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Angiographic and Midterm Thrombosis of Bioresorbable Vascular Scaffold for Coronary Bifurcation Narrowings

We have read with interest the important paper published in the *American Journal of Cardiology*[1] concerning the angiographic and midterm thrombosis of bioresorbable vascular scaffold for coronary bifurcation lesions. The authors admitted that the 3.9% scaffold/stent thrombosis rate at 1 year was apparently higher than reported with second-generation drug eluting stents. They attributed, this higher rate, to device-specific and/or procedure-related factors, flow disturbance and high/shear stress, extensive vessel preparation that induces higher response to platelet adhesion, acute side-branch occlusion, strut thickness, location of bifurcation, and the presence of ostial stenosis.

However they did not elaborate on the bioresorbable scaffold components that can induce such milieu intérieur pathophysiologic disturbances that can lead to scaffold thrombosis.

Indeed, the embedded bioresorbable poly (L-lactide) coated by bioresorbable poly (D,L-lactide) polymers are eventually degraded into lactic acid and finally into carbon dioxide and water, through metabolism in the Krebs cycle that can induce: enhancement of local acidosis by the carbon dioxide which can cause thrombosis as has been seen in open thorax surgery,[2] diminishing of activated partial thromboplastin time facilitating thrombosis,[3] and decrease of clot lysis that maintains thrombus formation.[4] Furthermore, the decreased pH of the surrounding intima, media, and adventitia, by accumulation of lactic acid, stimulates lactic acid sensors on sensory neurons innervating the heart[5] and induces the same pain as in angina and myocardial infarction.

Bioresorbable scaffolds bear 4 platinum marker beads, 2 embedded at both the proximal and distal ends for fluoroscopic visualization that have been

incriminated as inducing hypersensitivity reaction leading to stent thrombosis.[6] Bioresorbable poly (L-lactide) acid screws, used in orthopedics, have induced systemic hypersensitivity reactions proven by positive skin tests and necessitated to remove the screws.[7] Bioresorbable poly (L-lactide) gel injections can induce also granulomatous reactions.[8] The eluted everolimus substance from absorb bioresorbable stent has been already associated with the development of hypersensitivity pneumonitis, atopic dermatitis, exanthema, and generalized as well as lingual angioedema.[9]

Therefore, efforts to avoid and/or prevent locally induced acidity, local hypersensitivity inflammation, and foreign body reaction, together with technical and structural improvement seem to be of paramount importance for prevention the so feared scaffold thrombosis.

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Prevalence of Diabetes Mellitus in Patients With Takotsubo Syndrome According to Age and Sex

The pathophysiology of takotsubo syndrome (TTS) remains elusive. A plausible pathomechanism, currently considered, is that TTS is mediated by an autonomic sympathetic nervous system (ASNS) surge and/or blood-borne catecholamines from adrenal oversecretion. Diabetes mellitus (DM) via its underlying ASNS neuropathy exerts a halting effect on both direct stimulation of the heart via norepinephrine, and the release of epinephrine by the adrenal glands.[1,2] Consequently one should expect a lower prevalence of DM in cohorts of patients with TTS.[1-3] Kato et al,[4] in response to an inquiry,[3] about the prevalence of DM in the InterTAK (International Takotsubo) Registry of 1,613 patients, contributed by the Registry participants from 8 European countries and the United States,[5] have advanced the interesting concept of a differential in a plausible DM-mediated pathogenetic mechanism of TTS; they theorized[4] that, while the prevalence of DM in patients ≥60 years old with TTS is lower than the one of general populations, both in Europe and the United States, and thus DM may be "cardioprotective" (due to the underlying autonomic peripheral neuropathy), patients <60 years old with TTS in both continents have a higher prevalence of DM than the corresponding general populations (and thus DM predisposes them to develop TTS via an underlying microvascular impairment which they have, rather than ASNS neuropathy, which they had not yet developed).

To investigate this hypothesis, all 4,106 reports, published in Pubmed from its inception to December 31, 2018, were accessed through the MeSH term "takotsubo," and a meta-analysis was carried out on 2,667 suitable patients, who had individual patient-based data on age, sex, and history of DM. The original database of the world literature, without language restrictions, included 2,823 individually presented patients, but after the employment of "Google translate," help sought by native speakers with medical background, except on rare occasions when this could not be accomplished, and repeated contacts through e-mails, with the corresponding authors of reports, 156 patient cases had to be excluded, when information about age, sex, and history of DM could not be securely documented. More details on methodology can be found elsewhere.[1,2] Also very rarely there was information available about the particulars of DM, and that included that the patient had type 1 or 2 DM. In 2 patients the diagnosis of DM was made for first time in the setting of the patients' admission with TTS, and in 4 patients the diagnosis of having and being treated for "hyperglycemia," than DM, was provided. The assembled cohort of 2,667 patient cases was by an average age of ~6 years younger than the InterTAK Registry patients, with 39.6% being <60 years old, and with 84.4% being women (Table 1). What is new in this Reader's comment, compared with the previously published reports based on the same assembled database from the world literature,[1,2] is that more patients are included in the present work, and a new analysis of prevalence of DM according to sex, and the dichotomized brackets of <60 years and ≥60 years old of patients with TTS is provided herein, specifically for the purposes of an exploration of the hypothesis of Kato et al,[4] of an alleged pathophysiologic differential of DM mediation in the emergence of TTS in patients younger versus older than 60 years old.

The prevalence of DM in all patients, women, and men for the ages <60 and ≥60 years old, except for men ≥60 years old, was lower than in the general populations of Europe, the United States, and the world, as seen