Nephrol Dial Transplant (2010) 25: 862–867
doi: 10.1093/ndt/gfp577
Advance Access publication 5 November 2009

Original Articles

Is intra-operative blood flow predictive for early failure of radiocephalic arteriovenous fistula?

François Saucy[1], Erik Haesler[2], Claude Haller[1], Sébastien Déglise[1], Daniel Teta[3] and Jean-Marc Corpataux[1]

[1]Department of Thoracic and Vascular Surgery, Lausanne University Hospital, Lausanne, Switzerland, [2]Department of Vascular Medicine, Lausanne University Hospital, Lausanne, Switzerland and [3]Department of Nephrology, Lausanne University Hospital, Lausanne, Switzerland

Correspondence and offprint requests to: François Saucy; Email: Francois.saucy@chuv.ch

Abstract

Background. For over 50 years, radiocephalic wrist arteriovenous fistulae (RCAVF) have been the primary and best vascular access for haemodialysis. Nevertheless, early failure due to thrombosis or non-maturation is a major complication resulting in their abandonment. This prospective study was designed to investigate the predictive value of intra-operative blood flow on early failure of primary RCAVF before the first effective dialysis.
Methods. We enrolled patients undergoing creation of primary RCAVF for haemodialysis based on the pre-operative ultrasound vascular mapping discussed in a multidisciplinary approach. Intra-operative blood flow measurement was systematically performed once the anastomosis had been completed using a transit-time ultrasonic flowmeter. During the follow-up, blood flow was estimated by colour flow ultrasound at various intervals. Any events related to the RCAVF were recorded.
Results. Autogenous RCAVFs (n = 58) in 58 patients were constructed and followed up for an average of 30 days. Thrombosis and non-maturation occurred in eight (14%) and four (7%) patients, respectively. The intra-operative blood flow in functioning RCAVFs was significantly higher compared to non-functioning RCAVFs (230 *vs* 98 mL/min; P = 0.007), as well as 1 week (753 *vs* 228 mL/min; P = 0.0008) and 4 weeks (915 *vs* 245 mL/min, P < 0.0001) later. Blood flow volume measurements with a cut-off value of 120 mL/min had a sensitivity of 67%, specificity of 75% and positive predictive value of 91%.
Conclusions. Blood flow <120 mL has a good predictive value for early failure in RCAVF. During the procedure, this cut-off value may be used to select appropriately which RCAVF should be investigated in the operation theatre in order to correct in real time any abnormality.

Keywords: autogenous fistula; haemodialysis; maturation; thrombosis; vascular access flow

Introduction

For over 50 years, radiocephalic arteriovenous fistula (RCAVF) has demonstrated unquestionable superiority over all other types of vascular access for haemodialysis [1]. The main benefits of arteriovenous fistula (AVF) are better long-term patency and lower complication rate. Nevertheless, failure within the first 4 months after surgery occurs in 20% to 50% of AVF [1–11]. Early failure of AVF is defined as occlusion or insufficient development to support haemodialysis within the first 3 months [12]. Maturation of an AVF depends on flow volume and diameter of the vein used for cannulation. In this regard, Robbin *et al.* showed that the likelihood of sufficient growth was 95% if flow volume was 500 mL/min or greater in association with a diameter of 4 mm [13]. In most successful AVF, these flow and size parameters are generally met within the first few weeks after construction [12].

Several pre-operative factors have been shown to predict the risk for early AVF failure. The main predictors are the diameters of the artery and vein. Pre-operative ultrasound (US) mapping is a useful tool for the accurate measurement of vessel diameter as a basis for planning operative strategy. Female gender and diabetes may also be risk factors for early AVF failure. In the scoring system proposed by Lok *et al.* to predict failure to mature of AVF, the four main clinical predictors were age over 65, peripheral or coronary artery disease and white race [14]. During surgical exploration, the operator should take into account the quality and size of the artery and the vein when deciding whether or not to create the fistula at the site chosen during pre-operative workup.

Few studies have evaluated intra-operative factors to predict early failure immediately after construction of an AVF. Two previous studies evaluated the predictive value of intra-operative blood flow volume. Wong *et al.* were unable to demonstrate a link between intra-operative flow volume and the risk of early occlusion [10]. On the other hand, Johnson *et al.* showed that the failure risk was significantly higher if flow volume was less than 170 mL/min [15]. However, none of these studies were specifically aimed to assess the value of intra-operative blood flow measurements for the outcome of RCAVF. The purpose of this study was thus to investigate the value of intra-operative blood flow measurements in the prediction for early failure and/or adequate function of RCAVF in a cohort of patients about to start a chronic haemodialysis program in our institution.

Materials and methods

Between January 2005 and December 2007, we performed 120 first-time AVF including 67 RCAV, i.e. 56% of the total number. The study cohort included a total of 58 patients that benefited from a first-time RCAVF; nine patients were not included due to their previous vascular access by central venous catheter. The criteria for inclusion were indication for initial haemodialysis requiring first-time AVF and complete follow-up data up to the time of the first functioning dialysis. Follow-up was discontinued at the time of the first functioning haemodialysis but never exceeded 8 weeks. The functioning RCAVF was defined as the ability to use the fistula for dialysis with two needles and maintain a dialysis machine blood flow rate adequate for optimal dialysis (≥300 mL/min) according to the Dialysis Consortium Study (DAC) criteria [16]. During the follow-up, the occlusions and the RCAVF unable to reach DAC's criteria were defined as non-functioning. In accordance with our department's follow-up policy for patients undergoing AVF for haemodialysis, all cases were reviewed weekly at multidisciplinary staff meetings attended by the nephrologist, angiologist, radiologist, vascular surgeon and dialysis nurse. All patients underwent a pre-operative vascular mapping by means of duplex ultrasound.

Pre-operative physical examination

The upper limb, shoulder and neck were examined to detect any sign of previous trauma, muscle atrophy, venous hypertension related to proximal vein obstruction or chronic ischaemia. Pulses were palpated, and an Allen test was performed. Auscultation was focused on the neck as well as the subclavian and axillary spaces.

Pre-operative duplex ultrasound examination

Duplex US was performed by experienced clinicians from the vascular medicine department using 5 to 12 MHz linear transducers (Envisor and HDI 5000, Philips Medical Systems Switzerland, Gland, Switzerland; Vingmed System V, GE Medical Systems Switzerland, Glattbrugg, Switzerland). The arterial tree was assessed from the clavicle down to the wrist. Vessel diameters and anatomical variations were noted. Spectral Doppler waveforms were obtained at different levels. Presence of arterial plaque was recorded regardless of whether resulting narrowing was haemodynamically significant or not. The extent of diffuse vessel wall calcification was subjectively evaluated based on the echogenicity of vessel walls and graded as follows: (i) no sign of diffuse calcification; (ii) mild calcification causing increased echogenicity of vessel walls and shadowing as observed in the transverse plane; (iii) moderate calcification causing not only shadowing but also Doppler attenuation resulting in incomplete luminal filling using colour mode; and (iv) severe calcification with high echogenicity, marked shadowing and Doppler attenuation causing colour to be nearly absent or to fill only very short segments of the artery, showing a patchy pattern.

The anteroposterior diameters of the superficial veins and distal part of the brachial veins were measured in the transverse plane after inflation of a pressure cuff positioned as on the arm to 80–90 mmHg to interrupt venous return and induce maximal distal vein distension. Thrombosis of draining veins was detected by B-mode imaging and compression. Doppler waveforms of the internal jugular and subclavian or axillary veins were analysed. Proximal venous obstruction was considered as highly unlikely in patients presenting the following three criteria: Doppler waves in both internal jugular and subclavian veins exhibiting clear respiratory and cardiac phasicity with the maximal velocity curve crossing the zero line; absence of clinical signs such as distended veins and visible collaterals especially around the neck, the shoulder and along the trunk; and normal vein compressibility based on subjective assessment using the ultrasound probe in B-mode.

After completing the US examination, findings were used to map the anatomical features of vessels including not only course and diameter but also the location of any abnormalities (plaque, stenosis and occlusions), degree of wall calcification and characteristics of proximal venous flow. Using this map, the clinician proposed the most suitable site for AVF construction. The preferred minimal vein and artery diameters for RCAVF creation were 2.5 and 2.0 mm, respectively [9]. However, these size preferences were waived in some cases, e.g. young patients for whom slightly smaller vessels were sometimes used and patients with a high degree of arterial wall calcification for whom the artery size cut-off value was increased to 3.0 mm.

Surgical technique

All procedures were performed under local or regional anaesthesia using a same standardized technique for creation of AVF, i.e. the minimal touch technique with limited dissection of the cephalic vein and radial artery. The artery was clamped using a coronary artery clamp, and an end-to-side anastomosis was made using a continuous 7.0 polypropylene suture. Suturing was visualized through magnifying loupes (×3.5). At the operator's discretion, papaverine was used after clamp removal if there were signs of vasospasm. Systemic or local heparinization was not used. The patients were operated on by a single vascular surgeon or senior resident supervised by this surgeon.

Intra-operative measurement of blood flow volume

Intra-operative measurement of blood flow volume was systematically performed immediately after the construction of the AVF. In the case of vasospasm requiring the use of papaverine, the measurement was delayed for 5 min. Measurements were performed by placing a 3–4 mm handheld flowprobe (MediStim, Oslo, Norway) around the draining vein 2 cm downstream from the anastomosis. Direct readings in mL/min were recorded after stabilization for 30 s. At least three readings were made until consistent values were obtained usually within the first 5 min. Systolic and diastolic pressure was recorded concomitantly with flow volume measurements. All data were consigned to a dedicated study form immediately after the procedure.

Post-operative ultrasound

Post-operative US was performed at each follow-up examination at 1 week, 1 month and just prior to the first RCAVF cannulation. Blood flow was assessed by measuring mean flow velocity and luminal diameter in separate segments of brachial, ulnar, pre-anastomotic and post-anastomotic radial arteries. Spectral Doppler and mean velocity were obtained with a Doppler angle at 60° and a sample size covering the entire lumen. Access blood flow was then calculated by adding pre-anastomotic radial to post-anastomotic radial flow, in case of retrograde flow in the latter. If post-anastomotic radial flow was antegrade, it was subtracted from pre-anastomotic flow. During Doppler sonography, blood pressure was recorded several times on the controlateral arm by means of an automated oscillometric manometer.

After access blood flow determination, feeding arteries and draining veins as well as the anastomosis were checked for the presence of stenoses. First, a colour Doppler scan of arteries from the clavicle down to the anastomosis was performed while analysing any flow disturbance by spectral Doppler to obtain peak systolic velocity. The same was done for the veins, from the anastomosis up to the clavicle and internal jugular vein. Then, a precise B-mode image of each stenosis detected by colour Doppler was obtained, and minimal luminal diameter was measured. Study results were consigned to a dedicated form indicating access flow, mean systolic and diastolic blood pressures and a vascular map of the entire limb showing flow direction, vessel diameters and any stenosis with its peak systolic velocity and minimal luminal diameter.

Statistical analysis

Statistical analysis was performed using Stata version 9.2 (StataCorp, College Station, TX, USA). Results were expressed either as number of patients (percentage) or as mean (± standard deviation). Between-group

Table 1. Demographic features, comorbidities, surgical findings and vessel diameters in 58 patients who underwent first-time RCAVF

Variable	Number (%)/mean ± SD
Age (year)	63 ± 14.3
Gender	
Male	40 (69)
Female	18 (31)
Medical history	
Hypertension	39 (67)
Diabetes	33 (57)
Current smoker	7 (12)
Ischaemic cardiac disease	18 (31)
Peripheral vascular disease	12 (20)
Anticoagulation	15 (25)
Antiaggregation	30 (51)
Intra-operative data	
Intra-operative BF (mL/min)	203 ± 182
Artery diameter (mm)	2.9 ± 0.6
Vein diameter (mm)	3.1 ± 0.6
SBP (mmHg)	133 ± 24
DBP (mmHg)	76 ± 13
Papaverine	13 (22)
Left arm	38 (66)

BF, blood flow; SBP, systolic blood pressure; DBP, diastolic blood pressure. Continuous variables are presented as mean ± standard deviation (SD) and discrete variables as number with (percentage).

Table 2. Comparison of demographic features, surgical findings, vessel diameters and comorbid conditions in 58 patients with non-functioning (n = 12) and functioning (n = 46) RCAVF

Variable	Non-functioning RCAVF	Functioning RCAVF	*P* value
n	12	46	
Age (years)	57.5 ± 16.5	64.4 ± 13.5	0.12
Female gender	7 (58)	11 (24)	0.03
Medical history			
Hypertension	10 (83)	29 (63)	0.3
Diabetes	10 (83)	23 (50)	0.06
Ischaemic cardiac disease	3 (25)	12 (26)	0.94
Peripheral vascular disease	3 (25)	9 (19)	0.68
Anticoagulation	4 (33)	11 (23)	0.51
Antiaggregation	8 (26)	22 (47)	0.25
Current smoker	1 (8)	6 (13)	0.1
Pre-operative data			
Artery diameter (mm)	2.8 ± 0.6	2.9 ± 0.6	0.58
Vein diameter (mm)	2.9 ± 0.6	3.2 ± 0.8	0.21
Arterial calcification	5 (18)	12 (46)	0.83
Intra-operative data			
BF (mL/min)	98 ± 65	230 ± 194	0.007
SBP (mmHg)	134 ± 25	137 ± 25	0.82
DBP (mmHg)	75 ± 13	78 ± 13	0.86
Other			
Papaverine	3 (25)	10 (22)	1.00
Left arm	6 (50)	32 (70)	0.31
Local anaesthesia	13 (72)	32 (69)	0.51

BF, blood flow; SBP, systolic blood pressure; DBP, diastolic blood pressure.

comparisons were performed using the Wilcoxon test for quantitative data and Fisher's exact test for qualitative data. Threshold values were screened using the roctg function of Stata with 25 mL/min blood flow volume intervals. Specificity, sensitivity and predictive values were computed together with the respective 95% confidence intervals using the diatg function of Stata. A *P* value less than 0.05 was considered as statistically significant.

Results

Patient data including demographic characteristics, surgical findings, vessel diameters and comorbid conditions are presented in Table 1. The mean age of patients was 63 ± 14.3 years with 38% over the age of 70 years.

The mean duration of follow-up was 30 days (range, 15 to 45 days; median, 21 days). During follow-up, one patient (1.7%) died at home from causes unrelated to the RCAVF, and 12 patients (20.6%) presented events related to the RCAVF, i.e. either failure to mature in four cases or permanent occlusion in eight cases. All eight occlusions occurred within the first post-operative week (mean delay, 3.3 days; range, 1-6 days). In all cases, alternative vascular access sites were created in more proximal locations including ipsilateral brachiocephalic AVF in 63% and placement of a prosthetic loop on the forearm in 37%. Placement of a permanent dialysis catheter was necessary in four of the eight patients (50%) with inadequate RCAVF.

Table 2 compares patients who presented no events with patients who presented early failure due to occlusion or failure to mature. Female gender and low intra-operative flow volume were significantly associated with early failure. To gain further insight on the impact of female gender, the overall data were compared by gender (Table 3). Findings showed that the artery diameter was significantly smaller in women than men: 2.6±0.5 *vs* 3.0±0.6 mm, respectively (P = 0.03). The post-operative blood flow after 4 weeks was also statistically higher in men (P = 0.02). Vessel wall calcifications were identified in three patients (16%) in the non-functioning RCAVF and six (15%) in the functioning RCAVF group.

Flow measurements in all patent RCAVF at 1 month after the creation demonstrated a mean flow volume of 733± 296 mL/min, i.e. a mean increase of 261% in comparison with intra-operative findings. Figure 1 shows that during the first post-operative month, the non-functioning RCAVF flow volume only increased by 142% from 101± 87 to 245±412 mL/min, whereas blood flow of functioning RCAVF demonstrated an increase of 294% from 232 ± 194 to 915 ± 353 mL/min. The increase of blood flow developed mainly during the first post-operative week. Indeed, in the functioning RCAVF, the blood flow increased by 224% from 232 ± 194 to 753 ± 269 mL/min, and only by 125% from Weeks 1 to 4. These kinetics also occurred in the non-functioning RCAVF with an increase of 21% during the first post-operative week and only 7% from Weeks 1 to 4. Further analysis of flow volume data showed that the most sensitive cut-off value to discriminate functioning and non-functioning RCAVF was 120 mL/min. Nine of the 12 non-functioning RCAVF (75%) presented flow volumes less than 120 mL/min as compared to only 15 of the 46 (32%) functioning RCAVF. A flow volume greater than 120 mL/min exhibited good sensitivity and specificity, i.e. 67.4% (range, 51.9–80.5%) and 75% (range, 42.8–94.5%), respectively. The positive predictive value of this parameter was 91.2%, i.e. excellent (range, 76.3–98.1%). The negative predictive value was, however, only 37.5% (range; 18.8–59.4%).

Table 3. Comparison of demographic features, comorbidities, surgical findings and vessel diameters in men (n = 40) and women (n = 18)

	Women	Men	*P* value
n	18	40	
Age (years)	63.7 ± 17.3	62.6 ± 13	0.48
Medical history			
Diabetes	11 (61)	22 (55)	0.78
Hypertension	13 (72)	26 (65)	0.76
Ischaemic cardiac disease	6 (33)	12 (30)	0.80
Peripheral vascular disease	4 (22)	8 (20)	0.85
Current smoker	2 (25)	5 (12)	0.88
Anticoagulation	5 (27)	10 (40)	0.82
Antiaggregation	9 (50)	21 (52)	0.86
Blood Flow			
Intra-operative BF (mL/min)	142.7 ± 94.7	230.2 ± 205.6	0.13
Post-operative BF (mL/min)	513.6 ± 330.2	784.7 ± 278.9	0.02
Pre-operative diameter			
Artery diameter (mm)	2.6 ± 0.5	3.0 ± 0.6	0.03
Vein diameter (mm)	3.1 ± 0.7	3.1 ± 1.0	0.99
Other			
Papaverin	5 (27)	8 (20)	0.52
Left arm	11 (61)	27 (67)	0.77

BF, blood flow. Results are expressed as mean ± standard deviation or as number of subjects and (percentage). Statistical analysis by Wilcoxon test or Fisher's exact test.

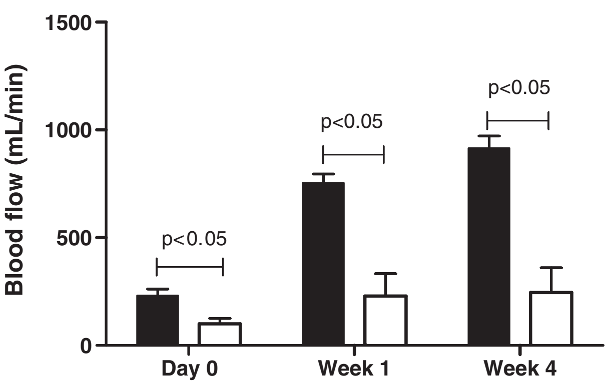

Fig. 1. Blood flow (in mL/min) in functioning (black box) and non-functioning RCAVF (white box).

Discussion

Our findings demonstrate that the intra-operative measurement of blood flow immediately after construction of a RCAVF was useful to predict early AVF failure. Statistical analysis identified a cut-off value of 120 mL/min for discriminating functioning and non-functioning RCAVF. Johnson *et al.* reported that a high intra-operative flow volume defined as 320 mL/min or greater was associated with a lower number of surgical revisions and longer access survival regardless of gender, race or presence of diabetes. The same authors reported that an intra-operative flow rate of less than 170 mL/min was correlated with a 56% risk for AVF failure within the first 50 days after construction [15]. In their 50-patient series, Won *et al.* also showed that an intra-operative flow rate of less than 160 mL/min was predictive of early failure of RCAVF [17]. A recent study including a cohort of 109 patients undergoing vascular access surgery for first-time haemodialysis showed that an intra-operative flow rate greater than 200 mL/min was associated with better middle-term outcome in terms of requirement for revision and early patency rate [18].

In this study, follow-up was limited to the period immediately after construction of the RCAVF up to the first haemodialysis. The goal was to eliminate the effect of puncture trauma associated with repeated puncture for venous access. This trauma may cause stenosis and/or haemorrhagic complications that are probably detrimental to AVF patency. Previous authors reported longer follow-up than ours but could not rule out the confounding effect of haemodialysis-related injury on their results. Moreover, the period prior to dialysis is crucial for AVF development that appears to be correlated with flow volume. Immediately after AVF construction, flow volume increases rapidly, reaching a maximum within 4 to 12 weeks [10,19–22]. Between 40% and 60% of the total increase in flow volume occurs within 24 h after creation of the AVF [10,19–22]. For most fistulas located on the forearm, maximum flow volume is reached within 4 weeks after construction [10,19]. The rate of the flow volume increase depends partly on the diameter of the vein lumen. In an earlier report, our group studied the size of the draining vein and observed that the lumen increased 86% after 1 week and 179% after 12 weeks in comparison with the lumen of the contralateral vein [22]. These results confirmed a previous study involving AVF located on the forearm that showed a 56% increase within the first 24 h after construction to 123% at 12 weeks in comparison with controls [10]. A fistula can be considered as mature or suitable to support haemodialysis when it allows insertion of two needles and can provide sufficient blood flow, i.e. at least 350–450 mL/min. Adequate flow volume is at least of 500 mL/min for an AVF [23]. There is currently no consensus as to criteria for predicting the outcome of AVF development. Some authors wait as long as 3 to 4 months before declaring an AVF non-functioning [16,24].

Several studies have attempted to identify predictors of AVF development. Pre-operative vascular mapping that we have been using routinely for many years has been shown to maximize the opportunities for autogenous fistulas and lower the need for prosthetic fistulas [9,25]. However, a reliable correlation has not been established between pre-operative evidence of adequate artery and vein diameter and AVF development [10,26,27]. A recent study [28] indicated that measurement of vein compliance was a good predictor of AVF development, but this finding was not confirmed in two subsequent studies [21,29]. Post-operative measurement of blood flow volume by duplex US has not been consistently shown to be useful in predicting AVF development [30,31]. Our data showed that the increase in flow volume during the first month after creation was 261% for functioning RCAVF as compared to only 142% for non-functioning RCAVF. This finding suggests that there is a good correlation between rapid flow volume increase in the first post-operative month and maturation of the RCAVF. Intra-operative and post-operative measurements showed that mean blood flow volume was significantly higher in functioning than non-functioning RCAVF. The intra-operative measurement of arterial dilation in response to reactive hyperaemia has also been identified as a predictor for AVF development with a sensitivity of 95%, a specificity of 61% and a positive predictive value of 87% [29]. In comparison, our results indicated that blood flow volume measurements with a cut-off point of 120 mL/min had a sensitivity of 67%, specificity of 75% and positive predictive value of 91%.

In agreement with previous studies [32,33], our data also showed that failure of an RCAVF to mature was frequently associated with females. Comparison of vessel diameters according to gender in our cohort demonstrated that arteries were significantly smaller in women than in men. However, it should be underlined that our findings are in contradiction with two recent studies showing no significant gender difference in the pre-operative diameters of veins and arteries [32,34].

Failure of an AVF to mature can have many aetiologies [35]. The most frequent cause is neointimal hyperplasia typically occurring in the juxta-anastomotic vein. Hyperplasia develops during the first post-operative month. In our study, all AVF occlusion occurred during the first post-operative week. Possible explanations include a defect in the surgical technique, poor vein quality or insufficient vessel diameter that was incorrectly estimated during US mapping. Pre-operative measurements should be made to detect possible sources of insufficient flow volume. US mapping could also decrease the functional maturation rate by the increase in performing complex procedures which were often secondary ones and by the use of smaller vein only detected by US but invisible during upper limb inspection [36]. Our vascular access improvement program provides for increasing the rate of autogenous vascular access and decreasing early failure. Pre-operative US mapping, early referral to vascular surgeon and surveillance program are some of the measures to achieve these goals. Despite the implementation of the Disease Outcomes Quality Initiative (DOQI) guidelines in our institution, 12 (20%) RCAVF failed to mature or occluded. The intra-operative surgical assessment of the vessels is the last possibility to choose the right strategy. To detect technical defects and identify poor artery or vein quality, Lin *et al.* proposed performing fistulography during the same procedure. The same authors pointed out that if a technical defect requiring surgical correction was not found, careful post-operative surveillance was necessary to allow early detection and prompt treatment of possible problems. They also proposed immediate construction of another fistula in diabetic patients presenting intra-operative flow volume less than 200 mL/min [18]. Finally, Berman *et al*. recommended that RCAVF with an intra-operative flow rate of <120 mL/min should either be immediately abandoned for another site or, at a minimum, evaluated for an immediate revision [37]. In view of these results, we intend to find out whether intra-operative haemodynamic and anatomical criteria may directly impact on the decision-making process in patients awaiting a functional AVF.

Our study may have a direct implication for practical clinical issue. Indeed, the intra-operative blood flow measurement should be carried out after each procedure to get a start value. A blood flow <120 mL/min has a good predictive value of early failure. This implies that we should aim for intra-operative investigations in order to look for a possible reason for this low blood flow. For instance, a fistulography with potentially a subsequent interventional procedure to re-establish a higher blood flow may be proposed. This hypothesis will be tested in a further study in our institution. In contrast, an intra-operative blood flow >120 ml/min may be interpreted as a safe result in terms of future RCAVF maturation. In conclusion, the findings of this study indicated that the intra-operative measurement of blood flow is a useful tool to predict the outcome of maturation in first-time RCAVF. A simple transit-time device can be used to obtain immediate readings that can be used to adapt operative strategy and thus improve outcome. These findings should be associated with blood flow value measurement just before the first puncture which is obviously an important criterion for making a decision. Whether this can be used to modify the intra-operative strategy, thus reducing the failure-to-mature rate, needs to be investigated.

Acknowledgements. The authors thank Dr Pedro Marques-Vidal of the Institute of Social and Preventive Medicine, Lausanne for his support in biostatistics.

Conflict of interest statement. None declared.

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Received for publication: 23.1.09; Accepted in revised form: 6.10.09

Nephrol Dial Transplant (2010) 25: 867–873
doi: 10.1093/ndt/gfp565
Advance Access publication 4 November 2009

Daily online haemodiafiltration promotes catch-up growth in children on chronic dialysis

Michel Fischbach, Joelle Terzic, Soraya Menouer, Céline Dheu, Laure Seuge and Ariane Zalosczic

Nephrology Dialysis Transplantation Children's Unit, University Hospital Hautepierre, Avenue Molière, 67098 Strasbourg, France

Correspondence and offprint requests to: Michel Fischbach; E-mail: Michel.Fischbach@chru-strasbourg.fr

Abstract

Background. In children, growth can be used as a measurable parameter of adequate nutrition and dialysis dose. Despite daily administration of recombinant human growth hormone (rhGH), growth retardation remains a frequent problem in children on chronic dialysis. Therefore, we performed an observational prospective non-randomized study of children on in-centre daily on line haemodiafiltration (D-OL-HDF) dialysis with the aim of promoting growth.

Patients and methods. Mean age at the start of the study was 8 years and 3 months, and all children had been receiving rhGH treatment for >12 months before enrolment. Mean follow-up time on D-OL-HDF was 20.5 ± 8 months (range, 11–39 months). Renal residual function was either <3 mL/