Lipoprotein(a), oxidized phospholipids, and aortic valve microcalcification assessed by ^{18}F -NaF PET/CT

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Introduction

- Elevated lipoprotein(a) (Lp[a]) levels is a major genetic risk factor for aortic stenosis (AS).
- Lp(a) is similar to LDL and consists of an apolipoprotein (apo)-(a) linked to an apo-B100 and is the preferential lipoprotein carrier of oxidized phospholipids (OxPL).
- Positron emission tomography combined with computed tomography (PET/CT) with the use of ^{18}F -Sodium fluoride (^{18}F -NaF) radiotracer is a noninvasive imaging technique that allows the identification and quantification microcalcification, which is associated with change in CT calcium score.

Objectives

- Determine whether patients with CAVS actively followed clinically by echocardiography had higher Lp(a), OxPL-apoB and OxPL-apo(a) levels compared to individuals without AS.
- Determine, in individuals without AS, whether those with elevated Lp(a) levels were characterized by aortic valve microcalcification assessed by PET/CT

Methods

Clinical assessment

Assessment of aortic valve macro- and microcalcification

- Participants without AS

Calcium score

Tissue activity

Blood pool activity

Tissue-to-background ratio; mean TBR

Results

Table 1. Clinical characteristics of patients with versus without aortic stenosis

	Controls (n=108)	Patients with SA (n=174)	p-value
Clinical characteristics			
Age, years	62.4 ± 7.4	65.3 ± 12.3	0.01
Men, n (%)	57 (53)	117 (67)	0.02
Body mass index, kg/m ²	28.1 ± 5.0	29.6 ± 5.8	0.02
Diabetes, n (%)	16 (15)	46 (26)	0.02
Coronary artery disease, n (%)	12 (11)	58 (33)	<0.0001
Hypertension, n (%)	36 (34)	123 (71)	<0.0001
Smoking (past or current), n (%)	56 (52)	122 (70)	0.002
Hyperlipidemia, n (%)	45 (42)	125 (72)	<0.0001
Laboratory data			
Total cholesterol, nmol/L	4.8 ± 1.1	4.3 ± 1.1	0.0005
Triglycerides, nmol/L	1.9 ± 0.9	1.6 ± 0.9	0.006
HDL-C, nmol/L	1.4 ± 0.4	1.4 ± 0.4	0.3
LDL-C, nmol/L	2.6 ± 1.0	2.2 ± 0.9	0.001

Data are presented as mean ± standard deviation or n (%).

Figure 2. Lp(a) (A), Ox-PL-apoB (B) and Ox-PL-apo(a) (C) levels in patients with aortic stenosis separated on the basis of estimated aortic valve calcium accumulation by Doppler echocardiography. 1 : Statistically different than the group with mild aortic valve calcium accumulation (p<0.05).

Table 4. Clinical characteristics of individuals without aortic stenosis with vs. without elevated Lp(a) levels.

	Lp(a) < 75 nmol/L (n=28)	Lp(a) ≥ 75 nmol/L (n=27)	p-value
Clinical characteristics			
Age, years	61.7 ± 6.4	59.8 ± 8.3	0.4
Men, n (%)	19 (68)	16 (59)	0.5
Body mass index, kg/m ²	28.5 ± 4.3	28.8 ± 4.8	0.8
Diabetes, n (%)	2 (7)	4 (15)	0.4
Coronary artery disease, n (%)	2 (7)	5 (19)	0.2
Hypertension, n (%)	9 (32)	13 (48)	0.2
Smoking (past or current), n (%)	19 (68)	10 (37)	0.02
Hyperlipidemia, n (%)	12 (43)	17 (63)	0.1
Doppler echocardiographic data			
Mean gradient, mmHg	4.4 ± 1.6	4.6 ± 1.9	0.6
Peak aortic jet velocity, cm/s	139.7 ± 25.6	144.8 ± 27.5	0.5
Indexed aortic valve area, cm ² /m ²	1.3 ± 0.3	1.7 ± 0.3	0.2
Laboratory data			
Total cholesterol, mmol/L	5.0 ± 1.0	4.8 ± 1.2	0.6
Triglycerides, mmol/L	2.1 ± 1.1	1.6 ± 0.7	0.05
HDL-C, mmol/L	1.3 ± 0.5	1.4 ± 0.5	0.6
LDL-C, mmol/L	2.7 ± 0.9	2.7 ± 1.0	1.0
Computed tomography data			
Aortic valve calcium, n (%)	14 (50)	11 (40)	0.5
Median aortic valve calcium, AU	0.5 (0 - 35)	0 (0 - 11)	0.8

Data are presented as mean ± standard deviation, median (interquartile range) or n (%).

Figure 3. A) Mean aortic valve calcium score in individuals with high vs. low Lp(a) levels. B) Mean ^{18}F -NaF uptake (tissue-to-background ratio) in individuals with high vs. low Lp(a) levels. C) Representative image of aortic valve microcalcification in a patient with a low Lp(a) level (at the left) and a patient with a high Lp(a) level (at top right).

Conclusions

- ✓ Patients with mild, moderate or severe AS are characterized by higher levels of Lp(a), OxPL compared to individuals without AS.
- ✓ In individuals without AS, despite having comparable macrocalcification on CT, those with high Lp(a) level had higher microcalcification in the aortic valve compared to individuals with low Lp(a) levels.
- ✓ Evaluation of the aortic valve microcalcification by ^{18}F -NaF PET/CT could be a point of interest in future clinical trials evaluating the impact of a therapy targeting Lp(a) on the development or progression of AS.