Specific organized substrates of ventricular fibrillation: comparison of 320-slice CT heart images in non-ischemic ventricular fibrillation subjects with non-ischemic sustained and non-sustained ventricular tachycardia subjects.

(心室細動における特異的基質の検討：非虚血性的心室細動症例における 320 列 CT 心臓画像、持続性、非持続性心室頻拍症例との比較)
Abstract

Purpose: If specific organized substrates of ventricular-fibrillation (VF) are identified, they may provide important-information for prevention of sudden-cardiac-death. To identify specific organized substrates of VF, we compared 320-slice CT heart images in non-ischemic VF subjects with non-ischemic sustained and non-sustained ventricular-tachycardia (VT) subjects.

Materials and methods: Retrospective analysis of a total of 103 subjects who had VF (17 subjects; age, 59±16 years), sustained VT (20 subjects; 62±19 years), or non-sustained VT (66 subjects; 60±15 years) underwent 320-slice CT (Aquilion one).

Results: After excluding 26 ischemic subjects with >50% stenosis in any coronary arteries on CT, myocardial infarction, or coronary vasospastic angina, a total of 77 non-ischemic subjects (12 VF subjects; age, 58±18 years), (13 sustained VT subjects; 55±20 years) or (52 non-sustained VT subjects; 58±15 years) were analyzed. On CT, myocardial abnormal-late-enhancement was significantly more frequent in the VF group (75%, all myocardial abnormal-late-enhancement in left-ventricle) than in the sustained VT group (31%) and the non-sustained VT group (35%) (both P<0.01).

Myocardial fatty change was significantly more frequent in the sustained VT group (54%) than in the VF group (17%) and the non-sustained VT group (12%) (both
P<0.01). Final diagnoses of the non-ischemic VF and sustained groups included four subjects in each case with normal cardiac structure on transthoracic echocardiogram; the former included two subjects who had abnormal-late-enhancement on CT without specific ECG findings.

Conclusions: Myocardial abnormal-late-enhancement and fatty change on CT may be substrates of VF or sustained VT in non-ischemic subjects. 320-slice CT can evaluate both coronary arteries and myocardium.
1. Introduction

The majority of sudden cardiac death (SCD) are caused by ventricular arrhythmias such as ventricular fibrillation (VF) and ventricular tachycardia (VT) [1]. As a result of the use of automated external defibrillators (AEDs) and implantable cardioverter defibrillators (ICDs), the number of survivors after occurrence of VF has increased. If we can accurately identify subjects at high risk for coronary disease and heart disease using non-invasive imaging and estimate their probabilities for future occurrence of VF or sustained VT (which may convert to VF), we may be able to develop strategies for preventive therapy in such subjects using antiarrhythmic drugs or implantation of ICDs. Therefore identification of specific organized substrates for occurrence of VF or sustained VT via non-invasive imaging is very important for prevention of SCD.

Late gadolinium-enhanced cardiovascular magnetic resonance (CMR) has enabled detection of myocardial abnormal late enhancement, suggesting presence of fibrosis non-invasively [2–6], but evaluation of coronary arteries by CMR is not still established. As a new non-invasive diagnostic modality for detecting myocardial fibrosis, multislice computed tomography (CT) is receiving increased attention. Because iodinated contrast materials used in CT have similar kinetics to gadolinium-based contrast media, enhanced CT can also visualize myocardial abnormal late enhancement in a manner
similar to CMR [7–9] since both contrast media show a defect in the early phase and abnormal enhancement in the late phase in the corresponding myocardium. In contrast, myocardial fatty change on CT reveals areas with <0 Hounsfield Units (HU) CT attenuation in both early and late phases [10]. Furthermore, evaluation of coronary arteries on CT has already been established with high accuracy compared with conventional coronary angiography, integrated backscatter intravascular ultrasound [11], or intravascular optical coherence tomography [12], if CT incorporating 64 or more detector rows is used; furthermore, among all new types of CT, 320 slice CT has the greatest number of detector rows and can acquire a whole heart image in only one conventional scan [13,14].

To identify specific organized substrates of VF, we compared 320 slice CT heart images in non-ischemic subjects who had VF with those who had sustained and non-sustained VT.

2. Materials and methods

2.1. Patient population

This is a retrospective analysis from January 2008 to April 2012, acquired from a total of 103 consecutive subjects who had VF (17 subjects; mean age, 59±16 years),
sustained VT (20 subjects; 62±19 years) or non-sustained VT (66 subjects; 60±15 years) underwent retrospective electrocardiogram (ECG) gated 320 slice CT (Aquilion one, Toshiba Medical) and transthoracic echocardiogram (TTE) (IE33, Philips) over a two-week period without any clinical events between examinations. Because of occurrence of critical ventricular arrhythmias with and without symptoms, CT was performed in all subjects to evaluate characteristics of coronary arteries, myocardium and cardiac function.

Survivors from VF who were confirmed with obvious ischemic findings such as preceding anginal chest pain and ST elevation on ECG with elevated Troponin T or I, first underwent invasive coronary angiography and such subjects were excluded in this analysis. For comparison, subjects with sustained VT and non-sustained VT were selected from recent Holter ECG data, but they also did not reveal obvious angina chest pain or ischemic ECG findings.

All CT acquisitions gave appropriate (50%) or uncertain (50%) indications in accordance with ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 appropriate use criteria for cardiac CT [15]. In addition to evaluation of coronary arteries, the main reasons for appropriate indications for cardiac CT were “evaluation of ventricular morphology and systolic function, evaluation of left ventricular (LV)
function, in heart failure subjects” (31%), “evaluation of ventricular morphology and systolic function, assessment of right ventricular morphology, suspected arrhythmogenic right ventricular cardiomyopathy (ARVC)” (7%), and “evaluation of Intra- and extracardiac structures, noninvasive coronary vein mapping, prior to placement of biventricular pacemaker” (5%), et al. The main reason for uncertain indications for cardiac CT was “arrhythmia etiology unclear after initial evaluation, non-sustained VT (49%).

On TTE, standard parameters were acquired in the customary fashion. On CT, when contrast defects were observed in myocardium in the early phase, late-phase acquisition was added six minutes after contrast injection.

After excluding ischemic subjects on CT, clinical information, or other diagnostic modalities, the non-ischemic subjects in each group were analyzed.

VF was defined as the presence of irregular undulations of varying contour and amplitude. Sustained VT was defined as VT lasting for 30 s or more. Non-sustained VT was defined as VT lasting for less than 30 s.

2.3. 320 slice CT protocol

All 103 subjects underwent 320 slice CT. Heart rhythm was controlled during CT acquisition in all subjects. Retrospective ECG gated conventional enhanced 320 slice
CT was performed with a slice thickness of 0.5 mm, tube voltage of 120 kV, and a tube current maximum of 580 mA as reported previously [13,14,16,17]. All subjects whose heart rates (HR) (beats per minute) were >60, received 10 mg propranolol (AstraZeneca) or 20 mg metoprolol tartrate (AstraZeneca) 1 h prior to the CT scan, except for those who had severe heart failure, bronchial asthma, hypotension, or bradycardia due to conditions such as atrioventricular block or sick sinus syndrome. Just prior to the scanning procedure patients were administered 2 doses of isosorbide dinitrate sublingually to facilitate dilation of coronary arteries and enable acquisition of clear images even in the small branches of coronary arteries.

We used a HeartNAVI® system which is a standard CT scanner protocol developed by Toshiba Medical Company. This system provides the best temporal resolution that can be optimized according to the HR during scanning. In this system, before performing actual acquisition, rehearsal of breath holding was carried out, and HR during scanning was estimated. Concerning the quantity of acquired heartbeat data, based on the estimates of HR, the following scanning conditions were established: When the estimated HR was b66, 1 heartbeat of data was acquired and half reconstruction was performed; when the estimated HR was 66–79, 2 heartbeats of data were acquired and 2 sector reconstruction was performed; when the estimated HR was
80–117, 3 heartbeats of data were acquired and 3 sector reconstruction was performed; when the estimated HR was 118–155, 4 heartbeats of data were required and 4 sector reconstruction was performed; if the estimated HR was >156, 5 heartbeats of data were acquired and 5 sector reconstruction was performed to obtain the best temporal resolution. If HR varied during the rehearsal of breath holding such as CAF or frequent premature beats, 1 extra heartbeat of data was acquired. Similarly, if there was no arrhythmia in the rehearsal of breath holds, but unexpected heartbeats occurred during the actual scanning, 1 extra heartbeat of data was also acquired.

Concerning the rotation speed, based on the estimated HR during the rehearsal of breath holds, in order to obtain the best temporal resolution, 4 rotation speeds were used, which were automatically selected from 0.35, 0.375, 0.40, and 0.45 s per rotation in combination with the number of acquired heartbeat data. Furthermore, if the estimated HR during the scan was <81, we utilized an ECG tube current dose modulation system to reduce radiation dose.

For contrast material injection, we employed a routine triphasic protocol. Right antecubital intravenous access was achieved using a 20- or 22-gauge needle and the system was connected to a dual-syringe injector with dual flow option (Dual Shot, Nemoto). In all phases of the study injection was performed at 4 ml/s whenever possible.
During the first phase we injected 50–70 ml of undiluted contrast agent, followed by 20 ml of a 50/50 saline/contrast material mixture and 30 ml of pure saline. Time-resolved (every 1 s) single section CT scans were acquired at the level of the mid-left ventricle during breath holding. Descending aortic time-resolved attenuation was then measured using the time-attenuation evaluation program accessible on the scanner, and when the CT values in the descending aorta had increased to 200 HU, we started the actual examination scan.

In subjects with normal sinus rhythm, volume data were reconstructed at every 5% of the ECG R-to-R intervals using half or multisector reconstruction, depending upon the number of the acquired heartbeat data in which the best temporal resolution could be obtained at the HR during rehearsal of the breath holding.

In subjects with arrhythmia, we checked the ECG information during the scan and selected the 1 heartbeat data with maximum R-to-R interval manually. Using this information, volume data were reconstructed using half reconstruction. If there were 2 or 3 phases which had similar ECG R-to-R intervals, in order to improve temporal resolution, volume data were reconstructed using 2 or 3 sector reconstruction. After acquisition, the reconstructed volume data images were transferred to a workstation (Virtual Place, Aze).
If there was a contrast defect in myocardium in the early phase, late phase acquisition was added using Target mode, one of the prospective ECG gating methods by which acquisition is completed during only one heart beat in spite of occurrence of arrhythmia and which accomplishes minimum radiation exposure; to evaluate presence of abnormal late enhancement in the corresponding myocardium (Fig. 1). If the contrast defect continued in the late phase with <0HU CT attenuation values, we diagnosed this site as myocardial fatty change (Fig. 2).

3. Statistics

All numeric results are expressed as mean ± standard deviation. Statistical analysis was performed with statistical software SPSS (SPSS Japan Inc., version 17.0). The chi square test was used to evaluate significant differences between types of final clinical or image diagnoses. Duncan's multiple comparison was used when comparing frequency of myocardial abnormal late enhancement and fatty change among the three arrhythmia groups in a patient-by-patient analysis. P values less than 0.05 were considered statistically significant.

4. Results
A total of 26 subjects (5 subjects with VF; age 61±8 years, 7 subjects with sustained VT; 74±8 years, and 14 subjects with non-sustained VT; 67±9 years) exhibited ischemic findings such as presence of myocardial infarction on ECG TTE or CT, either clinical or acetylcholine provocation test-confirmed coronary vasospastic angina, or >50% stenosis in any coronary arteries on CT.

The remaining total of 77 subjects did not exhibit these three ischemic findings and were assigned to the non-ischemic group (12 VF subjects; (age, 58±18 years), 13 sustained VT subjects (55±20 years) and (52 non-sustained VT subjects; 58±15 years)).

4.1. Final clinical or image diagnoses of non-ischemic subjects among three arrhythmia groups

The final clinical or image diagnoses of each non-ischemic group are shown in Fig. 3. There were variations in the final clinical or image diagnoses including HCM (as represented by the typical images in Figs. 1 and 2), ARVC (as represented by the typical images in Fig. 4), and cardiac sarcoidosis et al., in all of which the presence of myocardial abnormal late enhancement or fatty change could be evaluated on CT. In the chi square test, there were significant differences between the types of final clinical or image diagnoses and the three arrhythmia groups (P<0.001).
4.2. Frequency of myocardial abnormal late enhancement and fatty change on CT among three “non-ischemic” arrhythmia groups

In a patient-by-patient analysis, the frequency of myocardial abnormal late enhancement on CT was significantly higher in the non-ischemic VF group (75%, all myocardial abnormal late enhancement was in LV) than in the non-ischemic sustained VT group (31%) and the non-ischemic non-sustained VT group (35%) (both P<0.01) (Fig. 5). The frequency of myocardial fatty change on CT was significantly higher in the non-ischemic sustained VT group (54%) than in the non-ischemic VF group (17%) and the non-ischemic non-sustained VT group (12%) (both P<0.01) (Fig. 5).

4.3. Final clinical or image diagnoses and occurrence of abnormal late enhancement in LV myocardium on CT in non-ischemic VF group

The relationships between the final clinical or image diagnoses and the total numbers of subjects and the numbers of subjects with abnormal late enhancement in LV myocardium on CT in the non-ischemic VF group are shown in Fig. 6. This presentation differs partially from Fig. 3, specifically: a total of three subjects diagnosed as having J wave syndrome (1 subject), long QT syndrome (1 subject), or unknown diseases (1 subject), were all classified as having normal heart structure without LV dysfunction on
TTE. One subject diagnosed as having unknown diseases was classified as having normal heart structure with LV dysfunction on TTE. In this Figure, myocardial abnormal late enhancement in LV myocardium on CT occurred frequently and widely in the non-ischemic VF subjects in each clinical or image diagnostic subgroup.

More detailed composition of the non-ischemic VF group in this study is represented by the schema shown in Fig. 7, which presentation also differs partially from Fig. 3, as does Fig. 6. One subject who was diagnosed as having J wave syndrome and another as having long QT syndrome, did not have either abnormal late enhancement or fatty change in LV myocardium on CT. This was consistent with traditional knowledge data and such subjects should be diagnosed on the basis of their ECG, which is currently the case. However, the remaining one subject, who was diagnosed as having unknown disease and classified as having normal heart structure without LV dysfunction on TTE (sigmoid septum only on CT) had abnormal late enhancement in LV myocardium on CT, (as shown in Fig. 8) and was not diagnosed as abnormal on ECG and TTE, but only on CT. Also the one subject diagnosed as having unknown disease and classified as having normal structure with LV dysfunction on TTE had abnormal late enhancement in the LV myocardium on CT. As this subject revealed complete left bundle branch block on ECG, TTE assessors speculated that the presence of LV dysfunction on TTE could be
explained by dyssynchrony due to complete left bundle branch block. The latter revealed severe vasospastic angina pectoris and ST elevation on ECG confirmed by acetylcholine provocation test with normal coronary arteries on conventional coronary angiography. However, during the vasospasm, VF or ventricular arrhythmia did not occur and causes of occurrence of VF could not be explained by vasospastic angina; thus this subject was assigned to the non-ischemic VF group. In fact, these two subjects who had abnormal late enhancement in the LV myocardium on CT, but normal heart structure on TTE did not undergo CMR. Had these subjects undergone CMR, myocardial abnormal late enhancement would have been expected to be detected as clearly, or even more clearly than on CT. However, in the first instance, evaluation of coronary arteries should have priority over evaluation of myocardium in such VF subjects. 320 slice CT can evaluate coronary arteries much more accurately than ordinary CMR and therefore this subject had already been diagnosed as not having ischemic heart disease from information obtained of coronary artery status on 320 slice CT. Furthermore, adding late phase acquisition, we also succeeded in evaluating myocardium in which myocardial abnormal late enhancement was detected simultaneously on CT in the same phase of CT acquisition.
4.4. Final clinical or image diagnoses and occurrence of fatty change in myocardium on CT in non-ischemic sustained VT group

The relationships between the final clinical or image diagnoses and the total numbers of subjects and the numbers of subjects with fatty change in myocardium on CT in the non-ischemic sustained VT are shown in Fig. 9. This presentation partially differs from Fig. 3, specifically: a total of three subjects who were diagnosed as having either long QT syndrome (1 subject), or unknown diseases (2 subjects), were classified as having normal heart structure without LV dysfunction on TTE. Another subject who was diagnosed as having unknown diseases was classified as having normal heart structure with LV dysfunction on TTE.

More detailed composition of the non-ischemic sustained VT group is represented by the schema shown in Fig. 10, which presentation also differs partially from Fig. 3, as does Fig. 9.

Four subjects exhibited normal heart structure on TTE and of these, one subject was diagnosed as having long QT syndrome, and the remaining three subjects exhibited normal ECG and had neither abnormal late enhancement nor fatty change in LV myocardium on CT, nor were they diagnosed as abnormal on ECG, TTE, or CT; furthermore, even if they underwent CMR, such a procedure would also be unable to
diagnose such subjects as abnormal. Nine subjects exhibited organized heart disease on TTE and/or CT. Of these, four subjects were diagnosed as having ARVC, all of whom all had fatty change in the LV or right ventricular myocardium on CT.

5. Discussion

If specific organized substrates of VF are identified and sufficient clinical evidence is accumulated, these may provide important information for prevention of sudden cardiac death in the future, even though, at present recognition of abnormal late enhancement or fatty tissue in myocardium by means of CT may not alter common therapeutic management.

To our knowledge, our study is the first to describe evaluation of the myocardial substrates of VF, or sustained or non-sustained VT, based on 320 slice CT heart images in non-ischemic subjects. Our study revealed in a patient-by-patient analysis that among non-ischemic subjects who did not have myocardial infarction on ECG, TTE, or CT, either clinical or acetylcholine provocation test-confirmed coronary vasospastic angina, nor >50% stenosis in any coronary arteries on CT, the frequency of myocardial abnormal late enhancement on CT was higher in the VF group than in the sustained and non-sustained VT groups; in addition, the frequency of myocardial fatty change was
higher in the sustained VT group than in the VF and non-sustained VT groups. Until now, occurrence of critical ventricular arrhythmia has been thought to be associated with presence of irreversible myocardial damage even in non-ischemic subjects [18,19]. However, our results suggest some relationship between types of critical ventricular arrhythmia and the types of specific organized substrates in myocardium on CT in non-ischemic subjects; of course among critical ventricular arrhythmias, VF is the most important for prognosis of subjects.

The most important finding in this study was that in the non-ischemic VF group, two subjects with normal heart structure on TTE as shown in Fig. 8, had abnormal late enhancement in LV myocardium on CT. These subjects did not exhibit typical ECG findings of either Brugada syndrome, J wave syndrome, or long QT syndrome. From this result, in detection of subjects at high risk for occurrence of VF, the combination of ECG and TTE alone is not deemed to be sufficient.

CMR is the gold standard for detection of fibrosis in LV myocardium and the presence of myocardial fibrosis represented by late gadolinium enhanced CMR is known to be one of the predictors of SCD [20–23]; in addition, CMR is considered one of the initial diagnostic modalities for evaluating identification of substrate for ventricular arrhythmias [24]. However, ischemic heart disease is one of the most
frequent causes of VF, sustained and non-sustained VT. Ischemic subjects would be expected to be included frequently in cohorts with VF, sustained and non-sustained VT; in fact in this study, ischemic subjects were included: 29% in the VF group, 35% in the sustained VT group and 21% in the non-sustained VT group. Therefore the evaluation of coronary arteries is a necessity in such subjects with critical ventricular arrhythmia and initial use of CT is reasonable in such subjects with critical ventricular arrhythmia from this perspective. However, in cardiac CT studies, subjects with arrhythmias such as atrial fibrillation or frequently occurring ventricular arrhythmia were usually grouped in the exclusion criteria for cardiac CT examinations. Among several types of CT scanner, only 320 slice CT can acquire whole heart images in a single scan and even if arrhythmia frequently occurs during acquisition, clear heart images can be obtained [13, 14, 16, 17].

Our study showed that the presence of myocardial abnormal late enhancement and fatty change on CT might be related to occurrence of VF and sustained VT, respectively, in non-ischemic subjects. Myocardial fat is often observed on CT and CMR acquired from healthy adults and subjects with myocardial diseases [10, 25, 26]. Pathologic conditions associated with myocardial fat include healed myocardial infarction, ARVC [27], cardiac lipoma, lipomatous hypertrophy of the interatrial septum, tuberous
sclerosis complex, dilated cardiomyopathy, and cardiomyopathy with muscular
dystrophy. ARVC is characterized pathologically by RV myocardial atrophy and
fibrofatty replacement; furthermore, LV involvement has been reported in 76% of hearts
with ARVC, which was age dependent and was associated with clinical arrhythmic
events, more severe cardiomegaly, inflammatory infiltrates and heart failure [28]. In this
study (see Figs. 3 and 9) the non-ischemic sustained VT group included four ARVC
subjects all of whom had fatty change in RV and/or LV on CT (see Fig. 4); therefore this
matter might influence the finding that the frequency of myocardial fatty change on CT
was significantly more in the non-ischemic sustained VT group than in the
non-ischemic VF group and the non-ischemic non-sustained VT group (see Fig. 5). On
the other hand, the non-ischemic sustained VT group included four subjects whose
cardiac structure was normal on TTE, all of whom did not have either abnormal late
enhancement or fatty change on CT, without any specific ECG characteristics such as
long QT interval, J wave or Brugada syndrome, and who were not diagnosed using
modalities such as ECG, TTE, or CT; additionally, these subjects were not diagnosed as
abnormal, even if CMR were used.

Consideration of the use of iodinated contrast material and radiation exposure
associated with CT, CMR or TTE may of course, be preferable, especially in young
patients. If physicians merely wish to detect myocardial abnormal late enhancement, suggesting presence of fibrosis, CMR is a suitable diagnostic modality because of superior contrast resolution and absence of radiation exposure. However, ultimately, evaluation of coronary arteries is a necessity in such patients with critical ventricular arrhythmia, for example to detect coronary artery stenosis, vulnerable non-calcified coronary plaques, or malignant anomalous origins of coronary arteries, etc.; therefore, on this occasion we used CT instead of CMR. Furthermore if implantation of an ICD has already been performed, CMR cannot be performed in such subjects. An ICD was already implanted in some of the subjects in this study, in particular those who had already experienced VF. TTE does not allow complete visualization of complex morphological changes such as those seen in this study. In such subjects with critical ventricular arrhythmia, CT may be a useful tool for evaluation of coronary arteries, myocardium and in addition, complex anatomic structures of heart and great vessels simultaneously. Furthermore, when 320 slice CT is used, even if the subjects developed an arrhythmia during scanning, clear coronary artery and cardiac images can be obtained, which is not the case with other types of multislice CT.

6. Limitation
Our study population was small (N=103), retrospective and nonrandomized in a single center.

Strictly speaking, on CT, the area in which contrast defect is observed in the early phase and abnormal enhancement is observed in the late phase suggests the presence of interstitial tissue, and interstitial tissue includes fibrosis and edema due to inflammation, etc. Therefore among the subjects who were diagnosed as having myocardial abnormal late enhancement on CT in this study, there may have been some subjects who did not have myocardial fibrosis, but edema due to inflammation, which was in turn due to conditions such as active myocarditis or cardiac sarcoidosis. T2-weighted CMR or endocardial biopsy may be surrogate diagnostic modalities for differentiation of fibrosis from edema, but the utility of the former has not been established at present [29,30]; the latter is invasive and in addition there may have been sampling errors. Thus we could not strictly differentiate fibrosis from edema in this study. Therefore we feel it is better to use the term “abnormal late enhancement” instead of myocardial fibrosis in this study, even though most cases would be expected to be fibrosis rather than edema, in our clinical judgment.

Quantitative evaluation of myocardial abnormal late enhancement or fatty change on CT was not performed in this study and also inter-observer and intra-observer variances
for detection of myocardial abnormal late enhancement or fatty change on CT were not performed by multiple assessors.

As the gold standard for detection of myocardial abnormal late enhancement suggesting presence of fibrosis is still CMR, detection of myocardial abnormal late enhancement on CT should be compared with that detected on CMR, both qualitatively and quantitatively, to evaluate efficiency of CT for such detection.

Of course, traditional ECG parameters such as standard 12-lead ECG, signal-averaged ECG for detection of late potentials, Holter ECG, exercise loaded ECG, and head-up tilt test, are useful for evaluation of subjects at high risk of occurrence of VF or sustained VT. Furthermore, prognostic values from detection of myocardial abnormal late enhancement with information regarding coronary arteries on CT and from these traditional parameters should be evaluated for future occurrence of VF or sustained VT in prospective multicenter studies in larger populations over long periods.

7. Conclusion

After differentiating ischemic disease in non-ischemic subjects, myocardial abnormal late enhancement on CT may be a substrate of VF and fatty change on CT may be substrates of sustained VT. 320 slice CT can evaluate coronary arteries and myocardium
in subjects with arrhythmia and even with ICD, which cannot be acquired on CMR.

Acknowledgement

This work was supported by a Japan Heart Foundation Young Investigator's Research Grant. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

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2002;40:2156–64.


Fig. 1. Typical 320 slice computed tomographic (CT) images of myocardial abnormal late enhancement. A 76 year-old male diagnosed as Maron type 2 hypertrophic cardiomyopathy experienced ventricular fibrillation and recovered with use of automated external defibrillators. Short axis-enhanced CT images of left ventricle (LV) revealed two areas of massive abnormal late enhancement (arrows) in interventricular septum. As there were contrast defects in the interventricular septum in the early phase, late phase acquisition with prospective electrocardiogram gating was added and abnormal late enhancement was observed, which indicated presence of fibrosis. RV; right ventricle.
Fig. 2. Typical 320 slice computed tomographic (CT) images of myocardial fatty changes. A 79 year-old male diagnosed as apical-type Maron type 5 hypertrophic cardiomyopathy experienced non-sustained ventricular tachycardia. Long axis enhanced CT images of left ventricle (LV) revealed low CT area (arrows) in the apical anterior wall of LV in the early phase; late phase acquisition with prospective electrocardiogram gating was added and most of these areas still represented low CT areas <0 Hounsfield Units which indicates presence of fatty change. Compared with early phase, low CT area became smaller in late phase, and the area around fatty change may include presence of partial abnormal late enhancement. LA; left atria.
Fig. 3. Numbers of final clinical or image diagnoses of non-ischemic subjects among the three arrhythmia groups (ventricular fibrillation (VF), sustained and non-sustained ventricular tachycardia (VT)). In the chi square test, there were significant differences between the types of final clinical or image diagnoses and each of the three arrhythmia group types (P<0.001). HCM; hypertrophic cardiomyopathy, DCM; dilated cardiomyopathy, ARVC; arrhythmogenic right ventricular cardiomyopathy, and LV; left ventricle.
Fig. 4. 320 slice computed tomographic (CT) image of a non-ischemic sustained ventricular tachycardia subject with arrhythmogenic right ventricular cardiomyopathy (ARVC). A 23 year-old male with ARVC experienced sustained ventricular tachycardia. Three dimensional volume-rendered CT images revealed enlarged right ventricle (RV) with developed trabeculae in RV (Figure 4A). In the late phase axial source image, the fatty change could be observed in the mid portion of RV side interventricular septum (arrowhead) and left ventricular (LV) lateral wall (arrow Figure 4B).
Fig. 5. Comparison of frequency of myocardial abnormal late enhancement and fatty change on 320 slice computed tomography (CT) among the three “non ischemic” arrhythmia groups (ventricular fibrillation (VF), sustained and non-sustained ventricular tachycardia (VT)). The frequency of myocardial abnormal late enhancement on CT was significantly higher in the non-ischemic VF group (75%, all myocardial abnormal late enhancement was in the left ventricular myocardium) than in the non-ischemic sustained VT group (31%) and the non-ischemic non-sustained VT group (35%) (both $P<0.01$). The frequency of myocardial fatty change on CT was significantly higher in the non-ischemic sustained VT group (54%) than in the non-ischemic VF group (17%) and the non-ischemic non-sustained VT group (12%) (both $P<0.01$).
Fig. 6. Relationship between final clinical or image diagnoses and total numbers of subjects and numbers of subjects with abnormal late enhancement in left ventricular (LV) myocardium on 320 slice computed tomography (CT) in the non-ischemic ventricular fibrillation (VF) group. This presentation differs from Fig. 3. On this occasion, a total of three subjects diagnosed as having J wave syndrome (1 subject), long QT syndrome (1 subject), or unknown diseases (1 subject), were all classified as having normal heart structure without left ventricular (LV) dysfunction on transthoracic echocardiogram. One subject diagnosed as having unknown diseases was classified as having normal heart structure with LV dysfunction on transthoracic echocardiogram.

Myocardial abnormal late enhancement in LV myocardium on CT existed frequently and globally in the non-ischemic VF subjects in each clinical or image diagnostic subgroup. HCM, hypertrophic cardiomyopathy; DCM, dilated cardiomyopathy; ARVC, arrhythmogenic right ventricular cardiomyopathy; and AVR, aortic valve replacement.
Fig. 7. Detailed composition of the non-ischemic ventricular fibrillation (VF) group.

This presentation differs from Fig. 3. On this occasion, a total of three subjects diagnosed as having J wave syndrome (1 subject), long QT syndrome (1 subject), or unknown diseases (1 subject), were classified as having normal heart structure without left ventricular (LV) dysfunction on transthoracic echocardiogram (TTE) and one subject diagnosed as having unknown diseases was classified as having normal heart structure with LV dysfunction on TTE. The one subject diagnosed as having J wave syndrome and the other diagnosed as having long QT syndrome, did not have either abnormal late enhancement or fatty change in the LV myocardium on computed tomography (CT). However, the remaining one subject, diagnosed as having unknown
disease and classified as having normal heart structure without LV dysfunction on TTE (sigmoid septum only on CT) and not diagnosed as abnormal on electrocardiogram (ECG) and TTE, had abnormal late enhancement in the LV myocardium on CT. Also the one subject diagnosed as having unknown disease and classified as having normal structure with LV dysfunction on TTE had abnormal late enhancement in the LV myocardium on CT. As this subject revealed complete left bundle branch block on ECG, TTE assessors speculated that the presence of LV dysfunction on TTE could be explained by dyssynchrony due to complete left bundle branch block. The latter revealed severe vasospastic angina pectoris and ST elevation on ECG confirmed by acetylcholine provocation test with normal coronary arteries on conventional coronary angiography. However, during the vasospasm, VF or ventricular arrhythmia did not occur and causes of occurrence of VF could not be explained by vasospastic angina; this subject was assigned to the non-ischemic VF group.
Fig. 8. 320 slice computed tomographic (CT) image of a non-ischemic ventricular fibrillation subject with normal heart structure without left ventricular (LV) dysfunction on transthoracic echocardiogram. A 56 year-old female without any organized disease experienced ventricular fibrillation and CT revealed normal coronary arteries. Transthoracic echocardiogram revealed normal heart structure without LV dysfunction. The axial source CT image in the late phase revealed sigmoid septum and abnormal enhancement in the basal portion of the interventricular septum (arrow), suggesting myocardial fibrosis. RV; right ventricle.
Fig. 9. Relationship between final clinical or image diagnoses and total numbers of subjects and the numbers of subjects with fatty change in myocardium in the non-ischemic sustained ventricular tachycardia (VT) group. This presentation differs from Fig. 3. On this occasion, a total of three subjects diagnosed as having long QT syndrome (1 subject), and unknown diseases (2 subjects), were classified as normal heart structure without left ventricular (LV) dysfunction on transthoracic echocardiogram (TTE). The remaining subject diagnosed as having unknown diseases was classified as normal heart structure with LV dysfunction on TTE. The non-ischemic sustained VT group included four arrhythmogenic right ventricular cardiomyopathy (ARVC) subjects all of whom all had fatty change in the left ventricle (LV) or right
ventricle (RV) on computed tomography (CT); therefore this observation might

influence the result that the frequency of myocardial fatty change on CT was

significantly more in the non-ischemic sustained VT group than in the non-ischemic
ventricular fibrillation (VF) group and the non-ischemic non-sustained VT group (See
Fig. 5). HCM; hypertrophic cardiomyopathy and DCM; dilated cardiomyopathy.
Fig. 10. Detailed composition of the non-ischemic sustained ventricular tachycardia (VT) group. This presentation differs from Fig. 3. Four subjects exhibited normal heart structure on transthoracic echocardiogram (TTE). Of these, one subject was diagnosed as having long QT syndrome, and the remaining three subjects exhibited normal electrocardiogram (ECG) and had neither abnormal late enhancement nor fatty change in left ventricular (LV) myocardium on computed tomography (CT). Nine subjects exhibited organized heart disease on TTE and/or CT. Of these, four subjects were diagnosed as having arrhythmogenic right ventricular cardiomyopathy (ARVC), all of whom all had fatty change in the LV or right ventricular myocardium on CT.