

Opinion



The significance of family history in premature coronary artery disease: A call for early intervention

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Despite remarkable progress in the prevention and treatment of coronary artery disease (CAD), it remains the leading cause of death worldwide. The strong association between family history and premature CAD requires more attention. This association appears to be an avenue towards improved risk prediction and the creation of innovative treatments.

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The link between family history and early-onset coronary artery disease

Premature coronary artery disease (PCAD) remains a significant global health concern currently and frequently affects individuals before the age of 65 years in women and 55 years in men. Various risk factors may influence the development of PCAD and family history is a well-established, non-modifiable genetic risk factor that substantially increases an individual's susceptibility to PCAD.^{1,2} Despite advancements in cardiovascular medicine, deficiencies in early detection and preventive strategies leave many at-risk individuals undiagnosed or insufficiently treated. The present commentary emphasizes the urgent calls to proactive screening and individualized intervention among persons with a family history of PCAD.

Genetic predisposition and PCAD have well-established roles. Early studies show that subjects with one first-degree relative with PCAD face a substantially higher risk of developing the disease themselves³. This heightened risk is usually due to an inherited effect of genes, shared environmental effects, and familial clustering of modifiable risk factors such as obesity, hypertension, diabetes, and dyslipidemia. Genome-wide association studies (GWASs) have identified numerous common genetic variants linked to PCAD, with the majority attributed to single-nucleotide polymorphisms (SNPs) related to lipid levels and blood pressure.^{4,5}

Extensive genetic studies on large populations offer valuable insights into the hereditary factors influencing complex traits. Research on twins suggests that genetic factors contribute approximately 40%–60% to the risk of fatal CAD. Additionally, GWAS have so far identified 208 genetic regions associated with susceptibility to the disease.^{6,7}

Despite this knowledge, routine cardiovascular risk

assessment often underestimates the importance of family history; thus, a persistent need exists for improved familial risk prediction and the development of novel therapies. Standard risk score calculators, such as the Framingham Risk Score, the European "SCORE", and the ASCVD risk estimator, do not fully integrate family history into account. This oversight can lead to missed opportunities for early diagnosis and treatment.^{8,9}

Even though contradictory results in the realm of adding family history as a main variable to various risk estimators,^{8,10} the existing evidence supports the point that some details of family history parameters could be handy in assessing PCAD risk, especially in persons aged 35–55 years. To address this, clinicians must adopt a more comprehensive approach. Detailed family history including the number of affected first- and second-degree relatives and age of the relative at the time of PCAD should be integral to routine cardiovascular assessments.

Identifying individuals with a strong genetic susceptibility should encourage timely lifestyle changes, pharmacologic interventions, and, in select cases, advanced screening methods such as coronary artery calcium score scan, CT coronary angiogram or genetic testing.

Awareness programs in public health must also include campaigns on family history and its relevance to PCAD. Patients with a family history should be encouraged to organize periodic health checks, adopt a heart-healthy lifestyle, and watch out for potential symptoms as they develop.

Conclusion

Generally, a strong family history of PCAD should serve as a crucial red flag for appropriate intervention and is often accessible information that may assist clinicians in appropriate risk stratification of patients. Clinicians, researchers, policy and decision-makers, legislators,



and practitioners need to team up to highlight family history-based screening into routine practice, verifying timely recognition and managing high-risk individuals, particularly middle-aged persons. As we advance in precision medicine, leveraging genetic insights alongside traditional risk factors can pave the way for more personalized and effective cardiovascular care.

Authors' Contribution

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Investigation: Neda Roshanravan, Samad Ghaffari.

Validation: Samad Ghaffari.

Visualization: Neda Roshanravan, Samad Ghaffari.

Writing – original draft: Neda Roshanravan.

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Competing Interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. The authors declare that they are editorial board members of Biomedicine Advances at the time of submission. This had no impact on the peer-review process and the final decision.

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