

UPDATES IN CARDIOLOGY

Functional Aortic Root Parameters and Expression of Aortopathy in Bicuspid Versus Tricuspid Aortic Valve Stenosis

The aim of this prospective study is to analyze the correlation between the functional parameters of the ascending aorta and aortic pathology manifestation in patients operated for bicuspid aortic valve stenosis versus tricuspid valve. From January 1, 2012, until 31 December 2014, 190 patients underwent aortic valve replacement +/- proximal aortic replacement.

From January 1, 2012 until December 31, 2014, 190 patients (63 ~ 8 years, 67% male) underwent aortic valvular replacement +/- surgery on ascending aorta for aortic stenosis, bicuspid valve (n = 137, group BAV) and tricuspid (N = 53, group TAV). All patients were preoperatively examined using echocardiography and cardiac magnetic resonance imaging to assess morphological and functional parameters of the ascending aorta. The aortic tissue was collected during surgery based on the possibility of contact with the wall of the eccentric aortic blood flow, as determined by cardiac magnetic resonance (for example, jet sample and control sample jet). Lesions of the aortic wall were classified by using a histological sum score (0 to 21).

The largest cross-sectional aortic diameters were recorded in the middle segment upward in both groups and were higher in patients with BAV (40.2 ± 7.2 mm vs 36.6 ± 3.3 mm, respectively, $p < 0.001$). The histological sum score was 2.9 ± 1.4 in BAV group versus 3.4 ± 2.6 TAV group ($P = 0.4$).

The correlation was linear and comparable between aortic diameter and maximum angle between the left ventricular outflow axis and aortic root (LV / aorta angle) in both groups (BAV group: $r = 0.6$, $p < 0.001$ vs TAV group $r = 0.45$, $P = 0.03$, $z = 1.26$, $P = 0.2$). Through logistic regression was identified the angle between left ventricle / aorta as an indicator of indexed aortic diameter > 22 mm/m² (odds ratio: 1.2, $p < 0.001$).

The study shows association between functional / rheology parameters and aortic pathology and not provides definitive proof of causality. It remains to be determined whether these parameters are genetically influenced, or whether they simply represent a secondary phenomenon during progression of aortic valve stenosis associated aortopathy. It also shows comparable correlation patterns between

functional aortic root parameters and expression of aortopathy in patients with bicuspid aortic valve stenosis versus tricuspid. The current data support further the hypothesis that aortopathy in patients with BAV and TAV stenosis is a predominantly hemodynamically triggered phenomenon.

Evaldas Girdauskas, MD, PHD, Mina Rouman, MD, Kushtrim Disha, MD, Beatrix Fey, MD, Georg Dubslaff, MD, Bernhard Theis, MD, Iver Petersen, MD, PHD, Matthias Gutberlet, MD, PHD, Michael A. Borger, MD, PHD, Thomas Kuntze, MD Functional Aortic Root Parameters and Expression of Aortopathy in Bicuspid Versus Tricuspid Aortic Valve Stenosis-(J Am Coll Cardiol 2016;67:1786–96). (AP, RM)

Doppler echocardiographic measurements in Normal Chinese adult (EMINCE): a prospective, nationwide multicenter study

Currently, available Doppler echocardiography parameters reference are mainly from North America and Europe, which may not apply to the Chinese population. The aim of the study was to establish normal reference values of the Doppler echocardiography parameters in a healthy cohort of Chinese adults patients, across a wide range of ages. Since Han ethnicity is prevalent in China and represents almost 20% of world population, it is justified to establish some benchmarks.

Normal reference values of Doppler parameters are essential to distinguish normality from abnormality, and recent studies have reported a significant variation of these values with age and gender in healthy population. However, the normal reference values of Doppler velocities were never established by ASE guidelines, so it is difficult in practice to distinguish between a normal velocity and a slightly abnormal one.

Therefore, from January 2012 to December 2012, 1586 healthy volunteers were included in the study, at 43 collaborating echocardiography laboratories across China. Inclusion criteria required that all volunteers be aged between 18 and 79 years, of Han ethnicity, with normal blood pressure, a normal physical examination and normal electrocardiogram, and no history of cardiovascular disease.

Thus, a total of 1394 healthy subjects were qualified (mean age 47.3 ± 16.0 years, 678 men) and 37 transvalvular tissue Doppler parameters were obtained, analyzing the impact depending on gender and

age of each parameter. They found significant differences between men and women in 48.6% (18/37) of the analyzed parameters, and between different age groups at 83.8% (31/37) in men and 86.5% (32 / 37) in women.

From the mitral inflow spectra, they measured the peak velocities of early diastolic (E) and late diastolic (A) waves, E/A ratio, deceleration time (DT) of E wave and time duration of A wave (A-d). Similarity peak velocities of early diastolic (E-tv) and late diastolic (A-tv) waves, and E/A-tv ratio were measured from the tricuspid inflow spectra. The time duration of the right upper pulmonary venous reverse flow (Ar-d) was measured at atrial systole, and the time interval (Ar-A) between Ar-d and A-d was calculated. The peak systolic flow velocities at levels of LV outflow tract (LVOT-v), aortic valve (AV-v), right ventricular outflow tract (RVOT-v), and pulmonary valve (PV-v) were also measured.

Results showed that E-tv and E/A-tv were significantly higher in women than in men, which may be due to a much wider range of age and older population in the EMINCA study and also showed that values of E-tv and E/A-tv decreased, while A-tv increased with age in both genders. The age-stratified measurements of the mitral inflow E and E/A were decreased, whereas A and DT increased significantly with age groups in both genders ($P < 0.005-0.001$). Even though no differences between genders were found for the mean values of A-d, Ar-d, and Ar-A, the values of Ar-d and Ar-A increased with age groups in women ($P < 0.05-0.001$) but not in men. Measurements of peak systolic velocities across the aortic valve and the pulmonary valve were higher in women than in men ($P < 0.05-0.01$), whereas no gender differences were found for peak systolic velocities at LV outflow tract and right ventricular outflow tract. Velocities across the aortic valve, LV outflow tract, and right ventricular outflow tract in both genders and velocity across the pulmonary valve in men differed with age groups ($P < 0.05-0.01$), but these differences were not consistent across different age groups.

Therefore, the value of the mitral inflow E and E/A ratio decreased while A and DT increased gradually with ageing in both men and women. The age-related changes in these diastolic function parameters may reflect a prolonged LV myocardial relaxation, which may partially explain why older individuals are more prone to develop heart failure with preserved ejection fraction. On the other hand, values of the mitral inflow E and A in men were significantly lower than in women, which suggests that it is more appropriate to use gender-specified reference values in clinical practice.

An interesting finding is that as an index of LV relaxation, the septal, lateral, and average E' measurements did not differ between men and women in the whole population; however, they declined more rapidly with advanced age groups in women than in men.

The study has limitations, namely that has been applied only to Han ethnic group, in Chinese population, so it is difficult to apply to other racial groups, other studies on Chinese minorities to complete this study are needed.

In conclusion, the EMINCA study is the largest, prospective multicenter study conducted nationwide that established normal Doppler echocardiographic parameters reference in Chinese Han population of healthy adults. Most Doppler measurements differed with gender and age, and therefore the reference values set for women/men according to age should be recommended in everyday clinical practice.

Gui-Hua Yao, Mei Zhang, Li-Xue Yin, Cheng Zhang, Ming-Jun Xu, Yan Deng, Yan Liu, You-Bin Deng, Wei-Dong Ren, Zhi-An Li, Hong Tang, Quan-Bin Zhang, Yu-Ming Mu, Li-Gang Fang, and Yun Zhang, on behalf of the echocardiographic Measurements in Normal Chinese Adults (EMINCA) Study Investigators; *European Heart Journal – Cardiovascular Imaging* (2016) 17, 512–522. (AP, RM)

Temporal trends in the treatment and outcomes of elderly patients with acute coronary syndrome

The mortality rate related to coronary disease decreased over recent decades in many developed countries, even among older patients at high cardiovascular risk. Improving prevention helped reducing the incidence and improving adherence to guideline-treatment helped decrease the incidence of fatal cases. However, elderly patients with acute coronary syndrome continue to have an increased risk of mortality associated with complications.

Some studies and results on ACS (acute coronary syndrome) in older patients have suggested that negative results were attributable to poor adherence to guidelines recommended therapies. Current guidelines recommend the use of modern therapies for ACS, independent of age, but also recognize that less aggressive therapies can be justified to older patients with significant co-morbidities and reduced life expectancy. None of the current studies could not successfully answer this question, although some studies have suggested that the use of guideline-recommended therapies is unlikely beneficial in older patients.

The study presented is called AMI plus and is a prospective, cohort type of study, including patients with ACS admitted to hospitals from Sweden. AMIS Plus project includes 82 hospitals since 1977, ranging from regional hospitals to tertiary centers that are able to perform PCI or contract with another institution that can perform PCI. Patients included in the study were hospitalized with the following diagnoses: acute myocardial infarction with ST-segment elevation (STEMI), without ST-segment elevation (NSTEMI) or unstable angina.

The study population included all patients aged 70 years or older. They were enrolled 32500 ACS patients in the AMIS Plus study between January 1, 2001 and December 31, 2012 from 73 hospitals. Of these, 13 662 patients (42.0%) were patients aged 70 years or more and were included in this analysis. These patients were divided into 3 groups: 7974 septuagenarians (58.4%), 5009 octogenarians (36.7%) and 679 nonagenarians (5%). Guidelines recommendations were analyzed separately for each of the three age groups, according to three periods of 4 years (2001-2004, 2005-2008 and 2009- 2012) and an descriptive analysis has been applied for the general study population and separately for each age group; finally they were evaluated associations between use of PCI in hospital and mortality separately for the three 4-year period.

Regarding the evaluation of therapy use, they were selected seven therapies that were recommended by guidelines during the entire study period and irrespective of age. Therapies evaluated were: (i) use of acetylsalicylic acid in combination with either a P2Y₁₂ blocker or a glycoprotein IIb/IIIa inhibitor, (ii) use of heparins (unfractionated or low-molecular-weight heparins), (iii) use of b-blockers, (iv) use of angiotensin converting enzyme inhibitors (ACEIs) and/or angiotensin receptor blockers (ARBs), (v) use of statins, (vi) use of PCI during the index hospitalization, and (vii) use of a primary PCI in STEMI patients.

It has been considered only the drug treatment provided within 48 hours after the onset of symptoms or within 24 hours after being hospitalized. Primary PCI was defined as PCI performed in the first 24 hours after hospitalization. It was assessed in patients with STEMI subgroup because primary PCI is the therapy of choice in these patients.

The duration between onset of symptoms and hospital admission has decreased, so did the prevalence of STEMI at admission. Specific cardiovascular drug administration before admission, such as ACE inhibitors or

ARBs, beta blockers and statins increased in use over the 3 periods of 4 years in all age groups with the exception of beta-blockers in septua- and octogenarians, where its use decreased along with the declining importance of b-blockers for acute treatment of ACS. In contrast, use of b-blockers increased in nonagenarians, but the proportion of nonagenarians receiving b-blockers during the first 4-year period was markedly lower than that of septua- or octogenarians.

Regarding the PCI procedure, it showed significant increase in the first period (43.8%) and during the last period (69.6%) ($P < 0.001$). The increase in nonagenarians was more pronounced between the second and third 4-year period, whereas in septuagenarians a marked increase was observed earlier and thereafter plateaued. Between first and third 4-year period, PCI was used in increasingly older and co-morbid patients.

Temporal trends of in-hospital mortality study shows that the general lot mortality decreased from 11.6% in the first period to 10.0% in the last period of 4 years. ($P = 0.020$). The highest decrease mortality rate between the first and last period (22.7%) was found among octogenarians. The rate of cardiac or cerebral acute events and the duration of in-hospital stay has decreased significantly over the 4 periods, in general lot, due to the decrease among septua and octogenarians. Among nonagenarians, no statistically significant changes of in-hospital outcomes were observed, but numbers of within-group patients were low. Using a PCI procedure during hospitalization was associated with lower odds of in-hospital mortality.

This analysis in a contemporary group of 13 662 elderly patients with ACS showed that the use of guidelines recommended therapies increased from 2001 to 2012 in septuagenarians, octogenarians and nonagenarians. During hospitalization, the results of these patients have improved, despite the fact that in the last 4-year period patients were older and had more important co-morbidities than in previous periods. It has been found that the use of PCI was not associated with low efficacy in preventing death in the hospital, in spite of its use of increasingly older and with multiple co-morbidities patients. These results indicate that, during the last 4 years period, about 64 in-hospital deaths and 121 cardiac or cerebral acute events were preventable compared to the first period of 4 years.

Limitations of the study include that has been performed only on the territory of Sweden, a country with a high level of care and conditions for implementing the guidelines therapies independent of age, insu-

rance, income or residency. Another limitation is using a statistical approach of using regression modeling in a prospective cohort that does not prove a causal relationship between use of therapy and outcome.

In conclusion the study documented that older patients with ACS have experienced significant improvements in in-hospital evolution in 2001-2012 and that these improvements have been accompanied by increased use of guidelines recommended therapies. Therefore, this study suggests that more rigorous application of the guidelines recommended therapies was adequate.

Andreas W. Schoenenberger, Dragana Radovanovic, Stephan Windecker, Juan F. Iglesias, Giovanni Pedrazzini, Andreas E. Stuck, and Paul Erne, On behalf of the AMIS Plus Investigators European Heart Journal (2016) 37, 1304–1311. (AP, RM)

Interactions between mitral valve and left ventricle analysed by 2D speckle tracking in patients with mitral valve prolapse: one more piece to the puzzle

Two-dimensional echocardiography often reveals abnormal left ventricle (LV) lateral wall kinetics in patients presenting with mitral valve prolapse (MVP). However, relations between MVP and LV deformation are not clearly established. The goal of this study was to assess and quantify mitral valve chordae, leaflets, and LV myocardial interactions using speckle tracking echocardiography (STE) in patients presenting with various forms of MVP when compared with healthy subjects. Speckle tracking echocardiography (STE) allows a precise measure of myocardial segmental systolic deformation and also characterizes early-systolic stretch and post-systolic deformation. STE has been shown to reveal subclinical abnormal deformation and helps to evaluate the extent of myocardial stretch in case of severe primary MR.

A retrospective selection of patients with MVP was performed between 2010 and 2015. Prolapse was defined as a maximal end-systolic displacement of a mitral leaflet superior to 2 mm to the line connecting the annular hinge points.

Using STE-derived longitudinal strain curves, LV peak longitudinal strain (PLS, %), post-systolic index (PSI), and prestretch index (PST) were analysed in 100 patients with MVP and normal LV ejection fraction. Global, regional, and segmental values were compared according to mitral regurgitation severity and MVP location. Twenty healthy subjects served as control patients.

There was no significant difference among control and MVP group for global and regional PLS (223.7 ± 3.2 vs. 223.1 ± 2.2). In contrast, patients with MVP had significantly higher values of global PST (3.2 ± 4.1 vs. 1.3 ± 1.2 ; $P = 0.01$) and global PSI (3.2 ± 0.4 vs. 1.7 ± 1.1 ; $P = 0.05$) compared with controls, located mainly in the lateral wall and basal segments. Both anterior and posterior MVPs were responsible for PSI in basal inferior segments and PST in anterior ones. Mid-wall segmental deformation pattern changes were mainly observed at the level of the segments adjacent to the papillary muscle.

This study supports the hypothesis that pathological early-systolic shortening and late systolic, post-systolic deformation are attributed to an increased interaction between wall deformation and mitral valve events in patients with MVP. STE is a useful tool in the assessment of interplays between MV leaflets and myocardium and helps to demonstrate changes in temporal pattern of myocardial deformation. These findings suggest that mechanical interaction between MVP and wall papillary muscles and left ventricle chordae have the potential to change myocardial deformation patterns. Elongated chords and redundant leaflets interact with the endocardium region where they are attached, and this tension potentially affects the mechanical and electro physiologic function of the LV. The various models of deformation on the location of mitral valve prolapse may be explained by changes in the shape and size of the leaflets; chordae insert geometry and the relationship between chordae insertion, papillary muscles, and left ventricular wall.

Further studies are needed to demonstrate the direct link between myocardial stretch induced by prolapsing leaflet, deformation abnormalities, fibrosis, and susceptibility for ventricular arrhythmia.

Olivier Huttin, Sarah Pierre, Clément Venner, Damien Voilliot, Jean-Marc Sellal, Etienne Aliot, Nicolas Sadoul, Yves Juilliere, and Christine Selton-Suty-European Heart Journal-Cardiovascular Imaging Advance Access published April 20, 2016. (AP, RM)

Lipoprotein(a) is a risk factor for aortic and mitral valvular stenosis in peripheral arterial disease

High levels of lipoprotein a (Lp (a)) have been associated with aortic valvular calcification, and aortic stenosis. Prevalence and risk factors, including the level of Lp (a), for valvular disease (VHD) were investigated in patients with peripheral arterial disease (PAD). This

study offers the first report of the prevalence and risk factors, including levels of lipoprotein A level, for valvular heart disease analyzed by echocardiography in patients with peripheral arterial disease.

Cardiovascular disease is a major cause of death in patients with peripheral arterial disease. These patients often present complications such as diabetes, hyperlipidaemia and hypertension and may have severe systemic atherosclerosis leading to increased mortality due to coronary artery disease. PAD and low ankle-arm index were associated with acute coronary syndromes. These associations suggest that many causes of acute coronary events are linked to systemic atherosclerosis, including BAP, valvular pathology and hypertension.

The aim of this study is to investigate the prevalence of valvular pathology and abnormal ultrasound parameters and identify associated risk factors, including significant levels of lipoprotein A, in patients with peripheral arterial disease.

It is about a transversal single center study, that included 861 patients with peripheral arterial disease, with mean age of 73 years (66-78 years) and ABI <0.9. The final diagnosis was based on clinical symptoms and iliac or femoropopliteal artery stenosis >70%, quantified by angiography or ultrasound. They were determined serum level of lipoprotein, total cholesterol, LDL-C, HDL-C, triglyceride, albumin, glucose, glycated haemoglobin A1c (HbA1c), creatinine, remnant-like particle cholesterol, homocysteine, D-dimer, fibrinogen, thrombin-antithrombin complex (TAT), plasmin-a2 plasmin inhibitor complex (PIC), and high-sensitivity C-reactive protein (hs-CRP). Diabetes, hypertension, stroke and CAD were studied as risk factors for atherosclerosis.

Heart valve disease severity was classified into 4 degrees (none, mild, moderate and severe). Initially, the index was calculated Pearson correlation between disease severity and cardiac valvular all risk factors, including lipoprotein A. Next, factors with $P < 0.05$ in this analysis were evaluated using stepwise forward linear multiple regression analysis to examine relationships between the risk factors and severities of each VHD or Lp(a) levels.

The prevalence of regurgitation of the aortic valve (AR), the mitral valve regurgitation (MR), stenosis, aortic valve (AS), mitral valve stenosis (MS) and tricuspid regurgitation (TR) were 26.8, 19.7, 5.9, 1.3, and 9.4%. No patient had a history of rheumatic fever. Patients with valvular pathology included significantly more women and had low rates of association with alcohol

and tobacco, but increased significantly with age and with high homocysteine level, D-dimer, TAT and PIC; with a significantly lower body mass index, EGFR, albumin, total cholesterol, triglycerides. Drug treatment did not differ significantly between groups.

In Pearson correlation analysis, AR had positive correlations with age, TAT and PIC, and negative correlation with BMI, diabetes, eGFR, HbA_{1c}, triglycerides and albumin; MR had positive correlations with age, and negative correlation with eGFR, albumin, and triglycerides; AS had positive correlations with age, hemodialysis, and Lp (a), and negative correlation with eGFR; SM had positive correlations with age, female gender, and Lp (a), and negative correlations with ABI; and TR had positive correlations with age, fibrinogen, and PIC, and negative correlation with BMI, total cholesterol, LDL-cholesterol and triglycerides (all $P < 0.05$).

In stepwise multiple regression analysis of disease severity, AR was related to age, lower albumin and low eGFR; MR has been related to the decrease eGFR and age. AS it has been related to reduced eGFR, Lp (a) and age; MS has been linked to Lp (a) and female gender and TR was related to age, lower BMI, and lower total cholesterol.

Serum lipoprotein levels were significantly elevated in patients with AS compared to those without ($P=0.002$); in patients with mitral stenosis compared to those without ($P=0.037$) and in patients with SA and / or MS compared to those without SA or SM ($P=0.01$).

Older patients with aortic stenosis have a higher prevalence of peripheral arterial disease symptomatic compared with those without aortic stenosis and patients with calcification of the mitral ring have a higher prevalence of developing a lower index ankle-arm compared with healthy subjects. Data suggest a doubling of the prevalence of new onset heart failure in patients with PAD, and an index ankle-arm <1 in patients of middle age in the study is associated with an increased risk of heart failure, independent of already well known risk factors such as coronary heart disease, carotid atherosclerosis and myocardial infarction.

AR severity was related to age, albumin low value and low eGFR, and RM was linked to decreased eGFR and age. Age and chronic kidney disease are important risk factors for systemic atherosclerosis and diabetic renal patients have a higher prevalence of occurrence and severity of vascular and valvular calcification compared with healthy subjects. Degenerative aortic valve calcification and mitral were also it was reported to be

more common in patients with end stage renal failure.

A low serum albumin is associated with a higher risk of heart attack, stroke, and mortality from all causes. Moreover, malnutrition and chronic inflammation are common in patients with chronic renal failure. Thus, chronic kidney disease, lower albumin levels and aging may be risk factors for valvular regurgitation (aortic and mitral). The high rate prevalence of valvular pathology had especially mitral insufficiency and aortic and elevated lipoprotein A were associated with an increased risk of aortic stenosis and mitral stenosis in patients with peripheral arterial disease.

Limitations of this study include relatively small sample size and the conduct of a single center. This study design was by cross-sectional analysis. Also, SNPs was not analyzed and it was not used population-based data. Therefore, further studies are needed to determine the exact prevalence and risk factors of developing valvular pathology in patients with peripheral arterial disease.

Yoshiaki Hojo I, Hisao Kumakura, Hiroyoshi Kanai, Toshiya Iwasaki, Shuichi Ichikawa, and Masahiko Kurabayashi; *Lipoprotein(a) is a risk factor for aortic and mitral valvular stenosis in peripheral arterial disease; European Heart Journal – Cardiovascular Imaging* (2016) 17, 492–497. (AP, RM)

Lipoprotein (a): a promising target in the treatment of stenotic valvular diseases

The main findings this study are valvular pathology, in this case aortic insufficiency and mitral regurgitation, which are commonly found in patients with peripheral vascular disease and on the other hand, increased circulating levels of lipoprotein A, which combine an increased risk of aortic and mitral stenosis.

The study was developed in Japan, on 861 patients with peripheral arterial disease, 43.6% patients had valvular pathology at echocardiographic examination, from which 26.8% of them had aortic insufficiency, 19.7% mitral insufficiency, 5.9% aortic stenosis, 1.3% mitral stenosis and 9.4% tricuspid regurgitation. Older patients were associated with increased prevalence of valvular pathologies over all, but not mitral stenosis. Decreased glomerular filtration was associated with the presence of aortic regurgitation, mitral and aortic stenosis. However, the most surprising finding of the study was that elevated levels of lipoprotein A were independently associated with increased prevalence of developing stenotic valvular lesions but not of regurgitant lesions.

Previous studies have suggested that aortic stenosis is an active process involving pathogenic pathways as lipid infiltration, oxidative stress, inflammation and fibrocalcific remodelling of the aortic valve. Although retrospective studies and data obtained from animal models suggest that LDL cholesterol can be a key initiator of aortic stenosis, three randomized studies (Salt, SEAS, Astronomer) have failed to demonstrate the benefits of aggressive LDL-cholesterol-lowering therapy with statins and / or fibrates in patients with mild to moderate aortic stenosis. On the other hand, recent studies have shown that genetic variations of the LPA locus mediated by levels of lipoprotein A is associated with an increased incidence of aortic sclerosis and aortic stenosis in the general population.

In a substudy of Astronomer, Capoulade et al also have reported that elevated plasma levels of lipoprotein A is a strong independent predictor factor of rapid progression of aortic stenosis, especially in young patients. In contrast with aortic stenosis are relatively few published data about the pathophysiology of degenerative mitral stenosis. In this study, Hojo et al found that lipoprotein A is associated not only with aortic stenosis, but also with mitral stenosis. These correlations would suggest that degenerative mitral stenosis shares with aortic stenosis several etiologic factors, including Lp A. However, the study of Hojo et al. has some significant limitations such as: is a cross-sectional and retrospective nature study which provides a demonstration of cause-effect relationships between lipoprotein A and valvular stenosis; and the very small number ($n = 11$) of patients with mitral stenosis which considerably limits the statistical performance for the analysis of mitral stenosis.

About 20% of the general population have elevated lipoprotein A, and there is currently a wide range of evidence that supports its role in the development of coronary artery disease, peripheral artery disease and valvular pathology. Among lipoproteins, lipoprotein A, is the main carrier of oxidized phospholipids (OxPL) in the bloodstream. When OxPL accumulate in vascular tissue valve or they are recognized by the immune system as danger-associated-molecular-patterns (DAMPs).

Immune system response in an attempt to remove DAMPs is to generate inflammation, which then mediates atherosclerotic process. In addition, OxPL are converted into lizofosfatidylcoline (LPC) of lipoprotein associated phospholipases A2 (Lp-PLA2). Instead, LPC autotaxin provides a substrate for the enzyme

that produces lysophosphatidic acid (LPA). Both LPC and LPA has been shown to promote osteogenic differentiation and calcification of the valves and vascular cells. Therefore, lipoprotein A, and association with OxPL could, in terms of their pro-inflammatory and pro-atherosclerotic effect, contribute to the development of both the BAP and valvular pathology. On the other hand, these factors probably play a minor role in the pathogenesis of regurgitant valvular lesions involving myxomatous degeneration rather than degeneration by calcification. These findings may explain, at least in part, why in the study of Hojo et al, lipoprotein A was associated with aortic stenosis and mitral stenosis but not with IA, IM or IT.

Taken overall, the findings of the literature supporting the role of Lp (a) / OxPL / LPC / LPA in the development and progression of aortic stenosis, creating thus the achievement of a clinical trial on the therapy that decreases the serum levels of lipoprotein, reported in this population. However, circulating levels of lipoprotein A is largely genetically determined. Currently, there are a series of drug therapy, such as niacin,

but slightly reduce LPA levels and have significant side effects. Recently, antisense oligonucleotide directed to apolipoprotein A, was shown to reduce by >80% lipoprotein A level with minimal side effects. PCSK9 inhibitors of LPA also reduce the level with 20-30%. The next step is to test the efficacy of these new drugs on the progression of aortic stenosis.

The study provides further arguments to implement systematic screening of lipoprotein A in patients with peripheral arterial disease and / or pathology valve to conduct randomized trials to assess the effect of therapy by lowering levels of Lp(a) of patients with aortic stenosis. Also, it suggests that Lp (a) may be involved in the development of degenerative MS, but several studies with larger series of patients are needed to confirm this hypothesis.

Philippe Pibarot, Raphael Rosenhek, and Patrizio Lancellotti,- Lipoprotein (a): a promising target in the treatment of stenotic valvular diseases; European Heart Journal – Cardiovascular Imaging (2016) 17, 498–499. (AP, RM)

Rubrică realizată de Dr. Alina Popa, Dr. Rugina Mihaela.