Vascular Access Blood Flow Estimation Based On Standardized Extracorporeal Blood Flow in Hemodialysis Patients

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Research Article

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Abstract

Background: Measurement of vascular access flow (Qa) is a recommendation in the care of hemodialysis patients. We developed an observational study to answer the following question: Can access blood flow be estimated?

Methods: This observational study was carried out in the hemodialysis unit of the José Carrasco Arteaga Hospital in Cuenca-Ecuador. The sample calculation was 41 cases. Patients older than 17 years with stage 5d chronic renal failure and vascular access with arteriovenous fistula were included. The variables were descriptive of the population: Qa and extracorporeal blood flow (Qb). Qa measurement was performed with the Transonic® monitor. Qb was measured at dynamic arterial line pressures (DALPs) of -60 mmHg, -100 mmHg, -160 mmHg, and -200 mmHg. The correlation coefficient "r" was obtained between Qa and Qb. SPSS 22.0 was used to analyze the information and perform a linear regression equation to estimate access blood flow (eQa).

Results: Fifty-seven patients aged 62.9 ± 12.7 years with 29.4 ± 33 months on hemodialysis were included; 23 women (40.3%) and 45.6% had diabetic nephropathy. Fistulas were seen in 40 cases in the left upper limb (70.2%) and 17 (29.8%) in the right upper limb. The prevalence of aneurysms was 10.5%. The 50th percentile of Qb was 415 mL/min with a DALP of -200 mmHg. The mean access flow was 1516 ± 878 mL/min. The correlation between Qb and Qa was statistically more significant between Qb and DALP of -200 mmHg. The association had a coefficient $R_s = 0.643$ (IC 0.453 to 0.771) $P < 0.0001$. The estimated access flow $eQa = (Qb \text{ at DALP of } -200 \text{ mmHg (mL/min)} * 16.63) - 5449.71$.

Conclusions: It was possible to estimate access blood flow with parameters for easy intradialysis measurements. The equation obtained, if applied to the same patient with the same DALP, could become a useful parameter for monitoring vascular access.

Trial registration: *ClinicalTrials.gov Identifier: NCT00522704. Registered 14 March 2008, <https://clinicaltrials.gov/ct2/show/NCT00522704>*

Background

Patients who undergo hemodialysis have a cumulative survival time of less than 60 months [1]. One of the most important factors that negatively influences mortality is the low clearance dose of uremic toxins [2]. In dialysis, the clearance of uremic toxins directly depends on the characteristics of the solute or toxin (small or medium size), properties of the membrane, volume of the dialysate fluid, and extracorporeal flow of the hemodialysis circuit (Qb) [3]. This last factor is operator-dependent and can be optimized to obtain a better clearance of uremic toxins in each treatment.

The KDOQI (Kidney Disease Outcome Quality Initiative) guidelines establish Qb recommendations between 300 and 500 mL/min [4]. This flow is obtained with a peristaltic pump. The pressure generated by the pump draws blood from the vascular access continuously through an arterial extracorporeal line. In most hemodialysis systems, this measurement is performed in the segment prior to the peristaltic pump, so the pressure in this arterial line is considered negative. Due to the dynamic measurement in pump operation, this

pressure is called dynamic arterial line pressure (DALP) [5]. DALP is a negative pressure that has been used to determine dysfunction of hemodialysis catheters and is identified when an extracorporeal dialysis flow of 300 ml/min is not obtained in a catheter that previously gave 350 ml/min at a DALP (prepump) of -250 mmHg.

Extracorporeal flow depends on the development of venous vascular access, which has previously been arterialized through the artificial creation of an arterial-venous shunt, which in the course of 4 to 6 weeks can go from normal flow to access flow (Qa) from 600 to 1500 ml/min [6].

Measurement of vascular access flow is a determining factor in the survival of patients in hemodialysis programs [7]. An access flow greater than 600 mL/min leads to good survival of the patients, a good quality of hemodialysis, improves the metabolic control of phosphorus, and reduces blood volume. A flow below this limit is a strong predictor of mortality, thrombosis, and stenosis of the access, which forces the patient to intervene to prevent thrombosis and the deterioration of the quality of hemodialysis in patients [7].

Current guidelines [8, 9] recommend the development of vascular access flow monitoring programs with the aim of early diagnosis of vascular graft dysfunction with the ultimate goal of reducing the percentage of thrombosis and the number of catheters that are a potential risk of infections and vessel stenosis and have a lower performance than arteriovenous fistula [9].

The National Kidney Foundation Kidney Disease Outcome Quality Initiative (K/DOQI) guidelines recommend indirect measurement of Qa [9]. The best-known method is the dilutional method with saline solution using ultrasound—this approach was validated with direct measurements of Qa by Doppler ultrasound [10]. Although there are other methods for measuring Qa, such as body temperature monitoring (BTM) [11] and pre- and postfilter urea measurements, the standardized method is the use of the Transonic® monitor, which uses a previously mentioned dilutional method.

The measurement of the flow of vascular access leads to methodological problems due to the technological implementation that this requires. There are several methods to perform this measurement, and the gold standard is intradialysis quantification using an ultrasound monitor that is based on the intra-access saline injection method and measurement of the fraction of saline that recirculates in the vascular access followed by inversion of the hemodialysis lines and a new measurement of the inverted recirculation of saline solution.

Until now, there has been no regression study that provides an approximation equation to estimate the access flow, which would result in an easily accessible calculation for the health team in charge of the daily care of vascular accesses. Therefore, the objective of this study was to resolve the following question: Can the flow of vascular access be estimated? We developed an observational study to resolve this question.

Methods

The present study was observational and descriptive in which multiple variables were measured and a correlation was made between them. The duration of the study was 6 months from the approval of the ClinicalTrials.gov Identifier protocol: NCT00522704. Measurements were made from September 29, 2016 to

January 30, 2017 in the Hemodialysis Unit of the Hospital de Especialidades "José Carrasco Arteaga" in Cuenca-Ecuador.

Participants

Patients older than 18 years and with stage 5d chronic renal failure were included in hemodialysis programs with vascular access with arteriovenous fistula. We excluded patients who did not wish to participate in the study or in whom the vascular access flow measurement could not be performed due to obtaining very low-pressure values in the arterial line that stopped extracorporeal flow.

Cohort and sample

The cohort was patients with stage 5D chronic kidney failure who underwent hemodialysis treatments. Cuenca (Azuay, Ecuador) has approximately 480 patients in hemodialysis programs. For the calculation of the sample size, the equation corresponding to a nonfinite universe of correlation studies was used [12]: $N = [(Z\alpha + Z\beta) 0.5 \ln [(1 + r)/(1 - r)]]^2 + 3$. where $Z\alpha$ corresponds to the 95% confidence interval value of the population (1.96) and $Z\beta$ corresponds to 84%. In the r value for the present population is expected to have a coefficient greater than or equal to 0.8. The number of patients was 36, to which 10% was added due to possible losses, with a final sample of 45 patients.

Variables

Demographic variables such as age, weight, dialysis time, and etiology were measured. We also measured the flow of vascular access (Q_a), extracorporeal flow (Q_b) at 4 dynamic pressures of the arterial line (-600, -100, -160, and -200 mmHg), and pain in vascular access.

Measurement of Vascular Access Flow

The standardized method was applied and used a Transonic® monitor that was optimized before each measurement via details on hemodialysis lines as well as patient weight and height. The ultrasound transducers were placed on the arterial line coming from the patient as well as on the venous line coming from the hemodialysis machine at the distance recommended by the manufacturer of the Transonic® device. The extracorporeal flow was decreased to 300 ml/min, 10 ml of saline solution was injected through the venous line, and fistular recirculation was recorded. In a second step, the hemodialysis lines were inverted, and a 10 ml bolus of saline solution was injected; again, the module reported inverted recirculation. Each measurement lasted a period of 60 seconds. With these data, the module performed a calculation of the access flow with the equation $Q_a = Q_b * (1 - RX) (1 - Rn)/(RX - Rn)$.

Measurement of Standardized Extracorporeal Flow (Q_b)

Extracorporeal flows were measured at the start of hemodialysis. The peristaltic pump flow was decreased and/or increased enough to obtain dynamic arterial line pressures (DALPs) of -60 mmHg, -100 mmHg, -160 mmHg, and -200 mmHg. We waited 30 seconds between each pressure rise to obtain stabilization of the system and the "no change in value in the real extracorporeal flow." Decreasing the DALP to values of -200 mmHg was not dangerous for the patient [5] because the system normally works with negative pressures up to -300 mmHg.

Data handling

The data were collected in a form and transferred to an SPSS 20.0 electronic sheet for PC. The data quality control methods included personal supervision of the author in each measurement and registration process.

The general design of the first part of the study corresponded to a bivariate analysis where the association between Qb and Qa in the study group was described. The value of the correlation coefficient "r" between Qa and Qb was obtained. The association was significant and not determined by chance when the value of R was greater than 0.6 and the value of $P < 0.05$. The R^2 coefficient was obtained to obtain the percentage of explanation of change of variable by change of its correlated variable. The confidence interval for the Spearman correlation coefficient (R) was also obtained. A prior protocol [13] reported that if there was a correlation of variables, then a multiple linear regression was performed. According to the type of covariate, all the variables whose T value was greater than 1 or less than -1 with a P value less than 0.05 were introduced in block in the model. The covariates considered whose T values were greater than 2 or less than -2 with a P value less than 0.05 and without collinearity (< 15) were included for the final model of the regression equation. The 95% confidence interval and a Bland-Altman concordance analysis with an estimated Qa based on the resulting equation were included in the results.

Results

Participants

We included 57 patients from the hemodialysis program of the "Hospital de Especialidades "José Carrasco Arteaga"" in the city of Cuenca, Ecuador; 18 cases were discarded. In 10 cases, it was not possible to measure the access flow because the recirculation values could not be obtained due to technical problems with the extracorporeal flow, which was much lower than that recommended by the operating system. Measurements were made in 8 cases; however, the results were illogical with flows greater than 4 liters per minute or less than 300 ml/min with inconsistent results in a repetition of a new measurement (Fig. 1).

Characteristics of the patients

The age of the population studied averaged 62.9 ± 12.7 years, with an average time of 29.4 ± 33 months in the hemodialysis program (Table 1). There were 34 men (59.7%) and 23 women (40.3%); a high percentage (45.6%) had diabetic nephropathy as the etiology of chronic renal failure, and the etiology was not defined in 32% (Table 2).

Table 1
Descriptive statistics of the studied population

Variable	Mean $\pm$ SD
Age (years)	62 $\pm$ 12.7
Dry weight (kg)	62.5 $\pm$ 8.8
Weight pre-HD (kg)	64.0 $\pm$ 8.5
Size (meters)	1.57 $\pm$ 0.11
Body mass index (m/kg ²)	25.3 $\pm$ 3.4
Time on hemodialysis (months)	29.4 $\pm$ 33.1
Vascular access construction time (months)	26.1 $\pm$ 29.5
Categorical/nominal variables Frequency (%)	
Gender Female	23 (40%)
Diabetes mellitus type 2	26 (46%)
Unrelated cause	18 (32%)
Arterial hypertension	10 (18%)
Focal and segmental glomeruloesclerosis	2 (4%)
Primary glomerulopathy	1 (2%)
Legend Table 1: HD: hemodialysis.	

The presence of fistulas in the extremities was in the upper extremities: there were 40 cases in the left upper limb (70.2%) and 17 (29.8%) in the right upper limb. The vast majority were located in the proximal position of the limb 36/57 (63%) and in the distal position 21/57 (37%). There were six aneurysms (11%).

Hemodialysis machines

The patients received treatment in a volumetric hemodialysis machine from Fresenius (Germany). The models were 4008S in 28/57 cases (45.6%), 4008B 25/57 (43.9%), and 5008 6/57 (10.5%). The diameter of the impedance pump segment of the hemodialysis lines was 8 mm.

Main Results

Descriptive analysis of extracorporeal flow

The extracorporeal flow was taken at four negative ascending DALPs. Table 2 shows that the average maximum flow reached was 419 $\pm$ 34 ml/min, which represented an extracorporeal effective flow of 367 $\pm$ 27

ml/min at a pressure of -200 mmHg in the arterial line. The extracorporeal flow percentiles of the pump at the different pressures in the arterial line are shown in Figure 2.

Table 2
Measurement of vascular access blood flow

	No recirculation n=55	With recirculation n=2	<i>P</i>
DALP in measurement (mmHg)	-153 ±24	-140 ±0	0.230
DVLP (mmHg)	158 ±37	221 ±1.4	0.0103
Qb measured by transonic (ml/min)	316 ±32	298 ±40	0.210
Recirculation (%)	0.11 ±0.0	41±5.7	<0.0001
Inverted Qb (ml/min)	242 ±34	230 ±57	0.310
Inverted recirculation (%)	20.4 ±9.1	37.5 ±38.9	0.013
Qa (ml/min)	1507 ±785	1745 ±2256	0.350
DVLP/[Root(DALP)] ^{2*}	1.050 ±0.277	1.579 ±0.010	0.0048
Qb ^{DALP-60 mmHg} (ml/min)	183 ±32	195 ±42	0.305
Qb ^{DALP-100 mmHg} (ml/min)	253 ±32	245 ±35	0.372
Qb ^{DALP-160 mmHg} (ml/min)	346 ±34	338 ±46	0.362
Qb ^{DALP-200 mmHg} (ml/min)	419 ±34	405 ±70	0.274
DALP: Dynamic arterial line Pressure. DVLP: Dynamic venous line pressure, Qa: Vascular access blood flow. Qb: Extracorporeal blood flow.			

Descriptive analysis of the access flow

The mean access flow was 1516 ± 878 ml/min with a minimum value of 150 ml/min and a maximum of 4000 ml/min. There was no difference in access flow by sex, and there was no difference in flow by location in the limb or by anatomical position of the proximal or distal fistula. The frequency of the access flow was divided by percentiles: 0 to 399 ml/min 2/57 cases (3.5%), 400 to 800 mL/min 12/57 cases (21.1%), 801 to 1516 mL/min 16/57 cases (28.1%), 1517 to 2130 mL/min 13/57 cases (22.8%), 2131 to 2944 ml/min 12/57 cases (21.1%) and 2945 to 4000 mL/min 2/57 cases (3.5%). None of the measurements were painful for the patients.

Association between extracorporeal flow and access flow

The best association between the access flow and the extracorporeal pump flow was observed when the DALP was -200 mmHg. Additionally, all possible correlations with pressure variables of the venous and

arterial lines were made, and they were not significant (correlations not shown). These data are shown in Table 3.

Table 3
Significant correlations between extracorporeal flow and vascular access flow

Qa (ml/min)				
N=57	Rho Spearman	CI 95% LL	CI 95% UL	P
Qb ^{DALP-60 mmHg}	0.569	0.349	0.730	<0.0001
Qb ^{DALP-100 mmHg}	0.582	0.350	0.760	<0.0001
Qb ^{DALP-160 mmHg}	0.580	0.364	0.751	<0.0001
Qb ^{DALP-200 mmHg}	0.643	0.453	0.771	<0.0001
Qa: Access blood flow. Qb: Extracorporeal blood flow. DALP: dynamic arterial line pressure				

Linear regression

In the first model, the variables with collinearity were eliminated, leaving the most representative in the model because it had the highest correlation (QB with DALP -200 mmHg). The summary of the model was acceptable with statistical association ($P = 0.001$); however, there were two nonsignificant variables in the regression equation that were eliminated from the final model. These were pressure in the arterial line at the time of measurement and pressure in the venous line at the time of measurement with p value > 0.05 . The final model was discarded autocorrelation with the Durbin-Watson statistic, which was 1.754. The value of $R = 0.674$, $R^2 = 0.454$, $P < 0.0001$. The equation is shown in Table 4.

Table 4
Regression equation model to estimate vascular access flow.

	Non-standardized coefficients		Standardized coefficient	T	P	95% CI for B		Correlations (zero and partial order)
	B	SE	Beta			LL	UL	
Constant	-5449.71	1032.6		-5.28	<0.0001	-7519.0	-3380.3	
Qb ^{DALP-200 mmHg}	16.63	2.46	0.674	6.77	<0.0001	11.71	21.56	0.674
SE: Standard error, LL: lower limit, UP Upper limit.								

The regression equation was obtained to estimate the access flow (${}_eQa$) = (QBDALP -200 mmHg (mL/min) * 16.63) - 5449.71; here, ${}_eQa$ is the estimated access flow, and QBDALP -200 mmHg is the extracorporeal flow in the pump when the arterial line pressure is at -200 mmHg.

A new variable (${}_eQa$) was then created for Bland-Altman concordance analysis. This included the average of the ${}_eQa$ and the difference between the Qa and ${}_eQa$. The agreement between Qa and ${}_eQa$ was obtained with the standard deviation of the difference in $Qa - {}_eQa$ (Figure 3).

Discussion

Main findings of the study

Among the main findings, we show that there is a correlation between extracorporeal flow and vascular access flow—it was statistically more important between extracorporeal flow measured with an arterial line pressure of -200 mmHg. The association had a coefficient $R_s = 0.643$ (IC 0.453 to 0.771) $P < 0.0001$. The regression equation to estimate the access flow (${}_eQa$) was established with the variable “extracorporeal flow with pressure in the arterial line of -200 mmHg” after eliminating the variables with collinearity and the statistically nonsignificant variables and the final equation (Table 4). The estimated access flow was calculated as a new variable to obtain the Bland-Altman concordance analysis. Here, systematic error was discarded because the points are distributed randomly on either side of the line corresponding to the difference 0 between measurements (black horizontal line).

Importance of the findings

The meaning of obtaining a standardized extracorporeal flow pattern through the DALP is important because a scale is established for the first time that predicts the behavior of the extracorporeal flow to be compared against itself and its extracorporeal flow quality rating in the interdialysis periods of each patient. The simple measurement that is part of the hemodialysis process offers an early warning when the extracorporeal flow changes percentile or is located in dangerous percentiles such as the 25th percentile for risk of decreased flow or the 75th percentile for hyperdynamic flow risk. The association between access flow and extracorporeal flow has a coefficient of determination or R^2 of 0.46, which suggests that 46% of the access flow is explained by the variable “extracorporeal flow.” In this case, the flow prediction equation of the estimated access becomes very useful and versatile to apply in patients using Fresenius Medical Care hemodialysis machines to estimate the access flow.

Studies with related findings

The rationale for surveillance depends on the dysfunction hypothesis, which states that stenosis causes access dysfunction with decreased blood flow (Qa). This dysfunction reliably precedes and accurately predicts thrombosis [14–15]. The usefulness of Qa surveillance depends on accurately predicting thrombosis so that stenosis can be corrected before thrombosis. However, there is a wide hemodynamic variation during the measurements of Qa , which makes Qa a relatively imprecise predictor of thrombosis [16]; thus, an equation for the prediction of vascular access flow has not been established to date. A study published in 2015 reported that a fast 5-minute Doppler ultrasound of vascular access predicts vascular access

maturation [17]; sensitivity and specificity were not reported. Another study [18] in 2014 reported that with a 2-dimensional ultrasound algorithm, the access flow can be estimated with a positive predictive value of 87.8% and a sensitivity of 89%.

Alternative explanations

The fact that the concepts of Q_a and Q_b are related does not fully explain their causality. Under this conception, the extracorporeal flow would seem to depend on the access flow. A lower access flow leads to a lower extracorporeal flow standardized by the pressure in the arterial line. However, this statement is not true in all cases because the vascular access flow in a good percentage of cases does not depend on a single arterialized vein but on a confluent vascular group that shares a common flow. In those cases, the repeatability of the access flow measurement is more difficult since the measurement is dependent on the degree to which one puncture resembles another in the location and direction of the needles additional to the stenosis that occurs and the patient volume.

Clinical relevance of the findings

These findings have clinical relevance in the daily practice of hemodialysis units because the measurement of extracorporeal flow in a comparative interdialytic way at the same DALP (-200 mmHg) is established as a vascular monitoring pattern. Additionally, having a regression equation available to estimate the flow of access allows us to take preventive measures for vascular care early.

Study limitations

The main limitation of this study is that the estimation made by the equation includes recirculation and inverted recirculation of the access within the constant; no variable was statistically significant to be able to independently predict these variables. This fact was because when there is no recirculation in the access, the measurement system reports the data as "zero" in most of the measurements. However, when there was recirculation of the access, a DVLP/root ratio $[DALP^2]$ greater than 1.578 ± 0.010 was observed. This observation may help in future studies to estimate the recirculation of vascular access. A second limitation refers to the methodology, which is applicable to Fresenius Medical Care volumetric lines and machines.

Conclusions

We estimated the flow of vascular access with parameters from easy intradialysis measurements. The resulting equation could be applied to the same patient with the same dynamic pressure of the arterial line. This was then a useful parameter for monitoring vascular access.

List Of Abbreviations

DALP: Dynamic arterial line pressure

DVLP: Dynamic venous line pressure

Dif: Difference in $Q_a - eQ_a$

CI *: Confidence interval for the mean.

LI: Lower limit.

LS: Upper limit.

Qa: Vascular access blood flow.

$_{e}Qa$: Estimated vascular access blood flow.

Qb: Extracorporeal blood flow.

Declarations

Ethics approval

This study complies with the World Medical Association Declaration of Helsinki. The Research Ethics Committee on Human Beings (CEISH) of the Universidad San Francisco de Quito approved this research protocol with the code 2016-067E.

Consent to participate

Appropriate informed consent was obtained from participants.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors have no conflicts of interest to declare.

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The measurement and monitoring equipment belongs to the José Carrasco Arteaga Hospital. The authors contributed to the administrative costs of the research with their own funds.

Authors' contributions

FGBM carried out the research idea, study design, data collection, article writing, statistical analysis, and critical analysis. SCRG participated in the research idea, data collection, and critical analysis of the article. PTMT participated in the study design, data collection, and statistical analysis. MRU participated in the design of the study and in the critical analysis of the article.

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Figures

Figure 1

Flowchart of participants

Figure 2

Diagram of area under the curve and percentiles of extracorporeal flow and dynamic pressure of the arterial line.

Figure 3

Legend: T = 0.008, GL = 56, P = 0.994, difference of means 0.63544 (lc95% of the difference -163 to 164), Dif = Qa-eQa.