .087 | .138 | .593** | -.038 | .001 | 1.000 |
| | Sig. (1-tailed) | .201 | .103 | .000 | .355 | .494 | . |
| | N | 96 | 86 | 96 | 96 | 96 | 96 |

*. Correlation is significant at the 0.05 level (1-tailed).
**. Correlation is significant at the 0.01 level (1-tailed).

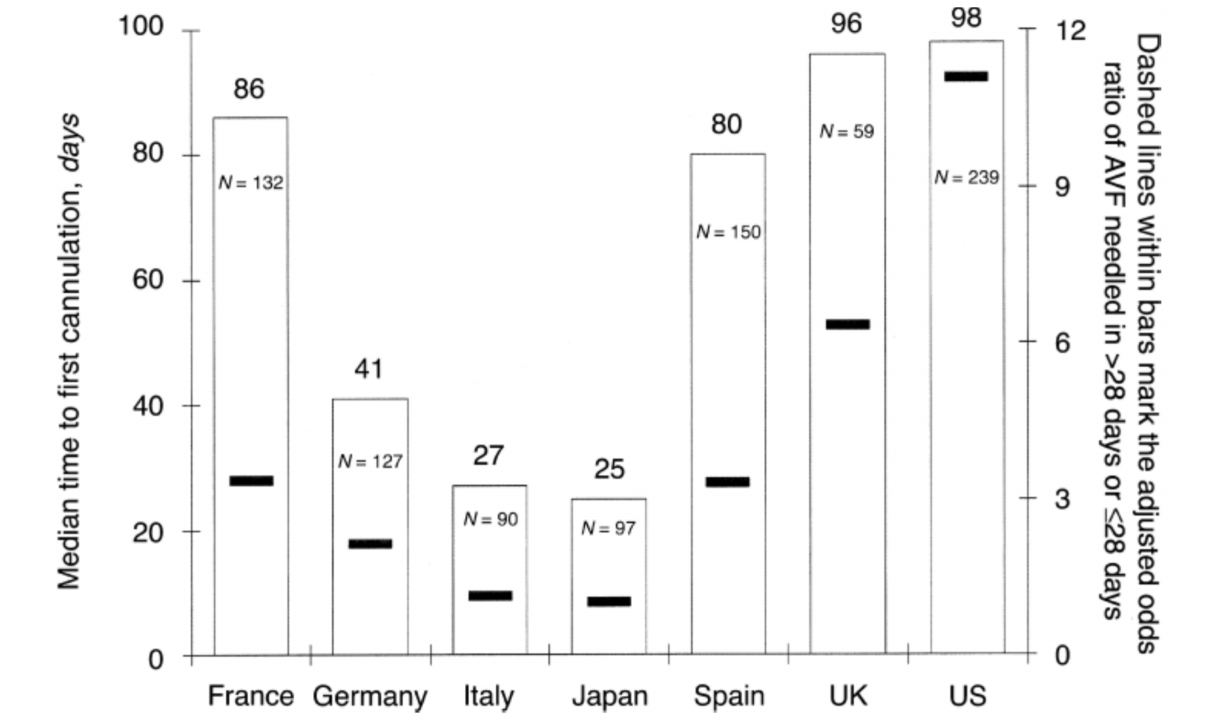


Fig. 2. The Median Time to First Cannulation of A-V Fistulae by Country (bars), and Adjusted Odds Ratio of an A-V Fistula being Cannulated ≤28 days versus>28 days after Creation Relative to Japan (dashed line within bar) (36)

## Discussion

There is much discrepancy between MT in various reports. In NKF-K/DOQI guidelines, the average time for fistula maturation is reported to be 1 to 4 months. Also, the median time to first fistula cannulation differed between countries, ranging from 28 days in Japan and Italy to 96 and 98 days in transplantation in UK and US, respectively (36) (Fig. 2).

This finding that the use of vein with larger stream diameters was associated with greater success rate is consistent with the following studies. These studies examined preoperative venous diameter and AVF adequacy for dialysis (37,38). Wong et al. (37) found no differences in the average venous diameter at the wrist between failed and adequate AVF, but reported that all AVF would fail if the diameter was 1.6 mm or less. Another study reported that 16% of AVF were adequate with a vein diameter of 2 mm or less compared to 76% of those >2 mm (39).

Using Spearman's correlation analysis (Table 1), we found that the maturation time of fistula (MT), was correlated with vein diameter. However, no correlation was observed between MT and diameter of the arteries in the previous research (9).

No correlation was found between MT and gender of the patients. Moreover, as there were only six patients over 80 years of age (label A80), no statistically significant relation was found between them. This study may help to identify those patients with higher risks for elongated vascular accessibility for the HD. Moreover, future studies should be conducted with larger sample sizes to evaluate these factors and other ones that can decrease the period of fistula maturation.

## Conclusion

Based on the results of this study, we concluded that in most patients, maturation time (MT) decreased when diameters of the vascular vein and artery were close to one another. In addition, the analysis revealed a Spearman's correlation coefficient for vein diameter with MT. The VDR ratio showed that in elderly patients, MT was reversely related to VDR (arterial>venous diameter), while this relation was direct in younger patients (arterial<venous diameter). Moreover, VDR had a notable role (Table 1) in diabetic patients. Thus, we recommend that more studies be conducted on this subject in the future. Based on our observation, a surgeon could choose a vein with a diameter closer to either brachial or radial artery in AVF creation.

## *Disclosure*

None of the authors and co-authors of this paper have any direct or indirect financial relation with the commercial identity, “Rapidminer” mentioned in this paper.

## *Conflict of interest*

The authors declare no competing interests.

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