Takotsubo cardiomyopathy, acute myocardial infarction and dyslipidaemia: a comparison of studies

Alfredo De Giorgia, Matteo Guarino, Benedetta Boaria, Rosaria Cappadona, Elisa Maietti, Fabio Fabbiana and Roberto Manfredinia

ABSTRACT

Background: Takotsubo cardiomyopathy (TTC) and acute myocardial infarction (AMI) share similar clinical presentation and risk of death, although one of the most important differences is the absence of obstructive coronary disease in TTC. We analysed the available literature and evaluated the prevalence of dyslipidaemia in patients with TTC compared with patients with AMI.

Methods: A MEDLINE literature search to identify relevant papers focused on TTC and AMI was performed, evaluating the prevalence of dyslipidaemia in both groups. Systematic reviews, meta-analyses, controlled trials, cohort studies and case-control studies were considered for inclusion. We focused on studies reporting precise data on the prevalence of dyslipidaemia for both groups.

Results: Out of a total of 511 articles found, 207 case reports, 24 comments, 56 letters and 57 articles in languages other than English were excluded. Of the remaining 167 papers, 23 articles providing the required information were selected. They included and compared 2247 TTC and 19,843 AMI patients. Cases with dyslipidaemia were 734 (32.7%) in the TTC group and 6592 (33.2%) in the AMI group.

Conclusions: Patients with TTC showed a prevalence of dyslipidaemia comparable with that of patients with AMI. The prevalence of dyslipidaemia and clinical outcome in TTC and AMI may represent unrelated issues. It is likely that for TTC patients, other conditions and comorbidities, rather than dyslipidaemia alone and/or other established risk factors, are responsible for a risk of death comparable with that of AMI.

© 2016 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

KEYWORDS

dyslipidaemia; takotsubo cardiomyopathy; myocardial infarction; comorbidity; risk factors; patient outcome

CONTACT  Roberto Manfredini  roberto.manfredini@unife.it

INTRODUCTION

Dyslipidaemia is an important risk factor for cardiovascular disease (CVD), cerebrovascular diseases and acute myocardial infarction (AMI), especially when associated with hypertension, diabetes, smoking and a family history of CVD.[1] However, the effect of these risk factors on incidence of AMI is different, and should be related to gender as well.

Takotsubo cardiomyopathy (TTC), also known as “stress cardiomyopathy”, “left ventricular apical ballooning syndrome” or “broken heart syndrome” was first described in 1990.[2] TTC is a unique acute syndrome characterised by transient left ventricular systolic dysfunction in the absence of significant coronary artery disease (CAD). [3] TTC and AMI share a similar clinical presentation, and one of the most important differences is the absence of obstructive coronary disease in TTC.[4] The diagnostic criteria must include all the following: (a) transient hypokinesis, akinesis or dyskinesia in the left ventricular mid segments with or without apical involvement; regional wall motion abnormalities that extend beyond a single epicardial vascular distribution; and, frequently but not always, a stressful trigger, (b) absence of obstructive CAD or angiographic evidence of acute plaque rupture, (c) electrocardiogram with new abnormalities (ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin, and (d) absence of myocarditis or pheochromocytoma.[4]

It is estimated that 1–2% of patients with suspected acute coronary syndrome may be eventually diagnosed with TTC.[5] Recent studies from the Sweden Heart Registry (2005–2013) and the United States National Inpatient Sample (NIS) (2007–2012) reported a > 3-fold increase in hospitalisation due to TTC,[6,7] possibly due to the introduction of a specific ICD-9-CM for TTC in 2006. TTC is more prevalent in elderly post-menopausal women (66–80 years of age); Asian and Caucasian patients [5] have an annual recurrence rate of TTC of about 1–2%. [8]
The pathophysiology of TTC is complex, involving the cognitive centres of the brain and the hypothalamic–pituitary–adrenal axis.

Cardiovascular responses are caused by the sudden sympathetic activation and surge in concentrations of circulating catecholamines, often following a physical or emotional stress. High levels of circulating epinephrine trigger a switch in intracellular signal trafficking in ventricular cardiomyocytes, from G(s) protein to G(i) protein signalling via beta(2)-adrenoceptors, with a final negatively inotropic effect greatest at the apical myocardium due to the increased sympathetic innervation of the apex.

Several common clinical conditions could activate the catecholaminergic system. TTC has been reported to be associated, among others, with localised or systemic acute infections, pulmonary diseases, allergic diseases, endocrine dysfunctions and neurological diseases. Moreover, different drugs, e.g. sympathomimetic drugs with direct or indirect action, some non-sympathomimetic drugs, and drug withdrawal, have been related with TTC.

Because of similarities between AMI and TTC, we analysed the available literature evaluating the prevalence of dyslipidaemia in patients with TTC compared with patients with AMI.

Methods

We performed a MEDLINE literature search to identify relevant papers focused on TTC and AMI, and then we evaluated prevalence of dyslipidaemia in both groups. The following search terms were used: “takotsubo (tako-tsubo) cardiomyopathy”, “stress-induced cardiomyopathy” and “apical ballooning syndrome” in combination with “myocardial infarction”, “acute myocardial infarction” and “acute myocardial ischemia”. Systematic reviews, meta-analyses, controlled trials, cohort studies, case-control studies were considered for inclusion. Case reports, comments, discussion letters, articles in languages other than in English, and conference abstracts or proceedings were excluded. Authors, years of publication, number of patients with TTC and AMI enrolled in every single study and prevalence of dyslipidaemia in the two groups were collected. Moreover, total numbers of patients with TTC and AMI and calculations of dyslipidaemia prevalence in the two groups were performed.

Regarding the definition of dyslipidaemia, five authors defined it as hypercholesterolaemia, one as history of hypercholesterolaemia, seven as hyperlipidaemia, two as treated hyperlipidaemia, one as treatment of dyslipidaemia and six as dyslipidaemia. Prevalence of dyslipidaemia in TTC and AMI patients was compared by chi-square test with Yates’ correction (GraphPad software available at https://www.graphpad.com/quickcalcs/contingency1.cfm). Data were combined using Odds Ratios (ORs) and in the combined measure each study was weighted using the inverse-variance of log[OR]. The latter analysis was carried out in order to adjust for variability in the estimates.

Results

We found a total of 511 articles. We excluded 207 case reports, 24 comments, 56 letters and 57 articles in languages other than English. Out of the remaining 167 papers, we selected 23 articles providing the requested information. One article was published in 2003, 2005, 2012 each, 2 articles in 2013, 4 in 2014, 8 in 2015 and in 2016. Seven hundred thirty-four TTC patients out of 2247 (32.7%) and 6592 AMI patients out of 19,843 (33.2%) had dyslipidaemia; this difference was not statistically significant. The difference in the prevalence of dyslipidaemia in the 23 papers analysed is reported in Table 1. The crude OR of dyslipidaemia in TTC group compared with AMI was 0.725 (95%CI 0.646–0.813), suggesting a significant reduction in the ORs of TTC compared with AMI (Figure 1). The great majority of weight (70%) in the combined measure was ascribed to only 5 out of 23 studies (Figure 1). The heterogeneity test was not statistically significant (p = 0.653), confirming the adequacy of combined measures.

Discussion

Dyslipidaemia is a common finding in TTC patients. A recent international collaborative systematic review has evaluated both the clinical characteristics and comorbidities of TTC patients. The analysis of risk factors showed that dyslipidaemia ranked second place: hypertension (54% of patients), dyslipidaemia (32%), smoking (22%), diabetes (17%) and obesity (17%). Similar results were reported in a study conducted in 14 non-academic hospitals in France: hypertension (57.9%) dyslipidaemia (33.0%), diabetes (11.5%) and obesity (11.5%). Age does not seem to make any difference. Data from an Italian cohort of TTC patients (92% women, median age 67.5 years), reported that hypercholesterolaemia was present in 34.2% of overall patients, with no significant differences in groups by age (<65 years: 35.8%; 65–74 years: 32.7%; >75 years: 33.3%).

Until a few years ago, TTC was considered as a benign cardiac disease, since TTC patients had generally a good short-prognosis. However, some recent studies on large cohorts of patients reported different results. Templin et al. in their multicentre study (1998–2014, 1750 patients) evaluated in-hospital complication and death, and did not find significant difference between TTC and AMI. Again, no difference in mortality between ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction...
(NSTEMI) and TTC was reported in a Swedish study (2005–2013), even after adjusting for cardiovascular risk factors (age, gender, diabetes mellitus, smoking, body mass index, hypertension, hyperlipidaemia, previous MI, previous percutaneous coronary intervention and previous coronary bypass surgery).[7] Torvall et al., in a case-control study from the Swedish Coronary Angiography and Angioplasty Register (2009–2013) showed that even though TTC patients were characterised by a low-cardiovascular risk factor profile, there was an association with a hazard ratio (HR) of 2.1 (95% confidence interval (CI): 1.4–3.2; \( p < 0.001 \)) for death compared with control subjects without CAD.[34] This excess risk was similar to that seen among the CAD control subjects compared with control subjects without CAD (HR): 2.5; 95% CI: 1.8–3.3; \( p < 0.001 \)), independent of adjustment for CAD risk factors.[34] Also, Stiermaier et al., in Germany, reported that TTC patients showed a significantly higher long-term (>2 years of follow-up) all-cause mortality compared with a matched STEMI cohort (24.7% vs. 15.1%; HR 1.58, 95% CI: 1.07–2.33; \( p < 0.001 \)), and only male sex, high Killip class on admission, and diabetes mellitus were identified as independent predictors of mortality in TTC patients after multivariable regression analysis.[22] This latter observation on male sex as an independent predictor of mortality is in agreement with results from Japan.[44] Moreover, data from the United States NIS, showed that, although the total in-hospital mortality rate for TTC was 2.4%, males exhibited more than a twofold rate (4.8%) than in women (2.1%) (\( p < 0.01 \), probably related to the increased prevalence of acute critical illnesses, ventricular arrhythmia and sudden cardiac arrest in men.[45]

To the best of our knowledge, this is the first comparison of available studies evaluating the prevalence of dyslipidaemia in TTC and AMI patients. The main finding is that patients with TTC have a lower prevalence of dyslipidaemia than patients with AMI. At the same time, even if rather surprisingly, TTC patients do not show significant differences in mortality risk compared with AMI. Dyslipidaemia and clinical outcome in TTC and AMI may be unrelated issues. In fact, a series of studies in TTC patients has shown that dyslipidaemia does not influence major cardiovascular events, such as acute heart failure, cardiogenic shock or in-hospital mortality.[46,47] Moreover, not only dyslipidaemia, but even hypertension and diabetes mellitus were not related to higher prevalence of events in TTC patients.[6] The INTERHEART Study has provided strong evidence on the effect of potentially modifiable risk factors associated with AMI.[48] Nine risk factors may account for a great proportion (>90%) of the risk of an initial AMI, and smoking and dyslipidaemia are the two most important. However, this study[48] showed the importance of psychosocial factors too, that gives great contribution to the multiplicative effect of risk factors on the ORs. In fact, the ORs reported in this study[48] for the various risk factors were, respectively: smoking (2.9), diabetes mellitus (2.4), hypertension (1.9), ApoB/A1 (3.3), all these four (42.3), + obesity (68.5), + psychosocial

**Table 1.** Prevalence of dyslipidaemia in TTC and AMI (review of the available studies).

| Author            | Year | TTC (2247) | AMI (19843) | Number of patients enrolled in each study (% of the whole study population, \( n = 22090 \)) | Number of patients with dyslipidaemia (% of the whole study population with dyslipidaemia, \( n = 7326 \)) |
|-------------------|------|------------|-------------|-----------------------------------------------------------------|-----------------------------------------------------------------|
| Ogura et al. [18] | 2003 | 13         | 13 (AMI)    | 26 (0.1%)                                                       | 7 (0.1%)                                                       |
| Inoue et al. [19] | 2005 | 18         | 85 (AMI)    | 103 (0.5%)                                                      | 49 (0.7%)                                                      |
| Kosuge et al. [20] | 2012 | 34         | 237 (AMI)   | 271 (1.2%)                                                      | 83 (1.1%)                                                      |
| Guerra et al. [21] | 2013 | 45         | 45 (AMI)    | 90 (0.4%)                                                       | 51 (0.7%)                                                      |
| Meimoun et al. [22] | 2013 | 28         | 28 (AMI)    | 56 (0.3%)                                                       | 22 (0.3%)                                                      |
| Prasad et al. [23] | 2014 | 12         | 571 (STEMI) | 583 (2.6%)                                                      | 244 (3.3%)                                                     |
| Meimoun et al. [24] | 2014 | 21         | 21 (AMI)    | 42 (0.2%)                                                       | 18 (0.2%)                                                      |
| Parkkonen et al. [25] | 2014 | 57         | 96 (STEMI)  | 153 (0.7%)                                                      | 84 (1.1%)                                                      |
| Randhawa et al. [26] | 2014 | 38         | 97 (AMI)    | 135 (0.7%)                                                      | 90 (1.2%)                                                      |
| Redfors et al. [7] | 2015 | 302        | 14802 (STEMI+nSTEMI) | 15104 (68.4%)             | 3632 (49.6%)                                                   |
| Novo et al. [27] | 2015 | 53         | 53 (AMI)    | 106 (0.5%)                                                      | 62 (0.8%)                                                      |
| Najib et al. [28] | 2015 | 216        | 1822 (AMI)  | 2038 (9.2%)                                                     | 1741 (23.8%)                                                   |
| Khalid et al. [29] | 2015 | 16         | 15 (AMI)    | 31 (0.1%)                                                       | 21 (0.3%)                                                      |
| Zorzi et al. [30] | 2015 | 31         | 30 (AMI)    | 61 (0.3%)                                                       | 23 (0.3%)                                                      |
| Daniel et al. [31] | 2015 | 25         | 56 (AMI)    | 81 (0.4%)                                                       | 9 (0.1%)                                                       |
| Venvaet et al. [32] | 2015 | 37         | 103 (STEMI) | 140 (0.6%)                                                      | 24 (0.3%)                                                      |
| Mugna et al. [33] | 2015 | 27         | 27 (AMI)    | 54 (0.2%)                                                       | 24 (0.3%)                                                      |
| Tornvall et al. [34] | 2016 | 505        | 1010 (AMI)  | 1515 (6.9%)                                                     | 544 (7.4%)                                                     |
| Stiermaier et al. [35] | 2016 | 286        | 286 (STEMI) | 572 (2.6%)                                                      | 198 (2.7%)                                                     |
| Dias et al. [36] | 2016 | 100        | 99 (STEMI)  | 199 (0.9%)                                                      | 105 (1.4%)                                                     |
| Frangieh et al. [37] | 2016 | 200        | 200 (AMI)   | 400 (1.8%)                                                      | 164 (2.2%)                                                     |
| Budnik et al. [38] | 2016 | 66         | 66 (STEMI)  | 132 (0.6%)                                                      | 67 (0.9%)                                                      |
| Vitz et al. [39] | 2016 | 97         | 81 (STEMI)  | 178 (0.8%)                                                      | 64 (0.9%)                                                      |

Abbreviations: AMI = acute myocardial infarction; STEMI = ST elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; TTC = Takotsubo cardiomyopathy.
A. DE GIORGI ET AL.

Compared with CAD patients, whereas they had similar rates of severe in-hospital complications, including shock and death ($p = 0.93$). Thus, it is likely that for TTC patients other conditions and comorbidities, rather than dyslipidaemia alone and/or other established risk factors, are responsible for a risk of death comparable with that of AMI. However, our conclusions have several limitations. For example, the definition of “dyslipidaemia” was not uniform and there are no details regarding treatment. The type of AMI differed between studies. The studies considered were also based on different ethnicities. It follows that there is a need for more research to establish the exact role of dyslipidaemia in the pathogenesis of TTC.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

[1] Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA. 2001;285:2486–2497.

[2] Sato H, Tateishi H, Uchida T. Takotsubo-type cardiomyopathy due to a multivessel spasm. In: Kodama K, Haze K, Hon M, editors. Clinical aspect of myocardial injury: from ischemia to heart failure. Tokyo: Kagakuhyouronsha; 1990. p. 56–64.

[3] Bossone E, Savarese G, Ferrara F, et al. Takotsubo cardiomyopathy: overview. Heart Fail Clin. 2013;9:249–266.

[4] Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. Am Heart J. 2008;155:408–417.

[5] Lyon AR, Bossone E, Schneider B, et al. Current state of knowledge on takotsubo syndrome: a position statement from the taskforce on takotsubo syndrome of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2016;18:8–27.

[6] Khera R, Light-McGroary K, Zahr F, et al. Trends in hospitalization for takotsubo cardiomyopathy in the United States. Am Heart J. 2016;172:53–63.

[7] Redfors B, Vedrad R, Angerås O, et al. Mortality in takotsubo syndrome is similar to mortality in myocardial infarction – a report from the SWEDHEART registry. Int J Cardiol. 2015;185:282–289.

[8] Singh K, Carson K, Usmani Z, et al. Systematic review and meta-analysis of incidence and correlates of recurrence of takotsubo cardiomyopathy. Int J Cardiol. 2014;174:696–701.

[9] Akashi YJ, Nef HM, Lyon AR. Epidemiology and pathophysiology of takotsubo syndrome. Nat Rev Cardiol. 2015;12:387–397.

[10] Lyon AR, Rees PS, Prasad S, et al. Stress (Takotsubo) cardiomyopathy – a novel pathophysiological hypothesis to explain catecholamine-induced acute myocardial stunning. Nat Clin Pract Cardiovasc Med. 2008;5:22–29.

Figure 1. Log[ORs] of the studies comparing the prevalence of dyslipidaemia in patients with acute myocardial infarction (AMI) and in those with Takotsubo cardiomyopathy (TTC).

(182.9), all these risk factors (+333.7). On the one hand, a condition of stress, either physical or psychological, is very frequent in TTC patients (even if in 28.5% of cases a stressful could not be documented), on the other hand, comorbidities are crucial to explain the high mortality risk of TTC patients. In particular, TTC patients show higher rates of neurologic or psychiatric disorders (55.8% vs. 25.7%, $p < 0.001$) compared with CAD patients, whereas they had similar rates of severe in-hospital complications, including shock and death ($p = 0.93$). Thus, it is likely that for TTC patients other conditions and comorbidities, rather than dyslipidaemia alone and/or other established risk factors, are responsible for a risk of death comparable with that of AMI. However, our conclusions have several limitations. For example, the definition of “dyslipidaemia” was not uniform and there are no details regarding treatment. The type of AMI differed between studies. The studies considered were also based on different ethnicities. It follows that there is a need for more research to establish the exact role of dyslipidaemia in the pathogenesis of TTC.
[11] De Giorgi A, Fabbian F, Pala M, et al. Takotsubo cardiomyopathy and acute infectious diseases: a mini-review of case reports. Angiology. 2015;66:257–261.

[12] Cappelletti S, Ciallella C, Aromatomo M, et al. Takotsubo cardiomyopathy and sepsis: a systematic review. Angiology. 2016 [Jun 14]. pii: 0003319716653886. [Epub ahead of print].

[13] Manfredini R, Fabbian F, De Giorgi A, et al. Heart and lung: a dangerous liaison? Tako-Tsubo cardiomyopathy and respiratory system diseases: a systematic review of published case reports. World J Cardiol. 2014;6:338–344.

[14] Boccafogli A, De Giorgi A, Parisi C, et al. May allergic syndrome represent valid trigger for Tako-Tsubo cardiomyopathy? A systematic review of reported cases. Exp Clin Cardiol. 2014;20:5074–5087.

[15] De Giorgi A, Fabbian F, Tiseo R, et al. Tako-Tsubo cardiomyopathy and endocrine disorders: a mini-review of case reports. Am J Emerg Med. 2014;32:1413–1417.

[16] Finsterer J, Wahbi K. CNS disease triggering takotsubo stress cardiomyopathy. Int J Cardiol. 2014;177:322–329.

[17] Izumi Y. Drug-induced takotsubo cardiomyopathy. Heart Fail Clin. 2013;9:225–231.

[18] Ogura R, Hiasa Y, Takahashi T, et al. Specific findings of the standard 12-lead ECG in patients with ‘Takotsubo’ cardiomyopathy: comparison with the findings of acute anterior myocardial infarction. Circulation. 2003;67:687–690.

[19] Inoue M, Shimizu M, Ino H, et al. Differentiation between patients with takotsubo cardiomyopathy and those with anterior acute myocardial infarction. Circulation. 2005;69:89–94.

[20] Kosuge M, Ebina T, Hibi K, et al. Differences in negative T waves between takotsubo cardiomyopathy and reperfused anterior acute myocardial infarction. Circulation. 2012;76:462–468.

[21] Guerra F, Rrapaj E, Pongetti G, et al. Differences and similarities of repolarization patterns during hospitalization for takotsubo cardiomyopathy and acute coronary syndrome. Am J Cardiol. 2013;112:1720–1724.

[22] Meimoun P, Clerc J, Vincent C, et al. Non-invasive detection of tako-tsubo cardiomyopathy vs. acute anterior myocardial infarction by transthoracic Doppler echocardiography. Eur Heart J Cardiovasc Imaging. 2013;14:464–470.

[23] Prasad A, Dangas G, Srinivasan M, et al. Incidence and angiographic characteristics of patients with apical ballooning syndrome (takotsubo/stress cardiomyopathy) in the HORIZONS-AMI trial: an analysis from a multicenter, international study of ST-elevation myocardial infarction. Catheter Cardiovasc Interventions. 2014;83:343–348.

[24] Meimoun P, Abouth S, Boulanger J, et al. Relationship between acute strain pattern and recovery in Tako-Tsubo cardiomyopathy and acute anterior myocardial infarction: a comparative study using two-dimensional longitudinal strain. Int J Cardiovasc Imaging. 2014;30:1491–1500.

[25] Parkkonen O, Allonen J, Vaara S, et al. Differences in ST-elevation and T-wave amplitudes do not reliably differentiate takotsubo cardiomyopathy from acute anterior myocardial infarction. J Electrocardiol. 2014;47:692–699.

[26] Randhawa MS, Dhillon AS, Taylor HC, et al. Diagnostic utility of cardiac biomarkers in discriminating takotsubo cardiomyopathy from acute myocardial infarction. J Card Fail. 2014;20:2–8.

[27] Novo G, Giambanco S, Bonomo V, et al. Troponin I/ejection fraction ratio: a new index to differentiate takotsubo cardiomyopathy from myocardial infarction. Int. J. Cardiol. 2015;180:255–257.

[28] Najib K, Boateng S, Sangodkar S, et al. Incidence and characteristics of patients presenting with acute myocardial infarction and non-obstructive coronary artery disease. Catheter Cardiovasc Interventions. 2015;86(Suppl 1):S23–S27.

[29] Khalid N, Iqbal I, Coram R, et al. Thrombolysis in myocardial infarction frame count in takotsubo cardiomyopathy. Int J Cardiol. 2015;191:107–108.

[30] Zorzi A, Baritussio A, ElMaghawry M, et al. Differential diagnosis at admission between takotsubo cardiomyopathy and acute apical-anterior myocardial infarction in postmenopausal women. Eur Heart J Acute Cardiovasc Care. 2016;5:298–307.

[31] Daniel M, Ekenbäck C, Agewall S, et al. Risk factors and markers for acute myocardial infarction with angiographically normal coronary arteries. Am J Cardiol. 2015;116:838–844.

[32] Vervaet FE, Christensen TE, Smeijers L, et al. Is it possible to differentiate between takotsubo cardiomyopathy and acute anterior ST-elevation myocardial infarction? J Electrocardiol. 2015;48:512–519.

[33] Mugnai G, Pasqualin G, Benfari G, et al. Acute electrocardiographic differences between takotsubo cardiomyopathy and anterior ST elevation myocardial infarction. J Electrocardiol. 2015;48:79–85.

[34] Tornvall P, Collste O, Ehrenborg E, et al. A case-control study of risk markers and mortality in takotsubo stress cardiomyopathy. J Am Coll Cardiol. 2016;67:1931–1936.

[35] Stiermaier T, Moeller C, Oehler K, et al. Long-term excess mortality in takotsubo cardiomyopathy: predictors, causes and clinical consequences. Eur J Heart Fail. 2016;18:650–656.

[36] Dias A, Franco E, Janzer S, et al. Performance of a novel clinic score in differentiating takotsubo cardiomyopathy from ST elevation myocardial infarction within the first 24 h. Int J Cardiol. 2016;203:12–14.

[37] Frangieh AH, Obeid S, Ghadri JR, et al. ECG criteria to differentiate between takotsubo (stress) cardiomyopathy and myocardial infarction. J Am Heart Assoc. 2016;5:pii: e003418.

[38] Budnik M, Kochanowski J, Piatkowski R, et al. Simple markers can distinguish takotsubo cardiomyopathy from ST segment elevation myocardial infarction. Int J Cardiol. 2016;219:417–420.

[39] Vriz O, Brosolo G, Martina S, et al. In-hospital and long-term mortality in takotsubo cardiomyopathy: a community hospital experience. J Community Hosp Intern Med Perspect. 2016;6:31082.

[40] Pelliccia F, Parodi G, Greco C, et al. Comorbidities frequency and markers for acute myocardial infarction with angiographically normal coronary arteries. Am J Cardiol. 2015;116:838–844.

[41] Yayehd K, N’da NW, Belle L, et al. Management of takotsubo cardiomyopathy and acute anterior ST-elevation myocardial infarction within the first 24 h. Int J Cardiol. 2015;180:255–257.

[42] Citro R, Rigo F, Previtali M, et al. Differences in clinical features and in-hospital outcomes of older adults with Tako-Tsubo cardiomyopathy. J Am Geriatr Soc. 2012;60:93–98.
[43] Templin C, Ghadri JR, Diekmann J, et al. Clinical features and outcomes of takotsubo (stress) cardiomyopathy. N Engl J Med. 2015;373:929–938.
[44] Murakami T, Yoshikawa T, Maekawa Y, et al. Gender differences in patients with takotsubo cardiomyopathy: multi-center registry from Tokyo CCU Network. PLoS One. 2015;10:e0136655.
[45] Krishnamoorthy P, Garg J, Sharma A, et al. Gender differences and predictors of mortality in takotsubo cardiomyopathy: analysis from the National Inpatient Sample 2009-2010 Database. Cardiology. 2015;132:131–136.
[46] Regnante RA, Zuzek RW, Weinsier SB, et al. Clinical characteristics and four-year outcomes of patients in the Rhode Island Takotsubo Cardiomyopathy Registry. Am J Cardiol. 2009;103:1015–1019.
[47] Citro R, Bossone E, Parodi G, et al. Clinical profile and in-hospital outcome of Caucasian patients with takotsubo syndrome and right ventricular involvement. Int J Cardiol. 2016;219:455–461.
[48] Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. The Lancet. 2004;364:937–952.