Altered myocardial characteristics of the preexcited segment in Wolff-Parkinson-White syndrome: A pilot study with cardiac magnetic resonance imaging

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Abstract

Purpose
The preexcited myocardium of Wolff-Parkinson-White (WPW) syndrome would have different characteristics from normal myocardium and these findings might be related to persistent left ventricular systolic dysfunction. We evaluated myocardial tissue characteristics at the preexcited segment in adult WPW syndrome patients and their implicated findings.

Methods
For this prospective study, we enrolled 22 adult WPW syndrome patients (16 male, mean 45.4 ± 17.8 years) with echocardiographic findings of regional wall motion abnormality in our electrophysiology clinic. Of these patients, 14 underwent radiofrequency ablation before cardiac magnetic resonance imaging. All patients underwent cardiac magnetic resonance imaging including cine and late gadolinium enhancement. The ventricular morphology, function and myocardial characteristics of the preexcited segment were analyzed.

Results
A relatively high prevalence of late gadolinium enhancement (9/22, 40.9%) was observed exclusively at the basal septum. The septal accessory pathway was significantly more prevalent in patients with late gadolinium enhancement (P = 0.011). The prevalences of regional myocardial wall thinning and regional akinesia were significantly higher (P = 0.001 for both) and left ventricular function was significantly decreased in patients with late gadolinium enhancement (P < 0.001). In addition, there were no significant relationships between radiofrequency ablation and regional akinesia (P > 0.999), regional myocardial wall thinning (P > 0.999), late gadolinium enhancement (P = 0.662) and low ejection fraction (P > 0.999).
Conclusion
Myocardial fibrosis was observed at the preexcited myocardium of adult WPW syndrome patients with septal accessory pathway, which could accompany regional akinesia and regional myocardial wall thinning and might be related to persistent left ventricular systolic dysfunction even after radiofrequency ablation.

Introduction
Wolff–Parkinson–White (WPW) syndrome is defined as a congenital condition involving an abnormal conductive accessory pathway between the atrium and ventricle that bypasses the atrioventricular node [1,2]. This syndrome is of clinical importance because it is frequently associated with supraventricular tachycardia. Furthermore, sudden cardiac death is potentially possible due to ventricular tachyarrhythmia from the associated atrial fibrillation with rapid anterograde conduction over the accessory pathway [3,4]. In addition, a rare cause of morbidity in WPW syndrome patients is heart failure, which may occur as a result of recurrent or sustained tachyarrhythmia [5]. Recently, several literatures have reported a possible direct association between WPW syndrome and heart failure, regardless of the related tachyarrhythmia [6–10]. Eccentric ventricular preexcitation through the accessory pathway results in premature contraction of that ventricle, and this has been well documented in echocardiography [11,12]. Regional premature contractions are thought to be a possible mechanism for heart failure in WPW syndrome by inducing progressive ventricular dilatation with cardiac dysfunction similar to functional aneurysm [6,13]. In addition, heart failure in WPW syndrome has been associated with the septal accessory pathway and has a reversible nature with a temporal relation after radiofrequency ablation (RFA) of the septal accessory pathway [7,8,10,14]. Cardiac magnetic resonance imaging (CMR) is a rapidly evolving technology that might now be the most powerful imaging tool for noninvasive myocardial characterization through the late gadolinium enhancement (LGE) and T1 mapping technique. Recent research has supported the value of these techniques for the assessment of myocardial characteristics under multiple conditions [15,16]. We thought that the preexcited segment in WPW syndrome could have different myocardial characteristics from the normal myocardium, especially in adult patients who are exposed to the accessory pathway for a long period of time, and we thought that the different characteristics could be related to left ventricular systolic dysfunction. However, as far as we know, CMR findings for myocardial characterization in WPW syndrome patients have rarely been studied. Therefore, we evaluated the myocardial characteristics of the preexcited segment using CMR in adult WPW syndrome patients and their implicated findings through this study.

Materials and methods
Study population
This prospective study was approved by our institutional review board and the local ethics committee. Written informed consent was obtained from all study participants. A cardiologist and a radiologist reviewed the electrical medical record database and searched for new adult WPW syndrome patients (age ≥ 20 years) who had undergone echocardiography at their first examination in our electrophysiology (EP) clinics between January 2010 and December 2014, and 327 patients were identified. Of them, 77 patients (23.5%, 77/327) who had abnormal echocardiographic findings of regional wall motion abnormality (RWMA),
which did not correspond with vascular territory and was noted at the expected preexcited segment, were selected. A flow diagram for the study population and exclusion criteria is summarized in Fig 1. After the exclusion criteria were applied, 22 patients (16 males with a mean age of 45.4 ± 17.8 years) were finally enrolled. All 22 patients underwent CMR prospectively from January 2014 to May 2015.

### Clinical characteristics

All available clinical data were recorded after reviewing electronic medical records and/or after interviewing each patient with a standard questionnaire. Clinical presentation in terms of palpitation, chest pain and syncope was reviewed. The 12-lead electrocardiography (ECG) during sinus rhythm at the time of diagnosis was reviewed. On ECG, we reconfirmed ventricular preexcitation by Kent fibers with a short PR interval, widened QRS complex with slurred upstroke and secondary repolarization changes. An automatic computerized system recorded the longest QRS duration exhibited by the leads and the accessory pathway location was determined [17]. All study records from patients who underwent an EP study with RFA were reviewed for accessory pathways and related tachyarrhythmia. Data on performance of RFA and the approach method chosen for the ablation of the accessory pathway were also recorded. The accessory pathway locations were determined again in the EP study. From the results of the ECG and EP study, accessory pathway locations were categorized into one of the following three groups: septal (anteroseptal, midseptal and posteroseptal), right (right anterior, right lateral and right posterior), or left (left anterolateral, left lateral and left posterior) [18]. In addition, the presence of significant coronary artery disease was evaluated based on coronary artery computed tomography or conventional coronary angiography records obtained within 3 years before CMR.

### CMR protocol

CMR was performed with a 3.0-T imaging system (Magnetom Trio; Siemens Medical Solutions, Erlangen, Germany) and an 8-channel cardiac coil. After a localized scan, ECG-gated
cardiac cine images were obtained with the following parameters: True fast imaging with steady-state free precession sequence, TR 3.31 ms, TE 1.44 ms, flip angle 50°, field of view 337 x 400 mm, matrix 216 x 216, 25 phases and slice thickness 8 mm without gap in the four-chamber, long-axis and short-axis planes encompassing the whole ventricles. LGE imaging was performed 10 minutes after injection of gadobutrol (0.2 mmol/kg, Gadovist; Bayer Schering Pharma AG, Berlin, Germany) at 2 ml/sec. Scanning parameters were as follows: segmented inversion recovery prepared turbo fast low-angle shot sequence, TR 9.9 ms, TE 4.9 ms, flip angle 20°, field of view 380 x 380 mm, matrix 320 x 320 and slice thickness 8 mm without gap in the four-chamber, long-axis and short-axis planes encompassing the whole ventricles. Data acquisition was synchronized with ECG in the mid-diastolic phase. An 11-heartbeat modified Look-Locker sequence with inversion recovery was used for T1 measurement of the myocardium [19]. Scanning parameters were as follows: TR/TE = 2.43/1.01 ms, minimum inversion time 100 msec with inversion time increment 80 ms, field of view 308 x 380 mm², acquisition matrix 126 x 192, flip angle 35°, and slice thickness 8 mm. Short-axis images were acquired at the apical, mid and basal levels of the left ventricle. Images for T1 measurements were obtained before and 15 minutes after contrast administration.

Image analysis

All CMR images were transferred to dedicated software (CMR 42; Circle Cardiovascular Imaging, Calgary, Alberta, Canada). Two observers (H.J.L and Y.J.K. with 9 and 12 years of experience in cardiac imaging, respectively) who were both blinded to each patient’s clinical findings reviewed the images in consensus. From the cine images, observers evaluated the presence of regional myocardial wall thinning, which was defined as a myocardial wall thickness of 5.5mm or less on the end-diastolic image [20]. To evaluate myocardial mechanics, a semi-automated feature tracking method was used to obtain information on the ventricular strains: radial, circumferential and longitudinal strains. Using the results for global strain, strain rate, and time to peak, observers determined the presence of RWMAs (Fig 2) [21]. Afterwards, both

Fig 2. Strain curves for the regional wall motion abnormalities. Representative longitudinal strain curves are shown with the blue curve representing a normal contraction, the red a premature contraction, and the green hypokinesia or akinesia. Regional premature contraction was defined with the early systolic peak during the systole with decreased time to peak (red solid arrow) and overall decreased absolute values of global strains compared to the normal curve. An additional systolic peak (second or third) (red open arrows) could also indicate premature contraction. Regional hypokinesia or akinesia was defined with decreased absolute values of global strains and mild increased time to peak.

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ventricular end-diastolic volumes with ejection fractions were calculated by semi-automatically tracing the endocardial contours at end-systole and end-diastole in each short-axis image from the apical to basal ventricle. Patients were regarded as having low ejection fraction if the left ventricular ejection fraction was < 50%. Myocardial LGE was defined as a region with an apparent high signal intensity of > 5 standard deviations of the remote normal myocardium. If LGE was detected, its pattern was further classified and the location was recorded. Myocardial extracellular volume fraction was measured using pre- and post-contrast T1 map images with the following equation: Extracellular volume fraction (%) = \( \frac{\Delta R_1_m}{\Delta R_1_b} \times (1 - \text{hematocrit}) \times 100 \), for which \( R_1_m \) is \( R_1 \) in the myocardium, \( R_1_b \) is \( R_1 \) in the blood, and \( \Delta R_1 \) is the change in relaxivity before and after gadolinium chelate administration, respectively [22].

**Statistical analysis**
Statistical analyses were performed using statistical software (SPSS version 23.0 for Windows, SPSS). Continuous variables were expressed as mean values with standard deviations and categorical variables were expressed as percentages. We divided the patients into two groups according to the presence of LGE, and compared clinical characteristic and other CMR findings between the two groups. Additional analyses were done in which the study population was divided into two groups according to the performance of RFA or the presence of RWMA. The Mann-Whitney U test was used to appraise the differences between the two groups for continuous variables and the chi-square contingency tables or Fisher’s exact test were used to evaluate the differences between the two groups for categorical variables. A \( P \) value of < 0.05 was considered to indicate statistical significance.

**Results**

**Clinical characteristics**
The clinical characteristics of the study population are summarized in Table 1. The mean age of the patients was 43.6 ± 17.2 years at first diagnosis. All patients underwent ECG at the time of diagnosis and had ventricular preexcitation caused by Kent fibers on ECG. Palpitations were present in all patients. Of the patients with palpitations, chest pain was additionally documented in 6 patients and syncope in 4 patients. Fourteen patients of the study population underwent an EP study with RFA due to documented supraventricular tachyarrhythmias prior to CMR. The median time interval from first diagnosis to RFA for the 14 patients was 65.5 (IQR, 54.8–87.5) days. Accessory pathways were classified based on mainly ECG findings because not all patients underwent an EP study. For the 14 patients who underwent an EP study, both the ECG and EP study classified the accessory pathways identically. There was no patient with multiple accessory pathways. No recurrence was observed in patients with RFA. In addition, we observed no significant coronary artery disease in 16 patients on coronary computed tomographic angiography or conventional coronary angiography. The other 6 patients did not undergo coronary evaluation.

**CMR findings**
Median time interval from first diagnosis to CMR was 499.5 (IQR, 352.8–754.0) days. Median time interval from RFA to CMR was 465.5 (IQR, 276.5–709.5) days for the 14 patients with RFA. The CMR findings from the study population are summarized in Table 2. On CMR, RWMA was noted at the preexcited segment in 13 patients (13/22, 59.1%) and all of these findings were observed at the basal septum. Regional premature contractions were noted in 6 patients with a septal accessory pathway and 1 patient with a right posterior accessory pathway.
Table 1. Comparison of clinical characteristics according to the presence of LGE.

|                               | All patients (n = 22) | LGE (-) (n = 13) | LGE (+) (n = 9) | P value |
|-------------------------------|-----------------------|------------------|-----------------|---------|
| Male sex                      | 16 (72.7%)            | 10 (76.9%)       | 6 (66.7%)       | 0.655   |
| Age at diagnosis (yrs)        | 43.6 ± 172            | 44.9 ± 19.5      | 41. ± 15.0      | 0.857   |
| Palpitation                   | 22 (100.0%)           | 13 (100.0%)      | 9 (100.0%)      | 0.376   |
| Chest pain                    | 6 (27.3%)             | 4 (30.8%)        | 2 (22.2%)       | > 0.999 |
| Syncope                       | 4 (18.2%)             | 4 (30.8%)        | 0 (0.0%)        | 0.115   |
| Age at MRI (yrs)              | 45.4 ± 17.8           | 46.9 ± 20.1      | 42.4 ± 15.4     | 0.756   |
| QRS duration (msec)           | 141.3 ± 19.7          | 134.9 ± 18.6     | 150.4 ± 18.4    | 0.021   |
| Tachyarrhythmia               | 14 (63.6%)            | 9 (69.2%)        | 5 (55.6%)       | 0.662   |
| AVRT                          | 10 (45.5%)            | 6 (46.2%)        | 4 (44.4%)       | 0.937   |
| AF                            | 4 (18.2%)             | 3 (23.1%)        | 1 (11.1%)       | 0.616   |
| RFA                           | 14 (63.6%)            | 9 (69.2%)        | 5 (55.6%)       | 0.662   |
| Retrograde aortic             | 3 (13.6%)             | 1 (7.7%)         | 2 (22.2%)       | 0.544   |
| Transseptal                   | 11 (50.0%)            | 8 (61.5%)        | 3 (33.3%)       | 0.387   |

Values are mean ± standard deviation or patient number (%).

LGE = late gadolinium enhancement; AVRT = atrioventricular reentrant tachycardia; AF = atrial fibrillation; RFA = radiofrequency ablation; AP = accessory pathway

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Table 2. Comparison of CMR findings according to the presence of LGE.

|                               | All patients (n = 22) | LGE (-) (n = 13) | LGE (+) (n = 9) | P value |
|-------------------------------|-----------------------|------------------|-----------------|---------|
| Wall thinning                 | 6 (27.3%)             | 0 (0.0%)         | 6 (66.7%)       | 0.001   |
| RWMA                          | 13 (5.1%)             | 4 (30.8%)        | 9 (100.0%)      | 0.002   |
| Premature contraction         | 7 (31.8%)             | 4 (30.8%)        | 3 (33.3%)       | > 0.999 |
| Akinesia                      | 6 (27.3%)             | 0 (0.0%)         | 6 (66.7%)       | 0.001   |
| LVEDV (ml/BSA)                | 90.8 ± 30.9           | 76.0 ± 8.3       | 112.4 ± 38.9    | 0.003   |
| LVEF (%)                      | 56.7 ± 12.0           | 64.1 ± 5.0       | 45.9 ± 10.8     | < 0.001 |
| RVEDV (ml/BSA)                | 78.8 ± 15.8           | 76.0 ± 14.3      | 83.0 ± 17.8     | 0.601   |
| RVEF (%)                      | 58.0 ± 5.8            | 61.6 ± 2.6       | 52.7 ± 5.0      | 0.001   |
| Low ejection fraction         | 7 (31.8%)             | 0 (0.0%)         | 7 (77.8%)       | < 0.001 |
| Native T1 (msec)              | 1253.9 ± 41.6         | 1222.5 ± 11.6    | 1300.0 ± 20.5   | < 0.001 |
| Septal*                       | 1287.0 ± 71.7         | 1230.7 ± 15.3    | 1368.4 ± 23.1   | < 0.001 |
| Lateral*                      | 1220.8 ± 25.8         | 1214.2 ± 16.3    | 1230.2 ± 34.3   | 0.284   |
| ECV (%)                       | 27.2 ± 1.8            | 26.1 ± 0.5       | 28.7 ± 1.8      | 0.006   |
| Septal*                       | 28.4 ± 3.4            | 26.0 ± 0.7       | 31.8 ± 2.8      | < 0.001 |
| Lateral*                      | 26.3 ± 1.0            | 26.2 ± 0.6       | 26.5 ± 1.4      | 0.793   |

Values are mean ± standard deviation or patient number (%).

*Reference values of the normal volunteers (N = 7) on the same CMR system are presented as mean values with standard deviations as follows: Native T1 = 1245.4 ± 52.7 msec; 1249.6 ± 34.0 msec and 1253.5 ± 35.9 msec for septal and lateral, respectively. Myocardial ECV = 26.3 ± 1.4%; 26.3 ± 1.3% and 26.2 ± 1.8% for septal and lateral, respectively.

LGE = late gadolinium enhancement; RWMA = regional wall motion abnormality; LVEDV = left ventricular end-diastolic volume; BSA = body surface area; LVEF = left ventricular ejection fraction; RVEDV = right ventricular end-diastolic volume; RVEF = right ventricular ejection fraction; ECV = extracellular volume fraction

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close to the inferior septum. Regional akinesia instead of premature contraction was noted in 6 patients with a septal accessory pathway. On the cine images, regional myocardial wall thinning was noted at the basal septum in 6 patients with a septal accessory pathway (6/22, 27.3%). The mean values of the end-diastolic volume were 90.8 ± 30.9 ml/BSA and 78.8 ± 15.8 ml/BSA, and ejection fractions were 56.7 ± 12.0% and 58.0 ± 5.8% for the left and right ventricles, respectively. From the functional results, 7 patients (7/22, 31.8%) were classified as having low ejection fraction with a decreased left ventricular ejection fraction of < 50%. LGE at the preexcited segment was present in 8 patients with a septal accessory pathway and 1 patient with a right accessory pathway (9/22, 40.9%). All demonstrated LGEs were detected at the basal septum (both the anterior and inferior septum in 5 patients and only the inferior septum in 4 patients). The patterns of LGE were as follows: ill-defined patchy LGE in 4 patients and linear endocardial and/or epicardial LGE not corresponding with vascular territory in 5 patients. All of the 6 patients who did not undergo coronary evaluation did not show LGE on CMR. The native T1 value of the myocardium was measured as 1253.9 ± 41.6 msec and myocardial extracellular volume fraction was measured as 27.2 ± 1.8%.

Differences in clinical and other CMR findings according to the presence of LGE

Among clinical findings, the QRS duration was significantly longer in patients with LGE compared to patients without LGE (P = 0.021). The prevalence of septal accessory pathway was significantly higher in patients with LGE compared to patients without LGE (P = 0.011). In addition, the prevalence of lateral accessory pathway was significantly lower in patients with LGE compared to patients without LGE (P = 0.046). Other findings did not show significant differences between the two groups. Among CMR findings, a significantly higher prevalence of regional myocardial wall thinning was observed in patients with LGE (P = 0.001). The prevalence of akinesia was also significantly different between the two groups (P = 0.001) with akinesia being more prevalent in patients with LGE. However, for premature contractions, there was no significant difference between the two groups (P > 0.999). The mean left ventricular end-diastolic volume was significantly larger (P = 0.003) and left ventricular ejection fraction was significantly decreased (P < 0.001) in patients with LGE. Likewise, the prevalence of low ejection fraction was significantly higher in patients with LGE (7/9, 77.8%) than patients without LGE (0/13, 0.0%) (P < 0.001). In addition, patients with LGE showed significantly decreased right ventricular ejection fraction compared to patients without LGE (P = 0.001). The mean values of myocardial native T1 and extracellular volume fraction were significantly higher in patients with LGE compared to patients without LGE (P < 0.001 and 0.006, respectively), especially at the septum (P < 0.001 for both), but not for the lateral wall of the left ventricle (P = 0.284 and 0.793, respectively).

Comparison of major findings according to performance of RFA

The major findings were compared according to performance of RFA and the results are summarized in Table 3. Among the 14 patients who underwent RFA before CMR, 9 patients showed no RWMA but 5 patients still had RWMA on CMR even after successful RFA. The prevalence of regional premature contractions was significantly lower in patients who underwent RFA (P = 0.002). However, we observed no significant differences in the prevalences of regional akinesia and regional myocardial wall thinning between the two groups (P > 0.999 for both). In addition, there were no significant differences in the prevalences of LGE and low ejection fraction between the two groups (P = 0.662 and > 0.999, respectively).
A set diagram was drawn to describe logical relations between the major findings (Fig 3). All 9 patients without RWMA received RFA before CMR and did not show low ejection fraction as well as LGE. Among the 13 patients with RWMA at the preexcited segment, 7 patients showed low ejection fraction and all these patients had LGE. Of the 7 patients with low ejection fraction, 1 patient had regional premature contractions and 6 patients had regional akinesia with myocardial wall thinning (Fig 4). Of the 6 patients without low ejection fraction from regional premature contractions, 2 patients showed LGE and 4 patients did not. All patients with regional akinesia had a septal accessory pathway; 4 patients underwent RFA and 2 patients did not. In addition, we observed that the prevalence of the septal accessory pathway (92.3%, 12/13) was significantly higher in patients with RWMA compared to patients without RWMA (22.2%, 2/9) \( (P < 0.001) \) from the diagram. The prevalence of LGE in patients with RWMA (69.2%, 9/13) was also significantly higher than in patients without RWMA (0.0%, 0/9) \( (P < 0.001) \).

### Table 3. Comparison of major findings according to performance of RFA.

|                | RFA (+) (n = 14) | RFA (-) (n = 8) | \( P \) value |
|----------------|------------------|-----------------|--------------|
| RWMA           | 5 (35.7%)        | 8 (100.0%)      | 0.006        |
| Premature contraction | 1 (7.1%)    | 6 (75.0%)      | 0.002        |
| Akinesia       | 4 (28.6%)        | 2 (25.0%)       | > 0.999      |
| Wall thinning  | 4 (28.6%)        | 2 (25.0%)       | > 0.999      |
| LGE            | 5 (35.7%)        | 4 (50.0%)       | 0.662        |
| Low ejection fraction | 4 (28.6%)  | 3 (37.5%)      | > 0.999      |

Values are patient number (%).
RFA = radiofrequency ablation; RWMA = regional wall motion abnormality; LGE = late gadolinium enhancement.

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### Relationships between major findings with a set diagram

A set diagram was drawn to describe logical relations between the major findings (Fig 3). All 9 patients without RWMA received RFA before CMR and did not show low ejection fraction as well as LGE. Among the 13 patients with RWMA at the preexcited segment, 7 patients showed low ejection fraction and all these patients had LGE. Of the 7 patients with low ejection fraction, 1 patient had regional premature contractions and 6 patients had regional akinesia with myocardial wall thinning (Fig 4). Of the 6 patients without low ejection fraction from regional premature contractions, 2 patients showed LGE and 4 patients did not. All patients with regional akinesia had a septal accessory pathway; 4 patients underwent RFA and 2 patients did not. In addition, we observed that the prevalence of the septal accessory pathway (92.3%, 12/13) was significantly higher in patients with RWMA compared to patients without RWMA (22.2%, 2/9) \( (P < 0.001) \) from the diagram. The prevalence of LGE in patients with RWMA (69.2%, 9/13) was also significantly higher than in patients without RWMA (0.0%, 0/9) \( (P < 0.001) \).

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Discussion

We evaluated myocardial characteristics of the preexcited myocardium using CMR in adult patients with WPW syndrome. In our results, we observed a relatively high prevalence of LGE in the study participants (9/22, 40.9%) exclusively at the basal septum. The prevalence of septal accessory pathway was significantly higher in patients with LGE. In addition, the prevalences of regional myocardial wall thinning and regional akinesia were significantly higher in patients with LGE. Left ventricular end-diastolic volume was significantly larger and both ventricular ejection fractions were significantly decreased in patients with LGE. The native T1 value and extracellular volume fraction were significantly increased in patients with LGE, especially at the septum, which might support the presence of myocardial fibrosis. In addition, there were no significant relationships between RFA and abnormal CMR findings such as regional akinesia, regional myocardial wall thinning, LGE and low ejection fraction in the present study.

Although we included patients with RWMA observed on echocardiography, only 13 patients (13/22, 59.1%) had RWMA on CMR. This is probably because the patients without RWMA on CMR underwent RFA before undergoing CMR. As ventricular preexcitation in the manifest WPW syndrome occurs at the myocardium close to the ventricular insertion of the accessory pathway, we thought that abnormal findings in the myocardium on CMR might be exclusively observed at the basal left ventricle [23]. In addition, all these abnormal findings were observed at the preexcited segment in patients with a septal accessory pathway, namely...
the basal septum, with the exception of 1 patient with a right posterior accessory pathway who had a preexcited segment close to the inferior septum. Hypothetically, this finding might be related to the relatively shorter conduction time between the sinus node and septal accessory pathway [7,8,13], which might have more effects on the myocardium compared to the right or left accessory pathways.

Recently published literatures have reported that non-physiologic activation through the accessory pathway can directly lead to heart failure [6–8,13,14,24]. According to this hypothesis, abnormally decreased local preload by premature contractions can decrease the workload of the preexcited myocardium, which might induce regional myocardial wall thinning [25–27]. Regional myocardial wall thinning could then induce the systolic bulging of the corresponding segment, which in turn progresses to heart failure. Likewise, these findings were exclusively observed at the basal septum in patients with a septal accessory pathway. Previous research has also reported that regional myocardial wall thinning and/or heart failure in WPW syndrome are reversible and that cardiac function can be restored after RFA. However, in the present study, we observed 9 patients (9/22, 40.9%) with LGE at the basal septum, which could suggest myocardial fibrosis. Also, regional myocardial wall thinning, regional akinesia and low ejection fraction were only present in patients with LGE. In addition, there were no significant differences between these abnormal findings and the performance of RFA. In the set diagram, we observed that 3 of the 7 patients with regional premature contractions showed LGE, with 1 patient showing low ejection fraction while the other 2 patients did not. The 4 patients with regional premature contractions without LGE did not present with low ejection fraction. From these findings, we deduced that continuous premature contractions might cause regional myocardial wall thinning, which might proceed to myocardial fibrosis and lead to gradual worsening of the RWMA from premature contractions to akinesia along with the occurrence of persistent left ventricular systolic dysfunction even after successful RFA.

The hitherto published literatures have almost all focused on echocardiographic findings in pediatric patients, whereas we focused on CMR for adult patients, who might be diagnosed later in life and who might be exposed to the accessory pathway for a long period of time. Hence, we observed different findings such as myocardial fibrosis that could be related to persistent left ventricular systolic dysfunction even after successful RFA. We thought that our research could also help explain why three pediatric patients in a previous study had irreversible heart failure in spite of RFA [6]. Expectably, we observed that premature contractions were not noted in patients with RFA except for 1 patient with right posterior accessory pathway, who had a short time interval between RFA and CMR. Prior studies have suggested that premature contractions of the ventricle can persist after successful RFA probably due to the existence of a cardiac memory, and that these abnormal contractions might gradually return to normal contractions over a 1-month period [28,29]. However, from the results of the present study, we assumed that a few patients could have myocardial fibrosis before RFA, which might progress to regional myocardial wall thinning and akinesia, and ultimately to persistent left ventricular systolic dysfunction in spite of RFA. From a different perspective, performing RFA would be a critical determinant of myocardial fibrosis. However, there was no significant difference in LGE according to RFA in the present study. In addition, RFA is usually applied to a very small area near the atrioventricular annulus after accessory pathway localization, but the areas of LGE were much larger than what would be expected with just ablation. Further prospective studies using CMR with a large study population might be necessary to confirm these findings.

This study has some limitations. First, we included a small number of patients in this preliminary study. Second, we selected eligible patients with grossly visible RWMA on echocardiography because non-visible RWMA can be related to very small areas of preexcited segment,
and it would be difficult to characterize myocardium on CMR considering spatial resolution. In actual practice, however, not all patients with WPW syndrome would undergo echocardiography. This ultimately raises the possibility of a selection bias, and consequentially the incidence of LGE might have been higher than its actual value. Third, although we prospectively performed CMR in this study, not all patients underwent the EP study and clinical follow-up varied among the patients. To investigate clinical findings related to myocardial fibrosis and heart failure in patients with WPW syndrome, further prospective studies with larger populations are necessary.

Conclusions
We observed a relatively high prevalence of myocardial fibrosis at the preexcited myocardium of adult WPW syndrome patients, exclusively at the basal septum with septal accessory pathway in the present study. In some cases, myocardial fibrosis accompanied regional akinesia and regional myocardial wall thinning. These abnormal findings might have occurred from continuous premature contractions by the septal accessory pathway and might be related to persistent left ventricular systolic dysfunction even after successful RFA. A further prospective study using CMR with a large population is necessary to identify myocardial characteristics at the preexcited myocardium in WPW syndrome, which might provide new perspectives for the disease and help develop management strategies in the future.

Author Contributions

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References

1. Ticzon AR, Damato AN, Caracta AR, Russo G, Foster JR, Lau SH. Interventricular septal motion during preexcitation and normal conduction in Wolff-Parkinson-White syndrome: echocardiographic and electrophysiologic correlation. Am J Cardiol. 1976; 37: 840–847 PMID: 1266749

2. Lebovitz JA, Mandel WJ, Laks MM, Kraus R, Weinstein S. Relationship between the electrical (electrocardiographic) and mechanical (echocardiographic) events in Wolff-Parkinson-White syndrome. Chest. 1977; 71: 463–469 PMID: 852320

3. Pappone C, Manguso F, Santinelli R, Vicedomini G, Sala S, Paglino G, et al. Radiofrequency ablation in children with asymptomatic Wolff-Parkinson-White syndrome. N Engl J Med. 2004; 351: 1197–1205. https://doi.org/10.1056/NEJMoa040625 PMID: 15371577

4. Santinelli V, Radinovic A, Manguso F, Vicedomini G, Gulletta S, Paglino G, et al. The natural history of asymptomatic ventricular pre-excitation a long-term prospective follow-up study of 184 asymptomatic children. J Am Coll Cardiol. 2009; 53: 275–280. https://doi.org/10.1016/j.jacc.2008.09.037 PMID: 19147045
5. Soria R, Fernandez F, Heller J, Birtile J, Cherif F, Barrillon A, et al. [Wolff-Parkinson-White syndrome and cardiopathies]. Arch Mal Coeur Vaiss. 1984; 77: 1468–1480 PMID: 6240236

6. Fazio G, Mongiovì M, Sutera L, Novo G, Novo S, Pipitone S. Segmental dyskinesia in Wolff-Parkinson-White syndrome: a possible cause of dilative cardiomyopathy. Int J Cardiol. 2008; 123: e31–34. https://doi.org/10.1016/j.ijcard.2006.11.109 PMID: 17292982

7. Kwon BS, Bae EJ, Kim GB, Noh CI, Choi JY, Yun YS. Septal dyskinesia and global left ventricular dysfunction in pediatric Wolff-Parkinson-White syndrome with septal accessory pathway. J Cardiovasc Electrophysiol. 2010; 21: 290–295. https://doi.org/10.1111/j.1540-8167.2009.01612.x PMID: 19804548

8. Udink ten Cate FE, Kruessell MA, Wagner K, Trieschmann U, Emmel M, Brockmeier K, et al. Dilated cardiomyopathy in children with ventricular preexcitation: the location of the accessory pathway is predictive of this association. J Electrocardiol. 2010; 43: 146–154. https://doi.org/10.1016/j.jelectrocard.2009.09.007 PMID: 19879594

9. Marti-Almor J, Bazan V, Morales G, Guerra JC. [Heart failure in a patient with Wolff-Parkinson-White syndrome]. Rev Esp Cardiol. 2011; 64: 1217–1218.

10. Yodogawa K, Ono N, Seino Y. Rapid recovery from congestive heart failure following successful radiofrequency catheter ablation in a patient with late onset of Wolff-Parkinson-White syndrome. Intern Med. 2012; 51: 277–280 PMID: 22293802

11. Chandra MS, Kerber RE, Brown DD, Funk DC. Echocardiography in Wolff-Parkinson-White syndrome. Circulation. 1976; 53: 943–946 PMID: 131657

12. DeMaria AN, Vera Z, Neumann A, Mason DT. Alterations in ventricular contraction pattern in the Wolff-Parkinson-White syndrome. Detection by echocardiography. Circulation. 1976; 53: 249–257 PMID: 1245032

13. Tomaske M, Janousek J, Razek V, Gebauer RA, Tomek V, Hindricks G, et al. Adverse effects of Wolff-Parkinson-White syndrome with right septal or posteroseptal accessory pathways on cardiac function. Europace. 2008; 10: 181–189. https://doi.org/10.1093/europace/eun005 PMID: 18256123

14. Dai CC, Guo BJ, Li WX, Xiao YY, Jin M, Han L, et al. Dysynchronous ven tricular contraction in Wolff-Parkinson-White syndrome: a risk factor for the development of dilated cardiomyopathy. Eur J Pediatr. 2013; 172: 1491–1500. https://doi.org/10.1007/s00431-013-2070-z PMID: 23812508

15. Cummings KW, Bhatta S, Javidan-Najad C, Bierhals AJ, Gutierrez FR, Woodard PK. A pattern-based approach to assessment of delayed enhancement in nonischemic cardiomyopathy at MR imaging. Radiographics. 2009; 29: 89–103. https://doi.org/10.1148/rg.291085052 PMID: 19168838

16. Ugander M, Oki AJ, Hsu LY, Kellman P, Greiser A, Aletras AH, et al. Extracellular volume imaging provides insights into overt and sub-clinical myocardial pathology. Eur Heart J. 2012; 33: 1268–1278. https://doi.org/10.1002/euhj.201111 PMID: 22279111

17. Cain ME, Luke RA, Lindsay BD. Diagnosis and localization of accessory pathways. Pacing Clin Electrophysiol. 1992; 15: 801–824 PMID: 1382283

18. Cosio FG, Anderson RH, Kuck KH, Becker A, Borggreve M, Campbell RW, et al. Living anatomy of the atrioventricular junctions. A guide to electrophysiologic mapping. A Consensus Statement from the Cardiac Nomenclature Study Group, Working Group of Arrhythmias, European Society of Cardiology, and the Task Force on Cardiac Nomenclature from NASPE. Circulation. 1999; 100: e31–37 PMID: 10430823

19. Lee JJ, Liu S, Naef MS, Ugander M, Han J, Kawel N, et al. Myocardial T1 and extracellular volume fraction mapping at 3 tesla. J Cardiovasc Magn Reson. 2011; 13: 75. https://doi.org/10.1186/1532-429X-13-75 PMID: 22123333

20. Shah DJ, Kim HW, James O, Parker M, Wu E, Bonow RO, et al. Prevalence of regional myocardial thinning and relationship with myocardial scarring in patients with coronary artery disease. JAMA. 2013; 309: 909–918. https://doi.org/10.1001/jama.2013.1381 PMID: 23462787

21. Schuster A, Hor KN, Kowallick JT, Beerbaum P, Kutty S. Cardiovascular Magnetic Resonance Myocardial Feature Tracking: Concepts and Clinical Applications. Circ Cardiovasc Imaging. 2016; 9: e004077. https://doi.org/10.1161/CIRCIMAGING.115.004077 PMID: 27009468

22. Diesbourg LD, Prato FS, Wisenberg G, Drost DJ, Marshall TP, Carroll SE, et al. Quantification of myocardial blood flow and extracellular volumes using a bolus injection of Gd-DTPA: kinetic modeling in canine ischemic disease. Magn Reson Med. 1992; 23: 239–253 PMID: 15490323

23. Lee HJ, Uhln JS, Joung B, Hong YJ, Hur J, Choi BW, et al. Detecting Regional Myocardial Abnormalities in Patients With Wolff-Parkinson-White Syndrome With the Use of ECG-Gated Cardiac MDCT. AJR Am J Roentgenol. 2016; 206: 719–725. https://doi.org/10.2214/AJR.15.15141 PMID: 26866341

24. Emmel M, Balaji S, Sreeram N. Ventricular preexcitation associated with dilated cardiomyopathy: a causal relationship? Cardiol Young. 2004; 14: 594–599. https://doi.org/10.1017/S1047951104006031 PMID: 15679994
25. Prinzen FW, Cheriex EC, Delhaas T, van Oosterhout MF, Arts T, Wellens HJ, et al. Asymmetric thickness of the left ventricular wall resulting from asynchronous electric activation: a study in dogs with ventricular pacing and in patients with left bundle branch block. Am Heart J. 1995; 130: 1045–1053 PMID: 7484735

26. Vernooy K, Dijkman B, Cheriex EC, Prinzen FW, Crijns HJ. Ventricular remodeling during long-term right ventricular pacing following His bundle ablation. Am J Cardiol. 2006; 97: 1223–1227. https://doi.org/10.1016/j.amjcard.2005.11.044 PMID: 16616030

27. Tsai IC, Huang JL, Ueng KC, Hung YW, Hung CF, Liao WC, et al. Global and regional wall motion abnormalities of pacing-induced heart failure assessed by multi-detector row CT: a patient and canine model study. Int J Cardiovasc Imaging. 2010; 26: 223–235. https://doi.org/10.1007/s10554-010-9684-2 PMID: 20730496

28. Ghosh S, Rhee EK, Avari JN, Woodard PK, Rudy Y. Cardiac memory in patients with Wolff-Parkinson-White syndrome: noninvasive imaging of activation and repolarization before and after catheter ablation. Circulation. 2008; 118: 907–915. https://doi.org/10.1161/CIRCULATIONAHA.108.781658 PMID: 18697818

29. Delelis F, Lacroix D, Richardson M, Klug D, Kouakam C, Brigadeau F, et al. Two-dimensional speckle-tracking echocardiography for atrioventricular accessory pathways persistent ventricular pre-excitation despite successful radiofrequency ablation. Eur Heart J Cardiovasc Imaging. 2012; 13: 840–848. https://doi.org/10.1093/ehjci/jes048 PMID: 22398658