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The clinical significance of perivalvular pannus in prosthetic mitral valves: Can cardiac CT be helpful?

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ABSTRACT

Background: The clinical significance of pannus in the prosthetic mitral valve (MV) is not well documented.
Objectives: To investigate the clinical significance of pannus on cardiac computed tomography (CT) in patients with a prosthetic MV.
Methods: A total of 130 patients with previous MV replacement who underwent cardiac CT were retrospectively included in this study. The presence of pannus, paravalvular leak (PVL) around the prosthetic MV and limitation of motion (LOM) of the MV were analyzed using CT. Between patients with MV pannus and those without pannus, CT, echocardiographic, and redo-surgery findings were compared. The diagnostic performance of CT and transesophageal echocardiography (TEE) for the detection of MV pannus was also compared, using surgical findings as a standard reference.
Results: MV pannus was observed on cardiac CT in 32.3% of the study population. Patients with MV pannus detected on CT more commonly had LOM (28.2% vs. 15.2%) and less frequently had PVL of the prosthetic MV (16.7% vs. 25%) than patients without MV pannus ($P > 0.05$). Prosthetic valve obstruction (PVO) due prosthetic MV pannus requiring redo-surgery was present in only five patients (11.9%). Cardiac CT detected MV pannus with sensitivity of 65.2% and specificity of 80.9% and showed better diagnostic performance than TEE ($P < 0.05$).
Conclusions: Prosthetic MV pannus can frequently be seen on cardiac CT. However, its clinical significance should be assessed with careful consideration, because PVO due to MV pannus is relatively uncommon, and pannus can be seen in patients without any clinical problems.

1. Introduction

Although the rate of mitral valve (MV) repair has increased in recent years, a number of patients with primary mitral regurgitation (MR) or mitral stenosis will still ultimately undergo mitral valve replacement (MVR) [1]. Prosthetic valve obstruction (PVO) remains a significant and life-threatening complication after valve replacement and can be caused by thrombosis, pannus, or both. Transthoracic echocardiography (TTE) is the primary modality to evaluate the prosthetic valve and can detect increased transprosthetic pressure gradients (PGs) and abnormal echogenicity around the prosthetic valve, both potential signs of PVO. However, precise determination of the underlying pathology can be limited by acoustic shadowing. Although transesophageal echocardiography (TEE) provides additional information for the prosthetic valve over TTE, sometimes it also has limitation, including evaluating the ventricular side of mitral prosthesis but not the atrial side [2].

Pannus in the prosthetic valve has received attention for being a potential cause of PVO, limitation of motion (LOM), or elevated transprosthetic PG [3]. Subaortic pannus is known to occur more frequently than mitral pannus and has been reported to have higher prevalence than expected [2,4,5]. Despite the higher number of patients with MVR than patients with aortic valve (AV) replacement, the prevalence and clinical significance of pannus in the prosthetic MV have not yet been well determined [6]. Only a few case studies have reported perivalvular pannus in the prosthetic MV as a cause of prosthetic valve dysfunction with LOM or valvular regurgitation [7–10].

Along with increasing focus on the detection of prosthetic valve abnormalities using imaging modalities, the application of cardiac CT for prosthetic valve evaluation has also drawn greater interest. Cardiac CT can provide excellent temporal visualization of the motion of the prosthetic valve leaflet and perivalvular structures, while also affording

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sufficient contrast and spatial resolution, overcoming acoustic shadowing artifacts seen with echocardiography. Many previous studies have reported the utility of cardiac CT for the detection of subprosthetic pannus in the prosthetic AV [4,5,11–17]. However, CT studies for prosthetic MV pannus are limited in number.

Therefore, the purpose of our study was to investigate the clinical significance of perivalvular pannus detected on cardiac CT in patients with a prosthetic MV.

2. Materials and methods

2.1. Patients

The Institutional Review Board of our institution approved this retrospective study, and informed consent was waived. We retrospectively searched the database for cardiac CT examinations performed between January 2014 and November 2015, and included 154 patients with previous MVR (Fig. 1). Among them, we excluded 24 patients who did not have an echocardiographic exam (either TTE or TEE) within 90 days of the CT scan. A total of 130 patients comprised our study population. Of these 130 patients, 54 were also included in a study by Suh et al. [18]. This previous study focused on the diagnostic performance of cardiac CT for the detection and localization of mitral paravalvular leak (PVL) in comparison with TTE and TEE. However, our study focused on the determination of the clinical significance of MV pannus found on cardiac CT. Demographic data and information on the prosthetic valves and surgical findings were collected from electronic medical records. Patients underwent cardiac CT exam for evaluation of prosthetic MV dysfunction (n = 46), coronary artery disease (n = 28), prosthetic valve dysfunction other than MV (n = 20), native valve disease (n = 14), the pulmonary veins and atrium before radiofrequency ablation (n = 13) and for detection of the cardioembolic source in stroke patients (n = 3), a coronary bypass graft evaluation (n = 3), a postoperative follow-up after MV surgery (n = 2), and evaluation of a left atrial thrombus (n = 1).

2.2. CT acquisition

All CT scans were performed with a dual-source CT scanner (SOMATOM Definition Flash, Siemens Healthcare, Forchheim, Germany). Scans were usually performed with in retrospective electrocardiogram (ECG)-gated data acquisition mode without ECG-based tube current modulation in order to allow the prosthetic valves to be imaged during the entire cardiac cycle. The triple-phase injection method was used with injection of 70 mL of iopamidol, followed by 30 mL of blended iopamidol/saline (1:1) and 20 mL of saline, all at 5 mL/s. From raw datasets, images were generated with a medium kernel using iterative reconstruction (I36f), and the reconstruction slice thickness was 0.75 mm, with a 0.5-mm increment between slices. For all patients, 10 transverse datasets were reconstructed every 10% of the cardiac cycle. Reconstructed images were transferred to an image server and analyzed using dedicated 3-dimensional software (Aquarius iNtuition, Ver 4.4.11, TeraRecon, San Mateo, CA, USA).

2.3. CT image analysis

All CT analyses were performed by two independent radiologists who were blinded to clinical information, the results of TTE or TEE, and the CT analysis results of the other reader. When disagreement in the CT analysis occurred between the two CT readers, the final decision was made through a consensus reading. Cardiac CT analysis included the presence of pannus, vegetation, thrombus, and PVL around the prosthetic MV, and the presence and type of LOM of the prosthetic MV. LOM was considered to be present when abnormal opening or closing of both leaflets or one leaflet of the mechanical valve was observed. When a prosthetic AV was present, the presence of subaortic pannus was also assessed. If MV pannus was present, the location of the pannus was recorded and classified as ventricular, atrial, or both.

2.4. TTE and TEE

Conventional 2D TTE examinations were performed on 125 patients (96.2%) within the 90-day period from the CT scan. The presence of PVL, transvalvular regurgitation, and LOM and the transvalvular PG were assessed. Transvalvular PG was considered to be elevated when it was ≥6 mm Hg [19]. TEE was recommended for each patient if PVL or LOM of the prosthetic valve was suspected from clinical or TTE findings.

Sixty-nine of 130 patients (53.1%) underwent TEE examination. The presence of PVL, transvalvular regurgitation, pannus, or thrombus around the prosthetic valve was assessed.

2.5. Surgical finding on redo-surgery

Among the patients who underwent redo-cardiac surgery for valves after CT scan, intra-operative TEE was performed for identification of abnormalities of the cardiac valves. For patients who underwent redo-surgery for the prosthetic MV, the presence of abnormalities such as MV pannus, PVL, thrombus, or vegetation was confirmed by visual inspection during surgery.

2.6. Statistical analysis

Statistical analyses were performed using a computerized statistics program (SAS version 9.2, SAS Institute Inc., Cary, NC, USA). Normally distributed data were identified using the Shapiro–Wilk W-test. Comparison of CT, echocardiographic, and redo-surgery findings was performed between patients with MV pannus and those without MV pannus. Continuous variables were presented as mean ± standard deviation and compared using the independent *t*-test for normally distributed data or the Mann–Whitney *U* test for non-normally distributed data. Categorical variables were compared using the Chi-square test or Fisher's exact test. The diagnostic performance of CT for diagnosing MV pannus was assessed using surgical findings as the standard reference. To compare the diagnostic performance of CT and TEE for the detection of MV pannus, the generalized estimating equation was used. Probability values <0.05 were considered statistically significant.

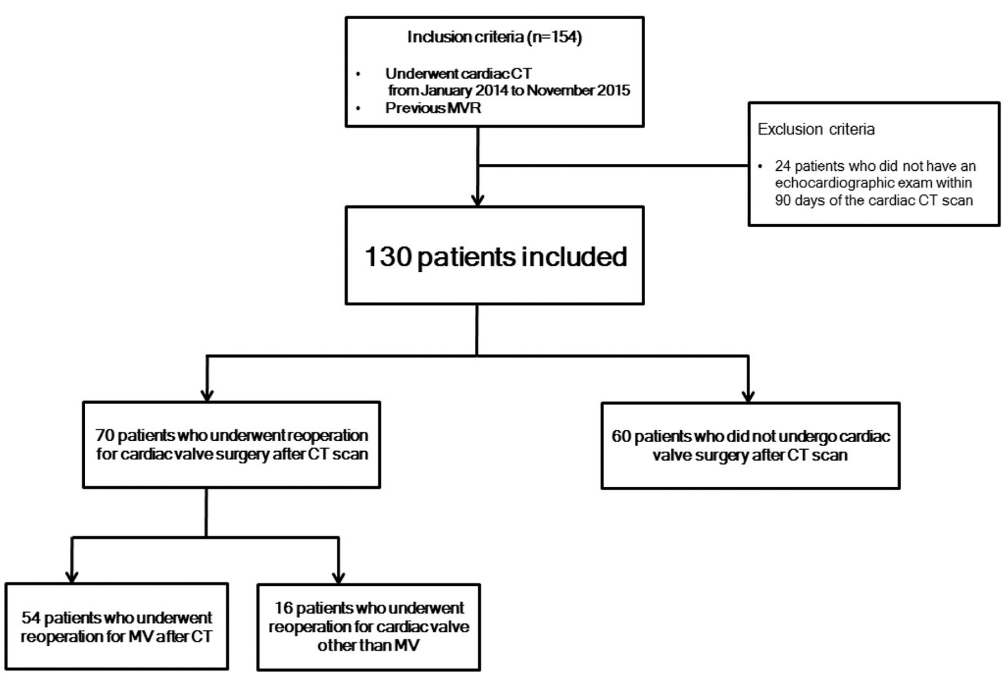

Fig. 1. Flow chart of the study population. CT, computed tomography; MVR, mitral valve replacement; MV, mitral valve.

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Table 1
Clinical characteristics and CT parameters of the study population.

Characteristics (n = 130)	Data
Male sex	47
Age at the time of cardiac CT (years)	63 (56–72)
Rheumatic heart disease	115 (88.5)
Age at MVR (years)	47.5 ± 14.0
Time after MVR (years)	15.4 ± 8.5
Initial surgery	
MVR only	55
With other valve replacement or repair	75
Presence of mechanical aortic valve	56
Prosthetic mitral valve type	
Tissue valve	17
Mechanical valve	113
Valve size (mm)	28.4 ± 2.1
Redo-valve surgery	
MV surgery	54
Other valve surgery	16

CT, computed tomography; MVR, mitral valve replacement.

3. Results

3.1. Patient characteristics

Clinical characteristics of the study population are presented in Table 1. Among the 130 patients in our study population, 70 underwent redo-surgery for a cardiac valve after CT scan: 44 patients had redo-surgery for the MV, 10 patents had MV pannus removal with other valve surgery, and 16 patients had other cardiac valve surgery. Indications for redo-MV surgery were suspected PVL (n = 27), infective endocarditis (n = 7), prosthetic MV obstruction due to pannus or thrombus (n = 6), or bioprosthetic MV dysfunction with degeneration (n = 4).

3.2. CT analysis

Cardiac CT revealed MV pannus in 42 patients (32.3%, Table 2). Evaluation of the presence of MV pannus was not possible on cardiac CT in nine patients due to poor CT image quality from motion or a severe metallic artifact, and these patients were considered to be negative for MV pannus for the purposes of data analysis. The interobserver agreement for the detection of MV pannus was excellent (weighed kappa value = 0.802, 95% confidence interval = 0.691–0.913). Among the 42 patients who had MV pannus on cardiac CT, pannus was present on the ventricular side or both sides in 37 patients (88.1%) and only on the atrial side in 5 patients (11.9%). Patients with MV pannus had a younger age at initial MVR and a longer time interval from initial MVR to cardiac CT than patients without MV pannus (P = 0.0475 and P = 0.0053, respectively). On CT, LOM was seen in 22 patients (17 mechanical valves and 5 tissue valves), and could not be assessed in 12 patients due to either prospective ECG-gated data acquisition covering only the mid-diastole or end-systole of the cardiac phase (n = 7), unknown valve type (n = 4), or poor leaflet visibility caused by a severe metallic artifact (n = 1). LOM was classified as symmetric in 11 mechanical valves and asymmetric in six. LOM was found more frequently in patients with MV pannus on CT than in those without MV pannus, however this difference was not statistically significant (28.2% vs. 15.2%, respectively; P = 0.263). Mitral PVL was less frequently observed in patients with MV pannus than in those without MV pannus (16.7% vs. 25%, respectively; P = 0.37). Subprosthetic pannus of the prosthetic AV was present in 37 patients and was more frequently detected in patients with MV pannus than in patients without MV pannus, although this difference was not statistically significant (85.0% vs. 61.1%, respectively; P = 0.119). After excluding patients with poor CT image quality, patients with MV pannus on CT had more LOM, less mitral PVL, and more prosthetic AV pannus, but these results were not statistically significant (Supplemental Table 1). MV pannus involving only the atrial side did not reveal any LOM.

Table 2
Comparison of clinical characteristics and CT findings between patients with MV pannus and those without pannus on cardiac CT. Bold values indicate statistical significance.

	MV pannus positive on CT (n = 42)	MV pannus negative on CT (n = 88)	P-value
Clinicals			
Age (years)	61 (54–70)	64 (56.5–72)	0.524
Sex (male)	11/42 (26.2)	36/88 (40.9)	0.15
Valve size (mm)	28.41 ± 3.65	28.4 ± 2.2	0.901
Rheumatic heart disease	39 (92.9)	76 (86.4)	0.236
Age at MVR (years)	**44.0 ± 12.1**	**49.2 ± 14.7**	**0.0475**
Time after MVR (years)	**18.4 ± 7.5**	**14.0 ± 8.6**	**0.0053**
CT			
Limitation of motion (n = 118)	11/39 (28.2)	12/79 (15.2)	0.152
Paravalvular leak	7 (16.7)	22 (25)	0.37
Prosthetic aortic valve pannus (n = 56)	17 (85.0, n = 20)	22 (61.1, n = 36)	0.119
TTE (n = 121)			
Mean transprosthetic pressure gradient (mm Hg)	4.7 (3.48–6.13, n = 41)	4.55 (3.4–6.8, n = 80)	0.58
Pressure gradient elevation (≥6 mm Hg)	14/41 (34.1)	27/80 (33.8)	0.873

MV, mitral valve; CT, computed tomography; MVR, mitral valve replacement; TTE, transthoracic echocardiography.

3.3. Clinical significance of MV pannus detected on re-operation

Upon redo-surgery, MV abnormalities were observed in 54 patients, including 23 with MV pannus (Supplemental Table 2). Only five patients among the 23 with prosthetic MV pannus on redo-surgery had clinically suspected PVO as a surgical indication (Fig. 2, Supplement Table 3). The group with surgically confirmed MV pannus revealed less frequent mitral PVL and more frequent LOM on both cardiac CT and TEE than patients without MV pannus on redo-surgery (Supplemental Table 4, P < 0.05). Patients with MV pannus on redo-surgery showed more frequent prosthetic AV pannus both on CT and in the surgical field; however, these differences were not statistically significant. Furthermore, there was no significant difference in the mean transvalvular PG between the two groups. The diagnostic performances of cardiac CT and TEE for the detection MV pannus are described in Supplemental Table 5. CT showed better sensitivity (65.2% vs. 13.3%, respectively; P = 0.0012) and negative predictive value (82.6% vs. 71.1%, respectively; P = 0.0389) than TEE.

4. Discussion

Our study demonstrates that MV pannus is frequently observed on cardiac CT (32.3% of this study population). However, LOM of the prosthetic MV and PVO due to MV pannus are observed only in 28.2% and 11.9% of patients with pannus seen on CT. Patients with MV pannus detected on redo-surgery more frequently had LOM and less frequently had PVL of the prosthetic MV compared with patients without MV pannus, with no significant difference observed in transvalvular PG elevation between the two groups. Cardiac CT can detect MV pannus with a sensitivity of 65.2% and a specificity of 80.9% when surgical findings as a standard reference.

Pannus around the prosthetic MV is considered one possible cause of PVO, which can be a fatal complication after valve replacement [20]. Nevertheless, the clinical significance of perivalvular pannus around the prosthetic MV has not been sufficiently investigated. As seen in prosthetic AV, MV pannus is thought to be a cause of LOM of prosthetic valves, such as a fixed leaflet or valvular regurgitation, and elevation of transprosthetic PG. When observed around prosthetic MVs, pannus has been reported to occur most often on the atrial side of the prosthesis [21]. On echocardiography, it typically presents as a very dense, immobile echo and is encountered in patients with a normal anticoagulation

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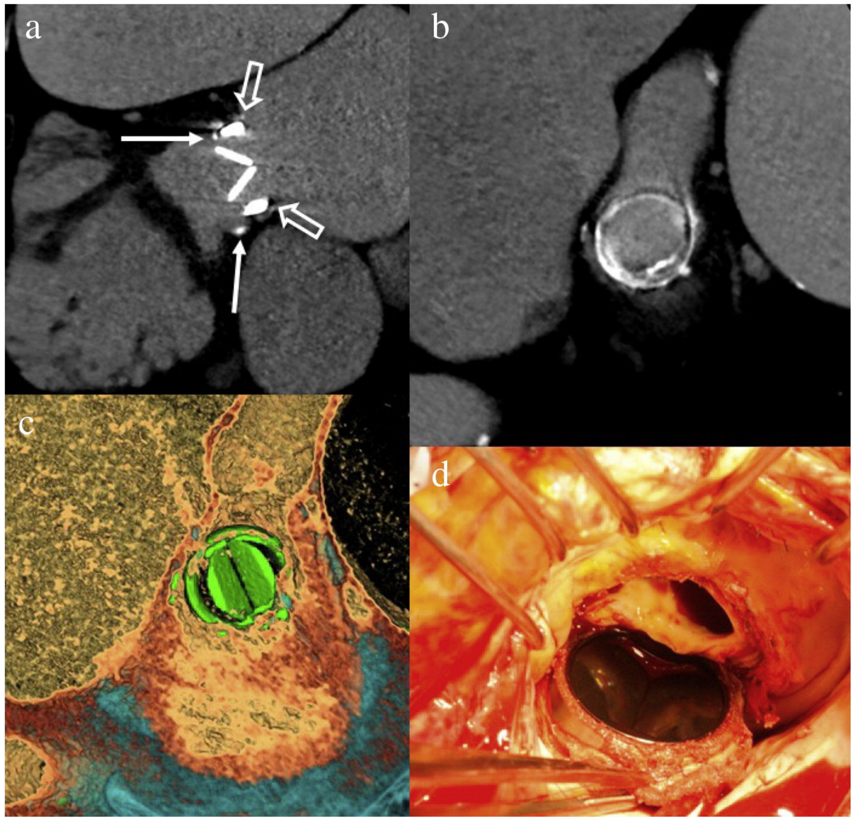

Fig. 2. Long axis CT multiplanar reformatted image of a 59-year-old female patient with a 29-mm Carbomedics valve showing calcified perivalvular pannus around the prosthetic MV (a, arrows indicating the ventricular side and open arrows indicating the atrial side) with a restricted opening (opening angle 52° and manufacturer value 78°). She underwent MV replacement 37 years before the CT scan because of rheumatic heart disease. CT images from the left ventricular side (b, multiplanar reformatted image and c, 3D image) showing circumferential pannus formation around the prosthetic MV ring. She underwent redo-MV replacement surgery due to prosthetic valve obstruction caused by pannus, and (d) circumferential pannus was identified on the surgical inspection and resected. CT, computed tomography; MV, mitral valve.

profile and with subacute or chronic symptoms, all of which can help differentiate pannus from thrombus. However, the differentiation between pannus and thrombus from clinical and imaging findings is usually not easy, because those two pathologies can occur together; the presence of pannus can predispose the valve to thrombosis, and chronic thrombosis of a valve can trigger pannus formation [22,23].

Although MV pannus was frequently seen on cardiac CT, clinically significant pannus requiring re-operation due to PVO was rare; only five of 42 patients with perivalvular pannus noted on CT required redo-surgery due to PVO. Moreover, MV pannus seemed to cause LOM rather than PG elevation. In this study, perivalvular pannus in a prosthetic MV was more frequently located on the ventricular side than the atrial side, and, interestingly, pannus involving only the atrial side never caused LOM nor transvalvular PG elevation.

These characteristics of perivalvular pannus in prosthetic MVs seem to be different from those of subaortic pannus. Although the prevalence and accompanying PVO of subaortic pannus have not been well reported, it is accepted that obstructive pannus shows a gradual increase of transvalvular PG compared with the baseline TTE, and leaflet restriction is common [3]. However, PVO seems to be less commonly associated with MV pannus compared with subaortic pannus and seems to present as the form connected with the subaortic pannus, with prosthetic AV pannus being observed in 85% of patients with prosthetic MV pannus on CT and in 83.3% of those with MV pannus on redo surgery. In prosthetic AV, flow turbulence has been suggested as a potential mechanism for the development of perivalvular pannus, such as that associated with a small body size (female sex or small body surface area) or the small size of the implanted valve [24]. Characteristics distinctive of the MV compared to the AV, such as large annular size and lower turbulent flow, might explain the low incidence of perivalvular pannus with clinical problems. The difference in wall shear stress in the vicinity of the prosthetic valve and lower pressure around a prosthetic MV than AV can explain this difference in pannus formation between the AV and the MV, because wall shear stress and transprosthetic pressure are thought to be a contributing factors for pannus formation [25,26].

No clear mechanism or etiology of pannus in a prosthetic MV has been elucidated; however, a young age at the time of initial MVR surgery and a long interval between the MVR and cardiac CT scan seemed to be potentially relevant factors in our study. In a previous study of prosthetic AVs, a young age at the time of initial valve replacement was found to be a significant predictor of the formation of significant pannus, possibly due to a more vigorous immune system and metabolism [5,27]. In our study, the postulated mechanism of pannus formation, in response to chronic inflammation caused by the prosthetic valve, might explain the relationship between the time interval from initial valve replacement and the rate of pannus formation.

One interesting point in our study was the possible negative relationship between perivalvular pannus and PVL. Among patients who underwent redo-surgery after cardiac CT scan, patients with positive pannus on surgical findings tended to be negative for PVL. This trend was also observed in patients who were positive for pannus on CT, although the difference was not statistically significant. This difference between CT and surgical results might be due to the comparatively high sensitivity of CT, which could lead to the detection of even clinically insignificant pannus. One possible hypothesis for the negative relationship between pannus and PVL is that sex plays a contributing role to the prevalence of these two phenomena. The male sex has been reported to be a risk factor for late occurrence of PVL in prosthetic MVs [28]; in contrast, the female sex, with a smaller average body size, has been

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considered to be a contributing factor to the development of pannus. Therefore, males, with larger average annular size, might be protected from the occurrence of pannus. Supporting this hypothesis, patients with perivalvular pannus in our study were less frequently male than those without pannus.

Our study is the first of its kind to report on the clinical significance of prosthetic MV pannus in a relatively large population. Few previous studies have investigated the epidemiology of prosthetic MV pannus, possibly because TTE and/or TEE have been accepted as the main imaging modalities for prosthetic valve evaluation. Acoustic shadowing from the prosthetic valve ring might hamper the detection of perivalvular structural abnormalities, especially pannus around the valve ring and the left ventricular side of the MV. The better sensitivity and NPV of CT for the detection of prosthetic valve pannus compared with TEE observed in our study provide supporting evidence for this point. However, given that the results of our study show that MV pannus can be associated with uncommon clinical events, such as PVO, the significance of prosthetic MV pannus detected on cardiac CT should be carefully considered. In clinical context, evaluation of clinically significant pannus would be of great concern. Unfortunately, however, we were unable to detect any characteristics as predictors of the development of PVO in association with pannus, probably due to the small percentage of patients with PVO in our study (3.8%). We suggest that further studies with larger populations will help solve this problem.

Our study has several limitations. First, it was a retrospective study from a single institution and included only patients who underwent cardiac CT. However, to avoid bias in patient selection, CT images were blindly analyzed, without knowledge of the clinical information of the prosthetic valve, echocardiographic data, or surgical findings. Second, some patients had poor quality CT images, which can affect the diagnostic accuracy of MV pannus detection. This poor quality might have been due to the large annular motion of the MV and the inferior temporal resolution of CT, which can trigger severe motion artifacts, especially in patients with arrhythmia. Further studies that use methods to reduce cardiac motion (e.g., a motion correction algorithm or an absolute delay) should address this problem. Finally, the high prevalence of rheumatic heart disease as the etiology of the original valve disease might have led to overestimation of the prevalence of perivalvular pannus, because rheumatic valve disease and pannus formation could be related in terms of chronic inflammation process via transforming growth factor-β1 [22,29,30].

5. Conclusions

Pannus around the prosthetic MV is frequently seen on cardiac CT. However, its clinical significance should be assessed with careful consideration, because PVO due to MV pannus is relatively uncommon, and pannus can be seen in patients without any clinical problems.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2017.09.169.

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