

# FUNCTIONAL ASSESSMENT OF MICROCIRCULATION IN TAKOTSUBO CARDIOMYOPATHY

a pilot study

V. Brazdil, M. Hudec, R. Stipal, O. Bocek, P. Jerabek, M. Poloczek, P. Kala





# Background



## Takotsubo cardiomyopathy (TTC)

- an acute reversible left ventricular dysfunction that often mimics myocardial infarction
- approximately 1–2% of all patients treated for acute coronary syndrom are actually experiencing TTC
- mortality during the acute phase in hospitalized patients is currently estimated at 5%
- diagnostic coronary angiography reveals normal coronary arteries in most patients (15% of patients can have coincident coronary artery disease)
- the pathogenesis of TTC is still not completely understood, coronary microvascular dysfunction (CMD) has been proposed as one of the mechanisms



### Takotsubo cardiomyopathy

Background

CONSENSUS PAPER

#### International Expert Consensus Document on Takotsubo Syndrome (Part I): Clinical Characteristics, Diagnostic Criteria, and Pathophysiology

Jelena-Rima Ghadri<sup>1</sup>, Ilan Shor Wittstein<sup>2</sup>, Abhiram Prasad<sup>3</sup>, Scott Sharkey<sup>4</sup>, Keigo Dote<sup>5</sup>, Yoshihiro John Akashi<sup>6</sup>, Victoria Lucia Cammann<sup>1</sup>, Filippo Crea<sup>7</sup>, Leonarda Galiuto<sup>7</sup>, Walter Desmet<sup>8,9</sup>, Tetsuro Yoshida<sup>10</sup>, Roberto Manfredini<sup>11</sup>, Ingo Eitel<sup>12</sup>, Masami Kosuge<sup>13</sup>, Holger M. Nef<sup>14</sup>, Abhishek Deshmukh<sup>3</sup>, Amir Lerman<sup>3</sup>, Eduardo Bossone<sup>15</sup>, Rodolfo Citro<sup>15</sup>, Takashi Ueyama<sup>16†</sup> Domenico Corrado<sup>17</sup>, Satoshi Kurisu<sup>18</sup>, Frank Ruschitzka<sup>1</sup>, David Winchester<sup>19</sup>, Alexander R. Lyon<sup>20,21</sup>, Elmir Omerovic<sup>22,23</sup>, Jeroen J. Bax<sup>24</sup>, Patrick Meimoun<sup>25</sup>, Guiseppe Tarantini<sup>17</sup>, Charanjit Rihal<sup>3</sup>, Shams Y.-Hassan<sup>26</sup>, Federico Migliore<sup>17</sup>, John D. Horowitz<sup>27</sup>, Hiroaki Shimokawa<sup>28</sup>, Thomas Felix Lüscher<sup>29,30</sup>, and Christian Templin<sup>1\*</sup>

International Experts: Jeroen J. Bax, Eduardo Bossone, Victoria Lucia Cammann, Rodolfo Citro, Domenico Corrado, Filippo Crea, Walter Desmet, Ingo Eitel, Leonarda Galiuto, Jelena-Rima Ghadri, Thomas Felix Lüscher, Alexander R. Lyon, Roberto Manfredini, Patrick Meimoun, Federico Migliore, Holger M. Nef, Elmir Omerovic, Frank Ruschitzka, Guiseppe Tarantini, Christian Templin, Shams Y-Hassan (European sites); Abhishek Deshmukh, Amir Lerman, Abhiram Prasad, Charanjit Rihal, Scott Sharkey, David Winchester, Ilan Shor Wittstein (USA sites); Yoshihiro John Akashi, Keigo Dote, Masami Kosuge, Satoshi Kurisu, Hiroaki Shimokawa, Takashi Ueyama, Tetsuro Yoshida (Asian sites); John D. Horowitz (Australian site)

<sup>1</sup>Uhienzity Heart Cetter: Department of Cardiology, University Hospital Zarich, Zurich, Settaradna, <sup>2</sup>Department of Medicine, Johns Hopkite University School of Medicine, Baitimore, MD, USA: <sup>1</sup>Division of Cardiosauchi Dissase Mayo Christen, MN, USA: <sup>1</sup>Cardiovanzolar Researd Division, Mimespolis Heart Institute Foundation, Mimespolis, NN, USA: <sup>1</sup>Department of Cardiology, Horolama Card, Kas Hospital, Teinolma, Japan, <sup>1</sup>Division of Cardiosauchi Peterson, Schwart of Istance Medicine, Schwartan University School of Medicine, Kawasaki, Japan: <sup>1</sup>Department of Cardiovascular Sciences, Cardiou Johnson, Belgium, <sup>11</sup>Department of Cardiovascular Medicine, University Joputal Lesen, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department of Cardiovascular Science, University of Leven, Leven, Belgium, <sup>11</sup>Department Science, Science Science,

#### Expert Consenus Document on Takotsubo Syndrome, Part I

#### Table I International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria)

- Patients show transient<sup>a</sup> left ventricular dysfunction (hypokinesia, akinesia, or dyskinesia) presenting as apical ballooning or midventricular, basal, or focal wall motion abnormalities. Right ventricular involvement can be present. Besides these regional wall motion patterns, transitions between all types can exist. The regional wall motion abnormality usually extends beyond a single epicardial vascular distribution; however, rare cases can exist where the regional wall motion abnormality is present in the subtended myocardial territory of a single coronary artery (focal TTS).<sup>b</sup>
- 2. An emotional, physical, or combined trigger can precede the takotsubo syndrome event, but this is not obligatory.
- 3. Neurologic disorders (e.g. subarachnoid haemorrhage, stroke/transient ischaemic attack, or seizures) as well as pheochromocytoma may serve as triggers for takotsubo syndrome.
- 4. New ECG abnormalities are present (ST-segment elevation, ST-segment depression, T-wave inversion, and QTc prolongation); however, rare cases exist without any ECG changes.
- 5. Levels of cardiac biomarkers (troponin and creatine kinase) are moderately elevated in most cases; significant elevation of brain natriuretic peptide is common.
- 6. Significant coronary artery disease is not a contradiction in takotsubo syndrome.
- 7. Patients have no evidence of infectious myocarditis.<sup>b</sup>
- 8. Postmenopausal women are predominantly affected.

<sup>a</sup>Wall motion abnormalities may remain for a prolonged period of time or documentation of recovery may not be possible. For example, death before evidence of recovery is captured.

<sup>b</sup>Cardiac magnetic resonance imaging is recommended to exclude infectious myocarditis and diagnosis confirmation of takotsubo syndrome.







2035

# \_\_\_\_\_

# Background



## Takotsubo cardiomyopathy











 $\mathbf{i}$ 

- 78-years-old female
- typical symptomatology of acute myocardial infarction
- coronary angiography revealed significant stenosis on the left anterior descending coronary artery
- ventriculography disclosed apical dysfunction and clinical course of the disease result in the diagnosis of Takotsubo cardiomyopathy











## **Functional assessment of coronary circulation**

Fractional Flow Reserve (FFR)

Background

- Coronary Flow Reserve (CFR)
- Index of Microcirculatory Resistence (IMR)

#### **Comparison of the indices**

FFR	iwFR	CFR	IMR
Epicardial	Epicardial	Epicardial + Microvascular	Epicardial + Microvascular
Pressure	Pressure	Doppler/ Thermodilution + pressure	Pressure + thermodilution
≤0.80	≤0.89	< 2.0	≥25







# **Methods**



### **Inclusion criteria**

- males and females, age > 18 years
- clinically indicated acute diagnostic cardiac cathetrization
- angiographically proved left ventricle wall-motion abnormality

#### **10** patients

diagnosed with TTC in line with interTAK Diagnostic Criteria

#### **Clinical follow-up**

with TTE in 3 month

#### **Exclusion criteria**

- cardiogenic shock
- the presence of mechanical complications
- allergy to adenosine/adenocor

#### FFR, CFR and IMR analysis

- Pressure wire and Pressure analyzer
- Adenosine 140ug/kg/min
- FFR < 0.8, CFR < 2.0 and IMR >25 were used as cut-off values











- non-obstructive findings in the epicardial coronary arteries assessed by FFR
- CFR and IMR repeatedly revealed pathological findings in our cohort
- TTE revealed dysfunction of the left myocardial ventricle in acute phase (normalisation after 3 month)







 We demonstrated the presence of dysfunction of the coronary microcirculation in patients with TTC

 Further research could provide novel insights on the role of microvascular dysfunction in pathogenetic mechanisms of TTC









absence of control group

no specific cut-off point to define CMD in patients with TTC











