ANNEXES TO CHAPTER 4

Clinical Question XIII. Which non-invasive monitoring or surveillance screening method for haemodialysis arteriovenous fistula presents predictive power of stenosis and thrombosis and increased patency of the native arteriovenous fistula in the prevalent patient and what is the frequency?

There are two main non-invasive monitoring options for patients with grafts on haemodialysis. The first is normal clinical monitoring of the vascular access, based on physical examination and/or presence of clinical signs of dysfunction; signs such as difficulty inserting the cannula or prolonged bleeding after dialysis.

The second option involves different variants of active surveillance, including measuring blood flow in the AVF (Qa) and measuring venous blood pressure during dialysis. In both tests, when the results cross a certain predetermined threshold, patients are referred for intervention to try to correct the stenosis.

There is fairly broad consensus on the utility of clinical monitoring, but not on regular active surveillance with measuring of vascular access flow and/or static dialysis venous pressures, or with ultrasound scanning. While some guidelines (KDOQI 2006/2009; Polkinghorne 2008) recommend active surveillance with the above tests, other authors question their routine use for all vascular access sites and argue that the measuring of blood flow or venous pressure are useful tests when there is clinical suspicion of stenosis or access dysfunction (Paulson 2012, 2013).

Predictive power of the various methods for detecting stenosis and thrombosis of vascular access

The prospective study by Asif (2007) with 142 patients with AVF analysed the precision of the physical examination for detecting stenotic lesions by comparison with angiography, which is considered the *gold standard* test. The sensitivity and specificity of physical examination were 92% and 86% respectively for *outflow stenosis* and 85% and 71% for *inflow stenosis*.	**Low quality**
The Campos study (2008) investigated the precision of physical examination and measurement of pressure within the access for detecting stenotic lesions by comparison with Doppler ultrasound, which they use in the study as standard technique. Of the 84 patients analysed, 50 (59%), were positive for stenosis by Doppler ultrasound imaging. In the physical examination, 56 patients were positive, meaning a sensitivity of 96% for the test, a specificity of 76%, a positive predictive value of 86% and a negative predictive value of 93%. In the measurement of pressure within the access, 34 patients (40%) tested positive, meaning a sensitivity of 60% for the test, a specificity of 88%, a positive predictive value of 88% and a negative predictive value of 60%.	**Low quality**

Clinical benefit of screening compared to routine practice	
We found two systematic reviews, both published the same year, with meta-analyses that address the clinical effects of these two options: Tonelli (2008) and Casey (2008). The Tonelli review only includes randomised clinical trials (RCT), whereas Casey also includes non-randomised studies. Both articles identified the same RCT and came to the same conclusions. For these CPG, we refer to the Tonelli meta-analyses (2008) as they provide more complete data on the stratified analysis for patients according to whether they had AVF or graft and, separately, we present the results of the latest RCT (Scaffaro, 2009), published after the Tonelli review, which is included in the review by Kumbar (2012). The Tonelli systematic review with meta-analysis (2008) found four RCT that compared active surveillance of the vascular access (using flow measurements or ultrasound) to routine clinical monitoring in patients with AVF (Sands 1999; Tessitore 2003; Tessitore 2004; Polkinghorne 2006). The studies included a total of 383 patients (206 in active surveillance and 177 in routine care). Only one of the studies had a low risk of bias in relation to areas such as blinding of allocation or double blinding. The Scaffaro RCT (2009), which included patients randomised by means of sealed envelopes, was not blinded.	
Risk of thrombosis in the vascular access In the meta-analysis with data from four RCT and 360 patients, Tonelli (2008) found the risk to be decreased with active surveillance by ultrasound, with the difference being statistically significant (Relative Risk 0.47; 95% CI: 0.28 to 0.77). The RCT by Scaffaro (2009), with 108 patients, found a lower rate of thrombosis in the intervention group (17.0% vs 24.1%), but the differences were not statistically significant (p=0.49).	**Low quality**
Time to thrombosis Performing a meta-analysis with data from two RCT and 158 patients, Tonelli (2008) found that the time to onset of thrombosis was much longer in screened patients (Hazard Ratio 0.30; 95% CI: 0.16 to 0.56), but did not specify the duration of follow-up.	**Low quality**
Loss of access In the meta-analysis with data from two RCT and 141 patients, Tonelli (2008) found no statistically significant differences (Relative Risk 0.65; 95% CI: 0.28 to 1.51).	**Low quality**
Time to loss of access With data from one RCT and 60 patients, Tonelli (2008) found differences with slight statistical significance (Hazard Ratio 0.38; 95% CI: 0.14 to 0.99).	**Low quality**
Patients' values and preferences *No relevant studies related to this aspect have been identified.*	

Use of resources and costs

No specific cost-effectiveness studies were found that analyse these interventions in the environment in which the Guidelines are to be applied. There are also no studies on the budgetary impact that would potentially derive from widespread continuous and periodic use of active surveillance techniques by ultrasound scanning in patients with AVF in our setting. It would probably represent a significant increase in the costs of caring for this group of patients and it is likely that the incremental cost-effectiveness ratio would be high.

With data from one RCT and 60 patients, providing low quality evidence, Tonelli (2008) found statistically significant differences in relation to number of catheter insertions (RR 0.20; 95% CI: 0.04 to 0.88; data from one RCT and 60 patients) and the number of hospitalisations (RR 0.37; 95% CI: 0.16 to 0.87; data from one RCT and 60 patients).

However, the differences were not statistically significant in relation to number of angiograms, number of percutaneous angioplasty procedures, number of surgical interventions or number of revisions.

The RCT by Scaffaro (2009), with 108 patients, providing low quality evidence, found the need for central venous catheters for dialysis to be lower for the intervention group (7.5% vs 25.9%; p=0.021).

Summary of evidence

Monitoring by means of physical examination is a test with high sensitivity and acceptable specificity, providing high positive and negative predictive values.	**Low quality**
Active surveillance by measuring flow rates and ultrasound scanning reduces the risk of thrombosis.	**Low quality**
Active surveillance by measuring flow rates and ultrasound scanning reduces the need for central venous catheters for dialysis.	**Low quality**
Active surveillance by measuring flow rates and ultrasound scanning does not reduce the rate of loss of vascular access.	**Low quality**
There are no studies on the cost effectiveness or the budgetary impact that would potentially derive from widespread continuous and periodic use of active surveillance techniques by measuring flow rates and ultrasound scanning in these patients in our setting.	**Low quality**

Recommendations [Proposal]

Weak	We recommend routine clinical monitoring by means of physical examination in patients on haemodialysis via AVF.
Weak	In patients on haemodialysis with AVF, we recommend that the use of surveillance techniques with flow measurements and ultrasound be restricted to patients whose physical examinations are positive and for subjects enrolled in studies to evaluate the validity of the surveillance technique.

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Table 1. STUDIES EXCLUDED

Study	Cause for exclusion
Thomsen 1985	Does not analyse any non-invasive monitoring or surveillance methods. It compares clinical and radiological signs in the preoperative assessment of patients with uraemia and vascular access fistula problems.
Rose 2013	Expert opinion.
Tessitore 2013	Does not compare different non-invasive AVF monitoring or surveillance strategies. The aim of the study, as expressly stated by the authors, is to question the recommendations or guidelines, such as the Kidney Disease Outcomes Quality Initiative (KDOQI), that propose intervening only when there is significant stenosis (>50%) and/or inflow Qa (<300-500 ml/minute.) The study by Tessitore (2013), is an RCT which compared the effectiveness of early intervention (by surgery or percutaneous angioplasty) in fistulae with subclinical stenosis and inflow (Qa) greater than 500 ml/minute versus the option to wait and treat only patients who develop significant stenosis in the fistula and have signs of access dysfunction or inflow (Qa) less than 400 ml/minute. The 58 patients included in this study had fistulae with subclinical significant stenosis confirmed by angiography (>50% reduction in the vessel diameter compared to adjacent segment on biplane angiography) and a Qa >500 ml/min, after being previously identified by a surveillance programme based on criteria considered highly sensitive in the detection of stenosis: the combination of a positive physical examination and a Qa <900 ml/min or a derived static venous pressure (vascular access pressure ratio: VAPR) >0.5. They measured the Qa using the ultrasound dilution method with the HD03 monitor within 30 to 150 minutes after starting dialysis, in a dialysis session with no cardiovascular haemodynamic instability. The Qa values were the mean of the measurements made in triplicate and the VAPR values were the mean of five measurements taken during a single dialysis session. None of these fistulae had had any surgical and/or endovascular treatment within the three months prior to the assessment. The results, that they present as interim or preliminary, were that the option of acute management of fistulae with stenosis and flow >500 ml/minute showed statistically significant better outcomes with regard to the risk of thrombosis (RR 0.37; 95% CI: 0.12 to 0.97; p=0.033) and loss of access (RR 0.36; 95% CI: 0.09-0.99; p=0.041), and also favourable outcomes with regard to the risk of access failure (RR 0.47; 95% CI: 0.17 to 1.15; p=0.090), although this last difference was not statistically significant. Not significant differences were found between the two strategies in costs.

GRADE TABLES

Date: 2013-10-20
Question: Should ultrasound monitoring vs standard care be used for patients on haemodialysis with AVF?
Settings: hospital
Bibliography: Tonelli M, James M, Wiebe N, Jindal K, Hemmelgarn B; Alberta Kidney Disease Network. Ultrasound monitoring to detect access stenosis in hemodialysis patients: a systematic review. Am J Kidney Dis. 2008 Apr; 51(4):630-40.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ultrasound monitoring	Standard care	Relative (95% CI)	Absolute		
Thrombosis												
4	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	RR 0.47 (0.28 to 0.77)	-	LOW	CRITICAL
								0%		-		
Thrombosis (surveillance every 3 months)												
1	randomised trials	serious	no serious inconsistency	no serious indirectness	serious	none	9/53 (17%)	14/58 (24.1%)	RR 0.70 (0.33 to 1.49)	72 fewer per 1000 (from 162 fewer to 118 more)	LOW	CRITICAL
								0%		-		
Access loss												
2	randomised trials	very serious	no serious inconsistency	no serious indirectness	serious[2]	none	-	-	RR 0.65 (0.28 to 1.51)	-	VERY LOW	CRITICAL
								0%		-		
Need of central venous dialysis catheters (follow-up mean 3 months)												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	-	RR 0.29 (0.1 to 0.82)	-	MODERATE	IMPORTANT
								0%		-		

[1] Allocation concealment and double blinding only done in one of the four studies.

[2] Wide confidence interval.
[3] No blinding.