I hope that future studies with inclusion of ‘novel’ biomarkers will help us to understand this complex and life-threatening complication.

References


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Apical ballooning syndrome, emotional stress and women

In their systematic review, Gianni et al. described clinical characteristics of the transient left-ventricular apical ballooning syndrome or takotsubo cardiomyopathy. They found that the disease onset is preceded by emotional stress in 26.8% and physical stress in 37.8% of cases. However, two largest and most comprehensive studies in western populations strongly have pointed toward the stunning female predominance, but also toward the importance of emotional stress as a possible external triggering event, observed in 86 and 100% of cases. Moreover, the shift in epidemiology due to the redefinition of myocardial infarction is unlikely to leave the incidence of early malignant arrhythmias unaffected.

I fully agree with the authors that the prediction of such events, albeit of major scientific and health economic interest, still remains a challenge. As our data suggest, the susceptibility of patients with non-ST-segment elevation myocardial infarction for such events is not explained by factors which have been shown to have good discriminatory power for other acute adverse events. Similarly, a recent meta-analysis could not elicit any risk factors for primary ventricular fibrillation other than ST-elevation and time from onset of symptoms, with the latter being a major confounder for other previously reported risk factors. In agreement with the authors, representing protracted or re-iterated emotional stress, excess in risk of infarction in both sexes is associated with natural catastrophes or stressful mass events such as earthquakes and war threats (e.g. missile attacks), again more prominently among women.

We have speculated that men and women respond differently to emotional stress or that there may be sex-specific pathophysiological mechanisms involved in triggering, as those suggested for apical ballooning syndrome. Furthermore, we have also previously observed a greater association of emotional stress with non-Q-wave than Q-wave myocardial infarction and proposed that transient vasospasm may be an important triggering mechanism associated with an emotional stress. Multiple vasospasm is one of the mechanisms postulated to underlay apical ballooning syndrome.

Gianni et al. noted several putative explanations for the sex difference in pathophysiology of triggering of apical ballooning syndrome including sex hormones-related influence on the sympathetic neurohormonal axis and on coronary vasoreactivity, women’s susceptibility to sympathetically mediated myocardial stunning, and postmenopausal alteration of endothelial function. However, further mechanisms may involve a sigmoid interventricular septum or a smaller left-ventricular outflow tract and reduced left-ventricular volumes predominantly found in women. In conclusion, in spite of data from the present review on the more frequent presence of physical stress before the onset of apical ballooning syndrome, there is evidence convincingly suggesting the pivotal role of emotional stress in triggering of this disorder that predominantly affects women. Still, the existence of such a phenomenon should be evaluated by controlled data (such as case-crossover methodology), whereas eventual underlying pathophysiological mechanisms are yet to be fully clarified.

References

Apical ballooning syndrome, emotional stress and women: reply

In our systematic overview, we found that apical ballooning syndrome is preceded by an emotional stressor in ~27% of cases and by a physical stressor in 38%. Ćulić suggests that emotional stress may be a more frequent trigger, especially in women. Indeed, in his meta-analysis of triggers of acute myocardial infarction (MI), Ćulić observed a greater association between emotional stress and MI in women vs. men. However, this finding relates to MI in general and not to Takotsubo cardiomyopathy in particular. Ćulić cites a couple of specific studies, conducted in western populations, which did indeed report a higher prevalence of emotional stressors as triggers for apical ballooning syndrome cases, and a report from Japan linking the stress associated with earthquakes to this syndrome in Japan. We thank Ćulić for drawing the readers’ attention to the interesting report from Japan, which was not incorporated in our systematic overview, as it was published in brief as a research letter and did not meet the a priori criteria set for the inclusion of studies in our meta-analysis.

The ascertainment of triggers for cases of apical ballooning syndrome is difficult, often based on patients’ recall, and we cannot exclude a more dominant role for emotional stressors. However, scientific rigour requires the careful consideration of the totality of the available evidence, rather than emphasis on specific reports. In our review, we attempted to capture all reliable and detailed studies reporting on this syndrome. It is possible that the role of emotional stress may differ in different populations [an emotional stressor was reported in 50 of 81 (63%) Caucasian patients, but only in 18 of 173 (9.3%) Japanese patients], and in women vs. men (we did not have access to individual patient data and could not analyse potential triggers in women and men separately).

Ćulić suggests that multiple vasospasm may be an important, emotional-stress-mediated, trigger mechanism for this syndrome and that the presence of a sigmoid septum or a small left ventricular (LV) outflow tract, both leading to low LV volumes, may also be important underlying pathophysiological mechanisms. We believe this to be unlikely. In the published literature to date, only three of 212 evaluated patients (1.4%) experienced multivessel epicardial spasm during coronaryography spontaneously and only 24 of 84 evaluated patients (28.6%) experienced multivessel epicardial spasm after infusion of a provocative agent. We identified no reports linking a sigmoid septum or a small LV outflow tract to the apical ballooning syndrome, and such conditions leading indeed to lower LV volumes may cause syncope, but would not be expected to trigger acute ischaemic events.

However, we fully agree that our current knowledge regarding the apical ballooning syndrome is scarce and that more research is needed to better understand this condition.

References


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The combination of anticoagulant and anti-platelet therapy in patients with atrial fibrillation: a comment on the recent ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation

In the recently published guidelines, all the aspects concerning the management of patients with atrial fibrillation are extensively and exhaustively discussed. Several assertions about the combination of anticoagulant and platelet-inhibitor therapy, however, appear questionable. First, a prominent role of clopidogrel in itself for the maintenance of coronary and stent patency can hardly be asserted because of the lack of specific evidence-based data. Instead, dual blockage of the ADP- and cyclooxygenase-mediated pathways of platelet aggregation, as obtained by the combined administration of clopidogrel and aspirin, is known to be necessary for optimal prevention of coronary artery thrombosis after an acute coronary syndrome or stent implantation. Therefore, the ideal anti-thrombotic treatment after coronary artery stenting in patients with atrial fibrillation appears to be represented by the combination of dual antiplatelet treatment and oral anticoagulation (OAC), rather than the suggested association of clopidogrel and OAC. Indeed, in small observational studies including patients with an indication for OAC undergoing coronary stent implantation, such triple therapy has been shown highly effective in totally preventing thrombo-embolic and thrombotic events, both at short- and long-term follow-up. The safety of triple therapy is undoubtedly an issue, since a relevant incidence of both minor and major bleedings
