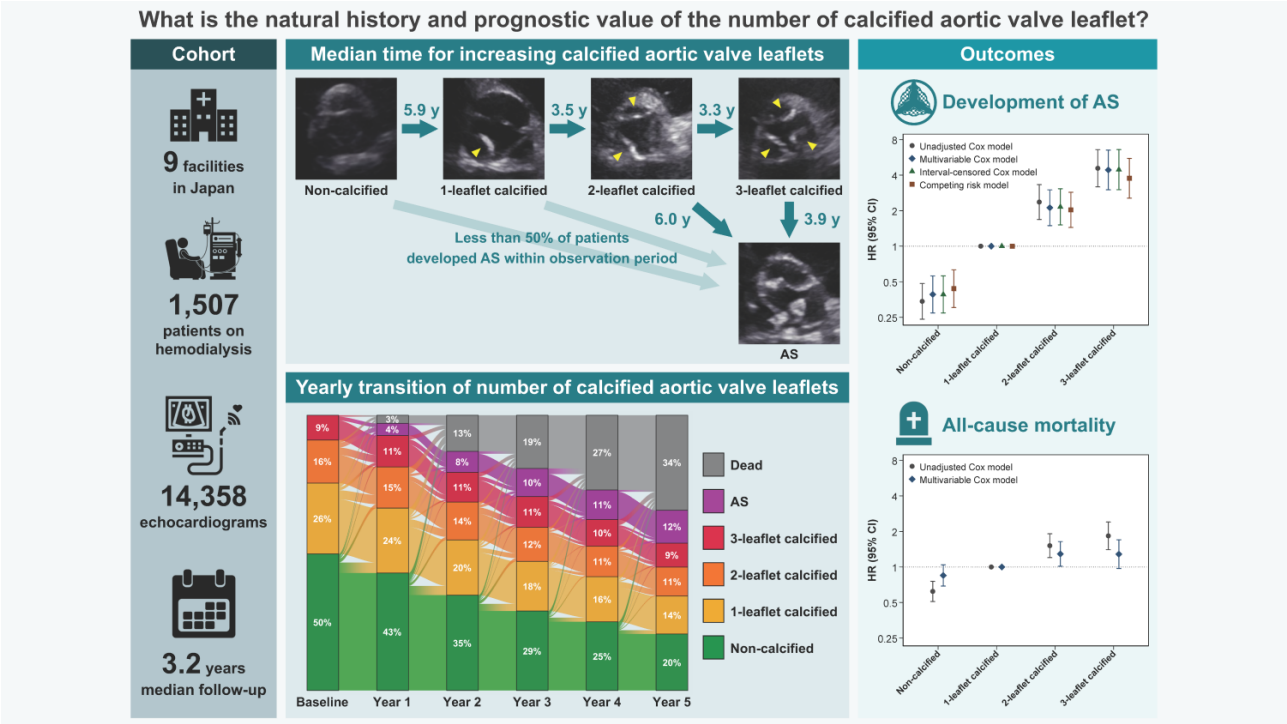

News Release

Title

Number of calcified aortic valve leaflets: natural history and prognostic value in patients undergoing haemodialysis

Key Points

- We evaluated the development of aortic valve calcification separately for each trileaflet and found that calcification of aortic valve leaflet typically increases by one in 3–4 years in patients undergoing hemodialysis.
- We demonstrated that ‘the number of calcified aortic valve leaflets’ predicts the development of aortic stenosis and mortality.
- The number of calcified aortic valve leaflets can be easily evaluated by echocardiography noninvasively, and this simple staging is expected to be used for risk stratification of patients with aortic sclerosis in practice and as an index to evaluate the effectiveness of some treatment to halt aortic valve calcification at an early stage in future clinical trials.

Summary

A research group led by Shimon Kurasawa, Takahiro Imaizumi, Shoichi Maruyama of the Department of Nephrology, Nagoya University Graduate School of Medicine, in collaboration with the Kaikoukai Healthcare Group

(Nagoya Kyoritsu Hospital, Hirotake Kasuga), has investigated development and progression of aortic valve calcification in patients undergoing hemodialysis, separately for each trileaflet. As a result, it was found that ‘the number of calcified aortic valve leaflets’ is a useful indicator for predicting the development of aortic stenosis and mortality.

Patients with kidney failure and undergoing hemodialysis are prone to calcification of the heart’s aortic valve, and as calcification progresses, valve opening is restricted, leading aortic stenosis, a serious disease with a high mortality rate. Therefore, it is desirable to develop treatment to halt calcification progression. However, there are not enough evaluation method to detect high risk patients and assess the degree of calcification in patients with aortic valve calcification. It was necessary to establish a method that is noninvasive and can be performed repeatedly.

The group analyzed more than 14,000 longitudinal data on echocardiography performed comprehensively and frequently on approximately 1,500 patients undergoing hemodialysis in multiple centers. It was found that aortic valve leaflets are not always calcified simultaneously and are typically calcified by one in 3–4 years. It was also found that ‘the number of calcified aortic valve leaflets’ predicts the development of aortic stenosis and mortality; an increase in one calcified leaflet was associated with a more than two-fold increased risk of developing AS and an approximately 20% higher risk of mortality.

The number of calcified aortic valve leaflet can be easily and noninvasively assessed using echocardiography. This simple staging is expected to be used for risk stratification of patients with aortic sclerosis in practice and as an index to evaluate the effectiveness of some treatment to halt CAVD progression at an early stage in future clinical trials.

Research Background

The number of patients requiring dialysis treatment due to kidney failure continues to increase worldwide, exceeding 300,000 in Japan. Patients undergoing hemodialysis are known to be prone to calcification of heart valve and blood vessels due to various factors such as mineral and bone disorders. When aortic valve calcification progresses, the valve opening is restricted, causing aortic stenosis. Aortic stenosis is a life-threatening disease that makes it difficult for blood to be pumped through the body and is also a burden on the heart. There is no established treatment to halt aortic valve calcification, and the only available treatment, aortic valve replacement, has poorer results in patients undergoing hemodialysis. As well, many patients are unable to undergo aortic valve replacement due to their poor general

condition. Therefore, it is desirable to clarify which patients are particularly prone to calcification and to develop treatment to halt calcification progression in these patients.

The research group has previously found that more than half of hemodialysis patients have aortic valve calcification, that one in ten patients has calcific aortic stenosis, and that even aortic sclerosis, a precursor of aortic stenosis, is associated with mortality. At the same time, further research was deemed necessary to determine how aortic valve calcification progresses and to detect patients with higher risk to develop aortic stenosis.

The aortic valve consists of three valve leaflets, namely the non-coronary cusp, left coronary cusp, and right coronary cusp. However, there have been no studies to date that have examined the development of aortic valve calcification separately for each trileaflet. The research group focused on this point and conducted this study, hypothesizing that ‘the number of calcified aortic valve leaflet’ might be an indicator of the degree of progression of calcification.

Research Results

The group analyzed more than 14,000 longitudinal data on echocardiography performed comprehensively and frequently on approximately 1,500 patients undergoing hemodialysis in multiple centers of Kaikoukai Healthcare Group. The study investigated the natural history of the development of each of the aortic valve trileaflet and whether the number of calcified aortic valve leaflet predicts the development of aortic stenosis and mortality.

Distribution of calcified aortic valve leaflets in aortic sclerosis

Of the patients with aortic sclerosis, approximately half had calcification in only one leaflet, 30% in two leaflets, and 20% in all three leaflets. When distinguishing the site, the non-coronary cusp was most frequently calcified, and the left and right coronary cusps were calcified at almost the same frequency.

Natural history of aortic valve calcification progression

Aortic valve calcification develops at approximately 6 years in patients without aortic valve calcification and progresses by one leaflet in 3–4 years. Aortic stenosis developed approximately 4 years after all three leaflets are calcified, while less patients without 3-leaflet calcified developed aortic stenosis.

Association between the number of calcified aortic valve leaflets with development of aortic stenosis and mortality

During observation period, 251 (17%) patients developed aortic stenosis. The incidence rates (per 100 person-years) were 1.7, 4.8, 10.7, and 19.1 in patients without aortic valve calcification and with 1-, 2-, and 3-leaflet calcified, respectively. In the multivariable analysis, an increase in one calcified leaflet was associated with a more than two-fold increased risk of developing AS.

The mortality rates (per 100 person-years) were 4.8, 7.8, 11.6, 13.7 in patients without aortic valve calcification and with 1-, 2-, and 3-leaflet calcified, respectively. In the multivariable analysis, an increase in one calcified leaflet was associated with an approximately 20% higher risk of mortality.

In summary, the higher the number of calcified aortic valve leaflets, the higher the risk of aortic stenosis and mortality. There was no significant difference in these associations between the sites of the calcification: non-coronary, left coronary, and right coronary cusps.

Research Summary and Future Perspective

This study demonstrated the usefulness of assessing calcification for each valve leaflet separately using echocardiography; the number of calcified aortic valve leaflet can be easily and noninvasively assessed. This simple staging is expected to be used for risk stratification of patients with aortic sclerosis in practice and as an index to evaluate the effectiveness of some treatment to halt CAVD progression at an early stage in future clinical trials.

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