The natural history of autogenous radio-cephalic wrist arteriovenous fistulas of haemodialysis patients: a prospective observational study

Carlo Basile, Giovanni Ruggieri, Luigi Vernaglione, Alessio Montanaro and Rosa Giordano
Division of Nephrology, Hospital of Martina Franca, Italy

Abstract

Background. Clinical practice guidelines have supported vascular access surveillance programmes on the premise that the natural history of the vascular access will be altered by radiological or surgical interventions after vascular access dysfunction is detected. The primary objective of this study was to assess the actual risk of thrombosis of autogenous radio-cephalic (RC) wrist arteriovenous fistulas (AVFs) without any pre-emptive interventions.

Methods. We enrolled 52 randomly selected adult Caucasian prevalent haemodialysis (HD) patients, all with autogenous RC wrist AVFs, into this prospective, observational study aimed to follow the natural history of their AVFs for 4 years. The protocol prescribed avoiding any surgical or interventional radiological procedures until access failure (AVF thrombosis or a vascular access not assuring a single-pool \( Kt/V \geq 1.2 \)). The subjects underwent yearly assessments of vascular access blood flow rate by means of a saline ultrasound dilution method.

Results. All failures of vascular access were due to AVF thrombosis; none were attributed to an inadequacy of the dialysis dose. AVF thrombosis occurred in nine cases; a rate of 0.043 AVF thrombosis per patient-year at risk. The receiver operating characteristic curve, evaluating the diagnostic accuracy of baseline vascular access blood flow rate values in predicting AVF failure, showed an under-the-curve area of \( 0.82 \pm 0.05 \) SD (\( P = 0.01 \)). The value of vascular access blood flow rate, identified as a predictor of AVF failure, was \(< 700 \text{ ml/min} \) with an 88.9% sensitivity and 68.6% specificity. When subdividing the population of AVFs into two groups according to the baseline vascular access blood flow rates, two out of the nine thromboses occurred among the AVFs that had baseline blood flow rates \( >700 \text{ ml/min} \) (\( n = 31 \)), whereas seven occurred among the AVFs that had baseline blood flow rates \(<700 \text{ ml/min} \) (\( n = 21 \)). The 4 year cumulative actuarial survival was 74.36 and 20.80%, respectively (log-rank test, \( P = 0.04 \)). The 24 AVFs that remained patent at the end of the 4 years maintained a median blood flow rate \( \geq 900 \text{ ml/min} \) at all time points studied. Worth noting is that, five of them (20.8%) remained patent throughout the study with a blood flow rate consistently \( \leq 500 \text{ ml/min} \).

Conclusions. This study shows a very low rate of AVF thrombosis per patient-year at risk and a high actuarial survival of autogenous RC wrist AVFs, particularly of those having a blood flow rate \( >700 \text{ ml/min} \). Thus, a vascular access blood flow rate \( <700 \text{ ml/min} \) appears to be a reliable cut-off point at which to start a closer monitoring of this parameter—which may lead to further investigations and possibly interventions relevant to the function of the AVFs.

Keywords: autogenous radio-cephalic wrist arteriovenous fistula; haemodialysis; ultrasound dilution; vascular access blood flow

Introduction

Maintaining a functional haemodialysis (HD) is one of the important challenges nephrologists face today. Vascular access failure is associated with significant morbidity. There is also a significant cost associated with it—8000 US dollars per patient per year at risk in the United States, \( \sim 15% \) of Medicare’s expenditure for end-stage renal disease [1]. This, however, represents only the tip of the iceberg. Vascular access complications account for 16–25% of hospital admissions, and the type of vascular access in use is correlated with overall and cause-specific mortality [2].

The high cost of access failure calls for a closer look at strategies to prevent vascular access thrombosis. NKF K/DOQI clinical practice guidelines recommend regular monitoring of vascular accesses [be they arteriovenous grafts (AVGs) or arteriovenous fistulas]
(AVFs), by one of several methods, such as measurements of the vascular access blood flow rate [3]. A technique employing saline ultrasound dilution (USM) (Transonics Hemodialysis Monitor HD01; Transonics Systems Incorporated, Ithaca, NY, USA) has been developed [4], and published data support its efficacy for the regular monitoring of both AVGs and AVFs [3,4]. Such monitoring has received support [3] based on the premise that the natural history of the vascular access will be altered by radiological or surgical interventions after vascular access dysfunction is detected. The main point of our 4 year prospective observational study was to follow the natural history of mature AVFs without altering them by radiological or surgical interventions after detection of vascular access dysfunction. Thus, the aim of the present study was to assess the actual risk of thrombosis of AVFs while desisting from any pre-emptive interventions.

Subjects and methods

Patients

Our policy regarding vascular access includes two points: (i) the forearm, native-vessel AVF is considered the vascular access of first choice, and whenever possible must be attempted in every patient referred for surgery; (ii) all autogenous radio-cephalic (RC) wrist AVFs are constructed by the experienced nephrologists of our unit (A.M. and R.G.). Out of the 123 HD patients treated in our unit by 31 December 1998, 115 had native-vessel AVFs (93.5%) (112 autogenous RC wrist, three humerobasilic), five had AVGs (4.1%) and three had central venous catheters (2.4%). All AVFs are created in our unit after standardized vascular mapping, including both physical examination and colour Doppler sonography of the venous as well as of the arterial beds of the upper extremity.

We invited 112 adult Caucasian patients prevalent as of 31 December 1998 to participate in this study. All of them had mature autogenous RC wrist AVFs. For the purpose of the study, an AVF was defined as mature if it allowed a dialyser blood flow of at least 300 ml/min. Informed consent was obtained from 105 patients. We randomly selected 52 of them to undergo the present prospective observational study. Comorbidity scoring was performed by a single clinician (C.B.) familiar with the patient’s case histories, utilizing medical and nursing records and investigation data. A very simple comorbidity index was derived based on the presence (scored 1) or the absence (scored 0) of the following comorbidity domains: 1, diabetes mellitus; 2, heart disease (previous myocardial infarction, angina pectoris, atrial fibrillation, pacemaker, left ventricular dysfunction); 3, systemic or other significant pathologies—particular attention was paid to the presence of peripheral vascular diseases as detected by colour Doppler sonography or arteriography, or both. The highest the cumulative score could be was 3 [5] (Table 1).

Study protocol

The main point of our 4 year prospective observational study, which started on 1 January 1999, was to follow the natural history of the 52 mature autogenous RC wrist AVFs for 4 years without any surgical or radiological interventions until vascular access failure (AVF thrombosis or inadequacy of dialysis dose, i.e. single-pool Kt/V < 1.2). Thus, the primary objective was to assess the actual risk of thrombosis of AVFs in the absence of any pre-emptive interventions. All patients were dialysed three times per week with high- and low-flux membranes and standard bicarbonate dialysate using 15-gauge fistula needles. Patients were anticoagulated with systemic heparin.

Studies

At the baseline, the 52 patients were cannulated with two needles in the standard way; the distance between the tips, pointing in opposite directions, ranged from 13 to 21 cm, and the arterial needle faced upstream. Vascular access blood flow rate was evaluated by means of the ultrasound dilution Transonics Hemodialysis Monitor HD01 as previously described [4]. For the measurement of vascular access blood flow rate, the dialyser blood lines were reversed in a sterile manner and a temporary recirculation channel was created. The blood pump rate was set to 300 ml/min. The baseline vascular access blood flow rate was determined by averaging two separate measurements taken ~5–10 min apart during the first 30 min of dialysis. Subsequently, the patients underwent follow-up studies consisting of the periodic assessment —every 12 months for 4 years—of vascular access blood flow rate by means of USM conducted in the same manner as for the baseline measurements. Arterial blood pressure was measured immediately after vascular access blood flow rate measurement, and is expressed as mean arterial pressure (MAP).

All tests throughout the study were performed by the same operator (G.R.). Blood samples were collected for the determination of BUN, which was done using routine automated methods (Cobas Mira S, Roche, Italy). Single-pool Kt/V was estimated monthly.

Statistics

The survival of AVFs was evaluated by means of Kaplan–Meier analysis. The log-rank test was used for life-table
comparisons. To identify threshold values of vascular access blood flow rate that predict AVF failure, a receiver operating characteristic (ROC) curve was constructed [6] by plotting sensitivity vs the false-positive rate (FPR) at different cut-off levels of vascular access blood flow rate. Sensitivity was defined as the percentage of failed AVFs with positive test results; specificity was defined as the percentage of patent AVFs with negative test results, and FPR (equal to 1 – specificity) as the percentage of patent AVFs that tested positive. Friedman’s test was used for assessing the trends of repeated measures of MAP and of vascular access blood flow rate during the follow-up period. Data are expressed as means ± SD and median/range. All the statistical inferences were derived using the SPSS 10.1 (SPSS Inc., Chicago, IL, USA) software package. A *P*-value < 0.05 was considered significant.

**Results**

All vascular access failures resulted from AVF thrombosis, no non-thrombosed vascular access failed to allow an adequate dialysis dose, i.e. a single-pool Kt/V ≥1.2. AVF thrombosis occurred in nine patients; 19 cases were censored out of the study (14 deaths and five transplants). The rate of AVF thrombosis per patient-year at risk was 0.043 (Table 2). A thrombosed AVF was abandoned and a new vascular access was created either on the same or on the opposite arm.

Figure 1 shows the ROC curve for the diagnostic accuracy of baseline vascular access blood flow rate values in predicting AVF failure. The area under the curve was 0.82 ± 0.05 (*P* = 0.01) and the value of vascular access blood flow rate identified as a predictor of AVF failure was <700 ml/min with an 88.9% sensitivity and 68.6% specificity. When subdividing the population of AVFs into two groups according to baseline vascular access blood flow rates, two out of the nine thromboses occurred among the AVFs that had baseline vascular access blood flow rates >700 ml/min (*n* = 31), whereas seven occurred among those that had baseline vascular access blood flow rates <700 ml/min (*n* = 21). The 4 year cumulative actuarial survival was 74.36 and 20.80%, respectively (log-rank test, *P* = 0.04) (Table 3 and Figure 2). The 24 AVFs that remained patent at the end of the 4 years of follow-up kept a median vascular access blood flow rate ≥900 ml/min at all time points studied, and did not show any differences in MAP values (Figure 3). Worth noting is that five of them (20.8%) remained patent throughout the study with blood flow rates consistently ≥500 ml/min.

**Discussion**

Two main results derive from this study. The first, a very low occurrence rate of vascular access failures/AVF/year and a high actuarial survival of mature autogenous RC wrist AVFs is a reality we confirm. Two points need to be clarified about this outcome. (i) We had a low prevalence of diabetic patients in our population (11.5%). As is known, diabetes is a risk factor for vascular access thrombosis. (ii) We studied a population of prevalent AVFs. Thus, it is possible that we selected a series of AVFs with different thrombotic and survival rates than would be present in an incident population of AVFs. All of the above considerations notwithstanding, a number of studies have shown that mature AVFs have superior performance, when compared with AVGs, in terms of patency rates and the incidence of infection [7,8]. Thus, the first message of the present study is that autogenous RC wrist AVFs perhaps should be the initial type of permanent vascular access in the majority of HD patients. Two recent papers support our thesis: Rodriguez et al. [9] showed that AVFs have longer survival than AVGs and that, among AVFs, RC ones have the highest long-term function rate (45% at 10 years and 38% at 12 years). Furthermore, Konner et al. [10] published on a series of 748 consecutive primary AVFs made at a single center. The thrombosis rates were 0.03 and 0.07 per patient-year at risk for non-diabetics and diabetics, respectively. Despite these data, the number of
synthetic grafts placed in the United States has been increasing relative to AVFs [8,11]. The high rate of maturation failure of the RC AVFs (13–70%) [12,13], late referral to surgeons, timing of dialysis, the economics related to the type of access, and the inadequacy of veins for distal AVFs have all been implicated in the preference given to AVGs [7,8,11].

Our second result, that a vascular access blood flow rate $< 700$ ml/min appears to be a reliable cut-off point at which to implement a policy of closer monitoring of this parameter, may lead to further investigations and possibly interventions relevant to the function of AVFs. For both AVFs and AVGs, it is recommended that vascular access blood flow rate measurements be performed monthly [3]. The guidelines further suggest that a vascular access with a blood flow rate $\leq 600$ ml/min or $\leq 1000$ ml/min that has decreased by more than 25% over 4 months should be referred for a fistulogram [3]. Recommendations [3] have supported such monitoring on the premise that the natural history of the vascular access will be altered by radiological or surgical interventions after vascular access dysfunction is detected. However, there is no clear evidence that such a strategy of prospective monitoring of vascular access blood flow rate followed by radiological or surgical intervention significantly improves patency [14–20]. Most studies that have evaluated surveillance, whether done by vascular access blood flow rate or venous pressure, suggest that prophylactic repairs of vascular access reduce thrombosis rates and increase cumulative graft survival; however, those studies have used historic control groups or sequential groups, or have been retrospective [14–16]. Actually, some very recent randomized controlled studies in AVGs have not confirmed that the prophylactic repair of vascular access reduces thrombosis rates and increases

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**Table 3.** Events occurring during the 4 year prospective observational study in the 52 patients with autogenous RC wrist AVFs: the latter were subdivided into two groups, one including those AVFs with a baseline vascular access blood flow rate (VA BFR) $< 700$ ml/min, the other including those AVFs with a baseline VA BFR $> 700$ ml/min

<table>
<thead>
<tr>
<th>VA failures</th>
<th>Cumulative survival (%)</th>
<th>Transplants</th>
<th>Deaths</th>
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<tr>
<td>VA BFR $&lt; 700$ ml/min ($n = 21$)</td>
<td>7</td>
<td>20.80</td>
<td>2</td>
</tr>
<tr>
<td>VA BFR $&gt; 700$ ml/min ($n = 31$)</td>
<td>2</td>
<td>74.36</td>
<td>3</td>
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**Fig. 2.** When subdividing the population of 52 autogenous RC wrist AVFs into two groups according to the baseline vascular access blood flow rate (VA BFR), two out of the nine thromboses occurred in the group of AVFs which had a baseline VA BFR $> 700$ ml/min ($n = 31$), whereas seven occurred in the group of AVFs which had a baseline VA BFR $< 700$ ml/min ($n = 21$). The 4 year cumulative actuarial survival was 74.36 and 20.80%, respectively ($P = 0.04$).
cumulative graft survival [17–19], whereas a preliminary report on a randomized controlled study of AVFs shows that the pre-emptive correction of subclinical stenoses improves AVF longevity [20]. Our study did not clarify this issue, because its design does not include a second arm (regular monitoring of vascular access blood flow rate coupled with early intervention), which might have given the answer that, even at the very low rate of AVF thrombosis per patient-year at risk shown in this study, a policy of regular monitoring of vascular access blood flow rate coupled with early intervention could be worthwhile. Nonetheless, we think that our data (the very low rate of AVF thrombosis per patient-year at risk associated with the long-term patency of five AVFs with a consistent blood flow rate \( \leq 500 \text{ ml/min} \) on the one hand, and the different outcomes of AVFs associated with different baseline blood flow rates on the other hand) allow us to suggest that: (i) performing monthly blood flow rate measurements in all AVFs as recommended by the NKF K/DOQI guideline may be excessive; (ii) a vascular access blood flow rate <700 ml/min appears to be a reliable cut-off point at which to implement a policy of closer monitoring of this parameter.

In conclusion, our present prospective observational study shows a very low rate of AVF thrombosis per patient-year at risk and a high survival of autogenous RC wrist AVFs, particularly of those with vascular access blood flow rates >700 ml/min. Thus, a vascular access <700 ml/min would appear to be a reliable cut-off point at which to start closer monitoring of this parameter, which can culminate in further investigations and perhaps in eventually initiating interventions relevant to the function of AVFs.

Conflict of interest statement. None declared.

References

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Fig. 3. Comparison of vascular access blood flow rate (VA BFR) and of the MAP in the 24 patients with mature autogenous RC wrist AVFs which remained patent during the 4 year follow-up. No statistically significant difference was found when using Friedman’s test (\( P = 0.09 \) for VA BFR; \( P = 0.63 \) for MAP). The median VA BFR was \( \geq 900 \text{ ml/min} \) at all time points studied.


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