

Activity Report

2014

An integrated approach to cardiovascular function for outcome prediction in severe aortic stenosis: the role of exercise echocardiography

Contract no. 21/29.08.2013

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The main objective of our study is to evaluate prognostic markers of clinical outcome in asymptomatic patients with severe AS and preserved LVEF, using an integrated approach to assess the vascular, left ventricular and left atrial function, both at rest and at exercise. We want to assess for the first time the predictive value of exercise induced response of LV myocardial deformation parameters, LV untwisting, E/E' ratio, BNP serum level and impaired LA functional reserve in asymptomatic patients with AS using exercise echocardiography. In these patients we also intend to evaluate the prognostic role of arterial stiffness, LV torsion/untwisting and LA dysfunction evaluated at rest by state-of-the-art echocardiographic techniques.

Our secondary objectives are:

- to perform a **comparative assessment of both vascular and cardiac function in asymptomatic versus symptomatic patients with severe AS and preserved LVEF**, with a particular interest in studying the parameters related to arterial stiffness, LV torsion/untwisting and parameters of LA function.
- to assess **the impact of AVR on a range of parameters of cardiac function in symptomatic patients with AS** focusing on LV torsional deformation parameters, LV untwisting and LA function parameters, that were not studied yet in this clinical setting.

The results obtained so far according to the project were:

1. *Recruitment of patients with severe AS and preserved left ventricular ejection fraction (LV EF)* - 86 patients with AS were examined between December 2013 - December 2014 and all of them underwent an initial clinical and echocardiographic evaluation to determine the study eligibility. Of these, a total of 42 patients were included in the study and evaluated according to the previously established protocol - 13 asymptomatic patients with severe AS and preserved LV EF (group 1) and 29 symptomatic AS patients with preserved LV EF (group 2) .

2. *Clinical and ECG evaluation of patients included in the study* : all patients were evaluated for symptoms and signs of heart failure, syncope or angina, and treatment in groups 1 and 2. A resting ECG was recorded for all patients to exclude arrhythmias or conduction disorders.

3. *Biological assessment*: blood samples were collected to determine the serum BNP in asymptomatic patients with severe AS before and immediately after echocardiographic exercise testing.

4. *Resting echocardiography* (for the 3 groups: group 1, group 2 and group 3- the control group with normal subjects) was performed according to the following protocol:

- ultrasound examination using a Vivid E9 (GE Healthcare, Horten, Norway) equipped with a M5S and 4V probe.

- BP measurement was made immediately before resting echocardiographic examination

- all image acquisitions were performed according to the EAE recommendations, digitally stored in raw-data format and exported to a separate workstation equipped with commercially available softwares for offline analysis (EchoPac BT12, GE Healthcare, Horten, Norway).

- in addition to the standard examination were carried out :

- short axis views of LV at the mitral valve (base), papillary muscles and apex with a frame rate of 50-90 fps, with similar heart rate, three cardiac cycles

- apical 4, 3 and 2 chamber views of the LV with a a frame rate of 50-90 fps, with similar heart rate, three cardiac cycles

- apical 4, 3 and 2 chamber views of the LA with a a frame rate of 50-90 fps, with similar heart rate, three cardiac cycles

- apical 4, 3 and 2 chamber views of the LV with color TDI with a frame rate >110 fps, similar heart rate, three cardiac cycles

- apical 4, 3 and 2 chamber views of the LA with color TDI with a frame rate >110 fps, similar heart rate, three cardiac cycles.

5. *Exercise echocardiography by supine cycloergometer* (for group 1 and group 3 - control)

- a symptom-limited exercise test on a supine bicycle ergometer (ErgoLine sistem) according to a standardized protocol (increments of 25 W every 2 min), with simultaneous recording of ECG and BP monitoring

- images were recorded at low workload (ie at a heart rate 20 bpm higher than at rest), at the end of each step and at peak exercise. Total exercise time, maximum workload, peak heart rate, blood pressure and the reason for stopping the test were recorded.

The following LV parameters were measured during exercise:

- CW Doppler across the aortic valve to measure the transaortic peak and mean gradients
- PW Doppler in the LV outflow tract
- Septal and lateral myocardial velocities using PW TDI
- Short axis views of the LV at the mitral valve and apex to assess LV basal and apical rotation and rotation rates, LV torsion and untwisting rate; short axis views of LV at papillary muscles to assess radial and circumferential deformation
- apical 4, 3 and 2 chamber views of the LV to assess LV EF by Simpson biplane method and GLS using speckle-tracking echocardiography (STE)
- apical 4 chamber view of the LA to assess LA function parameters using STE.
- LV and LA functional reserve were calculated according to the following formula:
Functional reserve = (Peffort-Prest) x [1-(1/Prest)] where P is the analyzed LA/LV parameter.

The reasons for stopping the exercise test were: achieving maximum cardiac frequency (calculated for age), intense dyspnea, angina accompanied by changes in LV segmental kinetics, drop of > 20 mmHg in BP, ventricular or supraventricular arrhythmias.

6. *Arterial stiffness parameter* were assessed, after 15 minutes of rest, by measuring carotid arterial diameter variations using an echo-tracking system. Time-velocity curve resulted from the correlation between carotid diameter variations and brachial blood pressure values. Measurements were made at the right common carotid artery level, ~ 2cm before the bifurcation, in a region free of plaque. The resulting pressure curve derived the arterial stiffness and distensibility parameters:

- stiffness index beta = $\ln(Ps/Pd)/(Ds - Dd/Dd)$
- arterial compliance, $AC = \pi (Ds \times Ds - Dd \times Dd)/4(Ps - Pd)$
- augmentation index, AIx
- pulse wave velocity, PWV
- pressure-strain elastic modulus, E_p

7. *Ambulatory blood pressure monitoring (ABPM)/24 hours* was performed in group 1 and group 2 – for 8 patients with symptomatic AS and uncertain history of arterial hypertension.
8. *Cardio-pulmonary exercise testing with determination of gas exchange* for the assessment of peak oxygen consumption was performed in group 1 (patients with asymptomatic AS).
9. *Patients in group 1 were followed-up at 3 months* after the enrollment, in 2014, by phone, and the adverse events were noted in patients records tracking.
10. *Patients in group 1 were followed-up at 6 months* after the enrollment: these patients underwent a clinical re-evaluation, ECG and echocardiographic re-examination.
11. *Patients in group 2 were followed-up at 3 months after aortic valve replacement*: these patients underwent a clinical reevaluation, ECG and echocardiographic reexamination
12. *Managing collected and recorded data*: clinical data, ECG, rest and exercise echocardiography were filed, and most of these data have been exported to an excel type file.
13. *Providing logistical support for the project* – we have made all steps to acquire the necessary equipment, inventory objects and materials for the proper development of the project; many of these objectives were achieved in 2013. In 2014 there were only medical materials and office supplies necessary for the proper development of the project.
14. *Internal evaluation of partial results of the project* - results were analyzed by team members
15. *Disemination of partial results*

In 2014 original papers regarding LV function in patients with aortic stenosis were accepted and presented at the National Congress of Cardiology – Sinaia, october 2014 and at the EuroEcho Imaging Congress 2-7 december 2014, Vienna.

These papers have been published as original abstracts in the *Romanian Journal of Cardiology* and *European Heart Journal - Cardiovascular Imaging*:

Călin A, Roșca M, Beladan CC, Crăciun Mirescu A, Gurzun MM, Mateescu A, Enache R, Ginghină C, Popescu BA. Dinamica torsiunii ventriculului stâng la pacienții cu stenoză aortică strânsă și fracție de ejeecție ventriculară stângă păstrată – relația cu statusul simptomatic; *Romanian Journal of Cardiology*; Supliment A, 2014; 177-178; ISSN: 1583-2996. Cod CNCSIS 379 (Categoria B+) (National Congress of Cardiology, Sinaia 2014. Oral presentation.)

Beladan CC, Călin A, Roșca M, Craciun A, Gurzun MM, Călin C, Enache R, Ginghină C, Popescu BA. Impactul severității hipertensiunii arteriale sistemice asupra statusului funcțional și al funcției ventriculare stângi la pacienți cu stenoză aortică strânsă. *Romanian Journal of*

Cardiology; BDI; Supliment A, 2014; 107-108. ISSN: 1583-2996. Cod CNCSIS 379 (Categoria B+) (National Congress of Cardiology, Sinaia 2014. Poster presentation.)

Călin A, Roșca M, Beladan CC, Crăciun Mirescu A, Gurzun MM, Mateescu A, Enache R, Ginghină C, Popescu BA. Left ventricular torsional dynamics in symptomatic versus asymptomatic patients with severe aortic stenosis and preserved left ventricular ejection fraction. *European Heart Journal Cardiovascular Imaging*, 2014, Suppl – Poster presentation at EuroEcho Imaging 2014

Beladan CC, Călin A, Roșca M, Craciun A, Gurzun MM, Călin C, Enache R, Ginghină C, Popescu BA. Systemic hypertension in patients with severe aortic stenosis: does the severity of hypertension make a difference? *European Heart Journal Cardiovascular Imaging*, 2014, Suppl – Poster presentation at EuroEcho Imaging 2014

Team members lectured on topics related to the current project at scientific international and national meetings:

Andreea Calin. "Stenoza aortica asimptomatica - continua provocare" Invited lecture. National Congress of Cardiology 10.10.2014 - Sinaia

Besides these, the team members were also involved in developing original papers and lecturing on topics related to the current project:

A.D. Mateescu, **R. Enache**, O. Nastase, D. Botezatu, A. Buture, **B.A. Popescu, C. Ginghină.** Proprietățile elastice ale vaselor mari la pacienții cu valva aortică bicuspidă. *Romanian Journal of Cardiology*; BDI; Supliment A, 2014; 49-50; ISSN: 1583-2996. Cod CNCSIS 379 (Categoria B+) (National Congress of Cardiology, Sinaia 2014. Poster presentation.)

R. Enache, A.D. Mateescu, O. Năstase, **B.A. Popescu**, A. Buture, **C. Ginghină.** Cuplarea ventriculo-arterială la pacienții cu bicuspidie aortică – evaluare ecocardiografică. *Romanian Journal of Cardiology*; BDI; Supliment A, 2014; 87-88; ISSN: 1583-2996. Cod CNCSIS 379 (Categoria B+) (National Congress of Cardiology, Sinaia 2014. Oral presentation.)

R. Enache, B.A. Popescu, D. Muraru, R. Piazza, **A. Călin, C.C. Beladan, M. Roșca, G.L. Nicolosi, C.Ginghină.** Influența remodelării ventriculare stânga asupra dinamicii torsionale la pacienții cu regurgitare aortică cronică și fracție de ejeție a ventriculului stâng normală. *Romanian Journal of Cardiology*; BDI; Supliment A, 2014; 108-109; ISSN: 1583-2996. Cod

CNCSIS 379 (Categoria B+) (National Congress of Cardiology, Sinaia 2014. Poster presentation.)

B.A. Popescu. Cardiomiopatia hipertrofica, Invited lecture during the session "Assessment of left ventricular function in different clinical scenarios", COMMON SESSION, Romanian Society of Cardiology– European Association of Cardiovascular Imaging (EACVI) - National Congress of Cardiology 2014

B.A. Popescu. B.A. Popescu. Evaluarea riscului și informarea pacientului, Invited lecture during the session "Guidelines on myocardial revascularization", COMMON SESSION, Romanian Society of Cardiology – European Association for Cardio-thoracic Surgery (EACTS) - National Congress of Cardiology 2014

Rosca M. Atrial function and ventricular cavity filling. Invited lecture at EuroEcho-Imaging Congress 2014

Rosca M. Imaging evaluation of left atrium. Invited lecture at EuroEcho-Imaging Congress 2014

In 2014 team members have written a review focused on the role of imaging in the evaluation of left ventricular function in patients with aortic stenosis. This article is currently under review for publication in Cardiovascular Ultrasound.

Project Manager

Assoc. prof. BA Popescu

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