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VIEWPOINTS

Paucity of Coronary Artery Calcium Research in Low-Middle Income Countries: A Call to Action

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Cardiovascular disease (CVD) is the most common cause of death globally, with over three-quarters of CVD deaths occurring in low- and middle-income countries (LMICs). Most of these deaths can be delayed if detected early. Despite the higher prevalence of CVD and CVD deaths in LMICs compared with high-income countries (HICs), the prevalence of traditional risk factors is unexpectedly similar in LMICs.[1,2] A higher prevalence may be because of disparities in health care and education but potentially also because of lack of clear delineation of significant risk factors such as coronary artery calcium (CAC). Thus, it is vital to perform high-quality, longitudinal studies to detect additional risk factors that may be leading to the higher rate of CVD in LMICs. CAC has been investigated to assess CVD since the 1990s. However, the longitudinal CAC studies referenced by the current guidelines were performed almost exclusively in HICs, neglecting relevant, and potentially divergent, clinical data from LMICs.

Therefore, the world regions where people are twice as likely to die from CVD when compared with HICs often lack any local, evidence-based guidelines, including CAC recommendations.[3] In this perspective piece, we shine light onto the lack of CAC research in LMICs and propose solutions to increase the availability of high-quality CAC studies from these regions.

CURRENT EVIDENCE

As a specific sign of atherosclerotic disease, CAC measured using noncontrast cardiac computed tomography has emerged as an important predictor of major cardiovascular outcomes in asymptomatic patients with coronary artery disease (CAD) and has shown superior risk predictive value compared with traditional CAD risk factors.[4] In fact, the MESA study (Multi-Ethnic Study of Atherosclerosis) showed that CAC had the highest predictive value of all the CAD risk factors studied. Guidelines have added CAC as an important noninvasive tool to risk-stratify patients with asymptomatic CAD, especially those with 5% to 20% 10-year risk of atherosclerotic CVD. Thus, CAC may be the determining factor needed to initiate pharmacologic and lifestyle preventive therapies for the prevention of CVD in intermediate-risk patients.[5]

The World Bank classifies world economies into 4 categories according to their income measured using gross national income per capita: 29 low-income, 50 lower-middle income, 56 upper-middle income, and 82 high-income economies.[6] Using this classification, a focused literature search in PubMed demonstrated the poor availability of research studies involving CAC and CAD performed in LMICs. The search criteria used were as follows: *Country[all] AND (cacs[all] OR cac[all] OR coronary artery calcium[all] OR calcium scoring[all]*

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OR calcium score[all] OR agatston[all]) AND (cad[all] OR coronary artery disease[all] OR MACE[all] OR major adverse cardiac events[all] OR cardiovascular disease[all] OR cardiovascular event[all] OR myocardial infarction[all] OR cardiac outcomes[all] OR cardiovascular outcomes[all] OR cardiovascular risk[all]), with the term "country" being replaced by the country in question. The search was performed with every country in the World Bank registry. From the resulting set of articles, we confirmed the country of origin and screened the abstract and occasionally the full text to confirm the studies were relevant to the topic of CAC and CAD.

There was only 1 CAC study published that included populations from low-income countries, a cross-sectional Ugandan study that found a lower prevalence of CAC in a local cohort compared with subjects in the United States.[7] In lower-middle income countries, 19 articles were published originating from 7 countries (14.0% [7/50]). The majority (84.2%) of these studies were cross-sectional. Most of these studies assessed the distribution of CAC according to clinical risk factors and according to coronary artery stenosis severity. The 3 remaining longitudinal studies assessed clinical end points using CAC as a predictor; however, only 1 was prospective.

The relatively small amount of CAC research was noticeable even in upper-middle income countries. Only 30.4% (17/56) of these countries had published relevant CAC data. A recent review further described CAC studies in upper-middle income countries and highlighted the lack of evidence involving CAC and event rate prediction in these regions.[8] Overall, a significantly smaller number of low-income countries had CAC research when compared with lower-middle and upper-middle income countries (0.03% [1/29] versus 14.0% [7/50] versus 30.4% [17/56], respectively; P=0.001 for trend) (Figure).

CONSEQUENCES

The lack of high-quality CAC studies to assess CAD in LMICs restricts generalizability. Efforts by North American and European studies to involve multiple ethnicities to improve the generalizability of their results are appreciated but are not sufficient to investigate differing environmental circumstances experienced in LMICs, which may have significant differences in CAC and CVD burden.[9] Most of the world territories remain unassessed, yet LMICs usually use North American and European clinical guidelines to screen patients and manage preventative measures in those at elevated risk of atherosclerotic disease. As a result, people from LMICs may not be receiving optimal cardiovascular care and preventative therapies, although the reasons for the suboptimal atherosclerotic CVD prevention in

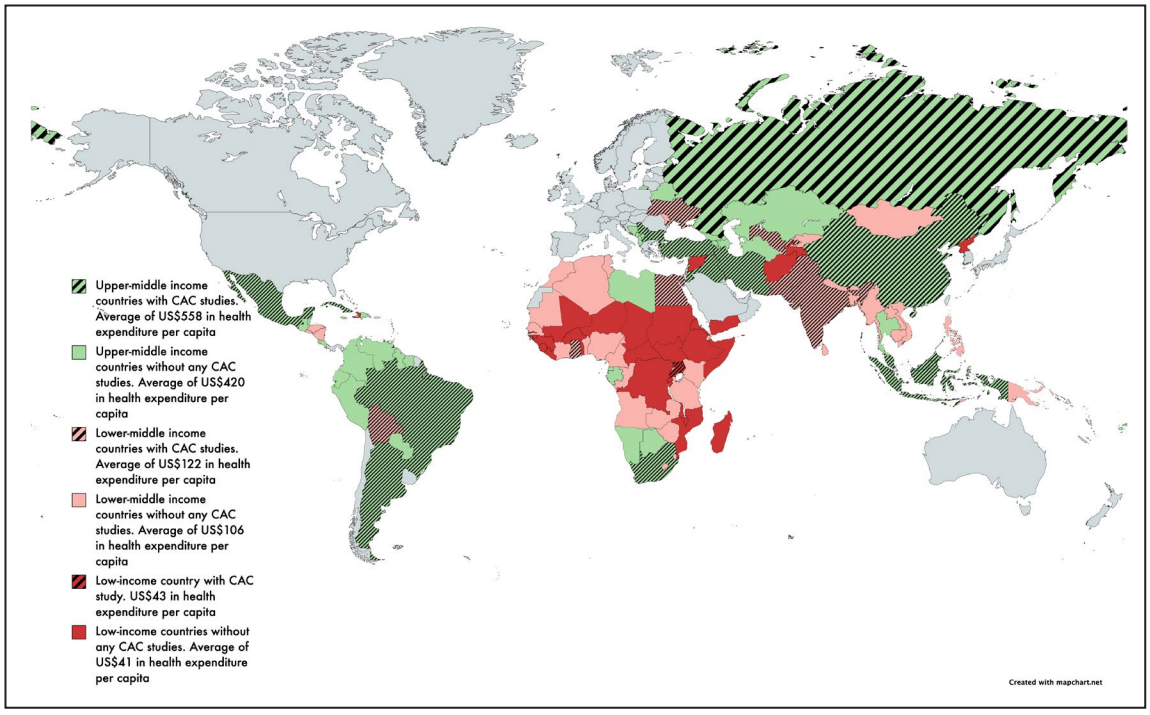

Figure. World map displaying low- and middle-income countries and the availability of coronary artery calcium and coronary artery disease studies found in a PubMed literature search.
Health expenditure per capita using 2018 World Bank data. CAC indicates coronary artery calcium.

LMICs are unclear and can only be speculated without prospective qualitative research.[10]

REASONS

Important deficiencies leading to limited CAC research in LMICs include a shortage of financial resources and a suboptimal research culture in comparison with HICs. World Bank data from 2018 show that health expenditure per capita is significantly lower as country income decreases. For instance, HICs spend US$3020 per capita; upper-middle-income countries spend US$436; lower-middle income countries spend US$124; and low-income countries spend US$41.[6] This potentially translates into scarcity of essential equipment to assess CAC, nullifying the possibility and usefulness of conducting CAC research to assess CAD in LMICs. Nevertheless, country wealth alone is not the only requirement to conduct research; the priority that government officials in these countries give to health care is crucial. For instance, according to the World Bank, LMICs allocate on average 5.4% of their total gross domestic product to health expenditure whereas HICs prioritize health care 130% higher on average (12.4% gross domestic product).

SOLUTIONS

To generate high-quality CAC data in LMICs, a significant research culture must be instilled, and sufficient resources must be allocated. The major catalyst to accomplish these goals is collaboration from HICs. Additionally, medical technology companies may benefit by providing private funding and hardware to academic institutions in LMICs, with the potential to test the performance of their technology in new markets. Research collaborations must involve different LMICs to further diversify the current evidence on CAC and CAD. For instance, the PURE (Prospective Urban Rural Epidemiologic) study recently published major findings describing the association between socioeconomic status and CVD risk from 20 LMICs and HICs.[11] The world would benefit from a similar collaborative effort to investigate CAC in LMICs.

BEYOND CAC

Although the focus of this perspective piece is centered on CAC because of its demonstrated incremental value over other clinical risk factors, the overarching ideas presented here could also be extended to other CVD risk stratification tools and clinical risk scores typically derived from prospective data in HICs.[12] In order to improve generalizability, prospective clinical trials must include a variety of LMICs.

CONCLUSION

Current literature contains limited CAC studies from LMICs, preventing us from having individualized data from the regions where three-fourths of global CVD deaths occur. We feel the main reasons are limited research culture and strained financial resources in LMICs. Collaboration from HICs and technology companies is key to improve availability of high-quality CAC research in LMICs.

ARTICLE INFORMATION

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