IDENTIFICATION OF EARLY BIOMARKERS OF ARTERIOVENOUS FISTULA (AVF) STENOSIS: THE ROLE OF CIRCULATING PLASMA MICROVESICLES (MV)

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TOPIC: Dialysis – vascular access

INTRODUCTION AND OBJECTIVES

A functional arteriovenous fistula (AVF) is the mainstay to perform adequate hemodialysis and to improve patient's survival. The primary complication that causes AVF failure is stenosis with subsequent thrombosis [1]. Surveying for stenosis can be performed by different ways: in this study, we first analyzed the role of Glucose Pump Test (GPT), an economic, quick and first level assay, to detect stenosis measuring access recirculation [2,3]; secondly, we evaluated correlations between some clinical parameters and novel biomarkers of microvascular injury such as circulating plasma microvesicles (MV) [4] and endothelial-derived von Willebrand factor (vWF) levels [5] in patients with significant (>50% of the access diameter) AVF stenosis.

METHODS

In the first part of the study, we retrospectively analyzed the results of 65 GPT performed in 31 hemodialysis patients with a critical AVF stenosis. Subsequently, 73 hemodialysis patients were enrolled: significant stenoses were identified by Doppler ultrasound (DUS) [6] and then correlated with socio-demographic parameters, clinical history and data from dialysis, AVF (including results of GPT) and laboratory (including MV phenotypic characterization and concentration of vWF).

RESULTS AND CONCLUSIONS

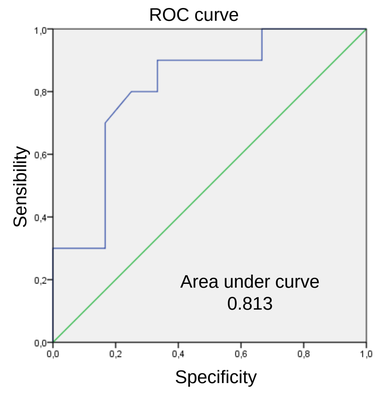
Retrospective analysis of 31 AVF showed a significant correlation between stenosis occurrence and GPT results (75th percentile value of 666 ml/min) or its variation when performed 6 months before angioplasty (66.1% of data with variation ≥ 25%). ROC curve revealed a cut off value of 687 ml/min for the diagnosis of AVF stenosis (**figure 1**).

DUS analysis of 73 patients showed 22 AVF with significant stenosis and 51 AVF with non significant or absent stenosis. We found a good correlation between significant stenoses and low achievement of prescribed blood flow (p<0.001), low Kt/V, bicarbonate hemodialysis (p 0.014) and previous angioplasty (p<0.001).

Concentration of plasma MV was significantly higher in patients with significant stenosis in comparison to non-complicated AVF (**figure 2**). Moreover, MV derived from stenotic AVF showed an increased expression of markers typical of endothelium (CD31, CD105, CD146) and platelets (CD41, CD42b, P-selectin) (**figure 3**).

Furthermore, we observed a significant increase in the concentration of vWF, an established marker of endothelial injury, in AVF stenosis group (p 0.001) (**figure 4**).

In conclusion, GPT may be considered as a valid first level test for monitoring AVF stenosis. However, in our experience the association between DUS and new biomarkers of microvascular injury, such as vWF and particularly endothelial-/platelet-derived MV, represents a new non-invasive diagnostic tool for monitoring AVF stenosis.



		Stenosis		Total
		Significant	No-significant	
GPT ≥ 687 ml/min	N° patients	8	3	11
	% in GPT687	72.7%	27.3%	100.0%
	% in stenosis	**80.0%**	**25.0%**	50.0%
	% of total	36.4%	13.6%	50.0%
GPT < 687 ml/min	N° patients	2	9	11
	% in GPT687	18.2%	81.8%	100.0%
	% in stenosis	**20.0%**	**75.0%**	50.0%
	% of total	9.1%	40.9%	50.0%
Total	N° patients	10	12	22
	% in GPT687	45.5%	54.5%	100.0%
	% in stenosis	100.0%	100.0%	100.0%
	% of total	45.5%	54.5%	100.0%

p. 0.01, odds ratio 12

Figure 1. GPT-ROC curve revealed a cut off value of 687 ml/min for the diagnosis of AVF stenosis

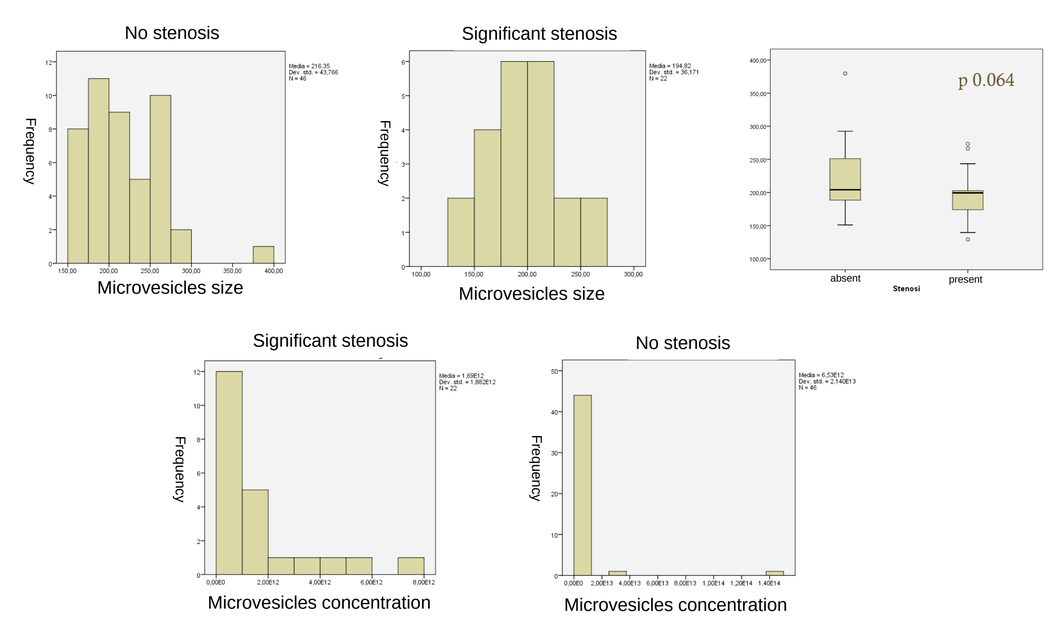
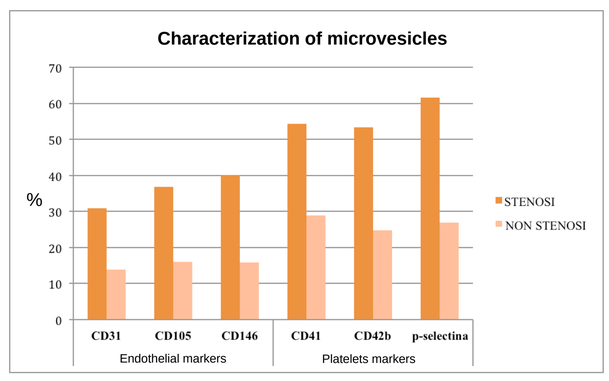


Figure 2. Size and concentration of plasma microvesicles in patients with and without significant AVF stenosis



	CD31	CD105	CD146	CD41	CD42b	p-selectina
Significant p	0.002	<0.001	<0.001	<0.001	0.002	0.002

Figure 3. Characterization of microvesicles

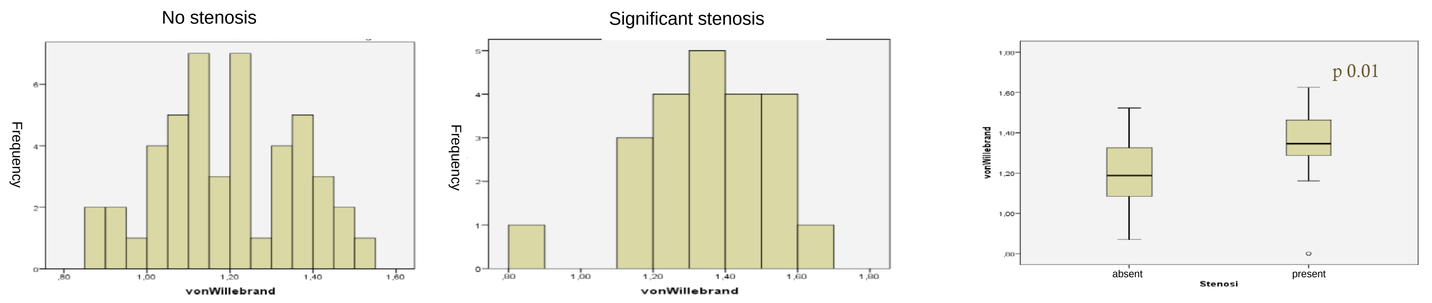


Figure 4. Concentration of vWF in patients with and without signifcant AVF stenosis

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DOI: 10.3252/pso.eu.54ERA.2017