UNVEILING THE NEXUS OF NON-MODIFIABLE RISK FACTORS IN ACUTE CORONARY SYNDROME: IMPLICATIONS FOR PERSONALIZED CARE AND PREVENTION

Abstract

Acute Coronary Syndrome (ACS) encompasses a spectrum of critical cardiovascular conditions, including unstable angina and myocardial infarction (MI), and represents a significant global health challenge. This review provides a comprehensive analysis of non-modifiable risk factors associated with ACS, shedding light on the importance of thorough risk assessment and tailored interventions for individuals with these risk factors. The review begins by emphasizing the profound impact of ACS on public health, especially in low and middle-income countries, with a focus on the escalating prevalence in India. Furthermore, the review delves into the mechanisms contributing to ACS, which include plaque rupture associated with inflammation, plaque rupture without significant macrophage accumulations, plaque erosion causing non-ST-segment-elevation MI, and vasospasm affecting both epicardial arteries and coronary microcirculation. The primary focus of this review is on non-modifiable risk factors, with a detailed exploration of age, gender, family history, and ethnicity as significant contributors to ACS risk. It also draws on recent studies to provide insights into the complex interplay of these non-modifiable risk factors and their implications for ACS management. It underscores the necessity for tailored, culturally sensitive healthcare approaches to improve ACS outcomes across diverse populations.

Keywords: Acute Coronary Syndrome (ACS), Unstable Angina, Myocardial Infarction (MI), Non-Modifiable Risk Factors, Risk Assessment, Tailored Interventions.

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I. INTRODUCTION

Acute Coronary Syndrome (ACS) is a significant cardiovascular condition encompassing a spectrum of clinical presentations such as unstable angina and myocardial infarction (MI). Identifying and understanding the risk factors associated with ACS is crucial for risk stratification, prevention, and early intervention [1].

Coronary artery disease (CAD) is the leading cause of death and disability worldwide, particularly impacting low and middle-income countries. In these countries, approximately 7 million deaths and 129 million Disability Adjusted Life Years (DALYs) are attributed to CAD annually [1–5]. India, in particular, has a higher age-standardized rate of cardiovascular disease (CVD) deaths compared to the global average (272 per 100,000 population versus 235 per 100,000 population), and there is considerable variation in the prevalence of coronary risk factors [2]. The prevalence of CAD has significantly increased in both urban and rural areas of India, rising from 2% to 14% in urban areas and from 1.7% to 7.4% in rural areas [3]. Several risk factors, such as smoking, diabetes, hypertension, abdominal obesity, psychosocial stress, physical inactivity, dyslipidemia, and an unhealthy diet, have been identified in case-control studies conducted in India [4]. Similar variations in the distribution of coronary risk factors have been reported among ethnic groups in Europe and Iran [5]. The Indian population is highly diverse, consisting of 4635 anthropologically defined groups [6].

ACS can be caused by four distinct mechanisms. The first mechanism is plaque rupture, also known as fissure, which has traditionally been considered the primary cause of ACS. Plaque rupture is often associated with local inflammation, represented by the presence of blue monocytes, as well as systemic inflammation, indicated by increased levels of C-reactive protein (CRP) in the blood and measured using a high-sensitivity assay [6]. However, there are cases where plaque rupture occurs in atheromas that lack significant accumulations of intimal macrophages (as determined by optical coherence tomography criteria) and do not result in elevated circulating CRP levels. In these cases, plaque rupture typically leads to the formation of fibrin-rich red thrombi [7]. Another mechanism contributing to ACS is plaque erosion, which is increasingly recognized as a significant cause; particularly in non-ST-segment-elevation MI. Plaque erosion involves the formation of thrombi over patches of intimal erosion, which typically exhibit characteristics of white platelet-rich structures. Lastly, vasospasm can also induce ACS. While vasospasm has long been known to affect the epicardial arteries, it can also impact the coronary microcirculation [4]. The four diverse mechanisms leading to ACS include plaque rupture associated with inflammation, plaque rupture without significant macrophage accumulations, plaque erosion causing non-ST-segment-elevation MI, and vasospasm affecting both epicardial arteries and coronary microcirculation (figure 1).

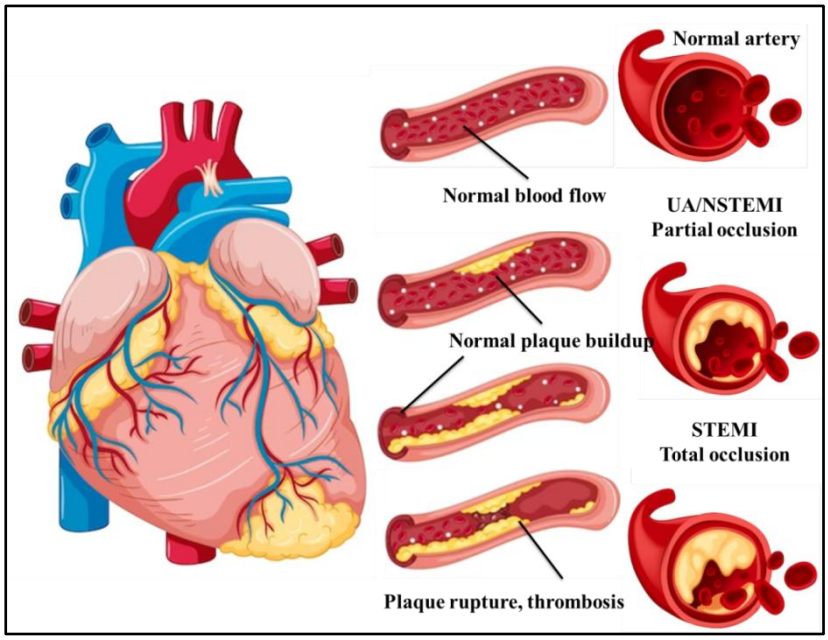

Figure 1: The Four Diverse Mechanisms Leading to ACS

The review draws on recent studies to provide insights into the complex interplay of these non-modifiable risk factors and their implications for ACS management. It underscores the necessity for tailored, culturally sensitive healthcare approaches to improve ACS outcomes across diverse populations.

II. NON-MODIFIABLE RISK FACTORS

1. **Age:** Age is a well-established risk factor for ACS, with advanced age consistently identified as a significant predictor of cardiovascular events. Numerous studies have shown that older individuals have a higher likelihood of developing ACS with each additional year of age. Cacciatore et al. (2023) highlight the importance of the American Heart Association's scientific statement on ACS management in older adults. They emphasize age-related changes contributing to ACS risk in older individuals, such as fibrotic degeneration, arterial stiffness, endothelial dysfunction, and pro-thrombotic tendencies. The statement emphasizes addressing geriatric syndromes like frailty, using tools like the Clinical Frailty Scale (CFS), and considering multimorbidity and polypharmacy. They also note limitations in frailty assessment in previous trials, underscoring the need for better therapeutic management understanding [7].Abdullah (2022) and Oberoi (2022) both discuss the complexity of managing ACS in older adults compared to younger patients. They cite factors like intricate anatomy, heightened physiological vulnerability, and increased risk due to geriatric syndromes [8, 9]. They highlight the challenges posed by a rising number of older ACS patients, leading to complications. Prompt PCI is recommended for STEMI patients of all ages, but NSTEMI management requires individualized risk assessment. Early invasive strategies for NSTEMI may benefit, but applicability varies due to selective trial populations and the influence of comorbidities and frailty. Boyraz et al. (2023) conducted a study on very old ACS patients (mean age 84.56 ± 5.01 years). They found PCI to be a safe treatment

option with low complication and mortality rates. Their study did not report any complications resulting in death or surgery. All-cause mortality was associated with heart failure, chronic pulmonary disease, shock, and C-reactive protein levels. Cardiovascular mortality correlated with heart failure, shock on admission, and C-reactive protein levels. These three studies collectively underline the challenges of managing ACS in older adults and the need for individualized approaches. Cacciatore et al. emphasize the importance of considering age-related changes, frailty, and comorbidities. Abdullah and Oberoi highlight the complexity of ACS management in older patients. Boyraz et al. provide valuable insights, suggesting that PCI is safe in very old ACS patients but emphasizing the importance of monitoring and managing heart failure, shock, and inflammation to reduce mortality risk. Further research is needed to establish precise standards of care for elderly NSTEMI patients [10].

2. **Gender:** The studies discussed in this comparison shed light on the significant sex differences in ACS and its management. Cenko et al. (2023) found that women with ACS face a higher mortality rate than men, regardless of the specific type of ACS, emphasizing the importance of considering these sex differences in risk assessment and treatment planning [11]. Meanwhile, Van Oosterhout et al. (2020) identified differences in symptom presentation, with women more likely to experience atypical symptoms, challenging the traditional classification of ACS symptoms as 'typical' or 'atypical [12].' Lunova et al. (2023) revealed that women with ACS often experience delays in receiving treatment and are less likely to undergo invasive procedures, highlighting disparities in care. However, adjusting for certain covariates can diminish gender-related differences in mortalit [13]. Lastly, Ronco et al. (2023) showcased disparities in out-of-hospital management, with women receiving fewer treatments but demonstrating a lower risk of long-term clinical events [14]. The common thread across these studies is the need for healthcare providers to recognize and address gender-specific factors in ACS management, ensuring adherence to clinical guidelines for all patients, irrespective of gender. Further research is necessary to better understand the underlying risk factors contributing to these disparities and to improve outcomes for ACS patients across the board.

3. **Family history:** Family history is an important risk factor for ACS. Assessing family history provides valuable genetic information that can enhance risk prediction, improve risk stratification, and enable personalized care for individuals with a history of myocardial infarction. Recognizing a familial predisposition to ASCVD allows healthcare professionals to implement targeted interventions to reduce the risk of recurrent cardiovascular events. Wahrenberg et al. (2021) demonstrated that a family history of early-onset ASCVD in first-degree relatives is associated with an elevated risk of recurrent ASCVD, even when traditional risk factors are accounted for. Incorporating family history into risk assessment tools improved predictive accuracy and risk stratification, suggesting its potential to guide intensified secondary prevention strategies for at-risk individuals [15]. Agarwal et al. (2018) found that patients with a family history of coronary artery disease (FHxCAD) experiencing STEMI had notably better in-hospital outcomes, including lower mortality rates and reduced adverse events. This observation suggests a potential protective effect of FHxCAD on STEMI outcomes, prompting the need for further research to elucidate the contributing factors, including lifestyle choices, medications, and interventions [16].Wahrenberg et al. (2020) highlighted that a family

history of CAD, particularly early-onset cases, is independently associated with an increased risk of ACS, particularly in younger patients and those with non-elevated initial cardiac biomarkers. This implies that considering a patient's family history, especially early-onset CAD, can be a valuable diagnostic tool, particularly in specific patient subgroups [17]. Prajapati et al. (2014) examined young patients and found that family history, along with other risk factors such as smoking and elevated lipid levels, played a significant role in the presentation of ACS at a young age. The study suggests that individuals with a family history of CAD, especially when combined with other risk factors, may face an elevated risk of experiencing ACS [18].Family history assessment can enhance risk prediction, improve risk stratification, and enable personalized care, particularly for individuals with a history of myocardial infarction. Further research is warranted to better understand the underlying genetic and environmental factors contributing to familial ASCVD and to develop tailored preventive measures for at-risk individuals.

4. **Ethnicity:** The studies discussed here collectively underscore the significant disparities in the prevalence, presentation, and outcomes of ACS among various ethnic groups. African Americans face a higher burden of comorbidities, such as obesity, diabetes, insulin resistance, and dyslipidemia, leading to a heightened incidence of cardiovascular disease [19]. They also exhibit distinct ACS symptomatology, with diaphoresis, left arm radiation, and palpitations being more commonly associated with the condition. However, these patients often experience longer delays in receiving timely treatment and are less likely to undergo certain procedures, despite potentially having lower in-hospital mortality rates [20].Asian Americans, on the other hand, present a diverse set of risk factors based on their specific ethnic backgrounds. South Asians, Japanese, and Filipinos have higher rates of diabetes and metabolic syndrome, while Filipinos are prone to hypertension and diabetes [21]. These groups often report different patterns of pain radiation and may exhibit higher rates of ST-elevation myocardial infarctions (STEMI). Interestingly, Asian Americans receive certain cardiac procedures at higher rates but still have worse overall outcomes and longer hospital stays [22].Hispanic patients, with their own set of risk factors, such as peripheral vascular disease, diabetes, hypercholesterolemia, obesity, and hypertension, may describe ACS symptoms differently. They often experience delays in reperfusion therapy and have lower rates of cardiac procedures, resulting in higher ACS mortality rates and extended hospital admissions [23-29].The study conducted by Sah et al. (2023) in India further highlights the importance of considering ethnicity as a factor in assessing cardiovascular risk [30]. They found significant differences in anthropometric and biochemical variables among different ethnic groups, with variations in risk factors like diabetes, smoking, hypertension, dyslipidemia, and family history of CAD. This research underscores the need for tailored prevention and treatment strategies for CAD patients based on their specific ethnic backgrounds. In conclusion, these studies collectively emphasize the imperative for culturally sensitive and tailored approaches to healthcare to address the disparities in ACS risk factors, presentation, and outcomes among diverse ethnic groups. Recognizing these differences is vital for improving ACS management and outcomes for all individuals, regardless of their ethnicity. Further research is essential to explore the underlying reasons for these disparities and to develop interventions specifically tailored to the needs of various ethnic groups.

III. CONCLUSION

In conclusion, this comprehensive review highlights the significance of non-modifiable risk factors in the context of ACS, emphasizing their impact on risk prediction, clinical presentation, and outcomes. This review will provide improved risk stratification. Healthcare professionals can use the insights from this review to refine risk prediction models for ACS, considering age, gender, family history, and ethnicity as crucial variables. This will enhance the accuracy of risk assessment and enable more personalized preventive measures. It underscored the need for tailored, culturally sensitive healthcare approaches for ACS management. Future clinical guidelines and interventions can incorporate these insights to address the unique needs of diverse patient populations. By recognizing and addressing disparities related to gender, age, family history, and ethnicity, healthcare systems can work towards reducing health inequities in ACS outcomes, ultimately leading to improved healthcare equity. This review will fill the gaps in our understanding of how these non-modifiable risk factors interact with ACS. Future research can delve deeper into the underlying mechanisms and genetic factors contributing to these disparities, paving the way for innovative treatments and preventive strategies.

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