Myocardial fibrosis in the right ventricle detected on ECG gated 320 slice CT showed a short term poor prognosis in subjects with pulmonary hypertension

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Presence of myocardial fibrosis in the right ventricular (RV) myocardium (RVM) may contribute to a poor prognosis in a subject with Tetralogy of Fallot [1]. If myocardial fibrosis in RVM can be detected in subjects who have other diseases with increased RV pressure, such as pulmonary arterial hypertension (PAH) or chronic thromboembolic pulmonary hypertension (PH) (CTEPH), a prognosis may be predicted.

Magnetic resonance imaging (MRI) can detect myocardial fibrosis in the left ventricular (LV) myocardium (LVM) [2], but some subjects with PAH or CTEPH cannot tolerate long acquisition time in the narrow space of an MRI scanner.

Recently, enhanced multislice computed tomography (CT), as well as MRI, was shown to detect myocardial fibrosis in LVM as contrast defect in the early phase and abnormal enhancement in the late phase [3].

In subjects with PAH and CTEPH, evaluation of the presence of thrombi in the pulmonary artery (PA) using CT is essential. Furthermore, quantitative evaluation of RV function by retrospective electrocardiogram (ECG) gating CT is determined as appropriate in the ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 appropriate use criteria for cardiac CT [4]. Since subjects with PAH and CTEPH show hypertrophied RVM, by adding late acquisition with prospective ECG gating CT, myocardial fibrosis can be visualized easily with minimum radiation exposure addition.

To evaluate the significance of presence of myocardial fibrosis in RVM on CT, as represented as an early defect in the early phase and conversely abnormal enhancement in the late phase on enhance CT, in PH subjects who underwent ECG gated enhanced 320 slice CT.

A total of 56 PH subjects confirmed on right heart catheterization (RHC) (15 males, age 57 ± 15 years, 33 CTEPH, 21 PAH, and 2 others) underwent ECG gated 320 slice CT (Aquilion one, Toshiba Medical) to evaluate PA, and transthoracic echocardiogram (TTE) within 3 months without any clinical incidents. Subjects were followed for a median of 9.5 months and all cause death was evaluated.

Two dimensional TTE was performed to evaluate RV and right atrial (RA) sizes, as well as RV systolic and diastolic functions. The parameters included a measure of tricuspid annular plane systolic excursion (TAPSE), estimated systolic PA pressure (sPAP), acceleration time per ejection time (AcT/ET), tricuspid valve (TV) systolic velocity (TV S′) and TV early diastolic tricuspid inflow velocity (E)/early diastolic tricuspid annulus velocity (E′) (TV E/E′), and cardiac output (CO).

To obtain not only images of the whole heart including RV and coronary arteries, but also images of the PA, all CT scans were obtained using a double volume conventional scan with retrospective ECG-gating using 320-slice CT with a 0.5 mm slice thickness and 0.35 s/rotation with a downward direction. Tube voltage was set at 120 kV and tube current was set at 580 mA with tube current dose modulation. We injected 60 ml of contrast material (350 mg I/ml) at 3.5 ml/s, followed by injection of a saline-to-contrast material mixture (40 ml contrast material at 2.0 ml/s and 30 ml saline at 1.5 ml/s), followed by injection of 20 ml pure saline at 1.5 ml/s [5,6]. All CT examinations were performed for a normal workup to diagnose or evaluate PH, with a scanning delay of 20–30 s for optimal PA visualization. Single volume conventional scan with prospective ECG-gating was added and if there was abnormal enhancement in RVM, we regarded this as myocardial fibrosis (Fig. 1).

All RHCs were performed by pneumologists with more than 5 years experience in managing PH patients. A Swan–Ganz thermodilution catheter was used and a jugular approach was preferred. sPAP, diastolic (dPAP) and mean PA (mPAP) pressures, RA pressure, CO and cardiac index (CI) were measured by thermodilution method and pulmonary vascular resistance.

Myocardial fibrosis in RVM was detected in 16 subjects (5 males, 56 ± 12 years old, 9 CTEPH, 6 PAH and 1 other). There were no significant differences of frequency of myocardial fibrosis in RVM among the three groups (Fig. 2).

Comparing subjects with and without myocardial fibrosis in RVM on CT (Tables 1–5), only CO (l/min) calculated on TTE was significantly lower, and the occurrence of all cause death during the observation period was significantly higher in subjects with myocardial fibrosis in RVM than in subjects without myocardial fibrosis in RVM (both $P<0.05$), even though there were no significant differences between the two groups in other factors, especially hemodynamic state parameters on TTE (Table 2), CT (Table 3), and RHC (Table 4). Furthermore the occurrence of all cause death was significantly higher in subjects with myocardial fibrosis in RVM than in subjects without myocardial fibrosis in RVM on CT ($P<0.05$) (Table 5).

Significant differences between subjects with and without myocardial fibrosis in RVM were observed at each time point when the whole follow-up period was compared by further Kaplan–Meier analysis and log rank test ($P=0.024$) (Fig. 3).

The presence of myocardial fibrosis in RVM detected on ECG-gated 320 slice CT may influence the short term poor prognosis in PH subjects, even though there were no significant differences in hemodynamic state parameters acquired from CT, TTE and RHC (except CO on TTE) between subjects with and without myocardial fibrosis in RVM on CT.

In contrast to hemodynamic state parameters, which tend to fluctuate, the presence of myocardial fibrosis in RVM is a permanent, irreversible, and organized morphological parameter that may be useful for accurately predicting the prognosis of PH subjects.

To our knowledge, our study is the first to describe the evaluation of myocardial fibrosis in RVM based on CT heart images in PH subjects.

Since the gold standard for the detection of myocardial fibrosis is MRI [2], the detection of myocardial fibrosis on CT should be compared with that detected on MRI, both qualitatively and quantitatively, to evaluate the efficiency of CT for such detection, even though subjects with PAH or CTEPH may not tolerate long acquisition time in the narrow space of an MRI scanner.

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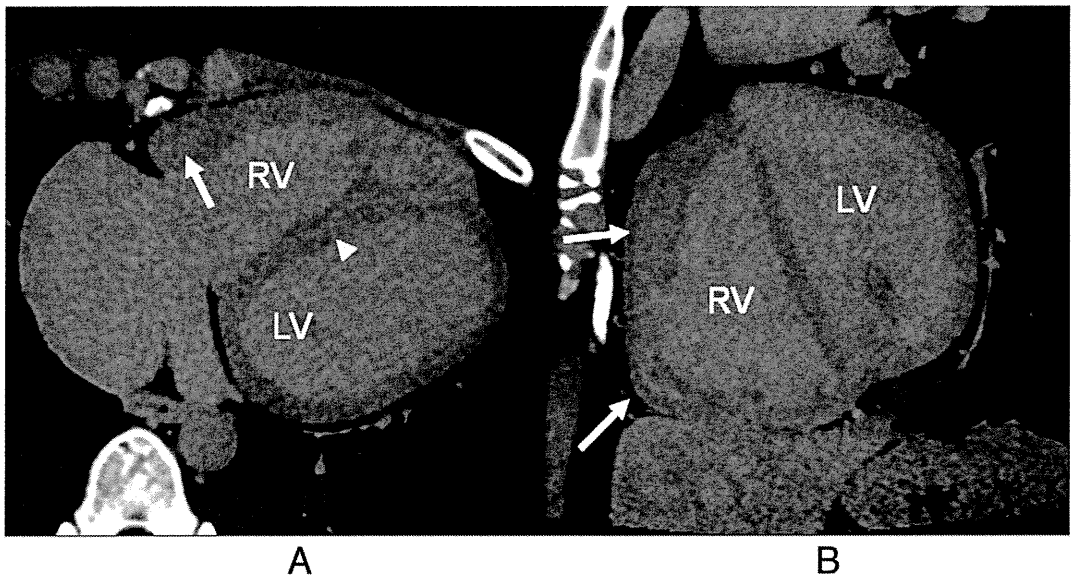

Fig. 1. Typical imaging of myocardial fibrosis (arrows and arrow head in right ventricular (RV) myocardium) in the late phase acquisition.A: Axial source image.B: Multiplanar reconstruction image of short axis of RV.Compared with the left ventricular (LV) myocardium, hypertrophied RV myocardium showed higher computed tomography attenuation in RV anterior to inferior wall (arrows) and RV sided inter ventricular septum (arrowhead).

Our study population was small (N=56), retrospective and non-randomized and located in a single center. The follow-up time was short (median of 9.5 months). Further prospective and long term studies are desired in a larger population. Compared with a non-ECG gated helical scan, the combination of double volume conventional scan with retrospective ECG gated in early phase and single volume conventional scan with prospective ECG gating requires a greater radiation dose, even though information of RV function and coronary arteries can be obtained.

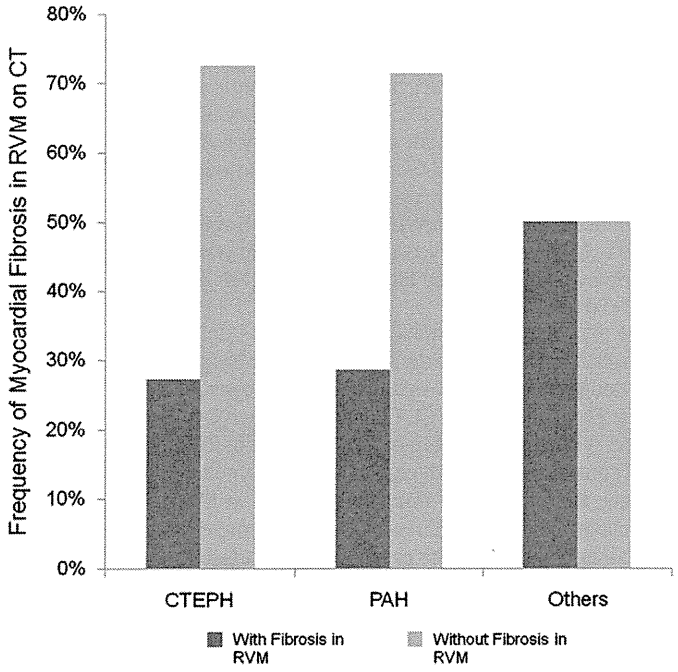

Fig. 2. Frequency of myocardial fibrosis in the right ventricular myocardium (RVM) on computed tomography (CT) in each group.There were no significant differences of frequency of fibrosis in RVM among the three groups: chronic thromboembolic pulmonary hypertension (CTEPH) (N=33), pulmonary arterial hypertension (PAH) (N=21), and others (N=2) (Chi square test P=0.788).

Table 1
Comparison of patient characteristics and general hemodynamic state parameters between subjects with and without myocardial fibrosis in the right ventricular myocardium (RVM) on computed tomography.
There were no significant differences in all these parameters between the two groups.

	With myocardial fibrosis in RVM N=16	Without myocardial fibrosis in RVM N=40	P value
Age (years)	56±12	57±16	0.788
Females (%)	11 (61.8%)	30 (75.0%)	0.633
Systolic blood pressure (mm Hg)	116±18	115±17	0.786
Diastolic blood pressure (mm Hg)	74±15	70±11	0.190
Brain natriuretic peptide (pg/ml)	179±252	181±293	0.987
Six minute walk test (m)	387±110	370±94	0.582

Table 2
Comparison of transthoracic echocardiogram (TTE) findings between subjects with and without myocardial fibrosis in the right ventricular (RV) myocardium (RVM) on computed tomography.
Only cardiac output was significantly lower in subjects with myocardial fibrosis in RVM than in subjects without myocardial fibrosis in RVM (P<0.05).
PASP, TAPSE, AcT/ET, TV S′ and TV E/E′ indicate pulmonary arterial systolic pressure, tricuspid annular plane systolic excursion, acceleration time per ejection time, tricuspid valve (TV) systolic velocity (S′) and TV early diastolic tricuspid inflow velocity (E)/early diastolic tricuspid annulus velocity (E′), respectively.

TTE findings	With myocardial fibrosis in RVM N=16	Without myocardial fibrosis in RVM N=40	P value
RV end diastolic diameter (mm)	40.5±6.7	43.0±8.6	0.417
RV end systolic diameter (mm)	32.6±9.3	34.5±1.7	0.565
Estimated PASP (mmHg)	74±23	68±24	0.419
TAPSE (mm)	20±6	17±6	0.206
RV outflow AcT/ET	0.26±0.06	0.27±0.08	0.654
Cardiac output (l/min)	3.5±1.0	4.4±1.1	0.011*
TV S′	9.6±1.9	11.9±2.5	0.108
TV E/E′	6.4±2.3	6.0±3.9	0.785

* P<0.05.

Table 3
Comparison of electrocardiogram (ECG) gated computed tomography (CT) findings between subjects with and without myocardial fibrosis in the right ventricular (RV) myocardium (RVM) on CT.
There were no significant differences in all these parameters between the two groups. RA indicates right atria.

ECG gated CT findings	With myocardial fibrosis in RVM N = 16	Without myocardial fibrosis in RVM N = 40	P value
RV wall thickness (diastolic) (mm)	3.8 ± 1.2	3.3 ± 1.1	0.165
RV wall thickness (systolic) (mm)	5.5 ± 1.9	5.1 ± 1.7	0.493
RV end diastolic volume (ml)	156 ± 75	138 ± 75	0.438
RV end systolic volume (ml)	106 ± 60	96 ± 70	0.238
RV ejection fraction (%)	34.6 ± 13	34.6 ± 14	0.992
RA end diastolic volume (ml)	121 ± 68	116 ± 61	0.768
RA end systolic volume (ml)	95 ± 61	93 ± 60	0.914

Table 4
Comparison of right heart catheter (RHC) findings between subjects with and without myocardial fibrosis in the right ventricular myocardium (RVM) on computed tomography (CT).
There were no significant differences in all these parameters between the two groups. sPAP, dPAP, mPAP and PVR indicate systolic pulmonary arterial pressure (PAP), diastolic PAP, mean PAP, and pulmonary vascular resistance, respectively.

RHC findings	With myocardial fibrosis in RVM N = 16	Without myocardial fibrosis in RVM N = 40	P value
sPAP (mm Hg)	78 ± 16	74 ± 27	0.571
dPAP (mm Hg)	26 ± 9	25 ± 10	0.744
mPAP (mm Hg)	46 ± 10	43 ± 16	0.497
Pulmonary capillary wedge pressure (mm Hg)	8.8 ± 3.4	8.5 ± 3.8	0.779
Cardiac output (l/min)	4.3 ± 1.2	4.5 ± 1.0	0.539
Cardiac index (l/min/m^2)	2.9 ± 0.9	2.8 ± 0.6	0.629
PVR (dyne · s · cm^{-5})	733 ± 84	701 ± 58	0.759

Detection of myocardial fibrosis in RVM on CT was very subjective and strict differentiation of myocardial fibrosis with myocardial edema due to inflammation cannot be achieved (additional performance of 18F-FDG-PET may be desired) [7,8].

Myocardial fibrosis in RVM as detected on ECG gated 320 slice CT in PH subjects is a permanent, irreversible, and organized morphological parameter that may be useful for accurately predicting the prognosis of PH subjects.

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Table 5
Comparison of occurrence of events during observation periods between subjects with and without myocardial fibrosis in the right ventricular myocardium (RVM) on computed tomography (CT).
The occurrence of all cause death was significantly higher in subjects with myocardial fibrosis in RVM than subjects without myocardial fibrosis in RVM (P<0.05).

	With myocardial fibrosis in RVM N = 16	Without myocardial fibrosis in RVM N = 40	P value
Event	5 (31.3%)	4 (10.0%)	0.05
Congestive heart failure	1	4	0.657
Stroke	2	0	0.023
Nonfatal myocardial infraction	0	0	–
All cause death	2 (12.5%)	0 (0%)	0.023*

* P<0.05.

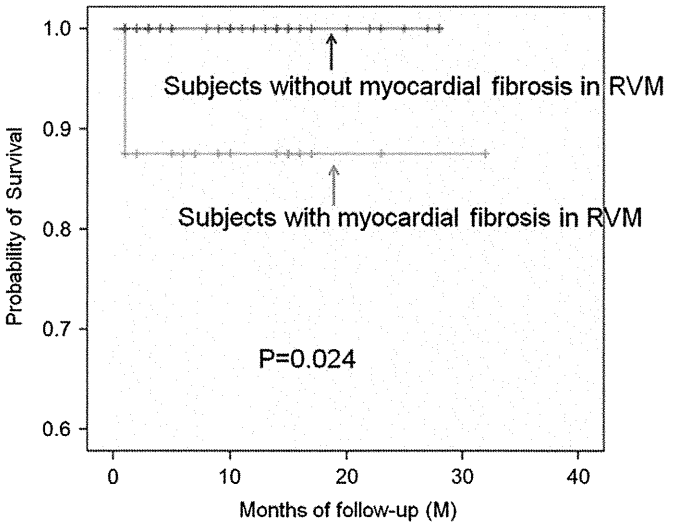

Fig. 3. Kaplan–Meier survival curves for occurrence of all cause death.All cause death was observed more frequently in patients with myocardial fibrosis in the right ventricular myocardium (RVM) on computed tomography (CT) than in those without myocardial fibrosis in RVM on CT (log-rank test, P = 0.024) during the observation period.

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