Sinus of Valsalva Sclerosis is Associated with Conduction Abnormalities on 12-Lead Standard ECG

Keywords: Sinus of valsalva sclerosis; Atrioventricular block; Conduction abnormality

Abstract

**Background:** Sclerosis of the sinus of valsalva correlates with cardiovascular disease burden. The anatomic proximity of the aortic root to the conduction system suggests potential association between sinus of valsalva sclerosis and conduction abnormalities.

**Methods:** ECGs and clinical records from 129 consecutive patients undergoing transesophageal echocardiography for routine stroke work-up were collected from a single centre database. TEE standard loops and standard 12-lead ECG recordings were analysed by 3 experienced cardiologists.

**Results:** Of 129 patients, sclerosis of the sinus of valsalva was detected in 72 (55.8%), 39 (30.2%) had aortic valve sclerosis and 67 (51.9%) showed plaques of at least grade 1 in the ascending aorta. Conduction abnormalities and arrhythmias were found in 63 patients amongst others 30 with grade I, or higher AV-block. 10 patients with sinus node dysfunction, and 20 with atrial fibrillation. Sclerosis of the sinus of valsalva occurred in 42 of these 63 patients (p=0.022). 30 of 39 patients with AV-block grade I or higher, 26 presented a sinus valsalva sclerosis (p=0.001), 7 of 10 patients with sinus node dysfunction presented a sinus valsalva sclerosis (p=0.038) and 15 of 20 with atrial fibrillation (p=0.081).

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**Materials and Methods**

**Patient population and patient baseline characteristics**

We retrospectively analysed TEE studies and standard 12-lead ECGs of 129 consecutive patients at the Cardiology division of a tertiary care regional hospital in the greater Zurich area. Patient records were analysed for demographics, co-morbidities at or before the examination date, cardiovascular risk factors, and cardiovascular drug therapy. Patients undergoing TEE for endocarditis evaluation or with congenital heart disease were excluded. The cantonal ethics committee of Zurich acknowledged retrospective data analysis for research purposes (KEK-ZH-Nr. 2014-0529).

To characterize the study population and to identify a potential correlation between arrhythmias and sinus valsalva sclerosis, the following parameters were tabled as baseline characteristics: Age, BMI, heart disease divided in coronary heart disease (1-, 2- or 3- vessel), dilated cardiomyopathy and valvular cardiomyopathy, dyslipidaemia, smoking, type II diabetes mellitus, hypertension, history of ST-elevation myocardial infarction, cerebrovascular insult, transient ischemic attack, peripheral arterial occlusive disease, atrioventricular sinus area who underwent aortic valve replacement surgery are significantly more likely to need temporary cardiac pacing than those without annular calcification [8].

We analysed TEE loops and standard 12-lead ECGs of 129 consecutive patients, undergoing cardiologic work-up after TIA/stroke, for sclerosis of the sinus of Valsalva and the presence of conduction abnormalities such as atrioventricular blockage (AVB), right bundle branch blockage (RBB), left bundle branch blockage (LBB) and sinus node disease (SND).
sclerosis of the aorta, ICD or permanent pacemaker device, and medications.

**Transesophageal echocardiography**

Transesophageal echocardiography was performed according to the guidelines of the American heart association [9] and executed with Siemens Acuson SC2000, Z6Ms transducer. All procedures were digitally stored. Each loop was recorded over 3 ECG gated cycles and analysed independently by three experienced cardiologists. Sclerosis of the sinus of valsalva was defined as a hyperechogenic pattern of the sinus of valsalva with an acoustic shadow. Aortic valve sclerosis was defined as focal areas of valve thickening, typically located in the leaflet center with commissural sparing and normal leaflet mobility and evidence for impaired motility of at least 1 cusp with flow velocity below 2.5 m/s [10]. Plaques in the aorta were notified and classified according to the classification of Montgomery [11].

**ECG analysis**

All 12-lead standard ECGs were recorded with a Schiller Cardiograph model AT-10 Plus, at a paper speed of 25 mm/s. In our hospital we obtain standard ECG (10 electrodes) using the traditional configuration with the limb lead electrodes placed on the distal limbs. Conduction abnormalities were defined as, AV-block grade 1 or higher, LBB partial or complete, RBB partial or complete, sinus node dysfunction (refers to sinus bradycardia, chronotropic incompetence and/or sinus pause).

**Statistical analysis**

Quantitative variables were expressed as mean ± SD and categorical variables as frequencies or percentages. Different groups were compared with Chi-square tests, and exact fisher test, significance of correlation between two binary variables was checked with Pearson test of correlation, appropriate using SPSS 21.0 statistical software package (SPSS, Chicago, IL, USA). P values of < 0.05 were considered statistically significant.

**Results**

Patient baseline characteristics are shown in Tables 1 and 2. 72 patients had sclerosis of the sinus of valsalva, 39 had aortic valve sclerosis. 30 of those had as well sinus valsalva sclerosis as aortic valve sclerosis. 67 patients showed plaques grades I-IV in the ascending aorta (see Table 3). Of 63 patients with arrhythmia or conduction abnormality, 30 had grade I or higher AVB, LBB partial or complete, RBB partial or complete, sinus node dysfunction (refers to sinus bradycardia, chronotropic incompetence and/or sinus pause).

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sinus of valsalva what is not significant (p=0.764), whereby 7 showed a sclerosis of the aortic valve, what as well is not significant (p=0.075). 15 of 20 patients with atrial fibrillation showed a sinus sclerosis in the echocardiography, what is not significant (p= 0.081) only 7 presented an aortic valve sclerosis (p=0.480).

27 of the 39 patients with atherosclerosis showed a sinus sclerosis as well, what is a significant result (p=0.043, correlation coefficient 0.178), only 13 presented a sclerosis of the aortic valve what is not significant (p=0.656). 57 of 67 patients with plaques in the aorta ascendens present a sinus sclerosis what is highly significant (p<0.001, correlation coefficient 0.640), only 25 of the patients with aortic valve sclerosis showed plaques in the aorta ascendentes (p=0.965). 29 of 39 patients with atrial valve sclerosis show a sinus sclerosis as well (p=0.015, correlation coefficient 0.250). All other correlations between sinus sclerosis and the different parameters showed no significant results as visible in Table 5.

Discussion

In this study we describe for the first time a correlation between calcification of the sinus of valsalva and the presence of conduction system abnormalities and arrhythmia. Of particular interest is the significant correlation between sclerosis of the sinus of valsalva and AVB despite the rather small study population and the fact, that this was independent of aortic valve sclerosis. With a correlation coefficient of 0.342 we can even show a medium correlation of these two parameters what can be seen as great advantage in a retrospective trial with a relatively small study population. Drugs like calcium-channel inhibitors, betablockers and digoxin are known to be related with cardiac conduction abnormalities, but mostly, these abnormalities are not directly induced by drugs [12]. Anyway importantly, only 7 of the 30 patients with AVB were treated with betablockers or calcium-channel inhibitors and none with digitalis. In the population without AVB, 30 patients were treated with beta-blocker and 10 with calcium-channel blockers.

As other risk factors for AVB coronary heart disease and myocardial infarction are known [13], although the incidence of high grade AVB in patients with myocardial infarction is reduced since patients are treated with primary percutaneous intervention [14]. In this study, incidence of patients after myocardial infarction in the population with AVB is 3 of 30, incidence of patients with coronary heart disease is 6 of 30. We therewith can neglect that this is a major trigger for AVB in our population. However so far, no other study correlated sclerosis of the sinus of valsalva with arrhythmias and/or conduction abnormalities. There is indirect evidence from patients undergoing transcatheter aortic valve replacement that a thickened and calcified aortic root predicts AV conduction abnormalities on follow-up [15,16]. Similarly, a high incidence of left bundle branch blockage was found after TAVI implantation [17]. In the context of transcatheter aortic intervention, however, the procedure requires the expansion of prosthetic devices, which might directly affect integrity of the adjacent conduction system in patients with aortic root calcification [18]. Accordingly, prosthesis depth and size were independent predictors for the occurrence of a new left bundle branch block. Moreover, it is not surprising that aortic root sclerosis is predictive for conduction abnormalities in TAVI. The relevance of sinus of valsalva sclerosis, however, has not been evaluated yet in this context.

In our cohort, analysis of conduction abnormalities also pointed to an association between sclerosis of sinus of valsalva and atrial fibrillation. These observations, however, are more difficult to interpret. The question therefore arises, whether sinus of valsalva sclerosis represents readout for structural atrial remodelling affecting the cardiac conduction system and electric activation in general. This is a striking hypothesis, but larger and prospective studies are certainly warranted to specifically address this question.

Sclerosis of the sinus of valsalva had been recognized as predictor for atherosclerosis. We could show a significant association between those two parameters nevertheless the correlation coefficient points only to a low correlation between them. This might be due to our rather small study population. Moreover, an inverse association between lumbar bone mineral density and atherosclerotic arterial calcium could be identified [3,19]. Interestingly, osteoporosis and...
atrioventricular-conduction abnormalities. However in this study we were not classified mutually exclusive. This however would be necessary for patients with sinus valsalva sclerosis and aortic valve sclerosis were getting significant results despite the relatively small study population, in patients with sclerosis of the sinus of valsalva as well as atrial fibrillation is much higher in the descending aorta (B; white arrow). The role of this noninvasive test in the geriatric population. Geriatrics 58: 30-34; quiz 35.

Alwaqfi NR, Ibrahim KS, Khader YS, Baker AA (2014) Predictors of temporary epicardial pacing wires use after valve surgery. J Cardiothoracic Surg 9: 33.

11. (1996) Atherosclerotic disease of the aortic arch as a risk factor for recurrent ischemic stroke. The French Study of Aortic Plaques in Stroke Group. N Engl J Med 334: 1216-1221.

12. Zeltzer D, Justo D, Halkin A, Rosso R, Ish-Shalom M, et al. (2004) Drug-induced atrioventricular block: prognosis after discontinuation of the culprit drug. J Am Coll Cardiol 44: 105-108.

13. Goldberg RJ, Zevallos JC, Zarzebski J, Alpert JS, Gore JM, et al. (1992) Prognosis of acute myocardial infarction complicated by complete heart block (the Worcester Heart Attack Study). Am J Cardiol 69: 1135-1141.

14. Gang UJ, Hvelplund A, Pedersen S, Iversen A, Jans C, et al. (2012) High-degree atrioventricular block complicating ST-segment elevation myocardial infarction in the era of primary percutaneous coronary intervention. Europace 14: 1639-1645.

15. Karbasi-Afshar R, Jonaidi-Jafari N, Saburi A, Khosravi A (2014) Atrioventricular block as the initial presentation of calcified bicuspid aortic valve. ARYA Atherosclerosis 10: 59-64.

16. Sekimoto Y, Nishizaki Y, Sesoko M, Sai E, Yamashita H, et al. (2014) Syncope due to paroxysmal complete atrioventricular block in a patient with atrial valve stenosis. Intern Med 53: 1347-1349.

17. Boerlage-Van Dijk K, Kooman KM, Yong ZY, Wiegierink EM, Damman P.
et al. (2014) Predictors and permanency of cardiac conduction disorders and necessity of pacing after transcatheter aortic valve implantation. Pacing Clin Electrophysiol 37: 1520-1529.

18. Ghadimi K, Patel PA, Gutsche JT, Sophocles A, Anwaruddin S, et al. (2013) Perioperative conduction disturbances after transcatheter aortic valve replacement. J Cardiothoracic Vasc Anesth 27: 1414-1420.

19. Hyder JA, Allison MA, Criqui MH, Wright CM (2007) Association between systemic calcified atherosclerosis and bone density. Calcif Tissue Int 80: 301-306.

20. Maichuk Elu, Voevodina IV, Mitrokhina TV, Makarova IA, Iureneva SV (2014) The risk of atherosclerosis and osteoporosis development in post-ovariectomy syndrome women during hormone replacement therapy. Ter Arkh 86: 75-79.

21. Prasad M, Reriani M, Khosla S, Gossl M, Lennon R, et al. (2014) Coronary microvascular endothelial dysfunction is an independent predictor of development of osteoporosis in postmenopausal women. Vasc Health Risk Manag 10: 533-538.

22. Parhami F, Morrow AD, Balucan J, Lettinger N, Watson AD, et al. (1997) Lipid oxidation products have opposite effects on calcifying vascular cell and bone cell differentiation. A possible explanation for the paradox of arterial calcification in osteoporotic patients. Arterioscler Thromb Vasc Biol 17: 680-687.