Guidelines for Diagnosis of Takotsubo (Ampulla) Cardiomyopathy

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Background  It is important to differentiate takotsubo cardiomyopathy from other types of transient ventricular dysfunction. These guidelines, resulting from a workshop sponsored by the Ministry of Health, Labour, and Welfare, Idiopathic Cardiomyopathy Research Committee, outline the steps necessary for diagnosis of takotsubo cardiomyopathy.

Methods and Results  The survey was conducted by mailing a questionnaire to the researchers of the 203 institutions that had made presentations on this disease at scientific meetings of the Japanese Circulation Society from November 1989 to October 2002. The questionnaires were sent and collected on January 10, 2003. Based on the results of the questionnaire, the first edition of the guidelines for diagnosis of takotsubo cardiomyopathy was prepared and evaluated at the 2003 group meeting of the Research Committee. Out of 33 researchers in Japan who had published research papers on this disease, 21 responded to the request and provided their opinions. The guidelines were revised and were approved at the 2004 group meeting.

Conclusions  This summary provides standard guidelines for patients with takotsubo cardiomyopathy. (Circ J 2007; 71: 990–992)

Key Words: Apical ballooning; Myocardial stunning; Ventricular dysfunction

The diagnostic criteria were developed by a consensus conference initiated by the Research Committee of Idiopathic Cardiomyopathy (Dr Akira Kitabatake, Former Chief Researcher; Dr Hitonobu Tomoike, Present Chief Researcher). To reflect the opinions of physicians who had actual experience with patients with takotsubo cardiomyopathy, 203 institutions were asked to cooperate in the preparation of the guidelines. These institutions had made presentations on this disease at scientific meetings of the Japanese Circulation Society from November 1989 to October 2002. Questionnaires asked for the observed numbers of cases (by sex), disease names in Japanese, sites of abnormal ventricular wall motion, obstruction of the ventricular outflow tract, exclusion criteria, electrocardiographic findings, symptoms, triggers, biochemical markers of myocardial damage, prognosis, fatal cases, and cases with severe sequelae. Questionnaires were sent and collected on January 10, 2003. Based on the results, the first edition of the guidelines for diagnosis of takotsubo cardiomyopathy were prepared. At the 2003 group meeting of the Idiopathic Cardiomyopathy Research Committee, an evaluation was considered necessary to determine whether this disease should be treated as a distinct clinical entity. To make the proposal more effective for the diagnostic guidelines, 33 researchers in Japan who had published research papers (original articles, reviews, and case reports, in English or Japanese) on this disease were asked to check the “Guidelines for diagnosis of takotsubo cardiomyopathy, 1st edition”. The contents were: disease names in Japanese, disease names in English (including those corresponding to Japanese names), should inverted takotsubo phenomenon be included in the definition, sites of ventricular contraction abnormalities (whether or not apical ballooning alone is acceptable, should takotsubo be specify only in cases with hypercontraction of the ventricular base, and should normal contraction of the ventricular base be included), and the clinical importance of coronary angiography.

Twenty-one researchers responded to the request and provided their opinions, based on which the diagnostic guideline was revised. At the 2004 group meeting of the Research Committee of Idiopathic Cardiomyopathy, the revisions were reviewed by the members, who approved them.

For the sites of ventricular contraction, many questionnaire participants stated, “only apical ballooning is necessary”. Eleven participants indicated, “cardiac base has normal contraction” and “includes a transient decrease including that in the base”. Therefore, “the contraction of the cardiac base is well preserved and some cases even have the tendency for hyperkinesis” was deleted from the draft. An overwhelming number of questionnaire participants (20/21) were of the opinion that the inverted takotsubo phenomenon should not be included.

There was lack of agreement on the indication for coronary angiography; 12 researchers insisted upon acute-stage angiography and 9 stated that chronic-stage angiography was acceptable. For this reason, the following statement was incorporated into section A of the exclusions: “urgent coronary angiography is desirable for imaging during the...
Table 1  Guidelines for Diagnosis of Takotsubo (Ampulla) Cardiomyopathy

I. Definition
Takotsubo (ampulla) cardiomyopathy is a disease exhibiting an acute left ventricular apical ballooning of unknown cause. In this disease, the left ventricle takes on the shape of a “takotsubo” (Japanese octopus trap). There is nearly complete resolution of the apical akinesis in the majority of the patients within a month. The contraction abnormality occurs mainly in the left ventricle, but involvement of the right ventricle is observed in some cases. A dynamic obstruction of the left ventricular outflow tract (pressure gradient difference, acceleration of blood flow, or systolic cardiac murmurs) is also observed. Note: There are patients, such as cerebrovascular patients, who have an apical systolic ballooning similar to that in takotsubo cardiomyopathy, but with a known cause. Such patients are diagnosed as “cerebrovascular disease with takotsubo-like myocardial dysfunction” and are differentiated from idiopathic cases.

II. Exclusion criteria
The following lesions and abnormalities from other diseases must be excluded in the diagnosis of takotsubo (ampulla) cardiomyopathy.
A. Significant organic stenosis or spasm of a coronary artery. In particular, acute myocardial infarction due to a lesion of the anterior descending branch of the left coronary artery, which perfuses an extensive territory including the left ventricular apex (An urgent coronary angiogram is desirable for imaging during the acute stage, but coronary angiography is also necessary during the chronic stage to confirm the presence or absence of a significant stenotic lesion or a lesion involved in the abnormal pattern of ventricular contraction).
B. Cerebrovascular disease
C. Pheochromocytoma
D. Viral or idiopathic myocarditis
E. Hypertrophic cardiomyopathy
F. Pericarditis
G. Myocardial radionuclear study: Abnormal findings in myocardial scintigraphy are observed in some cases.
H. Prognosis: The majority of the cases rapidly recover, but some cases suffer pulmonary edema and other sequelae or death.

III. References for diagnosis
A. Symptoms: Chest pain and dyspnea similar to those in acute coronary syndrome. Takotsubo cardiomyopathy can occur without symptoms.
B. Triggers: Emotional or physical stress may trigger takotsubo cardiomyopathy, but it can also occur without any apparent trigger.
C. Age and gender difference: Known tendency to increase in the elderly, particularly females.
D. Ventricular morphology: Apical ballooning and its rapid improvement in the ventriculogram and echocardiogram.
E. Electrocardiogram: ST segment elevations might be observed immediately after the onset. Thereafter, in a typical case, the T-wave becomes progressively more negative in multiple leads, and the QT interval prolongs. These changes improve gradually, but a negative T-wave may continue for several months. During the acute stage, abnormal Q-waves and changes in the QRS voltage might be observed.
F. Cardiac biomarkers: In a typical case, there is only modest elevations of serum levels of cardiac enzymes and troponin.
G. Myocardial radionuclear study: Abnormal findings in myocardial scintigraphy are observed in some cases.
H. Prognosis: The majority of the cases rapidly recover, but some cases suffer pulmonary edema and other sequelae or death.

Note: For the exclusion of coronary artery lesions, coronary angiography is required. Takotsubo-like myocardial dysfunction could occur with diseases such as cerebrovascular disease and pheochromocytoma.

References

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Acute stage, but coronary angiography is also necessary during the chronic stage to confirm the presence or absence of a significant stenotic lesion or a lesion involved in the abnormal pattern of ventricular contraction”.

The following pathological conditions are of interest.
1. Onset with symptoms suspicious of acute myocardial infarction (recent increase in asymptomatic cases and cases with dyspnea at onset).
2. Apical ballooning with akinesis and basal hyperkinesis.
3. ST segment elevation in the electrocardiogram (longer duration of ST elevation than from coronary spasm), T-wave inversion (giant negative T-wave), QT prolongation, and lack of reciprocal changes.
4. Slight elevation of cardiac enzymes (low values not proportional to the hypokinetic area).
5. Lack of significant coronary artery stenosis. Low provocation rate of coronary artery spasm (approximately 1/3).
6. Rapid normalization of the abnormal pattern of ventricular contraction, the electrocardiogram, cardiac enzymes and troponin, and the myocardial scintigram.
7. Higher incidence in elderly females (7-fold that of males).
8. Trigger factor of emotional stress1,2 (predominantly emotional stress in females and physical stress in males).
9. Presence of myocardial tissue damage. Some cases might have the sequel of ventricular aneurysm.
10. Reversible outflow tract obstruction might be observed in both ventricles.
11. Some cases may have an elevation in serum catecholamine levels.
12. The pathological conditions change and improve in response to various types of drugs: intracoronary verapamil improves coronary blood flow; intracoronary nicorandil improves ST elevation; intravenous propranolol or cibenzoline improves the outflow tract gradient and ST elevation.
13. The apical region is not opacified on contrast echocardiography.
14. There is an abnormality of coronary flow reserve in Doppler flow-wire studies.
15. In severe cases, respiratory failure can occur.
16. Fatal cases exist (eg, from cardiac rupture).
Appendix 1
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