Old and new enemies: psychological stress, occupational stress, COVID-19, and a glimpse of the future

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patients across the spectrum of renal function. About 36,000 subjects with newly diagnosed AF from Scream (Stockholm Creatinine Measurements), a healthcare utilization cohort of Stockholm residents, were included. Predictive performance of the AFI, CHADS2, Modified-CHADS2, CHA2DS2-VASc, ATRIA, and GARFIELD-AF was evaluated across three strata of kidney function: normal [estimated glomerular filtration rate (eGFR) >60 mL/min/1.73 m²], mild (eGFR 30–60), and advanced CKD (eGFR <30). Performance was assessed with discrimination and calibration. Discrimination was dependent on eGFR: the median c-statistic in normal eGFR was 0.75 but decreased to 0.68 for both mild and advanced CKD, respectively. The Modified-CHADS2 showed good performance across kidney function strata, both for discrimination (c-statistics 0.78, 0.73, and 0.74, respectively) and for calibration.

The authors conclude that predictive performance for most risk scores was poor in the clinically most relevant stages of CKD, increasing the risk of misclassification and thus over- or undertreatment. The Modified-CHADS2 performed best and consistently across all kidney function groups and would therefore be preferred for risk estimation in AF patients. The manuscript is accompanied by an Editorial by Ben Freedman from the Heart Research Institute in Sydney, NSW Australia, and David Brieger from the Concord Repatriation General Hospital in Sydney, Australia. The authors note that risk stratification tools abound in medicine, but most do not find a place in clinical practice. AF stroke risk scores stand out as being among the most widely adopted. The challenge is to complement this utilization with enhanced predictive accuracy, and the study by de Jong et al., through its examination of score performance in CKD, has provided some insights as to how to achieve this goal. However, they note that do not yet have the ideal AF-related stroke risk stratification tool for clinical decision-making.

The role of psychological stress in the aetiology of AF is unclear. The death of a child is one of the most severe sources of stress. In a clinical research article, ‘Death of a child and the risk of atrial fibrillation: a nationwide cohort study in Sweden’, Dang Wei from the Karolinska Institutet in Stockholm, Sweden, and colleagues aimed to investigate whether the death of a child is associated with an increased risk of AF. The authors studied parents with children born during 1973–2014 included in the Swedish Medical Birth Register (a population of 4,000,000 individuals). Information on death of a child, AF, and socioeconomic, lifestyle, and health-related covariates was obtained through linkage to nationwide population and health registers. They examined the link between death of a child and AF risk using Poisson regression. Parents who lost a child had a 15% higher risk of AF than unexposed parents. An increased risk of AF was observed not only if the child died due to cardiovascular causes, but also in the case of deaths due to other natural or unnatural causes. The risk of AF was highest in the first week after the loss and remained elevated on the long term.

Wei et al. conclude that the death of a child is associated with a modestly increased risk of AF. The authors’ finding that an increased risk is also observed after loss of a child due to unnatural causes confirms that stress-related mechanisms may be implicated in the development of AF. The manuscript is accompanied by an Editorial by Kim Smolderen from Yale University in New Haven, CT, USA. The authors conclude that through a valuable comprehensive national data asset, a potential link between stress and incident atrial fibrillation was demonstrated for the first time in parents who had faced
the devastating loss of a child. Assessment of the parents’ needs and activating support sources are important priorities when faced with bereavement due to loss of a child, along with an understanding of how we can tailor interventions to individuals in need. They conclude that the research of Wei and colleagues has highlighted the risk parents may face after losing a child, while also exposing evidence gaps that may be filled by mechanistic and efficacy research targeting pathways and interventions to mitigate the identified risk.

Leisure time physical activity is associated with reduced risk of CVD and all-cause mortality,16,17 while these relationships for occupational physical activity are unclear. In a clinical research article entitled “The physical activity paradox in cardiovascular disease and all-cause mortality: the contemporary Copenhagen General Population Study with 104 046 adults”, Andreas Holtermann from the National Research Centre for the Working Environment in Copenhagen, Denmark, and colleagues tested the hypothesis that leisure time physical activity is associated with reduced major adverse cardiovascular events (MACE) and all-cause mortality risk, while occupational physical activity is associated with increased risks.16 The authors studied >100 000 women and men aged 20–100 in the Copenhagen General Population Study with baseline measurements in 2003–2014 and median 10-year follow-up. Both leisure and occupational physical activity were based on self-report with four response categories. Compared with low leisure time physical activity, multivariable adjusted (for lifestyle, health, living conditions, and socioeconomic factors) hazard ratios for MACE were 0.86 for moderate, 0.77 for high, and 0.85 for very high activity; corresponding values for higher occupational physical activity were 1.04, 1.15, and 1.35, respectively. For all-cause mortality, corresponding hazard ratios for higher leisure time physical activity were 0.74, 0.59, and 0.60, and for higher occupational physical activity were 1.06, 1.13, and 1.27, respectively.

The authors conclude that higher leisure time physical activity is associated with reduced MACE and all-cause mortality risk, while higher occupational physical activity is associated with increased risks. The manuscript is accompanied by an Editorial by Martin Halle and Melanie Heitkamp from the Technische Universität München in Germany.19 The authors note that physical exercise performed during leisure time or occupational time is different in character, as leisure time exercise comprises more aerobic endurance exercise whereas occupational exercise primarily involves repetitive resistance exercise of short bouts and often insufficient recovery time. Moreover, those involved in heavy manual work may be particularly exposed to psychological factors (e.g. night shifts and environmental stressors such as noise or air pollution), which are less frequent in sedentary jobs (e.g. office work). These stress factors may clearly affect the relationship between occupational physical work and cardiovascular risk factors, e.g. arterial hypertension, increased inflammation, vascular dysfunction, atherosclerosis, and cardiovascular events. These factors may also be responsible for excess overall mortality in this group.

On 13 March 2020, the Danish authorities imposed extensive nationwide lockdown measures to prevent the spread of COVID-19 and reallocated limited healthcare resources. In a clinical research article entitled ‘All-cause mortality and location of death in patients with established cardiovascular disease before, during, and after the COVID-19 lockdown: a Danish Nationwide Cohort Study’, Jawad Butt from the Copenhagen University Hospital in Denmark, and colleagues investigated mortality rates, overall and according to location, in patients with established CVD before, during, and after these lockdown measures.20 Using Danish nationwide registries, the authors identified a dynamic cohort, comprising all Danish citizens with CVD (i.e. a history of ischaemic heart disease, ischaemic stroke, heart failure, AF, and peripheral artery disease) alive on 2 January 2019 and 2020, respectively. The cohort enrolling ~700 000 individuals was followed from 2 January 2019/2020 until death or 16/15 October 2019/2020. The in-hospital mortality rate was significantly lower and out-of-hospital mortality rate significantly higher during and after lockdown compared with the same period in 2019. These trends were consistent irrespective of sex and age (Figure 2).

The contribution is accompanied by an Editorial by Antonio Cannata from the King’s College Hospital London in the UK.21 Cannata notes that while it appears crucial to continue medical care for at-risk groups, including those with cardiovascular conditions, further research is needed to better understand the full scope of contributory factors to cardiovascular mortality during the COVID-19 pandemic, beyond infection rates. This information is essential to determine the best approaches to caring for patients, improving outcomes in extreme conditions, and minimizing collateral damage in future outbreaks. Novel analyses, such as the elegant one published in this issue of the journal, are needed and welcome in order to address direct and indirect consequences of the pandemic. However, while comprehensive research will help us better understand the implications for patients with CVD, for now, the full effect of the COVID-19 pandemic on CVD cannot be seen. Only history will reveal the depth of the iceberg.

The issue is further complemented by two Discussion Forum contributions. In a manuscript entitled ‘In-hospital resuscitation of COVID-19 patients is impeded by serious delays, but the
problem is obscured by poor time data. John Stewart from Seattle, WA, USA comments on the recent publication entitled ‘Cardiac arrest in COVID-19: characteristics and outcomes of in- and out-of-hospital cardiac arrest. A report from the Swedish Registry for Cardiopulmonary Resuscitation’ by Pedram Sultanian from the University of Gothenburg in Sweden, and colleagues. 22,23 Sultanian et al. respond in a separate comment. 24

The editors hope that this issue of the *European Heart Journal* will be of interest to its readers.

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