Monitoring of traditional atherosclerosis cardiovascular disease risk factors - is it enough to prevent premature acute coronary syndrome?

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Atherosclerotic cardiovascular disease is the leading cause of death worldwide, and the high prevalence of risk factors makes the occurrence of premature acute coronary syndrome a significant healthcare problem.[1] The prevalence of acute coronary syndrome <60 years of age is 3.8% and is three-fold greater above 60. 1 in 4 new cases of acute coronary syndrome is premature.[1,2]

In recent decades, discussion has focused on the profile of risk factors predisposing to premature acute coronary syndrome. In this issue of *The Lancet Regional Health-Europe*, Bugiardini et al., presented the results on 70,953 Caucasian patients with first acute coronary syndrome from 7 South Eastern European countries, participating in the International Survey of Acute Coronary Syndromes (ISACS) archives, who were compared with patients without any baseline traditional risk factors. The authors found the co-occurrence of smoking, arterial hypertension, diabetes, and hypercholesterolemia to be associated with a 5-year shorter life expectancy free of acute coronary syndrome.[3] Moreover, they found that current smoking increased the premature event risk almost 3–4 times (risk ratio [RR] for women 3.96, and for men 2.82), hypercholesterolemia by about 40% (women RR 1.31; men RR 1.39) and diabetes increased the risk of premature death due to acute coronary syndrome by 50–60% (women RR 1.52; men RR 1.63).[3] These results are consistent with those obtained in a meta-analysis with 12.7 million participants.[4] This confirms the critical role of preventive strategies, especially in countries with high prevalence.

The cut-off point for premature acute coronary syndrome was defined as ≤67 years in women and ≤63 years in men in the study, which limits the interpretation of the data and potentially overestimates risk, in the context to the generally accepted cut-off point of 60 years for women and 55 years for men.[1,2] The study included countries from South-Eastern Europe, which (besides Romania and Croatia), have the highest prevalence of cardiovascular disease risk factors, and the least-well organized healthcare systems. Of the countries analysed in the study, 2 are high income countries (HIC) and 5 are middle income countries (MIC).[3] A higher prevalence of risk factors and the rate of death due to acute coronary syndrome in MICs compared to HICs were recently observed in the Global Burden of Cardiovascular Diseases and Risks 1990–2022 analysis.[1] Expanding the definition of premature acute coronary syndrome also somehow contradicts the recent approach of preventive therapeutical interventions, which should follow *'the earlier the better and the longer the better'* strategy, which is especially important now that previously ignored risk factors (e.g., lipoprotein(a) (Lp(a))) are now monitored, and unknown risk factors for premature disease such as Covid-19 and long-Covid have emerged. These predictors of premature acute coronary syndrome, including also familial hypercholesterolemia (FH), and underweight/obesity were not investigated by the authors, which makes these results incomplete. Finally, they evaluated 30-day mortality,[3] which is also limited, with large effect of peri-event and in-hospital risk factors, and only 12–36 months follow-up on which to reflect the role of risk factors on cardiovascular disease outcomes.[5]

Well-recognized preventive methods effectively reduce the risk of premature cardiovascular events. Each 1 mmol/l LDL-C reduction is associated with a 23% reduction in atherosclerotic cardiovascular disease risk, and the long-term LDL-C control contributes to 29% cardiovascular risk reduction in the 7th year of lipid-lowering therapy and even 55% with 40-year LDL-C goal achievement.[6] Each 5-mmHg reduction in systolic blood pressure is associated with a reduction of cardiovascular risk by 9–11%.[7] Active smoking and second-hand smoke exposure determine >30% of coronary artery disease, and smoking cessation is associated with a 14–26% cardiovascular risk reduction.[8] Losing excess body weight is associated with a significant

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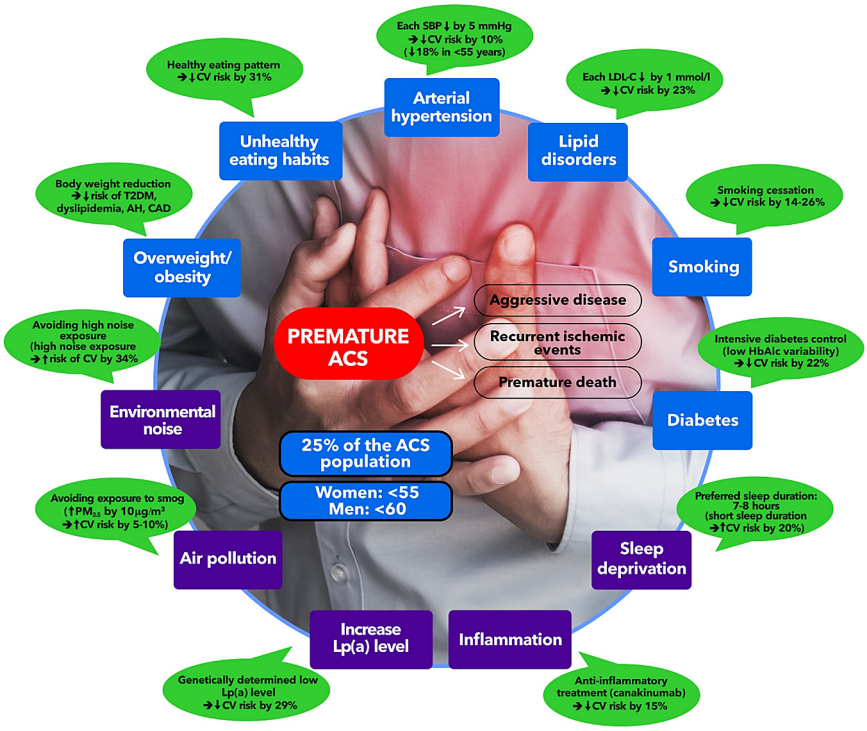

Fig. 1: Premature acute coronary syndrome - risk factors and possibilities for risk optimizing. Blue box – classic risk factors; purple box – non-classical risk factor. Figure was originally prepared based on information from [2,6–10, Front Cardiovasc Med 2022; 9: 930000; J Am Coll Cardiol. 2016; 68: 2761–72; Lancet Public Health 2022; 7: 890–1; Eur J Public Health 2023; 33: 725–31]. *Abbreviations: ACS – acute coronary syndrome; SBP – systolic blood pressure; CV – cardiovascular; LDL-C – low-density lipoprotein cholesterol; Lp(a) – lipoprotein (a); T2DM – type 2 diabetes mellitus; AH – arterial hypertension; CAD – coronary artery disease.*

improvement in cardiometabolic profile, thereby reducing cardiovascular risk.[9,10] Improving dietary habits can lead to a reduction in the risk of CVD by 31%.[6,9,10] and antidiabetic treatment has a documented preventive effect on cardiovascular disease and all-cause and cardiovascular mortality.[6,9,10] Also non-classical risk factors, including inflammation, infections, sleep deprivation and exposure to air and environmental noise should be considered.[1] One cannot forget the role of genetic predisposition, including FH and elevated Lp(a) levels. It has been shown that increased Lp(a) concentration is an independent risk factor for premature coronary artery disease, increasing the risk of myocardial infarction by 29%, peripheral artery disease by 31% and stroke by 13%.[6]

The analysis by Bugiardini et al.,[4] despite discussed limitations, carries an important message, showing clearly that effective prevention might significantly prolong life. The principles of premature acute coronary syndrome prevention are consistent with the "*Life's Essential 8*".[10] Thus, effective premature coronary syndrome prevention (and atherosclerotic cardiovascular disease in general) should be comprehensive and focus on classical and non-classical risk factors, and above all, those which are modifiable (Fig. 1).

Contributors

Maciej Banach: literature search, writing, supervision, preparing the final version of the paper; Stanisław Surma: literature search, first draft writing; preparing the manuscript's figure.

Declaration of interests

Maciej Banach: speakers bureau: Amgen, Adamed, Daiichi Sankyo, Exceed Orphan, KRKA, Polpharma, Mylan, Novartis, Novo-Nordisk, Pfizer, Sanofi, Teva, Zentiva; consultant to Adamed, Amgen, Daiichi Sankyo, Esperion, NewAmsterdam, Novartis, Novo-Nordisk, Sanofi, Teva; Grants from Amgen, Daiichi Sankyo, Viatris, Sanofi and Teva; Stanislaw Surma: honoraria from Novartis/Sandoz, Pro.Med.

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