

## The Influence of vascular access creation on plasma level of natriuretic peptide

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**BACKGROUND:** High access flow could lead to the development/worsening of chronic heart failure. Accesses with flow volume equivalent to  $>1/3$  of cardiac output are thought being hemodynamically significant. We hypothesized that also accesses with lower flow would lead to elevation of B-type natriuretic peptide (BNP), a marker of heart failure.

**SUBJECTS AND METHODS:** We included subjects with newly created, well functioning vascular access. All of them were examined before access creation (baseline) and 6 weeks after. BNP levels (6weeks vs. baseline) were compared using paired t-test.

**RESULTS:** We examined 30 subjects aged  $63.6 \pm 13.5$  years. Six weeks after surgery, access flow volume was  $709 \pm 311$  ml/min. BNP raised from  $231 \pm 144$  ng/L to  $428 \pm 438$  ng/L,  $p = 0.018$ .

**CONCLUSION:** Accesses with lower flow volumes also lead to heart overload. It is of clinical importance especially in subjects with chronic heart failure.

### Introduction

More than 50% of end-stage renal disease subjects treated by chronic hemodialysis die because of cardiovascular diseases. Chronic heart failure is one of the most important forms. Its high prevalence is influenced by many factors: accelerated coronary artery disease, intermittent volume overload between dialyses, anemia and also vascular access flow. The role of the latter is frequently underestimated (1). However, blood flow through normally functioning vascular access ( $Q_a$ ) is 500 –1500 ml/l, which represents 10-30% of normal resting cardiac output. These values are highlighted if taking to account the previously mentioned factors. Generally, it is thought that  $Q_a$  higher than  $1/3$  of cardiac output is clinically significant. We hypothesized that even lower  $Q_a$  would increase plasma level of brain natriuretic peptide (BNP), marker of heart failure. To confirm this hypothesis, we examined a group of subjects before and after access creation. In this article, we also describe 2 interesting case reports.

### Methods

Subjects coming to our hospital for creation of their first vascular access were asked to participate in this study. If agreed, they were examined within 4 days before

access creation, than 6 weeks after the surgery. Only subjects with any type of upper extremity accesses were included. All subjects were without manifest heart failure and assumed clinically stable either in the pre-dialysis phase or dialyzed via catheter. Subjects continued in the study only in case of well functioning access (defined by  $Q_a > 300$  ml/min).

During all examinations, vascular access ultrasonography was performed and blood drawn for BNP analysis.

All ultrasound examinations were performed by a linear array 11 MHz ultrasound probe of SONOS 5500 (Phillips, USA) device. First, the access was carefully examined for the presence of stenosis or other complications, as described earlier(2).

$Q_a$  was calculated as  $\pi r^2 v_{\text{mean}}$ , where  $r$  is radius of the examined vessel and  $v_{\text{mean}}$  is the time-velocity integral of averaged velocity layer during cardiac cycle. We have previously validated the accuracy of fistula flow volume measurement by ultrasonography (3). Results obtained by ultrasound tightly and significantly correlated with values obtained by thermodilution technique ( $r = 0.89$ ,  $p < 0.01$ ). Mean difference of values obtained by these 2 methods was 10%.

## Results

We included 30 subjects aged  $63.6 \pm 13.5$  years, (17 women, 18 diabetics). Four subjects had to be excluded because of access failure (2 cases), unwilling to continue (1 case) and death (1 patient).

Access flow was  $709 \pm 311$  ml/min six weeks after the surgery. BNP raised from  $231 \pm 144$  ng/L to  $428 \pm 438$  ng/L,  $p = 0.018$ . None of the subjects developed overt heart failure after access creation in this period.

### Case 1

A lady aged 45 years had end-stage kidney failure because of hereditary polycystosis. She had no history of heart disease. Examination in our lab was performed due to 6 months lasting shortness of breath at mild exercise. She had dilated native brachiocephalic access. Flow volume was measured by ultrasound at the feeding artery and was 4700 ml/min! We were confused by this value, so performed echocardiography, where was dilated left ventricle with ejection fraction

35%, but measured cardiac output 11 l/min. Surgical banding of the outflow vein was performed and symptoms of heart failure disappeared together with echocardiographical abnormalities within 3 months.

## Case 2

A lady, aged 75 year, without diabetes mellitus, with treated hypertension had end-stage kidney failure because chronic pyelonephritis. Before access creation, she had normal size and systolic function of her left ventricle. She developed pulmonary congestion and repeated pulmonary oedema 3 months after access creation. Our colleagues from another department knew about our research and referred this lady to us, because they suspected high access flow. However, Qa was only 750 ml/min and her left ventricle ejection fraction was 60%. BNP was 5800 ng/L. During the ultrasound examination, she developed again a pulmonary oedema with blood pressure on the upper extremity without access 120/65 mmHg (taking non-invasively). She was moved to coronary care unit, where the blood pressure was monitored invasively from the femoral artery. Surprisingly, we obtained values around 270/160 mmHg, which clearly explained pulmonary oedema. Subsequent examinations revealed bilateral stenosis of subclavian arteries, causing falsely low blood pressure values. Her status improved after new lipid-lowering drugs.

## Discussion

These preliminary data of our research of the impact of vascular access on heart failure have shown that creation of vascular access leads to increase of BNP even in "normal" values of Qa. It documents clinically silent changes in heart physiology, which could, together with other factors mentioned in Introduction play a role in the development of subsequent heart failure. Heart disease is very frequent in hemodialyzed subjects - Parfrey et al. observed normal echocardiographic findings in only 16% of hemodialyzed subjects(4).

One of possible deteriorating mechanisms could be increased sympathetic tone. Tamura et al.(5) observed increased sympathetic tone in end-stage renal disease subjects with lower hematocrite. Lower hematocrite leads similarly as creation of vascular access to hyperkinetic circulation. Hayano et al. documented higher mortality in subjects with increased sympathetic tone(6).

Vascular access is, of course, crucial for subjects treated by hemodialysis. Higher Qa is associated with longer access patency and this is the reason, why sometimes Qa around 2000ml/min is maintained until it causes any symptoms of heart failure. Further research should confirm if this strategy is or is not associated with higher morbidity and/or mortality. It is also an argument for routine Qa monitoring, which is still not provided in all hemodialysis centers. Fortunately, hyperkinetic heart failure is reversible, if treated without delay, as shown by Chemla et al.(7) or our Case 1.

To conclude, Qa should be kept in mind in both research and clinical care of subjects with heart failure, despite its impact is sometimes overestimated (Case 2).

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