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PSYCHOLOGICAL ASPECTS OF CARDIOVASCULAR DISEASES (A STEPTOE, SECTION EDITOR)

Psychosocial Factors and Recovery After Acute Myocardial Infarction in Younger Women

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Abstract

Purpose of Review To explain sex and gender approaches to studying acute myocardial infarction (AMI) risk and outcomes in younger women (18–55 years). More specifically, by looking at the AMI care pathway—from AMI risk to receiving acute and follow-up outpatient care to longer term AMI outcomes—we will examine where potential psychosocial factors may be associated with inequalities in AMI care and outcomes in younger women.

Recent Findings Despite recent declines in AMI incidence, morbidity, and mortality rates, younger women stand out as a group whose incidence has risen and who face worse outcomes following AMI, as compared with other groups. A focus on gender, rather than the binary, biological sex construct, allowed researchers to better understand potential pathways as to why younger women are facing this risk. Feminine traits and disproportionate exposures to psychosocial stressors in society at large may be correlated with inequalities in AMI care and further AMI outcomes in younger women. Psychosocial interventions in women with AMI that have proven to be successful have embraced this wider gender concept.

Summary Adopting a wider gender-concept to understand roles and demands that are placed on individuals that make them more at risk to experience psychosocial stressors and make it more challenging to organize self-care, get access to care, and equitable care may be needed.

Keywords Sex · Gender · Acute myocardial infarction · Younger women · Psychosocial factors

Introduction

As incidence, morbidity, and mortality rates for acute myocardial infarction (AMI) have decreased over the past decade, an interesting phenomenon stands out [1, 2]. Women, especially younger women (18–55 years), are the demographic group that has seen an increase in AMI incidence and have also been observed to be facing worse outcomes following AMI as compared with any other demographic [1, 2].

Major efforts have been directed towards understanding younger women's AMI risks that have focused on the biological underpinnings of these occurrences, different pathophysiologic pathways that are associated with the rise in obesity, and diabetes rates that disproportionately affect younger women, access to care, and quality of care issues, as well as psychosocial factors that may impede the timely recognition and recovery process following an AMI [3••]. In this review, we focus on describing the psychosocial aspects as it relates to AMI risk, recovery, and the role that sex and gender play in these associations, and specifically focus on the risk group of younger women in this context.

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As we are considering potential differences by sex and gender for the association between psychosocial factors and AMI risk and recovery, it is important to emphasize that a more nuanced understanding of the constructs sex and gender is necessary. Whereas sex differences typically refer to the biological meaning, the construct gender has typically been used to understand social roles assumed and attributed to individuals and that may be characterized along the masculinity versus feminity spectrum [4, 5, 6••]. In this review, we highlight the usefulness of a gender-based framework to post-AMI care as we consider psychosocial factors associated with AMI risk, recovery, and outcomes. However, it should be noted that both the sex and gender effects are likely hard to disentangle and often, multifactorial explanations to explain psychosocial differences in AMI risk and outcomes may be needed.

The specific objectives of this review are as follows (Fig. 1): first, to discuss the sex and gender frameworks that may be used to study psychosocial and AMI risk and outcomes. Secondly, we discuss whether psychosocial factors and risk of AMI occurrence have a differential relationship as a function of patients' sex or gender. Third, we examine whether a differential presentation by sex or gender exists as it relates to presentation for AMI symptoms and receiving quality AMI care, and whether psychosocial factors play a role in the potential differential or timely treatment of AMI symptoms. As we consider quality of AMI care, we also focus on early recognition and support for psychosocial stressors that may complicate the recovery pathway and outcomes following an AMI. Fourth, we then move into discussing recent insights into the risk of experiencing adverse outcomes following AMI and whether psychosocial factors are implicated and differential effects for men and women can be found. As we then combine these insights (Fig. 1), we conclude by discussing steps for future research and future intervention work to help erradicate differences in vulnerabilities and sex- and gender-based inequalities in outcomes following AMI.

Definition of Sex and Gender

Sex and gender differences play a very important role and influence clinical outcomes [4, 5, 6••]—yet both aspects are generally overlooked and under-reported. As sex and gender are not independent, exclusively assessing one or the other fails to account for identified variations in health. As per the Canadian Institutes of Health Research (CIHR) [7], the term sex should be used when reporting biological factors, while gender captures more complex aspects of individuals including identity, psychosocial, or cultural factors. Sex is defined as a biological construct and is often understood as a binary variable where one identifies as a man or a woman. Biological sex variables refer to the objectively measurable organs, hormones, genes, anatomy, and physiology [4, 5, 6••]. When considering gender in the evaluation of clinical research, the first hurdle for scientists originates from the apparent lack of standardized method to measure the complexities of all that gender encompasses. Gender represents a social construct that is linked to power, economic, and social status. It is culturally specific and varies over time. It has several dimensions including gender identity (how individuals/groups perceive and present themselves), gender norms (dynamics in the family, workplace, institutional, or global culture that influence attitudes/behaviors), and gender relations (the power relations between individuals) [4, 5, 6••, 7–10] (Fig. 2). As we are reviewing sex and gender differences for psychosocial factors that matter in the context of AMI risk and recovery, we will expand our scope beyond the "sex" definition that solely refers to biological differences but rather emphasize "gender" differences when referring to adopted and assigned roles.

The group that has done pioneer work adopting this vision is the research group around the GENESIS-PRAXY (Gender and Sex Determinants of Cardiovascular Disease: From Bench to Beyond - Premature Acute Coronary Syndrome) study [10]. In the Pelletier et al. (2015) study [6••], a gender index was constructed by looking at data from GENESIS-PRAXY. As a part of this study, variables measured through self-administered questionaires contributed towards most of the four gender aspects outlined by the Women Health Research Network of the Canadian Instutitute of Health Research: gender roles, gender identity, gender relations, and institutionalized gender [6••]. The authors developed and validated a method to derive a gender index score. As part of their validation work, they found that higher gender scores (scores on the "feminine" end of the gender continuum) were associated with cardiovascular risk factors such as hypertension and diabetes as well as heightened levels of depressive and

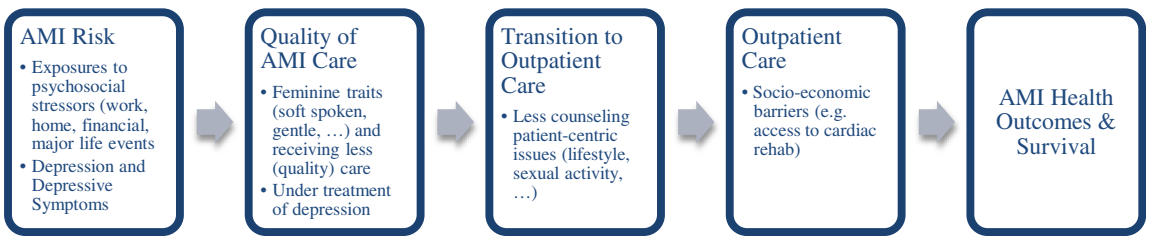

Fig. 1 Acute myocardial infarction (AMI) pathway and potential psychosocial factors associated with inequalities in AMI care and outcomes in younger women. (Adapted from Dreyer et al. [3])

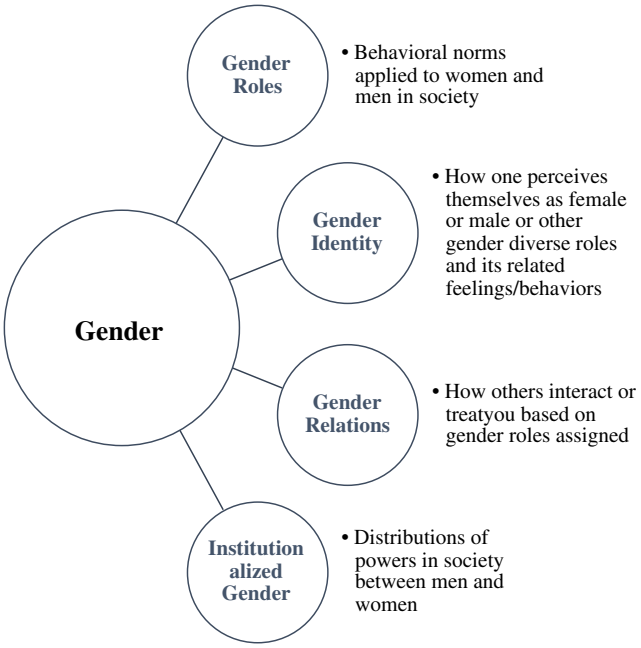

Fig. 2 Aspects that constitute gender [8]

anxious symptoms, associations they were not able to replicate using the biological construct sex. Studying gender roles along this continuum of masculinity and femininity as well as using appropriate terminology (sex vs. gender) and as prior work has shown a key to better understanding differences in risk psychosocial risk profiles and AMI outcomes [11••, 12]. While making this sex/gender distinction in the context of studying cardiovascular outcomes is a fairly recent approach, standardized assessment tools to quantify gender roles and relations and identify have been successfully developed and validated in a coronary population through the GENESIS-PRAXY questionnaire [6••, 11••].

Sex and Gender Differences for Psychosocial Factors and Risk of AMI: Are Younger Women at Highest Risk?

"Psychosocial factors" refer to a broad term that covers anything from intra- and interpsychic factors, "state" vs. "trait" concepts, and typically, these factors interact in complex ways with each other as well as with biological factors. Different conceptualizations of "stress" have been widely studied in the context of cardiovascular disease (CVD). The next most studied factor is depression. It is important to know that concepts such as social support, loneliness, hostility, anger, anxiety, and socio-economic status, as well as certain personality characteristics are all relevant concepts as we are trying to understand AMI risk and the role of gender and sex [13].

As many of these potential risk factors can be understood as contributing to increased exposure to stress, we are highlighting its role in AMI. Stress occurs when there are environmental demands to an individual that exceed a person's perceived personal resources. The experience of stress comes with negative emotions and physiological arousal as well as a higher tendency towards poor adaptive health behaviors (i.e., poor sleep, smoking). Continued exposure to stress increases one's risk of both physical disease as well as the risk of experiencing a psychological disorder. Different types of stress have been studied in the context of CVD ranging from daily stressors, chronic stress, stress in the workplace, to stressful life events. Stress causes cardiovascular reactivity, and through this mechanism, it can contribute to damaging the endothelial cells which then further promotes the deposit of lipids, inflammation, until atherosclerotic lesions are formed [14]. Cardiovascular reactivity due to stress may also contribute to a longer recovery period from sympathic activity. After being exposed to stress, vagal rebound is important to regulate recovery from sympathetic reactivity. Individuals with a diminished vagal rebound during recovery and decreased heart rate variability can be measured, which is a risk factor for CVD. Acute stress situations, for example, when experiencing extreme excitement or anger, can also trigger clinical events, such as a an AMI, possibly due to plaque rupture [15]. While these are mechanisms that have been studied in men and women, we are still trying to understand the specific nuances as to how sex and gender influences interact in these mechanisms and how these mechanisms are specifically at play in vulnerable groups such as younger women.

According to a 2006 meta-analysis looking at various models of work-related stress and its relation to CVD, the influence of workplace stressors represented by job strain, effort-reward imbalance, and organizational injustice is shown to account for a predictive association of about 50% with CVD occurrence [16]. As for private stressors, an accumulating body of research has demonstrated a marked societal increase in self-reported loneliness and social isolation, perhaps attributable to the dawn of the digital era and subsequent degradation of social networks [17]. In a 2012 literature review and meta-analysis conducted by Steptoe and Kivimaki, it was found that the long-term stress generated from social isolation may account for a 50% increase in CVD occurrence, comparable to the increase associated with work-related stress [17]. Additionally, INTERHEART, a 2004 case-control study conducted in 52 different countries with 15,152 cases and 14,820 controls enrolled, looked at risk factors and their association with CHD. Stress at work, and at home, financial stress, and major life events in the past year have all been found to be more frequent in AMI cases versus controls. Depression was also more frequently reported among cases than among controls. Furthermore, higher levels of locus of control were observed to have a protective effect for AMI. The effects of stress were similar for men and women and observed across all ages and geographic regions. The size of the effects

observed is comparable to the effects of hypertension and abdominal adiposity for the occurrence of AMI [18]. Developing standardized assessments to understand which sources of stress—e.g., family conflict, work/home balance, etc.—contribute to patients' risk associated with stress would help us to develop more targeted interventions to lower their risk.

A subgroup of individuals that are especially exposed to chronic stress are the ones who are dealing with depressive symptoms or depression. Both depressive symptoms and a major depressive disorder have been linked with an increased risk of AMI. Clear differences by sex and gender exist for the presence of depressive symptoms and depression [19, 20]. It has been shown that on a societal level, young women are a cohort uniquely prone to depressive symptoms when compared with older women and men; a study by Mallik et al. investigated whether this heightened rate of depression in young women was present during AMI hospitalization as well. Women enrolled in the study who were 60 years and younger displayed a significantly higher prevalence for depression during and after AMI [20].

It is known that individuals with a more compromised socio-economic status are particularly vulnerable to experiencing stress and be exposed to various psychosocial risk factors. As women may disproportionately take up multiple demanding roles, face gender pay gaps, and constitute the largest proportion of single parent families, exposure to related stress from these gaps may partially explain as to why we are seeing an increased prevalence of depression and associated cardiotoxic effects among women [21]. While psychosocial risk factors and risk of AMI seem to affect both men and women, the prevalence of risk factors such as depression seems to particularly manifest itself among younger females.

Younger Women and Quality of Treatment of AMI: Do Psychosocial Factors Play a Role?

Clear sex- and gender-based differences have been documented as it relates to symptom presentation for AMI. Young women in particular report more atypical symptoms, in addition to chest pain, and experience delays in presentation and treatment for AMI [3••]. While different disease pathophysiology (e.g., smaller infarcts, unknown mechanisms that caused the AMI) may partially explain a differential presentation and delayed recognition, disparities by sex and gender in treatment have been noted even after patients presented [22]. Less aggressive invasive tratments, medications, and delays in receiving percutaneous coronary intervention have been observed, as compared with men [23]. Psychosocial factors such as increased anxiety, housework, and feminine traits as measured by the BEM Sex-Role Inventory like being softly spoken and gentle have been shown to be predictors of delayed diagnostics and treatment for AMI [24]. These factors may be linked to the likelihood with which one is to receive care, but also the likelihood to use offered care, as well as the degree to which ones perceives the need to receive care [25].

Other quality of care concerns as it specifically relates to psychosocial risk factors is that psychosocial problems, such as depressive symptoms, remain largely under recognized in the AMI treatment pathway both among women and men, thereby leaving patients at risk of adverse outcomes associated with these psychosocial factors following the experience of their AMI [26, 27]. These disparities further extend to the post-AMI care pathway as women are less likely to receive referrals for cardiac rehabilitation, are less likely to be counseled about lifestyle choices (e.g., when to resume sexual activity), or face socio-economic barriers to participation in cardiac rehabilitation [28].

Adverse Outcomes Following AMI: the Role of Psychosocial Factors, Gender, and Sex

It has been replicated in several studies that depressive symptoms and depressive disorders, which may either be intensified by or are displays of psychosocial stress, are an independent predictor of both cardiac and all-cause mortality following AMI [29]. In a study by Reese et al., it was shown that both minor and major cases of depression, as defined by DSM-IV criteria, were significant predictors of hospital readmission after AMI, confirming what a number of other findings using self-report inventories of depressive symptoms have also concluded [29]. In addition, failure to recognize depressive symptoms when patients are admitted for an AMI is associated with an increased mortality risk, whereas in patients whose depressive symptoms were recognized and treated, such increased mortality was not observed [27]. These associations were observed in a cohort of 4062 patients who were admitted for an AMI; a total of 18.7% screened positive for clinically relevant depressive symptoms on the 9-item patient health questionnaire [30], and only one third received further follow-up or treatment. Patients' 1-year all-cause mortality outcomes with a positive depression screening that went on to receive treatment were similar to those who were not depressed (6.1% vs. 6.7%), whereas mortality outcomes in the untreated were 10.7%. These findings were replicated in a younger cohort of 3324 AMI survivors while focusing on adverse health status outcomes [26]. Not recognizing and treating depressive symptoms is associated with worse health status outcomes following AMI [26]. Other studies looking at the impact of stress have also found an increased risk of dying and for those exposed to higher levels of perceived stress; it has also been found that they face a higher risk of dying as well as worse health status outcomes [31]. While sex or gender interactions for the association between stress and adverse

outcomes were not reported, documentations of the increased prevalence of depressive symptoms and stress exposures in women may suggest that these risks disproportionally may extend to women over men. Currently, we are still trying to further understand whether and how sex or gender differences in psychosocial factors explain why we are seeing a higher vulnerability for women as compared with men as it relates to AMI outcomes.

Indeed, in recent years, studies have highlighted a concerning trend in public health—while prevalence of CVD and rates of mortality from AMI in the general population are on the decline, rates of AMI are shown to have increased in young women (≤ 55 years), with significantly higher rates of in-hospital and long-term mortality when compared with similarly aged men [3••, 32, 33]. The Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO) study has been the largest prospective cohort to date of young patients with AMI and investigated outcomes across the continuum of care for young women and men with AMI. In a study conducted by Dreyer et al., data from the VIRGO study was used to examine gender differences in the trajectory of health status (symptoms, functioning, quality of life) over a period of 12 months following AMI. Findings showed that despite women and men recovering similarly, young women reported lower health status outcomes than men over the first year post-AMI [34]. The VIRGO study has not been able to look at clinical outcomes (e.g., readmissions) as a function of psychosocial factors present in women versus men yet, but will have the ability to look into these questions with their data.

The GENESIS-PRAXY study, a multicenter prospective cohort study, involved a combination of self-administered questionairres and medical chart reviews that were collected and analyzed from 1163 patients with premature acute coronary syndrome (ACS) [32]. Considering the cohort's younger age group, findings showed unusually high rates of major adverse cardiac events and rehospitalization among both men and women within 12 months after ACS [35]. Consistent with VIRGO study findings, men and women experienced similar long-term outcomes following AMI; however, rates of all-cause rehospitalization 12 months following AMI, as opposed to cardiac-related rehospitalization, were higher in younger women [35, 36].

Bridging the Gap: Focus on Sex- and Gender-Specific Interventions to Optimize AMI Outcomes

While interventions that recognize psychosocial factors as relevant risk criteria to modify with the specific goal of improving AMI outcomes have been limited, a 2001 study by Cossette et al. demonstrated that further investigations to develop a modified approach are warranted. In the study, the psychological distress profiles of 433 patients from the M-HART study program were regularly measured using a General Health Questionnaire (GHQ). A secondary analysis showed that patients whose GHQ scores indicated a short-term reduction of psychological distress were less likely to die of cardiac causes, have high depression and anxiety, and to be readmitted for both cardiac and other causes at 1 year [37]. In The Stockholm Women's Intervention Trial for Coronary Heart Disease [38], randomized 237 women who were hospitalized for AMI or coronary procedures to a psychosocial group intervention program or usual care. Elements addressed in the program were psycho-education, relaxation exercises, self-monitoring and cognitive restructuring, learning how to cope with stressors associated with different roles, and compliance with clinical recommendations. A protective effect for mortality was associated with the intervention during the mean follow-up of 7 years, and effect that was almost threefold in favor of the intervention. These findings suggest that even though mechanisms for these observations remain unclear, there is promise in extending these interventions to our most vulnerable patients to directly help address some of the barriers and obstacles women face when dealing with receiving proper care and awareness for an AMI and its recovery trajectory.

While these interventional studies have focused on women in general and implicitly addressed gender-based differences for their targeted intervention, it is warranted to acknowledge its use against a wide range of gender diversities and rather to look along the spectrum of masculinity versus feminity traits and roles that may be associated with quality of care and outcome concerns in AMI. A 2015 study by Beckie et al. compared the biopsychosocial characteristics of young women and older women enrolled in cardiac rehabilitation, as well as the characteristics of those who prematurely terminated cardiac rehab participation. It was found that women ages 55 years and younger displayed significantly higher rates of anxiety and depression, reported significantly less optimism and hope, perceived less social support and more stress related to family, finances, work, and personal health, and demonstrated a significantly poorer quality of life overall when compared to older women [39]. Similar psychosocial profiles were shown among women who prematurely withdrew from cardiac rehabilitation, a notable finding given that their significantly higher rates of anxiety and depression deem them at greater risk for recurrent hospitalizations following AMI. Of the participants in the study, young women were more likely to be divorced or separated, employed full-time, disabled, on work leave without pay, or serving a caregiver role when compared with older women, characteristics that may begin to explain young women's heightened rates of depression and self-reported lack of social support [39].

Programs directly addressing these barriers—taking into account the unique stresses associated with the young woman's condition in today's society—and making it easier to find support as one tries to navigate the health care system to organize self-care to promote cardiovascular health, in concert with policy changes that would discourage inequities and inequalities in care as it relates to sex and gender are needed to effectively eradicate some of the concerning sex- and gender-based trends in AMI that we are observing. A one-size-fits-all approach for cardiac rehabilitation and improving vascular health that we historically have been promoting will not work as we try to address these inequities. This same observation may also apply to other social minorities as we are trying to understand their unique set of health concerns and come with custom solutions to address barriers that may hinder them from getting equitable care.

Conclusion

This review reviewed recent studies documenting sex and gender gaps in care and outcomes and how psychosocial factors may play a role. Recent worrisome trends in younger women who are the demographic group in whom AMI trends have been increasing against an overall background of decreasing AMI rates in general, and the documentation that women experience worse outcomes as compared with males point to a changing face of some of the risk profiles associated with an AMI. Investing in these issues and addressing them against a wider societal context are important as they affect not only the women and their families involved, but also hold implications to the costs of public health alone—financially, the cost of readmission for ACS is estimated between $13,000 and nearly $30,000 per patient [40–43]. The stakes are high considering that of those patients who survive the index hospitalization for ACS, 21–33% are re-hospitalized within 1 year [29].

Adopting a wider gender concept to understand roles and demands that are placed on individuals that make them more at risk to experience psychosocial stressors and make it more challenging to organize self-care, get access to care, and equitable quality of care may be needed to successfully address the gaps and inequalities observed. Successful examples of interventions directly addressing these demands can lead the way in how we think about organizing preventive efforts and integrate in our cardiac care and rehabilitation services against a quickly changing societal context.

Compliance with Ethical Standards

Conflict of Interest Anna Brush and Rachel P. Dreyer declare that they have no conflict of interest.

Kim G. Smolderen reports grants from Merck, Boston Scientific, Abbott Vascular, and Terumo. She is also co-founder of Dynamo Health LLC.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Ethical approval For this type of study (review of existing literature), formal consent is not required.

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