Prevalence and Clinical Features of Focal Takotsubo Cardiomyopathy
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Background: Because it is difficult to distinguish between focal takotsubo cardiomyopathy and aborted myocardial infarction, there is little information about the prevalence and clinical features of focal takotsubo cardiomyopathy.

Methods and Results: Our cardiac catheterization databases were queried to identify patients with focal takotsubo cardiomyopathy and other types of takotsubo cardiomyopathy. We defined focal takotsubo cardiomyopathy as hypo-, a- or dyskinesis in both anterolateral and septal segments without obstructive coronary artery disease explaining the wall motion abnormality. A total of 10 patients were diagnosed with focal takotsubo cardiomyopathy. The control group comprised patients with takotsubo cardiomyopathy with apical, mid-ventricular, or basal ballooning. Clinical features and in-hospital outcomes were compared between patients with focal takotsubo cardiomyopathy and those with other types of takotsubo cardiomyopathy. Among the 144 patients with takotsubo cardiomyopathy, the apical, mid-ventricular, basal, and focal types occurred in 85 (59.0%), 49 (34.0%), 0 (0%), and 10 patients (6.9%), respectively. The left ventricular ejection fraction was significantly higher in the focal group compared with the apical and mid-ventricular group (56±13 vs. 45±13 vs. 46±12%, P=0.03). In-hospital outcome was not significantly different among the 3 groups.

Conclusions: Focal takotsubo cardiomyopathy is not rare. Biplane left ventriculography is useful for its diagnosis. (Circ J 2016; 80: 1824–1829)

Key Words: Acute coronary syndrome; Apical ballooning syndrome; Left ventriculography; Takotsubo cardiomyopathy

Takotsubo cardiomyopathy is classically described as apical ballooning, but other types of takotsubo cardiomyopathy, such as mid-ventricular and basal ballooning, have been demonstrated. Several case reports have shown focal takotsubo cardiomyopathy. Recently, the International Takotsubo Registry reported that focal takotsubo cardiomyopathy was identified in 1.5% of patients with takotsubo cardiomyopathy. The transient nature of left ventricular (LV) dysfunction is one of the most important characteristics of takotsubo cardiomyopathy. However, aborted myocardial infarction (MI) may exhibit transient LV dysfunction and it can be difficult to distinguish between focal takotsubo cardiomyopathy and aborted MI in the absence of obstructive stenosis or clear thrombus in the corresponding artery. Thus the prevalence of focal takotsubo cardiomyopathy may be underestimated. It is important to distinguish focal takotsubo cardiomyopathy from aborted MI because patient follow-up and medical management are different. Therefore, it is imperative to establish a method of distinguishing focal takotsubo cardiomyopathy from aborted MI. Based on the present study, we propose a method of diagnosing focal takotsubo cardiomyopathy using biplane left ventriculography (LVG), and we also evaluated its prevalence and clinical features.

Methods

Patients and Inclusion Criteria
The International Takotsubo Registry showed that, in most cases, an anterolateral segment is involved in patients with focal takotsubo cardiomyopathy. As a result, the cardiac catheterization databases of Chiba University Hospital, Chiba Emergency Medical Center, and Kimitsu Chuo Hospital from June 2007 to May 2015 were queried to identify consecutive patients with hypo-, a- or dyskinesis in the anterolateral segment and basal, mid-inferior, and apical sparing in the right anterior oblique projection on LVG (Figures 1A,B;
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Patients excluded were those with obstructive coronary artery disease (CAD) or acute plaque rupture in the diagonal branch, because MI in the diagonal branch area shows LV wall motion (LVWM) abnormality in the anterolateral segment and apical sparing. Patients with pheochromocytoma or myocarditis were also excluded, leaving a total of 20 patients fulfilling the criteria. However, patients with aborted MI in the diagonal branch area might be included, so to definitely exclude them we also evaluated LVWM in the septal segment using the left anterior oblique (LAO) projection on LVG, because MI in the diagonal branch area does not show a wall motion abnormality in the septal segment. In total, 3 patients were excluded because of absence of the LAO views, and 7 patients were also excluded because of normal contraction of the septal segment. A total of 10 patients were diagnosed with focal takotsubo cardiomyopathy with LVWM abnormality in both anterolateral and septal segments.

The control group comprised patients with takotsubo cardiomyopathy with apical, mid-ventricular, or basal ballooning in the same time period according to the following criteria: (1) transient hypokinetic, akinetic, or dyskinetic LV; regional wall motion abnormalities extend beyond a single epicardial vascular distribution; (2) absence of obstructive CAD or angio-

**Figure 2.** Prevalence of the types of takotsubo cardiomyopathy. Of 144 patients with takotsubo cardiomyopathy, apical, mid-ventricular, basal, and focal types were observed in 85 (59.0%), 49 (34.0%), 0 (0%), and 10 patients (6.9%), respectively.
graphic evidence of acute plaque rupture; (3) new ECG abnormalities or modest elevation in cardiac troponin; and (4) absence of pheochromocytoma or myocarditis. Resolution of LVWM abnormality was confirmed by echocardiography. Apical type was defined as apical wall motion abnormalities with or without mid-ventricular involvement and basal hyperkinesis. Mid-ventricular type was defined as bilateral mid-ventricular wall motion abnormalities with basal and apical sparing. Basal type was defined as bilateral basal with or without mid-ventricular involvement with apical sparing. Clinical and laboratory information as well as in-hospital outcome data were obtained from hospital charts, which were reviewed by independent research personnel who were unaware of the objectives of the study. The ethics committee of Chiba University approved the study.

Table 1. Baseline Clinical Characteristics of the Patients With Focal Takotsubo Cardiomyopathy

|                          | Apical (n=85) | Mid-ventricular (n=49) | Focal (n=10) | P value |
|--------------------------|--------------|------------------------|--------------|---------|
| Age (years)              | 71±12        | 70±9                   | 69±18        | 0.88    |
| Female                   | 72 (85%)     | 41 (84%)               | 10 (100%)    | 0.56    |
| BMI (kg/m²)              | 21.6±3.8     | 20.8±3.5               | 21.5±3.0     | 0.58    |
| Hypertension             | 43 (51%)     | 24 (49%)               | 6 (60%)      | 0.90    |
| Dyslipidemia             | 32 (38%)     | 18 (37%)               | 4 (40%)      | >0.99   |
| Diabetes mellitus        | 22 (26%)     | 9 (18%)                | 2 (20%)      | 0.47    |
| Smoking                  | 10 (12%)     | 8 (16%)                | 2 (20%)      | 0.59    |
| Symptoms                 |              |                        |              |         |
| Chest pain               | 36 (42%)     | 27 (55%)               | 7 (70%)      | 0.15    |
| Dyspnea                  | 18 (21%)     | 13 (27%)               | 1 (10%)      | 0.53    |
| Trigger                  |              |                        |              |         |
| Emotional stress         | 12 (14%)     | 9 (18%)                | 2 (20%)      | 0.71    |
| Physical stress          | 41 (48%)     | 26 (53%)               | 3 (30%)      | 0.45    |
| No apparent trigger      | 33 (39%)     | 14 (29%)               | 5 (50%)      | 0.32    |
| ECG findings             |              |                        |              |         |
| ST elevation             | 61 (72%)     | 37 (76%)               | 4 (40%)      | 0.10    |
| T-wave inversion         | 53 (62%)     | 31 (65%)               | 7 (70%)      | 0.89    |
| QTc (ms)                 | 489±66       | 478±50                 | 503±64       | 0.37    |
| Troponin elevation*      | 67 (84%)     | 44 (92%)               | 8 (87%)      | 0.42    |

*Measured in 137 patients. BMI, body mass index; ECG, electrocardiography. There was no significant difference in baseline clinical characteristics between 3 types of takotsubo cardiomyopathy.

Figure 3. Incidence of ST-segment elevation and/or T-wave inversion in each lead in patients with focal takotsubo cardiomyopathy. In leads V2–V4, ST-segment elevation and/or T-wave inversion are observed in most of the patients. Approximately half of the patients had ECG changes in leads I, aVL, V5, and V6.
The main results of this study were: (1) focal takotsubo cardiomyopathy was observed in 6.9% of patients with takotsubo cardiomyopathy; (2) biplane LVG was useful to diagnose focal takotsubo cardiomyopathy; and (3) LVEF was higher in patients with focal takotsubo cardiomyopathy compared with those with apical or mid-ventricular takotsubo cardiomyopathy.

Takotsubo cardiomyopathy was named after noticing the resemblance of the LV to a Japanese octopus pot (takotsubo), which has a round bottom and narrow neck. Although apical ballooning is the most common, variant forms such as the mid-ventricular and basal type have been demonstrated. The mid-ventricular type is present in approximately 4–40% of patients with takotsubo cardiomyopathy. The basal type is rare and seen in only 1–3%. There does not appear to be a difference in the clinical characteristics of patients with the apical, mid-ventricular or basal type. Segmental wall motion abnormalities involving the apical right ventricle may be observed in patients with takotsubo cardiomyopathy. Right ventricular dysfunction is a marker of the severity of takotsubo cardiomyopathy and associated with lower LVEF and a higher incidence of severe HF. In contrast, the higher LVEF and lower LV end-diastolic pressure in patients with focal takotsubo cardiomyopathy may be associated with smaller LV area with wall motion abnormality. The exact pathophysiology of takotsubo cardiomyopathy is still uncertain, although several hypotheses, such as sympathetic excitation, multivesSEL coronary spasm, and microvascular impairment, have been postulated. Thus, differences in pathophysiology among the 3 groups were not significantly different among the 3 types of takotsubo cardiomyopathy.
types of takotsubo cardiomyopathy are also unknown. Several case reports have demonstrated focal takotsubo cardiomyopathy, especially using cardiovascular magnetic resonance imaging (CMR). Estehardi et al showed that focal type in 3 (7%) of 41 patients with takotsubo cardiomyopathy. Recently, the International Takotsubo Registry reported the clinical features and outcomes of 1,750 patients with takotsubo cardiomyopathy. Focal type was observed in 1.5% of the patients, which is lower than in the present study (6.9%). However, neither study showed how they distinguished it from aborted MI. The difference between the present study and other studies in the prevalence of focal takotsubo cardiomyopathy might be because of misdiagnosis of focal takotsubo cardiomyopathy as acute coronary syndrome (ACS) caused by transient thrombotic occlusion or severe coronary artery spasm. It is important to distinguish focal takotsubo cardiomyopathy from ACS, because patient follow-up and medical management, such as with antiplatelet agents, β-blockers, and angiotensin-converting enzyme inhibitors, are different.

CMR may be useful to distinguish between focal takotsubo cardiomyopathy and ACS. However, it may not be routinely performed in patients with focal ballooning. Patel et al have shown that the presence of systolic dysfunction in the posterolateral segment in the LAO projection on LVG most accurately distinguishes the apical type of takotsubo cardiomyopathy from aborted anterior MI. The posterolateral segment represents the territory that is generally perfused by the circumflex artery, and occasionally by a large dominant right coronary artery, which accounts for the lack of regional wall motion abnormality in anterior MI. In the present study, focal takotsubo cardiomyopathy was diagnosed in patients with regional wall motion abnormality in both the anterolateral and basal-septal segments and apical sparing. Apical sparing means that the left anterior descending coronary artery is not the culprit vessel. The anterolateral segment is perfused by the diagonal branch and the basal-septal segment by a septal branch, which means that a regional wall motion abnormality in both the anterolateral and basal-septal segments and apical sparing extends beyond a single epicardial vascular distribution. Because regional wall motion abnormalities extending beyond a single epicardial coronary artery distribution represents one of the most important features distinguishing takotsubo cardiomyopathy from CAD, biplane LVG should be routinely performed in patients with suspected takotsubo cardiomyopathy. However, CMR or single-photon emission computed tomography (SPECT) using 123I-metaiodobenzylguanidine (MIBG) or 123I-β-methyl iodophenyl pentadecaanoic acid (BMIPP) may be considered for distinguishing patients with focal takotsubo cardiomyopathy from those with ACS, if biplane LVG is not available in catheterization laboratory. CMR may show LVWM abnormality beyond a single epicardial vascular distribution in patients with focal takotsubo cardiomyopathy. SPECT may demonstrate reduced uptake of 123I-MIBG or 123I-BMIPP beyond a single epicardial vascular distribution.

In the present study, in-hospital outcomes were not significantly different among the 3 groups, which was consistent with the result in a previous study that showed no significant difference in long-term outcomes between the apical and non-apical types.

**Study Limitations**

The number of patients was relatively small. Focal takotsubo cardiomyopathy was diagnosed in patients with regional wall motion abnormality in both the anterolateral and basal-septal segments. There may be patients with focal takotsubo cardiomyopathy who have regional wall motion abnormality only in the anterolateral segment or the basal-septal segment. Furthermore, focal takotsubo cardiomyopathy might be observed in other segments. The prevalence of focal takotsubo cardiomyopathy might be underestimated. However, the International Takotsubo Registry showed that in most cases of focal takotsubo cardiomyopathy the patient had LVWM abnormality in the anterolateral segment.

**Conclusions**

Focal takotsubo cardiomyopathy is not rare and biplane LVG is useful for its diagnosis, which will affect the medical management of these patients.

**Conflict of Interest**

None declared.

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**Supplementary Files**

**Movie S1.** Left ventriculography in the right anterior oblique projection shows dyskinesis in the anterolateral segment and basal, mid-inferior, and apical sparing.

**Supplementary File 2**

**Movie S2.** Left ventriculography in the left anterior oblique projection demonstrates akinesis in the basal-septal segment.

Please find supplementary file(s); http://dx.doi.org/10.1253/circj.CJ-16-0360