Validation of QB stress test as a useful tool in the detection of native arteriovenous fistula stenosis: results after 22 months of follow-up

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Abstract

Background. Access flow (QA) surveillance is the best method recommended for early stenosis detection, but in native arteriovenous fistula (AVF), the literature is conflicting about the real need for monthly monitoring of QA, as suggested by the K-DOQI Guidelines.

Methods. From 1 January 2006 to 31 October 2007 (mean 18.0 ± 4.9 months), we prospectively followed up 224 patients with monthly AVF monitoring by means of clinical examination and QB stress test (QBST). Suspected malfunctioning AVFs were referred to ultrasound dilution technique (UDT) and imaging techniques (Doppler ultrasonography, angiography), with eventually further percutaneous angioplasty (PTA) or surgical revision.

Results. We observed a good correlation between QBST and QA measurement obtained by the UDT. Patients with positive QBST had a lower QA than negative QBST subjects (433 ± 203 vs 1168 ± 681 ml/min, P < 0.0001). Fifty-four out of 224 (24%) patients were selected for possibly malfunctioning AVF. We found no stenosis in 13 out of 54 (24%) patients, inflow stenosis in 29 out of 54 (54%) patients and outflow stenosis in 12 out of 54 (22%) patients.
patients. The QBST positive predictive value for inflow stenosis was 76.3%. The interventional radiologist performed 38 PTA procedures in 33 patients (11 PTA per 100 patient-years) and we surgically created 13 new AVF (3.7 per 100 patient-years). Only five thrombosis episodes occurred in five patients during the follow-up (1.5 thromboses per 100 patient-years).

Conclusions. QBST is a simple, low-cost, not time-consuming test, able to select, together with clinical evaluation, malfunctioning AVF with stenosis located specifically in the inflow tract. Our follow-up data demonstrated that it is possible to achieve a low AVF thrombosis rate by adding QBST in an AVF monitoring program, thus reducing the surveillance burden.

Keywords: arteriovenous fistula (AVF); haemodialysis; stenosis; vascular access surveillance

Introduction

Arteriovenous fistulas (AVF) created with native vessels are currently regarded as the gold standard for haemodialysis access because of their lower infection and thrombosis rates compared with other types of haemodialysis accesses [1–5].

According to Schwab et al. [6], in most cases, the thrombotic event is due to unrecognized stenosis located preferentially in the juxta-anastomotic segment (JAS), within 2 cm from the anastomosis, and this observation has been confirmed by several authors [7–11].

The rationale for AVF surveillance is based on the slow growth of the stenosis over time, causing a variable period of malfunction before halting the flow definitively. Thus, an early diagnosis permits saving the access, correcting the underlying malfunctioning conditions [5].

Many monitoring techniques have been described, of which the accepted gold standard is the access flow (QA) measurement using the ultrasound dilution technique (UDT) according to Krivitski (Transonic HD01) [12].

In the native AVF, however, this parameter is not always possible to measure; moreover, the studies available in the literature are conflicting about the real need for monthly monitoring of QA, as suggested by the K-DOQI Guidelines [4,5], because of the lower rate of AVF stenosis and the more complex AVF anatomy compared with grafts [13].

It is difficult to apply a vascular access monitoring program using routinely time-consuming techniques, like UDT, requiring well-trained and dedicated staff in a modern haemodialysis unit, with an increasing elderly population.

The primary aim of this pilot observational and prospective study is to analyse the results of an application of a new zero-cost screening test, the QB stress test (QBST), created to select, together with clinical evaluation, the group of low-flow AVF to refer to more detailed and specific study techniques (UDT, Doppler ultrasonography, angiography).

We first studied 286 patients with native AVF on chronic haemodialysis three times a week in our haemodialysis unit and then followed them up prospectively for 22 months in order to assess the efficacy of QBST and to evaluate native AVF thrombosis and malfunctioning rates.

Materials and methods

The ‘swing segment’ is defined as the native vein tract mobilized during the surgical intervention for a distal or proximal arm AVF [8]. Stenoses that develop in the proximal area (also called the ‘outflow segment’) are different from the JAS stenoses because they are not associated with surgical mobilization [14].

JAS stenosis belongs to the ‘inflow stenosis’ class, defined as a stenosis occurring within the arterial system and the artery–vein anastomosis. A ‘distal arm AVF’ has the anastomosis located in the forearm, below the elbow, and is created by using the ulnar or the radial artery as inflow tract. A ‘proximal arm AVF’ has the anastomosis located above the elbow and is created by using the brachial artery as inflow tract.

Rationale

It is accepted that a well-functioning AVF is characterized by a QA ≥500 ml/min at least [4,5]. Most of native AVF are well-functioning; therefore,
the AVF surveillance program should be focused only on low-flow accesses in order to improve the cost–benefit relation.

Since the most common site of stenosis occurrence is located at the JAS segment, it could be possible to detect two classes of patients on the basis of the aspiration pressure alarm setting a blood pump flow (QB) at 400 ml/min. We observed that the same effect can be obtained by applying a ‘stress’ to the fistula, i.e. raising up the patient's arm to 90° compared to the normal arm (0°) while setting the QB to 400 ml/min during the haemodialysis session (QBST). Elevating the arm to 90° causes a QA reduction dependent on the different position of the arm.

To verify the QA modification during the raising test (0° to 90°), we initially measured the QA in 10 patients with well-functioning AVF (no recirculation, good QB achieved) from at least 2 years using the UDT during a standard haemodialysis session (Figure 1).

The QA was the mean of three measurements obtained during the first hour of haemodialysis by appositely trained nursing staff.

The QB stress test: procedure

The test must be executed during the first haemodialysis hour in order to avoid interference of possibly occurring hypotensive episodes (Figure 2A and B).

While regulating the arterial pressure alarm to −250 mmHg and the venous pressure alarm to +250 mmHg, the patient's QB is set...
to 400 ml/min and the pressure levels are registered with the arm in the usual supine position (0°).

The AVF is then stressed by raising the patient's arm to 90° for 30 s. The test was considered negative or positive depending on the arterial pressure alarm appearing within the established time (30 s). The test is repeated after progressively lowering the QB to 300, 200 and 100 ml/min, and it is considered positive if the alarm goes on (2+, 3+ and 4+, respectively). A QBST positive at a QB of 100–200 ml/min (low flow) is considered an increased risk of stenosis.

The dialysis session is then conducted on the nephrologist's prescription schedule.

The QBST results are registered in a dedicated paper form by the attending nurses and then transcribed on a computerized database.

We validated our test by investigating the correlation between the QA measurement obtained by the UDT, maintaining the needles in the correct position to avoid recirculation (usual fashion) and the different positivity degrees of the QBST in 202 patients with native AVF (163 distal arm and 39 proximal arm fistulas).

Follow-up

Between 1 January 2006 and 31 October 2007, we prospectively followed up all our patients with AVF (n = 286). All of these subjects underwent monthly AVF monitoring by means of clinical examination and QBST (Figure 3).

We included in the analysis only patients with a follow-up ≥6 months (n = 224). We addressed to imaging only patients with QBST positive at lower QB (QBST 3+, 4+), and the others (QBST 0, 1+, 2+) continued the monitoring protocol.

The malfunction clinical criteria were: arm swelling, collateral veins, problematic cannulation making it impossible to achieve the prescribed QB and prolonged bleeding after cannulation.

The ultrasound stenosis criteria were: turbulence of flow (aliasing), visible narrowing of the vessel lumen ≥50% and a peak systolic velocity >100% compared with that found in adjacent normal segments [15–17].

The angiographic stenosis criterion was a reduction in the vessel lumen ≥50% compared with that in adjacent normal segment or, more precisely, a 50% defect in the balloon [11].

This study has been approved by the local ethics committee.

Statistical analysis

Data are expressed as the mean ± standard deviation (SD).

The QA variation after postural modification (raised-arm effect) was assessed with two-tailed Student's t-test for paired data.

QA differences in QBST positive and negative patients were investigated with two-tailed Student's t-test for unpaired data.

QA reductions depending on the positivity degree of QBST were evaluated by means of the analysis of variance.

The percentage of QA assessment (using UDT) depending on AVF location (distal arm, proximal arm) and the percentage of stenosis detected with clinical examination and QBST were analysed by means of the chi-squared test.

A P-value lower than 0.05 was considered statistically significant.

All computations were carried out using SPSS version 11.5 (SPSS Inc., Chicago, IL).

Results

The stress effect

First, we confirmed the QBST rationale (the stress effect) with the QA data achieved in 10 patients with a well-functioning AVF. In fact, from the supine (0°) to the raised-arm (90°) position, we observed a QA change from 1699 ± 549 to 1386 ± 557 ml/min. QA was always reduced (delta mean 313 ± 43 ml/min, range 250–400 ml/min, P < 0.001) (Figure 1), not depending on the AVF location considered (distal or proximal arm).

QBST validation

We then validated our test by comparing QBST results with the QA values obtained by UDT in 202 consecutive patients.
Maintaining the needles in the usual fashion, it was possible to obtain a QA measurement in only 138 out of 202 (68.3%) of the patients. We could not obtain the QA in 64 out of 202 (31.7%) subjects due to the needles being positioned on non-communicating venous branches [17]. In particular, the AVF location was significantly associated with the possibility of obtaining a QA measurement. In fact, we could not measure the QA in 53.8% (21 out of 39) of proximal arm fistulas and in 26.3% (43 out of 163) of distal arm fistulae studied (chi-squared test 14.9, \( P < 0.001 \)). On the contrary, we were able to measure QBST in all 202 patients.

QBST resulted negative in 88.1% (178 out of 202) and positive in 11.9% (24 out of 202) of the patients. In particular, in 24 positive patients, eight had a QBST value of 3 + and 16 of 4+.

Patients with positive QBST had a distal QA compared to those with negative QBST (433 ± 203 vs 1168 ± 681 ml/min, \( P < 0.0001 \)) (Figure 4).

**Follow-up**

We executed QBST and clinical monitoring in 286 patients with native AVF on chronic haemodialysis three times a week in our haemodialysis unit. We analysed data of patients with a follow-up ≥6 months (224 out of 286).

Clinical examination and QBST were always negative in 147 (66%) patients during the follow-up period (range 6–22, mean 18.0, SD ±4.9 months).

Twenty-three patients had a temporary QBST positivity due to needle misplacement; these were resolved by changing the cannulation site. Fifty-four out of 224 (24%) patients were selected for possibly malfunctioning AVF by means of QBST positivity (\( n = 34 \)), clinical evaluation (\( n = 16 \)) or both (\( n = 4 \)).

Seventy-nine imaging diagnostic procedures were performed (Doppler ultrasonography, angiography) in the 54 selected patients with the following results: 38 patients underwent one procedure each, while 16 patients underwent 41 procedures (on average 2.5 procedures per patient). We found no stenosis in 13 out of 54 (24%) patients, inflow stenosis in 29 out of 54 (54%) and outflow stenosis in 12 out of 54 (22%). The QBST positive predictive value (PPV) for inflow stenosis was 76.3% (29 out of 38), while the test was not able to identify outflow stenosis (PPV = 0%).

The clinical evaluation PPV for inflow stenosis was 20% (four out of 20) and for outflow stenosis was 60% (12 out of 20).

The overall PPV for both inflow and outflow stenoses was 80% (16 out of 20) and the NPV was 88% (179 out of 204), while sensitivity was 39% (16 out of 41) and specificity was 98% (179 out of 183) (Table 1). Combining the two tests, the PPV for all stenoses resulted to 75.9% (41 out of 54), while sensitivity was 100% (41 out of 41) and specificity was 93% (170 out of 183) (Table 1). It results that clinical evaluation alone was able to detect 39 of 100 patients with stenosis, while clinical evaluation plus QBST was able to detect all 100 patients with stenosis, with a gain of 61 correct diagnoses, reducing the specificity only by 5%.

Clinical examination was able to detect 39% (\( n = 16 \)) of the total number of stenosis, while the QBST detected 71%

### Table 1. Number of patients with and without stenoses according to clinical evaluation alone and clinical evaluation plus QBST

<table>
<thead>
<tr>
<th>Stenoses</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical evaluation</td>
<td>Positive</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>25</td>
<td>179</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>41</td>
<td>183</td>
</tr>
<tr>
<td>Clinical evaluation and QBST</td>
<td>Positive</td>
<td>41</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>0</td>
<td>170</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>41</td>
<td>183</td>
</tr>
</tbody>
</table>

\( n = 29 \). The chi-squared test, to compare the results of the two tests, was highly significant (\( P < 0.0001 \)).

Thirty-eight percutaneous angioplasty (PTA) procedures were performed by the same interventional radiologist in 33 patients (11 PTA per 100 patient-years); in five patients, it was necessary to perform a further surgical procedure to correct the stenosis (PTA success rate 84.8%). Thirteen new surgical AVF (3.7 per 100 patient-years) were created by the same interventional nephrologist team.

During 22 months of follow-up, only five thrombosis episodes occurred in five patients (1.5 thromboses per 100 patient-years). Three of them had positive QBST and documented stenosis, and thrombosis occurred before the correction procedures. Two patients had negative QBST and thrombosis was due to a subsequent infection.

### Discussion

The superiority of the native AVF as a vascular access for haemodialysis patients is a recognized fact, and it is due to its lower complication (infections, thrombosis) rates compared to arteriovenous polytetrafluoroethylene grafts. The major complication occurring in a native AVF is venous stenosis and it represents the main cause of access failure, negatively affecting patency and survival [6,7,19,20].

Analysing the various causes of AVF thrombosis, Schwab et al. reported that the thrombotic event can be mostly attributed to unrecognized stenosis [6].

Several authors described the JAS stenosis as the more frequent cause of AVF failure [7–9,11,20]. To summarize, the JAS area is a surgical swing site prone to developing stenotic issues. According to the K-DOQI Guidelines, it belongs to the ‘inflow stenosis’ group and theoretically could be detected with an accurate QA measurement.

The literature provides some agreement on the utility of QA assessment for grafts surveillance, while data available are conflicting about the real need of using it for monthly AVF surveillance, mainly because of the lower thrombosis rate characteristic of this type of vascular access [13,18] and because of the capability of AVF to maintain patency at a flow much lower than grafts [4,5]. However, it is not always possible to evaluate the QA measurement, in particular when there are multiple non-communicating outflow veins [17]. Moreover, it depends critically on the needles’ orientation [22], is time-consuming and requires a dedicated dialysis staff.
The K-DOQI Guidelines [4,5] recommend performing angiography in grafts if QA is <600 ml/min or <1000 ml/ min decreased by more than 25% over 4 months. However, until now, the literature has failed to provide consistent data about the QA threshold for intervention in native AVF.

According to Tonelli and colleagues [23], a QA <500 ml/min has a strong PPV for stenosis: 81% of the AVF with QA below this value improved with PTA. On the contrary, Tessitore et al. [24] reported a QA <700–1000 ml/min and/or a QA reduction of 25% as best predictors of stenosis (91% efficiency). Finally, some authors [25] believe that a single QA threshold for addressing angiography is an oversimplification. The optimal limit can change, depending on the various patient features (age, comorbidities, etc.) and on the AVF location.

To our knowledge, there are no controlled randomized studies able to provide evidence that QA assessment, together with frequent routine clinical monitoring, can significantly reduce thrombosis incidence rates.

According to some authors [26], the monthly clinical QA measurement in AVF is excessive compared to the low incidence of stenoses in the natural history of a native AVF. McCrory et al. [27] prospectively followed up 132 patients and reported a 2-fold thrombosis reduction rate using QA monitoring with UDT compared to no monitoring at all, but the result did not reach statistical significance. Others reported that adding QA assessment to the clinical examination does not reduce the stenosis rate. In particular, Shahin et al. [28] compared 76 patients monitored monthly with UDT with a historical control group of 146 subjects followed up with clinical examination alone and outlined that the monthly QA measurement caused a 7-fold PTA rate increase, without reducing the thrombosis incidence rate. Recently, Polkinghorne et al. [29], in a randomized study in 137 patients, pointed out that QA monitoring with UDT in addition to physical screening doubles the angiographic stenosis detection, but statistical significance is lacking.

The vascular access monitoring program is routinely performed by dialysis nurses and is very expensive [30,31]. The main purpose of this study is to demonstrate the utility of AVF monitoring with a new low-cost screening test: the QBST.

The main findings of our study are the following:

(i) the QBST is a simple screening test created to identify AVF stenosis and it has a good correlation with QA;

(ii) this test can only select malfunctioning AVF with stenosis located in the inflow tract (JAS stenosis);

(iii) our data demonstrated that it is possible to achieve a low AVF thrombosis rate with a surveillance program based on regular clinical monitoring and QBST, coupled with elective stenosis revision by PTA or surgery.

In our study, we propose an easy test, with simple premises, administered by the haemodialysis nursing staff during an ordinary haemodialysis session, without changing the needles’ position and without modifying the treatment for more than a few minutes, to monitor AVF performance.

For 2 years, the QBST has been performed monthly in our Dialysis Unit and Ambulatory Outpatient Haemodialysis Units, and it simplified native AVF surveillance, which represents the great majority of vascular accesses (about 86%) in our patients, like in other dialysis units in Europe [25,31].

Clinical examination and QBST were always negative in 170 (76%) patients, without requiring any other vascular access control procedure, since these subjects did not show any kind of clinical problem related to their AVF during the study period.

The application of our test makes it possible to perform a selective screening for inflow stenosis, in particular those at the JAS level. An inflow stenosis provokes a QA reduction indirectly detectable with the QBST: in fact, the earlier the arterial pressure alarm appears, the more haemodynamically significant is the stenosis, owing to a greater flow reduction and to the impossibility to generate higher QB values. Our follow-up data confirm that, more frequently, the stenosis location is at the AVF inflow, as previously reported by other authors [7–9].

Because of the early detection of malfunctioning AVF, we observed a very low incidence of thrombosis in our series during the follow-up (only five episodes over a 22-month period, equal to 1.5 events per 100 patient-years), similar to those reported by other authors like Basile et al. (4.3 AVF thromboses per 100 patient-years) [26].

The development of this test favoured the onset of a surveillance vascular access team (composed by interventional nephrologists, radiologists and dialysis nurses): the efficacy of the QBST could also be related to this dedicated vascular access team.

Limitations

This study has several limitations.

Firstly, our test was created starting from the clinical need to perform an efficient and simple AVF surveillance program, without adding further costs. This is a limit itself because all the efforts were concentrated on the positive patients.

Secondly, we could not evaluate the test sensitivity and specificity with respect to angiograms because angiograms were performed only in QBST positive patients, for ethical reasons (with or without clinical examination suspicion). Furthermore, we calculated sensitivity and specificity considering negative all patients without any fistula problem during the follow-up.

Conclusion

Considering the good correlation between QBST and QA measured with UDT, our study demonstrated that this test is simple, low-cost, not operator-dependent and could be a useful tool to identify the group of patients with malfunctioning AVF, with stenosis located specifically in the inflow tract. Our follow-up data demonstrated that it is possible to achieve a low AVF thrombosis rate by adding QBST in the AVF monitoring program, thus reducing the surveillance burden.
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Conflict of interest statement: None declared.

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