EDITORIAL

Diabetes Mellitus and Acute Coronary Syndrome: A Lethal Combination Requiring Better Therapeutic Strategies

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In this issue of the Current Vascular Pharmacology, Shehab et al. [1] have evaluated the impact of diabetes mellitus (DM) on all-cause death after acute coronary syndrome (ACS), at 30 days and 1 year using the Gulf COAST registry database. Among 3,576 ACS patients, 1906 (53.3%) had DM. Patients with DM were more likely to have hypertension, dyslipidaemia and a prior cardiovascular (CV) event [including myocardial infarction (MI), heart failure (HF), angina and stroke] than those without DM (p<0.001 for all comparisons) [1]. DM patients had a significantly higher in-hospital, 30-day and 1-year mortality than those without DM (by 4.8, 6.7 and 13.7%, respectively). Specifically, DM patients with ST-segment elevation myocardial infarction (STEMI) had poor short-term (30 days) outcomes, whereas DM patients with non-STEMI (NSTEMI) had poor long-term (1 year) survival [1].

The prevalence of DM in ACS patients is increasing (ranging from 20-40%) worldwide, following the DM epidemic and the improved survival of DM patients [2, 3]. In this context, the Global Registry of ACS (involving 16,116 patients in North and South America, Europe, Australia and New Zealand) reported that approximately 25% of these patients had DM [4]. In this registry, significantly more DM patients had a history of hypertension, MI, stroke, angina, HF, percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) than their non-DM peers. In the Taiwan ACS Full Spectrum Registry, DM prevalence was 36% (1,000 out of 2,766 patients) [5]. DM patients had significantly higher rates of dyslipidaemia, hypertension, prior CV disease [including coronary artery disease (CAD), stroke, peripheral artery disease (PAD), HF and unstable angina] and prior coronary interventions [i.e. PCI and CABG], as compared with non-DM patients.

DM prevalence in ACS patients seems to be higher in the Gulf region since Shehab et al. [1] found that 53.3% of their ACS patients had DM. The same authors reported earlier that 39.4% of the patients admitted for ACS in various hospitals in the United Arab Emirates (UAE) had DM; data were obtained from the 1st Gulf Registry of Acute Coronary Events (RACE) [6]. Furthermore, DM patients were significantly more likely to exhibit hyperlipidaemia, hypertension, CAD, PAD, stroke or a history of coronary artery revascularization [6]. Similarly, the Saudi Project for Assessment of Acute Coronary Syndrome (SPACE) study reported that 2,929 out of 5,055 ACS patients (58.1%) had DM [7]. These patients also had significantly higher rates of dyslipidaemia, hypertension, prior CV disease [including coronary artery disease (CAD), stroke, peripheral artery disease (PAD), HF and unstable angina] and prior coronary interventions [i.e. PCI and CABG], as compared with non-DM patients [7]. The observed higher percentage of DM patients among those with ACS in the Gulf region could be attributed to the high type 2 DM prevalence in the general population of these countries (31.6, 29, 25.4, 25.0 and 25.0% for Kingdom of Saudi Arabia, Oman, Kuwait, Bahrain and UAE, respectively) [8]. These findings highlight the importance of implementing health policies for DM prevention and management in these high-risk populations.

DM has been linked with an increased risk for major adverse cardiac events (MACE) and mortality in ACS patients [9, 10]. In this context, in the Taiwan ACS Full Spectrum Registry, after adjusting for confounding variables, DM patients had a significantly higher risk of the primary endpoint [i.e. recurrent MI, stroke and mortality] and 1-year all-cause death compared with those without DM [odds ratio (OR): 1.9, 95% confidence intervals (CI): 1.2-3.0; p=0.006, and, 1.6, 95%CI: 1.2-2.2; p=0.005, respectively] [5]. Similarly, in the Global Registry for ACS, DM individuals remained at a significantly increased risk for HF, cardiogenic shock and death during the acute hospitalization [4] as in the SPACE study [7]. These findings are in agreement with the Shehab et al. [1] study, highlighting the worse prognosis of DM patients following an ACS and the need for effective treatment and close monitoring during hospitalization and long-term.

A common finding in ACS registries worldwide is that DM patients experiencing an ACS are more likely to exhibit dyslipidaemia, hypertension, a history of CV disease or coronary intervention than those without DM [1, 4-7]. Therefore, DM patients in the general population should be more aggressively treated in terms of CV risk factors to avoid ACS. In this context, Shehab

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et al. [1] reported that 50.2% of the total ACS patient population had a HbA1c >7%, 68.2% had blood pressure >130/80 mmHg and 81.8% had low-density lipoprotein cholesterol (LDL-C) >70 mg/dl, thus stressing the need to improve treat-to-target therapeutic strategies in high-risk patients, especially those with DM. Furthermore, in the Shehab et al. study [1], both short-and long-term mortality was higher with increasing hyperglycaemia, irrespective of pre-existing DM. This finding supports the importance of evaluating glycaemia and achieving optimal glycaemic control in all ACS patients both in the short- and the long-term. In this context, the use of antidiabetic drugs with proven CV benefits in DM patients after hospitalization for an ACS is recommended by current guidelines [11]. These include sodium-glucose co-transporter 2 inhibitors (mainly empagliflozin, since canagliflozin has been associated not only with improved CV outcomes but also with a doubled risk for lower-extremities amputations) or glucagon-like peptide-1 receptor agonists (mainly liraglutide, since semaglutide and albiglutide are not available in the market yet) [11].

DM patients are more prone to renal dysfunction [12]. In this context, Shehab et al. [1] reported that ACS patients with DM had a significantly lower creatinine clearance than their non-DM counterparts. Similarly, in the Global Registry of ACS [4], the Taiwan ACS Full Spectrum Registry [5] and the SPACE study [7], serum creatinine levels were significantly higher in the DM group compared with the non-DM group. DM predisposes to the development of contrast-induced acute kidney injury (CI-AKI) [13]. CI-AKI could occur following coronary angiography/PCI and it has been related to prolonged hospital stay and increased CV and renal morbidity, as well as all-cause death, even in the long-term (data available up to 4 years) [14-16]. Strategies to prevent CI-AKI include hydration, some antihypertensives, statins, as well other options [17-19]. Of note, kidney function could deteriorate after exposure to contrast media, even in the absence of CI-AKI [20]. Thus, renal function should be monitored in the outpatient setting following an ACS, especially in the presence of DM. In this context, it would have been useful if Shehab et al. [1] had evaluated the occurrence of CI-AKI and if they had recorded any changes in creatinine clearance levels during follow-up.

Statin loading before PCI or CABG has been associated with improved outcomes [21]. Current guidelines recommend the administration of high-intensity statins pre-PCI to decrease the risk of peri-procedural MI in both statin-treated and naïve patients [22, 23]. Shehab et al. [1] do not mention if statin loading was performed in their study. This could have affected the results.

CONFLICT OF INTEREST

NK has given talks, attended conferences and participated in trials sponsored by Amgen, Angelini, Astra Zeneca, Boehringer Ingelheim, MSD, Novartis, NovoNordisk, Sanofi and WinMedica. NP has been an advisory board member of TrigoCare International, Abbott, AstraZeneca, Elpen, MSD, Novartis, Novo Nordisk, Sanofi-Aventis and Takeda has participated in sponsored studies by Eli Lilly, MSD, Novo Nordisk, Novartis and Sanofi-Aventis and received honoraria for a speaker for AstraZeneca, Boehringer Ingelheim, Eli Lilly, Elpen, Galenica, MSD, Mylan, Novartis, Novo Nordisk, Pfizer, Sanofi-Aventis, Takeda and Vianex; and attended conferences sponsored by TrigoCare International, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Novartis, Novo Nordisk, Pfizer and Sanofi-Aventis.

REFERENCES