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Vascular Access Maintenance:
A systematic approach to an unsolved question

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RESUMEN

El funcionamiento adecuado de los accesos vasculares de los pacientes en hemodiálisis, constituye un eslabón esencial para lograr la eficacia de los tratamientos sustitutivos renales. Desafortunadamente, no existieron avances importantes en este campo durante las últimas 3 décadas, y la falla del AV sigue siendo considerada como una de las principales morbilidades y causas de hospitalización.

Impulsados por esta realidad, establecimos en 1999 un programa de vigilancia, considerándolo como parte de un proceso más amplio de administración del ciclo de vida del AV, con un grupo de trabajo interdisciplinario como componente principal.

Diversos artículos bibliográficos reconocen las ventajas de la vigilancia de los AV sobre aspectos tales como la calidad de vida del paciente, la disminución de los procedimientos de urgencia, la planificación de medidas reparadoras o de nuevos accesos con más información y tiempo, asociándola paralelamente a una mejora en los costos. Pero en otros se reportan una serie de discusiones metodológicas, como las variables a medir y los valores a partir de los cuales actuar, la falta de eficacia de los programas de vigilancia en la extensión de la permeabilidad, e incluso referencias contradictorias sobre costos incrementados a raíz de la realización de angioplastías transluminales preventivas.

A partir de lo expuesto, realizamos un análisis de las posibles causas de las controversias planteadas:

- Si es necesaria la utilización de puntos de corte fijos para las mediciones efectuadas en la vigilancia, a partir de los cuales se define la funcionalidad del AV.

- El análisis de la efectividad de la acción reparadora (disminuida a partir del trabajo con AV ya trombosados, o la selección preferencial de angioplastías por sobre cirugías o viceversa), y de cuestiones de metodología estadística relacionadas con la potencia que tienen los estudios en la detección de diferencias significativas.

- Cómo efectuar la interpretación de los procesos de medición y comparación que surgen en los sistemas de vigilancia.

- El análisis ante la falta de descripción de los procedimientos utilizados en el monitoreo, la decisión y la reparación efectuada, que hace difícil la comparación directa de estudios o la lectura crítica de los mismos.

Luego, como soporte del análisis realizado de estas controversias, mostramos sus efectos utilizando un modelo biofísico simple. Sobre él presentamos las limitaciones de las aproximaciones actuales basadas en valores fijos, y la consideración de tendencias y la integración de distintas mediciones como una aproximación que permita predecir precozmente la falla y paralelamente maximizar la patencia del AV. Presentamos también los resultados de 6 años del programa de seguimiento utilizando estos conceptos.

ABSTRACT

The performance of hemodialysis (HD) strongly depends on a well functioning vascular access (VA). Unfortunately, there have been no major advances in this field through the last three decades, and VA failure is regarded as one of the most important causes of morbidity in the HD population.

Driven by this concern, we have established in 1999 an aggressive monitoring program, considered as a VA lifecycle administration process (strongly based on a Multidisciplinary Vascular Access Team, MVAT). In this paper, from this point of view, we analyze several controversial issues regarding VA monitoring and treatment to achieve a sustained patency. Using a simple biophysical model, we present the limitations of current fixed-values monitoring approaches, and the consideration of tendencies and integration of measurements as a more physiological approach. We also present the results of a six-year program using these concepts.

Key Words: *Hemodialysis, Vascular Access, Surveillance and Monitoring Techniques, Biophysics, Thrombosis, Hemodynamics, Preventive measures.*

INTRODUCTION

Maintenance of VA patency in hemodialysis (HD) patients is nowadays a major expense that consumes a significant fraction of the budget for healthcare, arousing the attention of more than just the patients and healthcare staff. Despite extensive clinical and scientific efforts, VA-related problems currently account for more than 25% of all hospitalizations in end-stage renal disease (ESRD) patients[1] totaling more than 1 billion dollars per year being spent on access-related care only in the United States[2].

The construction of native fistulae (VAF) is currently the preferred choice of VA for chronic HD in view of their superior patency and low complication rates[3]. However, VA grafts (VAG) are frequently utilized because of comorbid factors such as diabetes and/or age, which often limit the VAF implantation success rate. Accordingly, 20-60% of HD patients in Europe and the US, respectively, depend on VAG for permanent VA[4,5]. In view of the ongoing global diabetes growing population records[6], a sharp increase in ESRD incidence can be expected in patient groups likely to require VAG rather than VAF.

The VAG failure has a consistent pattern of fibromuscular intimal hyperplasia uncovered, most often at or near the venous anastomosis; the progressive venous obstruction just distal to the graft outflow tract (stenosis) caused by this lesion reduces blood flow and ultimately leads to thrombosis. Salvaging a thrombosed access is usually an emergent procedure that, if not immediately successful, causes delays in dialysis treatment and may require placement of temporary dialysis catheter with further endanger of the patient s life[7], added costs and the creation of inconvenience for the patient[8,9].

Up to now, all tested pharmacological and surgical interventions have not resulted in better outcomes for the HD patient s VA matter. On the other hand, periodically measuring access flow (Qa) plus dynamic and/or static venous and arterial pressure monitoring can identify failing grafts and fistulas before they thrombose, allowing elective intervention without interrupting the patient s dialysis schedule, and avoid other complications[10]. Several studies suggest that monitoring not only identifies VA that is more likely to fail but, when combined with timely intervention, also prolongs the access` life[11,12,13,14]. The tradeoff is an increase in angiography, angioplasty or vascular surgery revision, but the patient benefits from reducing hospitalizations and near elimination of temporary catheters[15]. The net economic effect is a considerable reduction in the provider s costs[16,17].

Driven by all these ideas, we have established in 1999 an aggressive surveillance (specific VA measurements: flow, pressure) and monitoring (clinical observations: thrill, pulse) program, with a main character: the Multidisciplinary Vascular Access Team (MVAT). Within MVAT, with the nephrologist´s coordinating activity[18,19], a group of specialists composed by the vascular surgeon, the interventional radiologist, the nursing staff[20,21] and óther support specialties (biomedical engineers, social workers), works very closely to analyze and decide the course of action regarding VA issues.

With our accumulated experience and results as well as the discrepancies observed over these years regarding the VA surveillance and monitoring (VA S/M) versus patency rates issue, we decided to face this controversial matter on the following pages:

1) Analyzing the controversial points from a systematic point of view,
2) And presenting our VA S/M program s
    a.   biophysical foundations
    b.   outcomes and results

Systematic analysis

In *figure 1* we can see a lifecycle systematic approach to the VA subject, and the relevance of S/M programs under MVAT management. In every stage there are some issues to consider, i.e., how much mapping to do, how much time to wait for first-using a VA, on which VA variables to rely on to monitor its function, what warning levels to use related to those variables, and so on. The overall VA patency depends on the result of each stage: a poor planning usually leads to a more frequent repairing or directly to a higher thrombosis rate, repairing interventions made by a vascular surgeon without deep experience on the dialysis field (usually in patients referred by social security agencies) could be less beneficial than those made by an specialized surgeon.

Hence, within each phase there are some critical subjects that must be properly addressed in order to maximize outcomes, measured as the ideal characteristics of VA for HD: a minimum blood flow must be reached so that an adequate dialysis[22] can be achieved, an extended (but in a reasonable timeframe considering several patient related factors) life or patency with minimum complications for the patient (no thromboses, no infections, no hemodynamic alterations).

Stating the VA S/M program as the tool for administration of VA´ lifecycle, we will focus on some methodological questions that we identify as controversial in the VA monitoring programs literature, and also as the reasons of some reported failures in this field.

Fig. 1 The concept of S&M program as VA´ lifecycle administration under management of MVAT
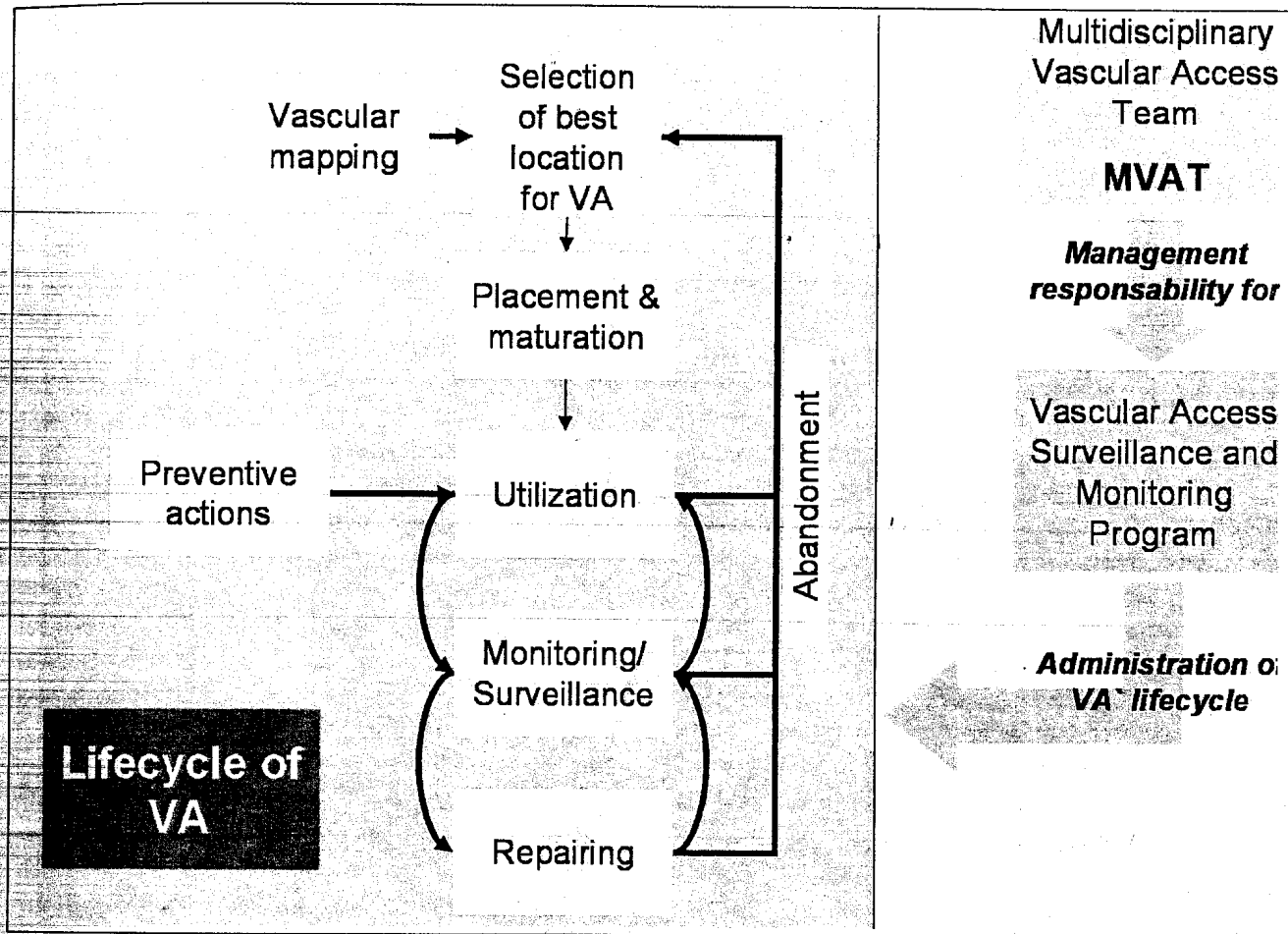
Controversial points analysis

1) Access flow and venous pressure values cut points:
The pathophysiological basis of VA failure implies a process with a high variability between patients[23,24,25], but a continuous process to the end, quite so using fixed values doesn t seem to be related to any physiological basic reason. The variability between VA starts at the construction of a VA graft: this results in increased tension of the venous vessel wall and altered shear stress levels caused by the higher flow velocities in the arterialized circulation[26,27,28], effects well dissimilar as a result of each surgery.

Also several studies have illustrated that these hemodynamic changes lead to turbulent flow patterns, specially at the anastomotic region[29,30]. This turbulence results in varying and/or reduced levels of shear stress during the pulsatile cycle[31] with a dramatic impact on the function of the endothelial lining, also with differences between patients and in different VA inside the same patient.

As recommended by the K/DOQI guidelines[32], a patient should be referred for a diagnostic fistulogram if the intra-access flow is less than 600 mL/min or if the blood flow is less than 1000 mL/min and has decreased by more than 25% over a 4-month period (some modifications have been made in the last published K/DOQI guidelines[10] regarding this issue). Both high and low flows depending on hemodynamic conditions, were seen in patients with fistulas and grafts[33]; but is clear that when the VAG flow falls below a given limit, the risk of graft thrombosis increases dramatically[34,35,36]. This limit could be found within the 600-800 ml/min range as stated in DOQI guidelines, but other investigators also found high thrombosis rates when the flow is ≤300 ml/min[37].

Krivitski[38] suggests in a recent work that this fixed points need to be modified to higher values, since a 50% stenosis were related to very different flows depending on the VA initial conditions considered. Correspondingly, regarding the pressures[39] (venous and arterial, both static and dynamic, and intra-access), there are similar problems; boosted by the fact that the fixed values cited by the literature are outdated (most investigations in the late 80`s and 90`s were done using 16G needles, and currently it s widespread the use of 15G needles).

There are other drawbacks, i.e., needle misplacement and orientation, patient arterial pressure variation; some of that were addressed by Besarab`s group defining the concept of intra-access to mean arterial pressure ratio[40]. All these pressure measures (also the method developed by Besarab), if used isolated (not correlated to flow measurement), do not detect stenosis in some typical places, and in more complicated lesions like multiple stenosis in series caused by repetitive catheter placement[16].

We will further analyze this point through a simple mathematical model, comparing two hemodynamical different VA. As we expected, the use of fixed points, regardless the value, could lead to a late or early intervention, always with increased costs (see "Simulation results"). Nevertheless, even the detractors of monitoring programs agree that measuring helps to detect the dysfunction prior to VA thromboses, and several studies show a good correlation between some measure of flow (value or variation) and/or pressure and an anatomical finding (outlet or inlet stenosis); but they find that when this lesions are treated by preemptive PTA (percutaneous transluminal angioplasty), the secondary (assisted) patency does not differ from the patients treated after thrombosis[65]. This is the second point in the "controversies analysis".

2) Repair effectiveness:

The relative lack of effectiveness of the repair procedures in achieving a longer VA life was recently established in some clinical trials. This conclusion is flawed by several methodological problems:

• The repair of the stenotic lesion can be done using either a surgical approach or a transluminal procedure. The success of PTA strongly depends on the elasticity of the lesion, and the feasibility of surgery depends on the lesion s site. High PTA rates were seen in those investigations, showing at least a strong preference for this method over a surgical approach. This preference could be based on several already stated advantages of intraluminal methods over the more invasive surgery (morbidity, economics), but in some cases the elastic recoil shown by stenosis treated by PTA should be addressed by surgery.

• The conclusion about a statistically significant non-difference between the groups (normally pressure and/or flow monitoring versus clinical control groups), could be severely skewed from a technical point of view. The recent Aggrenox (dipyridamole + aspirin) clinical trial design[41] discuses with some deepness this point, and more than 1000 patients were needed to show significant differences. A similar point was made by Besarab[14]: for a detection of a 33% survival difference at 3 years or a significant difference at 1 year, a sample of 700 patients is required.

• Several investigators have tried to salvage a thrombosed graft when the failure took place, and if this procedure was successful, generally from a radiographic point of view (which was questioned[42] regarding the predictive value), the patient was considered again within the original group. The graft surface thrombogenicity is impaired by the thrombotic event, since a complete "cleaning" of thrombus is hardly achieved[43] (and can t be assessed by typical imaging modalities). So, this salvaged VA has a higher probability of re-thrombosis, contributing more further to the poor result of the monitoring program[44].

• Normally a new measurement within the monitoring program should be made at the recently treated VA. If the new results are "outside" good values, then the corrective procedure can t be considered as successful. There are several reasons related to this functional failure: 1) failure to detect multiple stenoses (both in venous or arterial sites), and, 2) the elastic recoil normally seen in most lesions[45]. This issue isn t addressed in these studies.

3) Measures, concepts and interpretation:

A subject faced by all the clinical interventions which rely on measurements is the interpretation of the measured values. In physics sciences there is a huge amount of information[46] usually outside the scope of medical specialist, (and normally addressed by equipment manufacturers when they design and specify their products). The users concern arises when comparisons or decisions are made using these values.

The measurements normally used in VA programs have a wide range of error, such as (data from equipments manuals, or references included in each one):

a) Access flow by Transonic´s device: the bigger between 100 ml/min or 15% of reading value.

b) Venous pressure, 4008B Fresenius machine: 10 mmHg, but the "resolution" factor is 20 mmHg (due to the representation form of the measurement, which is the value that at the end reads the user).

c) Recirculation by Transonic´s device: 2% for measurement + 3% for reading.

d) Blood velocity by diagnostic ultrasound (US) devices: (best) 5%[47]; more than 6%[48].

e) Stenosis percent by angiography: 8%[49].

f) Flow by diagnostic US devices: 15 to 25%[50].

g) Fresenius´ BTM flow method: comparable to Transonic device[51,52].

Furthermore, the error for US devices depends mostly on the operator s skills; and stated in this way, the figure becomes more acceptable for the general medical community: it s common to hear comments about how much the results of Doppler studies depend on the operator ability.

What do these "errors" values mean? Let s take a common situation for a Doppler measurement setting, with a conservative 15% error:

    "Real" unknown value: 1000 ml/min
    Measurement 1: 1100 ml/min
    Measurement 2: 900 ml/min

But because of error, one must write these measurements as:

    Measurement 1: 1100 +/- 165 ml/min
    Measurement 2: 900 +/- 135 ml/min

Within the error theory frame, in spite of the apparent difference between 1100 and 900 ml/min as an absolute value, one must conclude that, because of measurement error, the two values are NOT really different (in the same sense that two statistical hypotheses are not different within a given "p"). Note that if the limit between a functioning and not-functioning access is 1000 ml/min, then the measurement 1 implies no action, and measurement 2 implies an angiography and/or PTA,

if no other considerations about errors are made. The same applies to every other physical magnitude used for VA S/M. Therefore, considering the variability of measures due to measurement technique itself, plus the intra-patient variation because of variable physiological adjustment, one must conclude that a better approach is to look at tendencies and the integration, than focus on isolated values and variables.

4) Monitoring and surveillance program

The composition and interaction within MVAT, the decisions made regarding the course of action for each VA, and the quality and timing of decision are determinants, both in our experience and in the others[53], for a program with good results. In the several papers that address the VA monitoring issue, there is no description of how, when and using which procedures the group in charge works. This is not a minor subject, since the whole success relies on the decisions made by the group.

Given the complexity of the mechanisms contributing to VA graft failure (such as hemodynamic and biophysics factors, compliance mismatch, endothelial damage, inflammation, platelet activation, growth factor release, etc), and until the science find different approach for treatments which could hold a promise for optimiz-
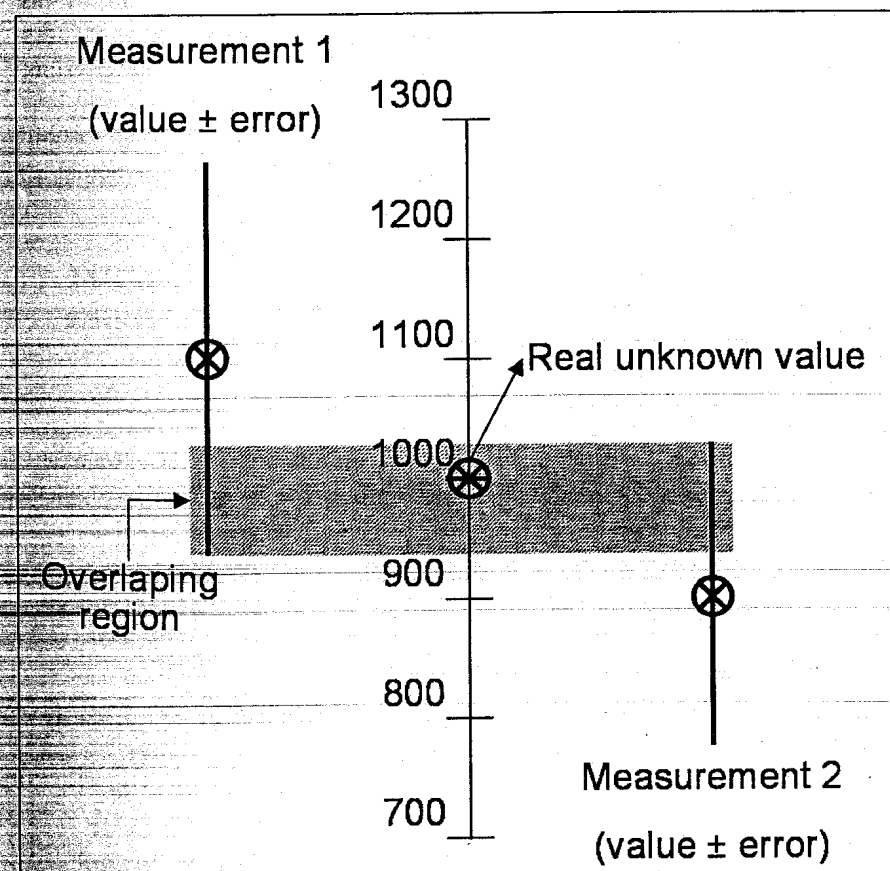

Fig. 2

Two measurements with real instruments (i.e. with errors). The real value lies on an overlapping zone which indicates that the two measured values, when correctly interpreted, are not really different.

ing AV graft patency rates, the surveillance programs are useful[54]. The thorough knowledge of every VA, and the decisions made on every step of its care, can be translated into huge improvements in both the health economics and a more specific measure of care: the patient s quality of life.

Biophysics approach of our S/M program and Simulation Results

We will introduce the fundaments and concepts behind our S/M program, and through a simulation, we will complete the analysis of the controversial points we have discussed about on the preceding pages. We have chosen to develop a graft model because a better and direct correlate between anatomical zones and model components along with failure sites can be shown. With some modifications, the model can be extended also to AVF.

The simulations use the well known fluid flow laws, which we present here rewriting the mathematical terms so that an immediate correspondence with anatomical and physiological entities could be stated:

$$Q = (Pi-Po)/Rh, \text{ with}$$
$$Rh = 8.\eta.L/(\pi.R^4)$$

(For an in-depth discussion and applications, see references[55, 56, 57, 58])

This way of writing the Hagen-Poiseuille law, allows an explanation of the flow from two standpoints:

a) the driving force, the differential pressure between the beginning (Pi) and the end (Po) of the vascular segment considered.

b) the opposition to this driving force, the hydraulic resistance (Rh) given by the vessel' geometrical characteristics (longitude L, radius R) and a blood related rheological parameter (blood viscosity η).

This law strictly deals with the linear components which dissipate energy within the hydraulic circuit. But in the human circulation, other non-linear dissipating entities are present, like the anastomosis and stenosis. One technique to consider these two effects is to modify the parameters in the Poiseuille equation conveniently, not to reflect just the linear components, but to include, in a simplified way, also the non-linear ones (i.e., considering some of the factors raised to 2nd, 3rd... power)

Other approach, and the one we have employed, is to start at typical measured pressures profiles[66] (which include all the effects within each physical "element" of the vascular access), and to compute from this normal profiles the normal hydraulic resistance of each VA' part. After this step, the variation of the resistances which reflects the pathology being simulated is calculated.

The prosthetic graft can be modeled splitting it into 3 segments: a resistance for the arterial anastomosis (Rart), one for the graft itself (Rg), and another one for the venous anastomosis (Rven). Flowing through the three resistances connected in a series topology, there is the access flow Qa.

In *figure 3*, we present also a typical pressure profile through the graft, beginning at the arterial pressure (as mean arterial pressure, MAP) and on the other end, the venous central pressure PVen. This is a simplification, but useful for our use of the model for comparison purposes.
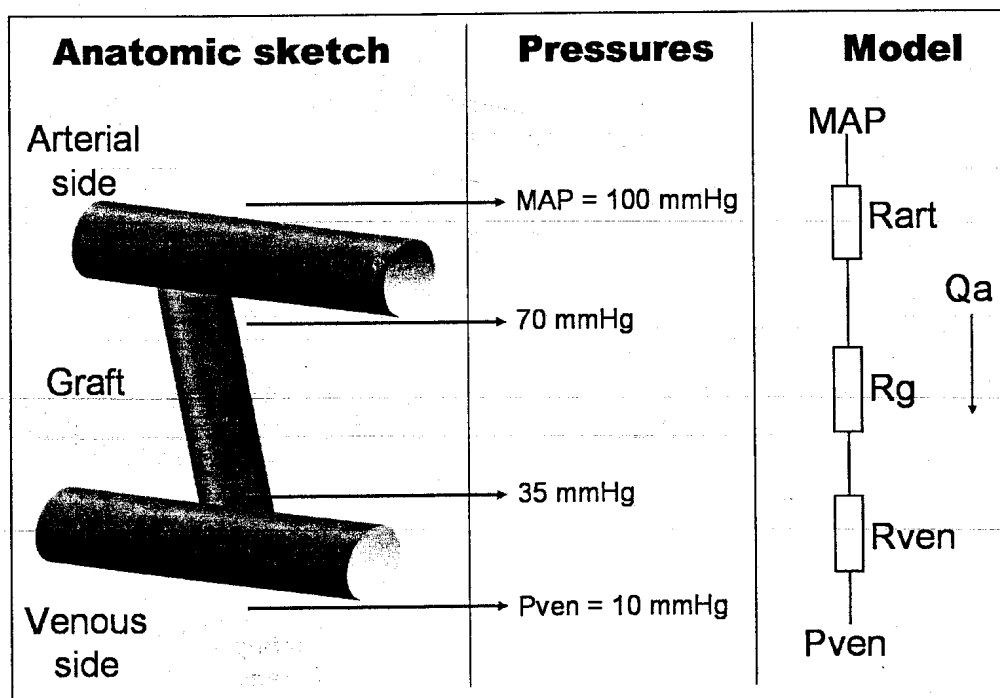

Fig. 3

Sketch of VAG, pressure profile and intravascular resistances model.

Finally, when the patient is connected to a HD filter, the blood circuit with all the components of the HD equipment is also depicted (*figure 4*): RNa and RNv (resistance for needles and tubing, typical value 0.28 mmHg. min/ml), R filter (resistance for HD filter), Qb eff (effective flow at blood pump, typical value 400 ml/min).

All the parameters normally used in VA S/M programs are shown on the *figure 4*, along with the resulting equations and initial conditions used in our model: recirculation as a percent of blood pump flow (Rec%), the pressures measured at HD equipment sensors, both arterial (PSArt) and venous (PSVen). Regarding the concept of recirculation (in our model we consider only the local, access related recirculation), only appears from a physical point of view when the flow trhough the access Qa is less than the flow through the external bloodlines Qb eff.

As the VA starts to develop the failure which finally ends (if nothing is done to correct it) in thromboses, one or various zones within the VA raises its hydraulic resistance (usually because of stenosis, and as consequence a diameter reduction can be found). As the final effect in our model, we concentrate the stenosis effect at Rven, so that it becomes a time-variant resistance (following a time-squared dependence). The constant we've used for simulating the effect of a time dependant increase for Rven is 0.00118 $1/s^2$.

The time in our simulation is parametric with arbitrary units, even though it can be considered as weeks, regarding our clinical experience. The same criteria (in accordance with clinical observations) was used to choose the time-squared dependence for stenosis development (and therefore for Rven).

We discuss the effect of a fixed value over the decisions made about VA care comparing the results obtained with two simulations. These simulation correspond to two hemodynamically different situations: a high-flow condition for "Case A" (e.g. a straight arm graft) and a low-flow condition for "Case B" (e.g. a forearm loop). As inicial conditions, we have chosen a flow of 2000 ml/min for case A, and 1400 ml/min for case B. As the thresholds in this hypothetical surveillance program, for the flow parameter we use 1200 ml/min, and for dynamic venous pressure, 200 mmHg.

Simulation results

The simulation, using the complete equations set, was made using the program Mathematica. The time dependant effects of Rven on variables (stenosis percentage, and other relevant model variables) are shown in *figure 5*.

Using the thresholds for flow mentioned above, the figure shows that in Case B an "early warning" is issued with a significant but low stenosis (32%), meanwhile for Case A the warning arrives at a more difficult situation, with a stenosis level over 50%. Recirculation, as stated also by several investigators in this field, is a very late warning, at least for VAG (and of limited utility in the VAF case). The only real application of isolated recirculation measurement (not as an intermediate tool for flow calculations is the correction of hemodialysis time to achieve the prescribed Kt/V[59].

In the pressures analysis case (*figure 6*), the PSVen (pressure at venous HD equipment sensor) is also poor as an indicator, in the sense that it fluctuates near the selected 200 mmHg level when stenosis still continues
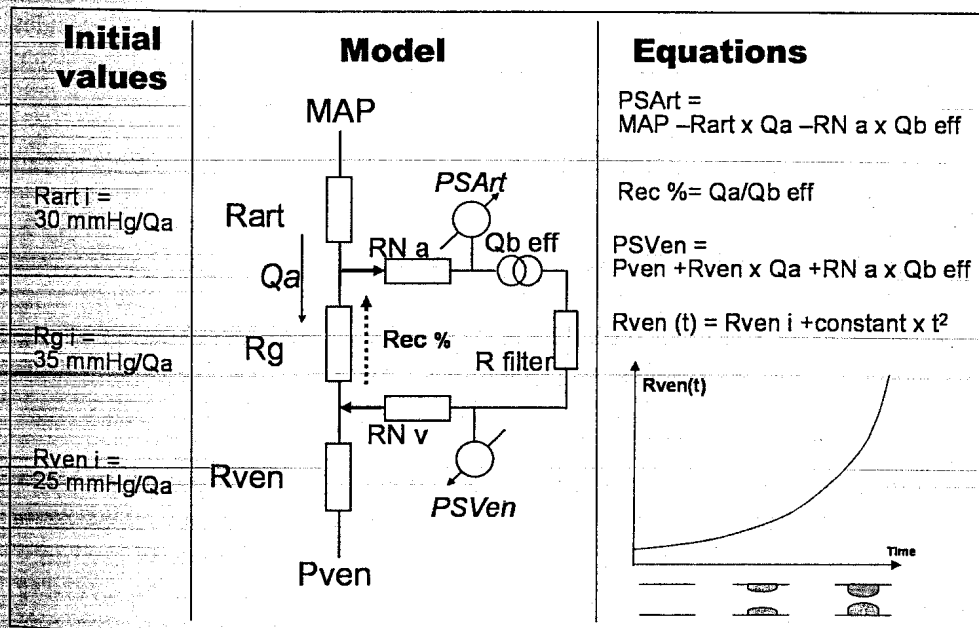

Initial values	Model	Equations
	MAP	PSArt = MAP −Rart x Qa −RN a x Qb eff
Rart i = 30 mmHg/Qa	Rart PSArt Qa RN a Qb eff	Rec %= Qa/Qb eff
Rg i = 35 mmHg/Qa	Rg Rec % R filter	PSVen = Pven +Rven x Qa +RN a x Qb eff
Rven i = 25 mmHg/Qa	Rven RN v PSVen	Rven (t) = Rven i +constant x t^2
	Pven	Rven(t) Time

Fig. 4

Initial values, model including extracorporaeal circulation and parameters, and governing equations, along the Rven dependence over time.

Fig. 5 The effect on variables Q and %Rec of two hemodynamically different VA. Note in (a) and (b) the imprecision zone for threshold determination due to the measurement error for flow.
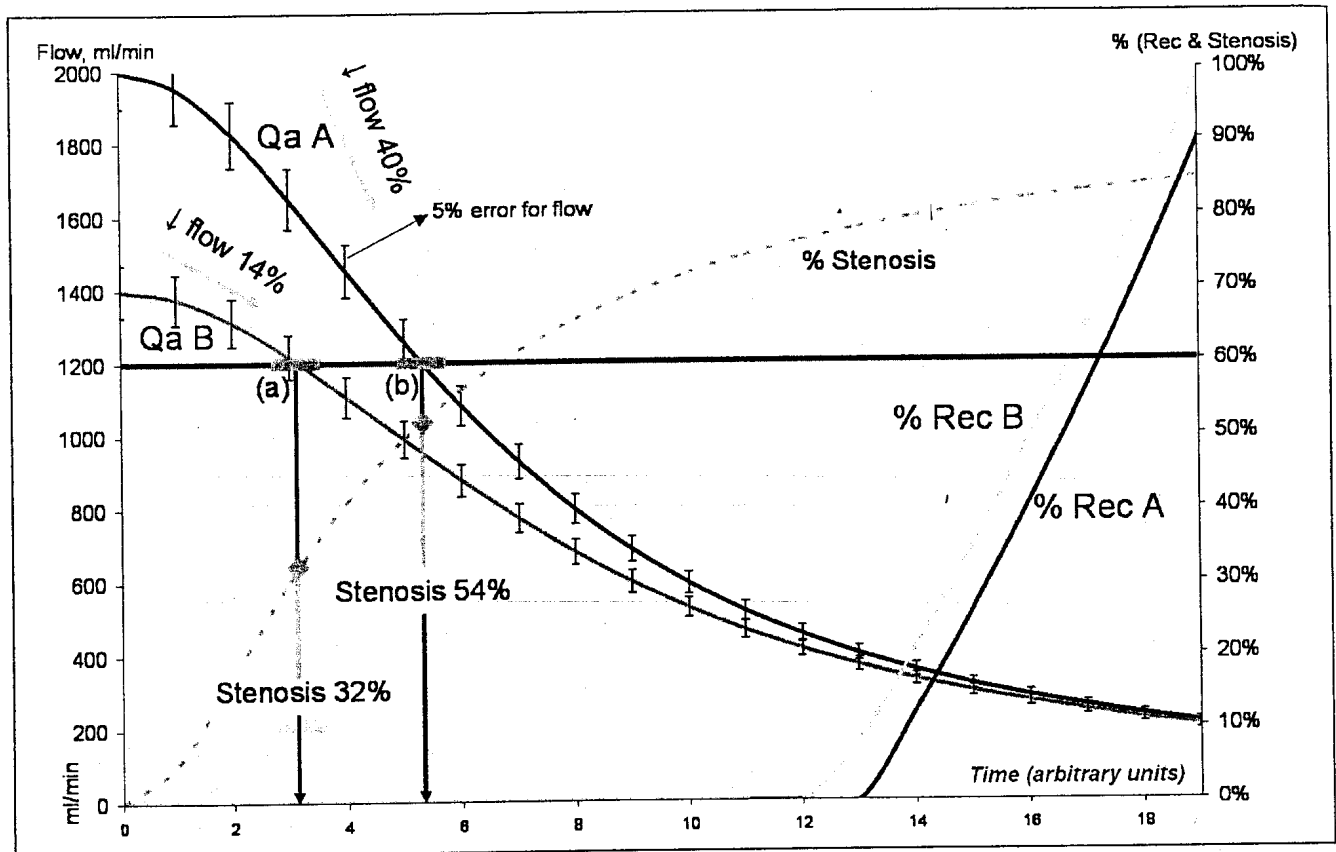
advancing, or even never reaches this level in case of medium-level stenosis, or in some cases of collateral branching. To overcome these sensing problems, some authors suggest a modification over the pressure method[60,61], all trying to find the value for Qb that improves some detection characteristic (sensitivity, specificity), but with no definitive results.

Outcomes of our S/M program

Since January-1999[62], we have established a S/M program (101 patients with 125 access, VAF: 74 and VAG: 51) based on a strong biophysical basis[63], aiming at stenosis prediction, detection, confirmation and treatment before a thrombotic event occurs. The basis of our program, as sketched in the model discussion above, is the trend analysis considering the history of the particular VA, and every time a significant reduction of flow[64] has been detected (using Blood Temperature Monitor BTM, Fresenius Medical Care), with a concomitant variation in pressures. This device employs a thermal bolus in the dialysate side, wich changes in turn the blood temperature, and this change is measured by the arterial sensor at the module when a recirculation ap-

pears (an artificially high recirculation is created by interchanging the patient´ needles). A closer surveillance over the implied VA is assumed.

When the MVAT has a confirmation of the variables movement towards an indication of stenosis, an imaging technique is carried out (preferred method angiography), and after the confirmation, the MVAT decides the angioplasty (transluminal or by surgery) if a lesion is detected, or decides the course of action for a new VA placement if necessary.

We introduce the results for the January-1999 to December-2004 period, using Kaplan-Meier survival analysis (KMSA). For KMSA an event is defined as VA placement, VA failure, surgery repair, PTA or VA replacement, without considering as an event the diagnostic studies (Doppler or angiography). We have taken as an occurrence for KMSA the VA failure or catheter, and as censored events: facility change, kidney transplantation, or death.

In *figure 7*, we present the cumulated survival curves, along a summary for assisted patency. These values for VAG are close to those suggested by DOQI.

Over the 6 year period to achieve this assisted patency, the 74 VAF have demanded 39 procedures (0.09 inter-
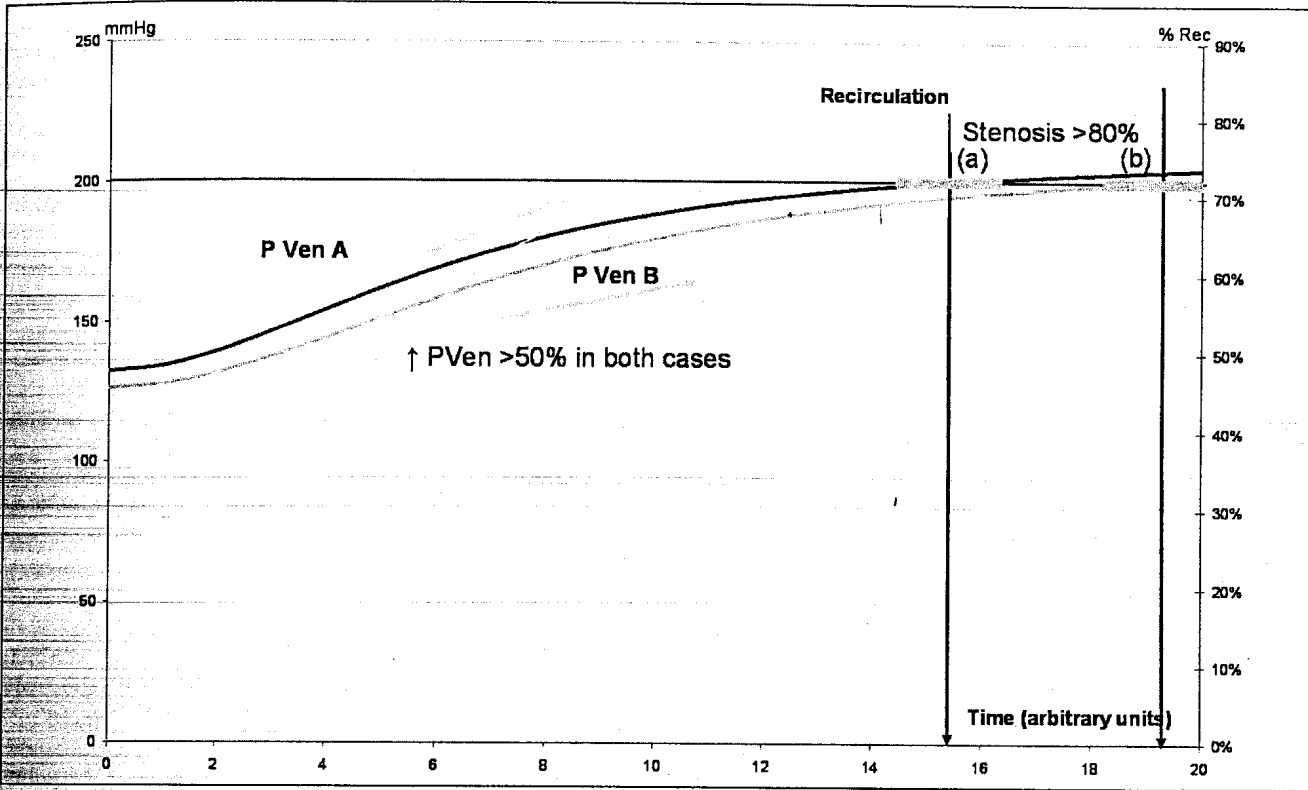
Fig. 6 The effect on variables PVen of two hemodynamically different VA. Note in (a) and (b) the imprecision zone for threshold determination due to the measurement error for flow.
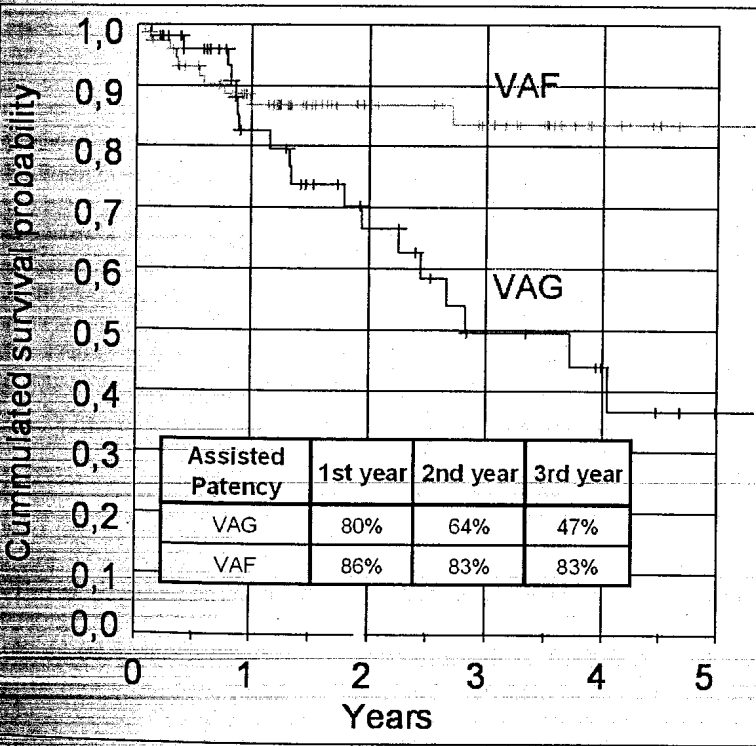

Fig. 7

Kaplan-Meier survival analysis. The marks in each curve represent censored events. Also the summary for assisted patency is presented.

Assisted Patency	1st year	2nd year	3rd year
VAG	80%	64%	47%
VAF	86%	83%	83%

vention/patient-year at risk), and the 51 VAG, 94 procedures (0.3 intervention/patient-year at risk). Other program quality indicator, the thrombosis rate, was 0.05 thrombosis/ patient-year at risk.

CONCLUSION

The understanding and use of basic hemodynamic principles within the VA context can help in planning an optimum approach to prevent and treat access failure.

The basis of this failure, triggering of thrombosis, is secondary to low flows[8] and the activation of different endothelial messaging signals at cellular level, which lead to a progressive increase of one or more segments of VA´ resistance, with all the concomitant variable alterations: lowering of flow, increasing of blood velocities and wall shear stress in some sites and lowering in others, and pressure alterations.

In the last 10 years there have been several papers addressing the different factors that finally lead to controversial statements about the real value of a VA S/M program: no better accumulated patency with more interventions and therefore expenditures.

We have identified and examined several methodological problems, such as including few patients in the study in order to draw statistically significant conclusions, and showing several design problems: which variables and values to use, how the inclusion of already thrombosed and salvaged VA affects the real outcome, and which exact and strict procedures to use to conduct the study.

One of the main problems, already stated by several investigators as Besarab, Vesely and Krivitski, is the use of fixed values as a decision point to trigger a corrective action. Instead, we have used a more physiological approach, which is the analysis of tendencies and integration of related variables to define the course of action of every VA, taking also into account its history.

Besides the "hard numeric" and good values related to assisted patency or survival curves we have obtained from our work, the main outcome of a well-designed and applied program (being the team work of MVAT the most important characteristic) is the falling of "VA problems" far low in the list of worries and fears of patients, nurses and nephrologists. During the consistent application of VA S/M program, several indicators show improvements: a better perceived quality of life for patients, a less global cost and almost the elimination of "crisis situation" that were seen after every thrombosis episode in the past.

The VA S/M programs must be considered as a "bridge" to a more radical solution in the future for the VA problem. In fact, it seems that the better approach will be the amelioration of tissue response to injury of endothelial wall vessel after shunt placement, following studies at molecular and genetic levels to block this response[23].

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Appendix

Here we show some details about formulae and further explanations for the equations and concepts used in the model.

The volume of a liquid substance that goes through a given surface perpendicular to this movement per time unit is called flow, and when this liquid is blood, then the units normally used in the biomedical field is ml/min. This flow is driven by the geometric characteristics of the vessel, the pressure diference between the the input and output, and some particular flow characteristics.

The Hagen-Poiseuille equation describes this relationship when the flow is laminar (ie, the trajectory of a particle inside the flow it´s a line). In some cases and depending on several factors, the blood flow goes from laminar to turbulent, and this equation loses validity. Anyway, it could be used with some considerations.

The components of this equation are as follows:

$$Q = (Pi - Po)/Rh, \text{ with}$$

$$Rh = 8.\eta.L/(\pi.R^4)$$

Q: blood flow, in ml/min.
Pi, Po: inlet pressure, outlet pressure, in mmHg.
h: viscosity, in Pa.s or Poise.
L: vessel length, in cm.
R: vessel radius, in cm.

For using this equation directly, is necesary to include the factors converting the used units to compatible ones. This equation states several useful informations, as examples:
• a short catheter has less resistance than a long one (affecting L in the equation);
• a VA located in upper arm, will have more flow than other located in the forearm, because of the diference in Pi, the "arterial" or inlet pressure for the shunt.

The model uses the equation sector by sector along the vascular access, and also for modelling the physics behind the extracorporeal system. The model shown in Figure 4, state also the equations we use for the calculation of several variables. As an example, the calculation of PSart:

Qa = 2000 ml/min, MAP =100 mmHg, Qb eff = 400 ml/min, Rna = 0.28 mmHg.min/ml

Vascular access resistances, initial values (time =0):
Rart i = 30 mmHg/Qa=30 mmHg/2000 ml/min= 0.015 mmHg.min/ml
Rg i = 35 mmHg/Qa = 0,0175 mmHg.min/ml
Rven i = 25 mmHg/Qa = 0.0125 mmHg.min/ml

From this values, the calculation for PSart is made:
PSart = MAP – Rart x Qa – RN a x Qb eff =
PSart=100 mmHg – 0.015 mmHg.min/ml x 2000 ml/min – 0.28 mmHg.min/ml X 400 ml/min
PSart= 100 mmHg – 30 mmHg – 112 mmHg = -42 mmHg.

Then, the pressure wich the machine measures at PSart is -42mmHg, a value that could be found in real situations when the patient has a very good VA (high Qa), and normal values for needles and tubing.

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