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Review

Gender-Related Factors Associated With Outcomes of Acute Coronary Syndrome in Young Female Patients

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ABSTRACT

Acute coronary syndrome (ACS) remains a significant global health concern, with a growing recognition of its impact on young adults, particularly young female adults. Although gender-related factors, defined as a social construct that encompasses 4 distinct dimensions (gender roles, gender identity, gender relations, and institutionalized gender) are undoubtedly relevant across age groups, young female patients with ACS face specific challenges and disparities in outcomes,

RÉSUMÉ

Le syndrome coronarien aigu (SCA) demeure un problème de santé préoccupant à l'échelle mondiale, avec une reconnaissance croissante de ses conséquences chez les jeunes adultes, plus particulièrement les jeunes femmes adultes. Les facteurs liés au genre, définis comme un construit social à quatre dimensions distinctes (les rôles liés au genre, l'identité de genre, les relations de genre et le genre institutionnalisé) sont indéniablement d'une grande importance dans tous les groupes

Lay Summary

Young female patientswith acute coronary syndrome (ACS), a sudden reduction or blockage of blood flow to the heart, face unique challenges influenced by the 4 dimensions of gender (roles, identity, relations, and institutionalized gender). Employment (gender roles) and a high level of social support (gender relations) improved outcomes. However, stress and depression (genderidentity) and low income and education (Institutionalized gender) were linked to worse outcomes. Addressing these gendered factors is key to improving acute coronary syndrome care for youngfemale adults.

Acute coronary syndrome (ACS) encompasses a spectrum of acute and potentially life-threatening conditions that result from a sudden reduction or blockage of blood flow to the myocardium, including unstable angina, non–ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction.^{1,2} ACS is a leading cause of mortality worldwide. In 2020, among all deaths caused by cardiovascular diseases, ACS accounted for 23% in male patients and

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18% in female patients globally.³ In developed countries, although the incidence of cardiovascular diseases has decreased among adults aged more than 50 years, it has either remained stable, or even increased, among younger adults over the past 2 decades.⁴

Although worldwide, age-standardized mortality rates for ACS were higher in male than in female patients,³ young female patients with ACS have a higher rate of 30-day allcause mortality,⁵⁻⁷ higher hospitalization rates,^{6,8-10} and higher readmission rates¹¹⁻¹⁶ than their male counterparts. Moreover, in the past 2 decades, the case fatality rate of ACS has shown a smaller reduction in young female patients than the rate in male patients.¹⁷ These patterns highlight the need to explore sex-specific influences on ACS, which particularly affect young female patients. In this context, sex, as assigned during birth, pertains to the biological dimension that allows a person to identify as a woman or man.

Moreover, previous studies have found important sex differences in etiology and presentation of ACS.¹⁸⁻²² To illustrate, in contrast to male patients or older individuals, young female patients might encounter coronary artery disease through distinct pathophysiological mechanisms that are related to hormonal changes,²³ differences in risk-factor profiles,²⁴ and conditions such as Takotsubo syndrome.²⁵ These factors make young female patients more susceptible to conditions that affect primarily the coronary microvasculature, such as spontaneous coronary artery dissection²⁶ and plaque erosion, rather than plaque rupture, the more common cause of ACS.¹⁸ The importance of integrating sex differences is being recognized increasingly by the scientific and medical

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compared to other populations. This narrative review examines the role of gender-related factors-specifically, gender roles, gender identity, gender relations, and institutionalized gender-in influencing objective and subjective ACS outcomes in young female patients. In the 5 articles identified, the objective outcomes included hospital readmission, "door-to-electrocardiography" time, and coronary atherosclerosis progression. Subjective outcomes, such as physical and mental functional status, quality of life, physical limitations, and vital exhaustion, were also examined. Being employed, which is a gender role, emerged as a protective factor against hospital readmission. Gender identity factors such as depression and stress were correlated with negative outcomes, and anxiety influenced "door-to-electrocardiography" times. Institutional factors, including income disparities. affected readmission likelihood. Strong social support decreased physical limitations post-ACS, whereas financial challenges and lower education negatively impacted quality of life and vital exhaustion. These findings underscore the intricate interplay of gender dimensions in shaping ACS outcomes among young female patients. Integrating these insights into clinical practice and research can enhance care, mitigate disparities, and foster improved cardiovascular health in this vulnerable population.

communities. Researchers, healthcare professionals, and policymakers have been acknowledging the significance of considering sex-specific factors in cardiovascular health research. This awareness has grown over time as a response to accumulating evidence and evolving perspectives within the field. In contrast, comparatively limited attention has been paid to how the multifaceted construct of gender influences health outcomes across various health conditions, including ACS.²⁷

Gender as a social construct pertains to the psycho-sociocultural attributes assigned to men and women within society, encompassing 4 distinct dimensions: gender roles, gender identity, gender relations, and institutionalized gender.²⁸⁻³⁰ In health research, consideration of the role of gender is crucial, as it interacts with biological sex and can influence the behaviour of patients, healthcare providers, and entire populations, ultimately affecting health outcomes. Sex and gender intersect and play a role in the diagnosis, management and outcomes of patients with ACS, especially among young adults.²⁰

Prior research has yielded a collection of review articles addressing varied aspects of ACS management inequalities,²⁰ socioeconomic inequities linked to ACS,^{31,32} racial and ethnic disparities therein,^{27,33} and the influence of nonstandard modifiable risk factors on ACS mortality.³⁴ In the context of young female patients, previous reviews have provided exploration of topics ranging from risk factors linked to ACS,²⁴ to psychosocial aspects of recovery following acute myocardial infarction,³⁵ alongside discussion on the d'âge, mais les jeunes patientes atteintes d'un SCA font face à des disparités et des défis particuliers à l'égard des résultats de santé par rapport à d'autres populations. La présente synthèse narrative propose un examen de l'influence des facteurs liés au genre (plus particulièrement les rôles liés au genre, l'identité de genre, les relations de genre et le genre institutionnalisé) sur les issues objectives et subjectives du SCA chez les jeunes patientes. Dans les 5 articles retenus, les issues objectives incluaient la réadmission à l'hôpital, le temps écoulé entre l'arrivée à l'hôpital et la réalisation de l'électrocardiographie et l'évolution de l'athérosclérose coronarienne. Les issues subjectives, comme le statut fonctionnel physique et mental, la qualité de vie, les limitations physiques et le syndrome d'épuisement, ont également été examinées. Être employé, qui est un rôle de genre, est apparu comme facteur de protection contre la réadmission à l'hôpital. Des facteurs liés à l'identité de genre, comme la dépression et le stress, étaient corrélés à des issues négatives et l'anxiété était liée au temps écoulé entre l'arrivée à l'hôpital et la réalisation de l'électrocardiographie. Les facteurs liés aux institutions, y compris les disparités de revenus, influençaient la probabilité de réadmission à l'hôpital. La présence d'un bon réseau social était associée à de plus faibles limitations physiques après le SCA, alors que les problèmes financiers et un faible niveau d'éducation avaient une influence néfaste sur la qualité de vie et le syndrome d'épuisement. Ces résultats font ressortir les interactions complexes entre les différentes dimensions du genre qui façonnent les issues du SCA chez les jeunes patientes. L'intégration de ces renseignements dans la pratique clinique et dans la recherche scientifique pourrait permettre d'améliorer les soins, de limiter les disparités auxquelles font face ces patientes et de favoriser une meilleure santé cardiovasculaire au sein de cette population vulnérable.

epidemiology, diagnosis, and treatment of acute myocardial infarction.^{23,36} Although gender-related factors are anticipated to continue to have an impact as individuals age, a review specifically focusing on the gender-related factors associated with ACS outcomes in young female patients has been lacking. This review aims to fill this gap by summarizing the evidence regarding gender-related factors explaining objective and subjective outcomes of young female patients with ACS. Understanding how gender factors influence patient outcomes allows us to inform decision-making regarding strategies for mitigating gender disparities experienced by young female patients with ACS.

Understanding Gender-Related Factors

The concept of *gender roles* encompasses a spectrum of behaviours and attitudes that are closely tied to an individual's biological sex and exert a substantial influence over various dimensions of their lives, including vocational choices, interpersonal relationships, attire preferences, and everyday interactions.²⁹ In the context of ACS research, delving into variables associated with gender roles traditionally ascribed to women can offer indispensable insights. These variables, ranging from primary-breadwinner roles to engagement in household chores, childcare responsibilities, and occupational pursuits, contribute to a holistic comprehension of how these gender roles intersect with ACS outcomes, especially among young female patients. By examining the intricate interplay between traditional gender roles and diverse facets of

individuals' lives, researchers contribute to a more nuanced analysis of the multifaceted societal dynamics that shape health disparities in the context of ACS.

The concept of *gender identity* is a deeply personal understanding of oneself in relation to gender, which may align with or diverge from the sex one is assigned at birth. This self-perception, whether as a woman, a man, or a nonbinary or "two-spirited," identity shapes emotional experiences and behavioural responses.²⁹ Studies have indicated that gender identity is intertwined intricately with mental health, as exemplified by feelings of depression, anxiety, and stress.³⁷ Therefore, the dimension of gender identity encompasses various psychological aspects that profoundly influence an individual's well-being and quality of life. Depression, anxiety, fatigue, and overall quality of life are integral components of this complex dimension.

The concept of *gender relations* refers to the intricate web of interactions that occur among individuals based on their gender.³⁰ These interactions encompass the ways people engage with each other. The study of gender relations involves analyzing how these interactions shape various facets of life, including social connections, health outcomes, resource access, and opportunities, contributing to a deeper understanding of human social experiences. In the ACS context, this arena involves understanding how interactions and relationships might impact symptom recognition, healthcare-seeking behaviours, treatment choices, access to medical services, and systems of support.²⁰

The concept of *institutionalized gender* encompasses the intricate distribution of power, resources, and opportunities across political, educational, and social institutions, based on gender.^{29,35} This facet of gender analysis acknowledges the systemic impact of gender norms on individuals' lives, spanning socioeconomic status and societal inequalities. The concept goes beyond the individual and interpersonal levels, to scrutinize how societal structures and cultural norms influence life decisions and access to resources, highlighting the need to address gender disparities at an institutional level.

We recognize that race and ethnicity are distinct constructs that encapsulate unique aspects of human diversity and intersect with gender in complex ways. Although race and ethnicity may influence ACS outcomes, our paper's main objective is to provide insights into gender-related disparities in the context of ACS.^{38,39} Therefore, in this review, race and ethnicity were not considered as gender-related factors associated with ACS in young female patients.

Methodology

This narrative review presents analysis of published articles concerning gender-related factors associated with outcomes in ACS. A targeted search for relevant literature was conducted across PubMed, using a combination of specific keywords, such as "ACS," "social determinants," "female sex," "young adults," and "outcomes" (see Supplemental Table S1). The study included exclusively original English-language peer-reviewed articles published from January 1, 2013 up to August 1, 2023. Moreover, we included studies that explicitly investigated and reported on the relationship or correlation between gender-related factors and ACS outcomes in young female patients, with an age cutoff of < 65 years. The

following types of publications were excluded: studies with an ambiguous age cutoff, editorials, letters to editors, conference proceedings, reviews, position statements, and short communications. Note that no medical subject heading (MeSH) terms exist for gender. Given that our review was not intended to be a formal systematic analysis, we did not apply risk-ofbias assessment to the articles we found in our search. Instead, our goal was to include pertinent existing literature. Furthermore, our search approach centred on specific genderrelated factors, such as social determinants of health, educational achievement, socioeconomic status, caregiving duties, marital situation, support networks, psychosocial factors, anxiety disorders, household size, and gender disparities. Consequently, we synthesized the available body of evidence concerning the impact of gender on objective and subjective ACS outcomes.

Studies Evaluating Gender-Related Factors Associated with Objective and Subjective ACS Outcomes in Young Female Patients

General characteristics of the included articles

Of the 248 abstracts identified through the PubMed search (Fig. 1), we excluded 104 as they were the wrong type of study—that is, they studied non-ACS outcomes or non-young adults. Moreover, after the full text was evaluated, 139 articles were excluded, and 5 original articles were finally included for this analysis⁴⁰⁻⁴⁴ (Table 1). Four articles included female patients aged under 55 years,⁴⁰⁻⁴³ and one study included female patients aged under 65 years.⁴⁴ Studies ranged in sample size from 103 to 2306 female participants with ACS. Three articles showed sex- and age-disaggregated data,⁴¹⁻⁴³ and 2 included only young female patients.^{40,44}

Description of the included research studies

These articles were drawn from 3 distinct research studies. Specifically, 2 of the articles stemmed from the Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO) study,^{40,41} 2 from the Gender and Sex Determinants of Cardiovascular Disease: From Bench to Beyond Premature Acute Coronary Syndrome (GENESIS-PRAXY) study,^{42,43} and 1 from the Stockholm Female Coronary Angiography Study⁴⁴ (Table 1).

VIRGO⁴⁵ is a large, prospective cohort study of the presentation, treatment, and outcomes of young female and male patients with acute myocardial infarction (AMI). The study enrolled 2985 female and male patients (ratio 2:1), aged 18 to 55 years, with AMI from 103 participating hospitals across the US between August 2008 and January 2012. Data were collected during the hospitalization, as well as at 1 month and 12 months after hospital discharge.

GENESIS-PRAXY⁴⁶ is a multicentre, prospective cohort study involving female and male patients with premature ACS (unstable or intermediate coronary syndromes and/or AMI). Data were collected from 24 centres—22 Canadian, 1 American, and 1 Swiss, between January 2009 and April 2013. Recurrent ACS, revascularizations, death, and healthcare system use were gathered by telephone interview and chart review at 12 months.



Figure 1. Flowchart of the included articles. ACS, acute coronary syndrome.

The Stockholm Female Coronary Angiography Study recruited participants from the Stockholm Female Coronary Risk Study, a case-control study conducted in Sweden, and enrolled female patients aged 65 or younger who were admitted to any of the 10 coronary care units in Stockholm due to either AMI, characterized by specific chest pain, enzyme patterns, and electrocardiographic changes, or unstable angina, indicated by newly intensified severe angina pectoris within the 4 weeks before admission, with elevated pain intensity and duration, or discomfort at rest or during minor physical exertion. For every patient, a control of the same age was chosen, free of heart disease symptoms and nonhospitalized for any health problem over the preceding 5-year period. Control subjects were selected from the census register of the wider Stockholm region. Participants were recruited between 1991 and 1994 and were examined 3 to 6 months after hospitalization. Among participants, 116 female patients underwent a second quantitative coronary angiography evaluation, on average, 3.25 years later.

Characteristics of the young female participants in the included research studies

The characteristics of the female participants included in the 3 studies are summarized in Supplemental Table S2. In the VIRGO study, almost half of the female participants were married (52.5%) and were primary income earners (73.9%), and 47.6% experienced low income. These female participants displayed engagement in the workforce (56.2%), showed a median score of social support of 27.0 (Interquartile range = 23-30, evaluated by the **En**hancing **R**ecovery in Coronary Heart Disease Patients (ENRICHD) Social Support Instrument (ESSI), which has a scale ranging from 8 to 32, and they exhibited varied states of mental and physical health. The GENESIS-PRAXY study involved female participants with a prevalence of depression and anxiety of 28% and 54%, respectively, substantially higher than the Canadian average of 7.6% and 5.2% who suffered from major depressive episode and generalized anxiety disorder in 2022.⁴⁷ In examining gender-identity factors, the VIRGO study utilized the Bem Sex-Role Inventory (BSRI). The BSRI uses a Likert scale from 1 to 7 for individuals to use to rate themselves on traits that are deemed culturally to be masculine or feminine; high scores in masculinity or femininity suggest strong identification with those respective traits. The VIRGO study found average femininity and masculinity scores of 6.0 and 4.8, respectively, alongside proportions of those who were employed (67%) and had social support (27%). The Stockholm Female Coronary Angiography Study⁴⁵ explored the characteristics of females aged below 65 years, revealing that 66.0% had education levels of 1-9 years, and 26% received vital exhaustion scores between 46 and 57, assessed using the Maastricht Vital Exhaustion Questionnaire, a tool developed to assess vital exhaustion as a symptom preceding myocardial infarction.

Author	Year	Study name	Settings	Study design	Inclusion and exclusion criteria	Sample size	Recruitment period and duration of follow-up	Outcomes examined
Dreyer et al. ⁴⁰	2023	VIRGO study	National network of hospitals in US, Spain, and Australia	Prospective cohort	Patients aged 18 to 55 y with AMI presenting to 103 hospitals in the	2007 female patients	August 2008 and May 2012; 1 y	Readmitted within 1 y
Beckman et al. ⁴¹	2016	VIRGOstudy	National network of hospitals in US, Spain, and Australia	Prospective cohort	1		August 2008 and May 2012; 1 y	 1-y physical functional status 1-y mental functional status Disease-related quality of life Perceived stress Depressive symptomatology
Leung Yinko et al. ⁴²	2014	GENESIS-PRAXY	Sites in Canada, US, Switzerland	Prospective cohort	Patients aged 18 to 55 y, admitted with a	761 male patients; 362 female patients	2009-2013; 12 mo	Physical limitation score
Pelletier et al. ⁴³	2014	GENESIS-PRAXY	Sites in Canada, US, Switzerland	Prospective cohort	diagnosis of ACS to the coronary care units of participating hospitals, fluent in English and/or French, and able to provide informed consent.	761 male patients; 362 female patients	2009-2013; 12 mo	"Door-to- electrocardiography" time within 10 min
Zimmermann-Viehoff et al. ⁴⁴	2013	The Stockholm Female Coronary Angiography Study	Sweden	Prospective cohort	All female participants younger than 65 y who were consecutively admitted for an acute coronary event (AMI and unstable angina pectoris) during a 3-y period in the greater Stockholm area.	103 female patients	February 1991 and February 1994; 6 mo after hospitalization	Baseline vital exhaustion score

ACS, acute coronary syndrome; AMI, acute myocardial infarction; GENESIS-PRAXY, Gender and Sex Determinants of Cardiovascular Disease: From Bench to Beyond Premature Acute Coronary Syndrome; VIRGO, Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients.

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Figure 2. Gender-related factors significantly associated with acute coronary syndrome (ACS) outcomes by gender dimensions. Down arrow indicates lower likelihood and/or values; **green** indicates subjective outcomes; **blue** indicates objective outcomes. D-ECG, "door-to-electrocardiography" time within the recommended 10 minutes; HospR, hospital readmission; LDN, luminal diameter narrowing after 3 years.

Gender-Related Factors and ACS Objective Outcomes in Young Females

Three studies investigating gender-related factors and their impact on ACS outcomes in young females were centred on 3 distinct outcomes (Supplemental Table S3), outlined as follows: (i) 1-year all-cause hospital readmission; (ii) door-toelectrocardiography (ECG) time within the recommended 10-minute window; and (iii) luminal diameter narrowing observed through angiography after a span of 3 years. A summary of the gender-related factors significantly associated with objective ACS outcomes is provided in Figure 2.

The "door to ECG" metric refers to the time interval from patients' arrival at the hospital to the moment they undergo ECG.⁴⁸ Although the "door to ECG" time is particularly emphasized in patients with ST-segment elevation myocardial infarction patients, due to the critical nature of timely intervention, its relevance extends to the broader spectrum of ACS. Rapid diagnosis via ECG can aid in distinguishing the type of ACS, guiding appropriate treatment strategies. Moreover, for young female patients with ACS, a demographic that already faces unique challenges and outcomes, timely diagnosis through prompt ECG becomes even more crucial. Delays can exacerbate complications and impact prognosis.

Gender roles and ACS objective outcomes in young female patients

Regarding gender roles (Fig. 2; Supplemental Table S3), according to Dreyer et al.,⁴⁰ being the primary income earner, working, and having a higher mean number of work hours per week were associated with a lower risk of hospital readmissions in young female patients with ACS. This finding suggests that employment status and work hours may play a role in the outcome of ACS in young female patients. However, an important point to note is that the relationship between gender roles and health outcomes is complex and can be influenced by many factors.

Gender-identity factors and ACS objective outcomes in young female patients

Concerning the gender-identity factors (Fig. 2; Supplemental Table S3) linked with ACS outcomes in young female patients, Dreyer et al.⁴⁰ identified substantially elevated median depression and perceived stress scores within the readmitted group. In particular, the readmitted group displayed a notably diminished median for physical limitation, quality of life, physical general health, and mental general health scores. Likewise, Zimmermann-Viehoff et al.⁴⁴

observed a negative correlation between vital exhaustion and its dimensions—fatigue and depressed mood scores—with luminal diameter change. However, when controlling for age, baseline coronary artery diameter, history of hypertension, smoking status, and high-density lipoprotein cholesterol, only depressed mood remained significantly associated with luminal diameter change. This finding suggests that depressed mood is linked to an accelerated progression of coronary atherosclerosis. Moreover, an inactive lifestyle escalated the likelihood of hospital readmission. Notably, Pelletier et al.⁴² established that anxiety was inversely related to achieving the recommended "door-to-ECG" time of within 10 minutes, underscoring anxiety as a clinical determinant of poorer access to care in patients with premature ACS.

Gender-relations factors and ACS objective outcomes in young female patients

In the context of gender-relations variables (Fig. 2; Supplemental Table S3), Dreyer et al.⁴⁰ revealed that female participants who were married or cohabiting with a spouse exhibited a reduced probability of hospital readmission compared to female participants who were not living with a partner. Regarding institutionalized gender (Fig. 2; Supplemental Table S3), Dreyer et al.⁴⁰ found a significant association between income and hospital readmission. That is, female patients with low income had a greater likelihood of being readmitted than female patients with high income.

Moreover, the risk-prediction model for 1-year hospital readmission proposed by Dreyer et al.²³ had 3 gender-related factors that included the following: physical health (gender identity), low income (institutionalized gender), and depressive symptoms (gender identity). A noteworthy point is that no gender-role or gender relations variables were included in the predictive model.

Collectively, these findings underscore the significant influence of gender-related factors on objective outcomes in young female patients with ACS. The studies included reveal that gender roles, including employment status and work hours, can impact the risk of hospital readmission. Genderidentity factors, such as depression and stress scores, are associated with both emotional well-being and the progression of coronary atherosclerosis. Furthermore, gender relations, including marital status and income, also play a role in determining the likelihood of hospital readmission.

Gender-Related Factors and ACS Subjective Outcomes in Young Female Patients

In the context of gender-related factors and their impact on the subjective outcomes of ACS in young female patients, this review found 3 pertinent articles (Supplemental Table S4). These articles reported on studies of subjective outcomes that encompassed physical and mental functional status, quality of life, perceived stress, depressive symptomatology, physical limitations, and vital exhaustion. This review also identified a restricted spectrum of 3 gender-related factors, namely social support (gender relations), financial barriers (institutionalized gender), and education level (institutionalized gender), which have been addressed across the existing body of literature. A summary of the gender-related factors significantly associated with subjective ACS outcomes is provided in Figure 2. An important point to highlight is that no gender-related factors were associated with ACS subjective outcomes in the dimensions of gender roles and gender identity.

Gender-relations factors and ACS subjective outcomes in young female patients

Leung Yinko's study⁴³ delved into the role of social support in influencing physical limitation scores among individuals with ACS. The study examined how different levels of social support affected the extent of physical limitations experienced by patients. Leung Yinko et al. found an interaction between sex and social support. Thus, the findings revealed a meaningful relationship between social support and physical limitation scores in female patients, but not in male patiens. Female patients with a high level of social support demonstrated a higher mean physical limitation score compared to those with a low level of social support. This association was statistically significant, indicating that female patients with robust social support networks tended to experience fewer physical limitations during their ACS recovery.

Institutionalized gender and ACS subjective outcomes in young female patients

Beckman's study⁴¹ explored the influence of financial barriers on various subjective outcomes in relation to ACS in young female patients compared to young male patients. The research examined the following 5 distinct subjective measures: 1-year physical and mental functional status; diseaserelated quality of life; perceived stress; and depressive symptomatology. The study found a consistent pattern in which higher levels of financial barriers were associated with unfavourable subjective outcomes across all measures. Specifically, individuals facing greater financial barriers experienced lower physical and mental functional status, reduced quality of life, higher perceived stress, and more severe depressive symptoms. This finding suggests that financial constraints have a significant impact on the overall well-being and mental health of patients recovering from ACS, which could, in turn, translate into worse health outcomes for those recovering from AMI, including an increased risk of hospital readmission.

Zimmermann-Viehoff et al.⁴⁴ studied the relationship between vital exhaustion scores and education levels in female patients with ACS. The investigation categorized participants based on their education levels and vital exhaustion scores. The study revealed that individuals with lower education levels consistently exhibited higher vital exhaustion scores across various ranges, whereas those with higher education levels consistently displayed lower vital exhaustion scores. Despite these trends, the statistical analysis indicated that the association between vital exhaustion scores and education levels was not statistically significant, suggesting that although a trend may be present, the relationship between education and vital exhaustion in ACS patients might be influenced by other factors that require further exploration.

These 3 studies collectively shed light on various genderrelated factors influencing subjective outcomes, including quality of life, in young female patients with ACS. Levels of financial barriers and social support were both shown to impact patients' well-being during their recovery, providing valuable insights for healthcare professionals aiming to enhance the holistic care of young female ACS patients.

Discussion

The objective of this review was to explore the impact of gender-related factors on the outcomes of ACS among young female patients in the contemporary scientific literature. Our findings revealed that gender-related factors had a noteworthy influence on both objective and subjective ACS outcomes in this population. The objective outcomes encompassed variables such as hospital readmission, "door-to-ECG" time, and the progression of coronary atherosclerosis. Moreover, subjective outcomes were examined, including aspects of physical and mental functional status, quality of life, physical limitations, and vital exhaustion. Within the gender-roles dimension, being a primary income earner and being a worker was associated with reduced hospital readmission rates among young female patients with ACS. In gender identity, the presence of conditions such as depression, anxiety, and stress was linked to unfavourable clinical outcomes, including prolonged "door-to-ECG" time and accelerated coronary atherosclerosis progression. Concerning gender relations, married female participants demonstrated a lower risk of hospital readmission compared to unmarried female participants. In the context of institutionalized gender, factors such as income and education level played roles in hospital readmission and vital exhaustion. Young female patients with lower income and education levels faced heightened risks, in contrast to their higher-earning and better-educated counterparts. The findings from this review emphasize the substantial influence of gender dimensions on specific outcomes of ACS in young female patients. These findings advocate for the incorporation of gender-sensitive considerations into both clinical practice and research endeavors, and they highlight the need for a comprehensive understanding of the complex interplay between gender-related factors and ACS outcomes among this population.

Young female patients with ACS are a uniquely vulnerable group with a predisposition to adverse outcomes compared to male patients.²⁴ The existing literature shows a significant lack of comprehensive studies exploring the intricate interplay of gender dynamics and their influence on ACS outcomes in this group, particularly in examining the roles, identity, relations, and structural aspects of gender.^{27,33} The focus has been predominantly on sex-based disparities, overshadowing the complex interaction of biological and sociocultural gender factors. This gap, accentuated by the absence of sex- and age-disaggregated data, reflects historical and societal biases in medical research and underscores the need for more nuanced and inclusive studies.

Historically, female participants, especially those in younger age groups, have been systematically underrepresented in cardiovascular studies.⁴⁹ This underrepresentation has deep roots in the misinformed notion that cardiovascular ailments afflict primarily older men. Consequently, the findings generated from such skewed research fail to capture the unique challenges that young female patients face concerning ACS. These challenges encompass a range of factors, including, but not limited to, hormonal influences,

pregnancy-related concerns, contraceptive choices, and overall cardiovascular well-being. Other gender-related challenges in young female patients with ACS encompass issues such as the underrepresentation of gender diversity, the need for gendersensitive mental health services, disparities in healthcare access, and the critical importance of addressing gender-based violence and abuse. Achieving equitable and effective healthcare for all requires a comprehensive approach that acknowledges and actively addresses these multifaceted gender-related challenges in both research and healthcare delivery.

A point imperative to recognize is that the neglect of agespecific and gender-sensitive data collection impedes our understanding of the intricate web of influences that shape ACS outcomes among young female patients. Therefore, addressing this research gap is not only an ethical imperative but also a scientific necessity. Incorporating gender-related perspectives into ACS research can unearth a wealth of insights into the ways in which societal norms, gender roles, and institutional biases intersect with medical outcomes. This work can pave the way for development of more-holistic interventions and treatments that cater to the unique needs of young female patients experiencing ACS.

Future directions

Future research should focus on the complex interplay of gender roles, identity, relations, and institutional factors in ACS outcomes among young female patients. Emphasis on intersectional and comprehensive data collection, including sex and age disaggregation, is essential. Advancements in healthcare for this demographic require integrating these insights into risk models and personalized interventions. Future strategies also should include tailored counseling, enhanced social support networks, and accessible mental health services to address the unique challenges faced by young female patients with ACS. Rigorous evaluation of these interventions will be crucial in improving this population's health outcomes and overall well-being.

Limitations

This narrative review has several limitations that warrant consideration. First, the restriction of including only Englishlanguage literature may have introduced a language bias that could have excluded relevant non-English studies. Second, the use of a single database, PubMed, may have resulted in the omission of pertinent articles available in other health-sciences databases, which could have led to a selection bias. The inclusion of articles published within the past 10 years aimed to emphasize recent developments, but this approach may have excluded valuable older studies offering historical context. Additionally, the review did not encompass reference list searches, which could have led to the oversight of relevant literature not identified in the initial search. Furthermore, the absence of a systematic review methodology, including a formal assessment of bias risk and evidence quality, poses a significant limitation. This gap may undermine the review's capacity to ascertain the validity and reliability of the findings, which is essential for drawing meaningful and robust conclusions. Last, the limitation of not considering aspects of intersectionality, particularly with regard to race and ethnicity, means that the review may not comprehensively address all

potential factors influencing ACS outcomes. Acknowledging these limitations is vital to contextualize the findings and underscores the need for more rigorous and systematic approaches in future research.

Conclusions

Gender-related factors are important determinants of ACS outcomes in young female patients. The findings suggest that gender-related factors, such as primary earner status, anxiety, marital status, income, financial barriers, and social support, can influence the risk of hospital readmission, "door-to-ECG" time, coronary artery narrowing, physical and mental functional status, quality of life, perceived stress, depressive symptoms, physical limitations, and vital exhaustion in young female patients with ACS. These factors can also interact with biological sex and other variables to create complex and nuanced patterns of health disparities. Therefore, integrating gender-related factors into clinical practice and research can help improve the care and outcomes of young female patients with ACS. This review also highlights the need for more studies exploring the mechanisms and implications of genderrelated factors in this population.

Ethics Statement

This narrative review has been conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. It synthesizes previously published data, adhering to relevant ethical guidelines for literature reviews.

Patient Consent

The authors confirm that patient consent is not applicable to this article. As this article is a narrative review, it synthesizes previously published data and does not involve any new studies of human or animal subjects performed by any of the authors.

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Disclosures

The authors have no conflicts of interest to disclose.

References

- Bergmark BA, Mathenge N, Merlini PA, Lawrence-Wright MB, Giugliano RP. Acute coronary syndromes. Lancet 2022;399:1347-58.
- Bhatt DL, Lopes RD, Harrington RA. Diagnosis and treatment of acute coronary syndromes: a review. JAMA 2022;327:662-75.
- 3. Timmis A, Kazakiewicz D, Townsend N, et al. Global epidemiology of acute coronary syndromes. Nat Rev Cardiol 2023;20:778-88.
- Andersson C, Vasan RS. Epidemiology of cardiovascular disease in young individuals. Nat Rev Cardiol 2018;15:230-40.
- 5. Ricci B, Cenko E, Vasiljevic Z, et al. Acute coronary syndrome: the risk to young women. J Am Heart Assoc 2017;6:e007519.
- 6. Izadnegahdar M, Singer J, Lee MK, et al. Do younger women fare worse? Sex differences in acute myocardial infarction hospitalization and early mortality rates over ten years. J Womens Health (Larchmt) 2014;23: 10-7.
- DeFilippis EM, Collins BL, Singh A, et al. Women who experience a myocardial infarction at a young age have worse outcomes compared with men: the Mass General Brigham YOUNG-MI registry. Eur Heart J 2020;41:4127-37.
- Arora S, Stouffer GA, Kucharska-Newton AM, et al. Twenty year trends and sex differences in young adults hospitalized with acute myocardial infarction. Circulation 2019;139:1047-56.
- **9.** Gupta A, Wang Y, Spertus JA, et al. Trends in acute myocardial infarction in young patients and differences by sex and race, 2001 to 2010. J Am Coll Cardiol 2014;64:337-45.
- Gabet A, Danchin N, Juillière Y, Olié V. Acute coronary syndrome in women: rising hospitalizations in middle-aged French women, 2004–14. Eur Heart J 2017;38:1060-5.
- 11. Davis M, Diamond J, Montgomery D, et al. Acute coronary syndrome in young women under 55 years of age: clinical characteristics, treatment, and outcomes. Clin Res Cardiol 2015;104:648-55.
- Dreyer RP, Ranasinghe I, Wang Y, et al. Sex differences in the rate, timing, and principal diagnoses of 30-day readmissions in younger patients with acute myocardial infarction. Circulation 2015;132:158-66.
- O'Brien C, Valsdottir L, Wasfy JH, et al. Comparison of 30-day readmission rates after hospitalization for acute myocardial infarction in men versus women. Am J Cardiol 2017;120:1070-6.
- Sawano M, Lu Y, Caraballo C, et al. Sex difference in outcomes of acute myocardial infarction in young patients. J Am Coll Cardiol 2023;81: 1797-806.
- Madan M, Qiu F, Sud M, et al. Clinical outcomes in younger women hospitalized with an acute myocardial infarction: a contemporary population-level analysis. Can J Cardiol 2022;38:1651-60.
- 16. Desai R, Mishra V, Chhina AK, et al. Cardiovascular disease risk factors and outcomes of acute myocardial infarction in young adults: evidence from 2 nationwide cohorts in the United States a decade apart. Curr Probl Cardiol 2023;48:101747.
- Camacho X, Nedkoff L, Wright FL, et al. Relative contribution of trends in myocardial infarction event rates and case fatality to declines in mortality: an international comparative study of 1.95 million events in 80.4 million people in four countries. Lancet Public Health 2022;7: e229-39.
- Haider A, Bengs S, Luu J, et al. Sex and gender in cardiovascular medicine: presentation and outcomes of acute coronary syndrome. Eur Heart J 2020;41:1328-36.

- Cader FA, Banerjee S, Gulati M. Sex differences in acute coronary syndromes: a global perspective. J Cardiovasc Dev Dis 2022;9:239.
- Mateo-Rodríguez I, Danet A, Bolívar-Muñoz J, et al. Gender differences, inequalities and biases in the management of acute coronary syndrome. J Healthc Qual Res 2022;37:169-81.
- Bugiardini R, Manfrini O, Cenko E. Female sex as a biological variable: a review on younger patients with acute coronary syndrome. Trends Cardiovasc Med 2019;29:50-5.
- 22. van Oosterhout REM, de Boer AR, Maas AHEM, et al. Sex differences in symptom presentation in acute coronary syndromes: a systematic review and meta-analysis. J Am Heart Assoc 2020;9:e014733.
- Dreyer RP, Sciria C, Spatz ES, et al. Young women with acute myocardial infarction: current perspectives. Circ Cardiovasc Qual Outcomes 2017;10:e003480.
- Siagian SN, Christianto C, Angellia P, Holiyono HI. The risk factors of acute coronary syndrome in young women: a systematic review and metaanalysis. Curr Cardiol Rev 2023;19:e161122210969.
- Assad J, Femia G, Pender P, Badie T, Rajaratnam R. Takotsubo syndrome: a review of presentation, diagnosis and management. Clin Med Insights Cardiol 2022;16:11795468211065782.
- 26. Hayes SN, Kim ESH, Saw J, et al. Spontaneous coronary artery dissection: current state of the science: a scientific statement from the American Heart Association. Circulation 2018;137:e523-57.
- 27. Khraishah H, Daher R, Garelnabi M, Karere G, Welty FK. Sex, racial, and ethnic disparities in acute coronary syndrome: novel risk factors and recommendations for earlier diagnosis to improve outcomes. Arterioscler Thromb Vasc Biol 2023;43:1369-83.
- Shannon G, Jansen M, Williams K, et al. Gender equality in science, medicine, and global health: Where are we at and why does it matter? Lancet 2019;393:560-9.
- 29. Tadiri CP, Raparelli V, Abrahamowicz M, et al. Methods for prospectively incorporating gender into health sciences research. J Clin Epidemiol 2021;129:191-7.
- Raparelli V, Norris CM, Bender U, et al. Identification and inclusion of gender factors in retrospective cohort studies: the GOING-FWD framework. BMJ Global Health 2021;6:e005413.
- Simoni AH, Frydenlund J, Kragholm KH, et al. Socioeconomic inequity in incidence, outcomes and care for acute coronary syndrome: a systematic review. Int J Cardiol 2022;356:19-29.
- Anand VV, Zhe ELC, Chin YH, et al. Socioeconomic deprivation and prognostic outcomes in acute coronary syndrome: a meta-analysis using multidimensional socioeconomic status indices. Int J Cardiol 2023;383:140-50.
- De Leon K, Winokur EJ. Examining acute coronary syndrome across ethnicity, sex, and age. J Nurse Practit 2022;18:31-5.
- 34. Kong G, Chin YH, Chong B, et al. Higher mortality in acute coronary syndrome patients without standard modifiable risk factors: results from a global meta-analysis of 1,285,722 patients. Int J Cardiol 2023;371:432-40.
- Smolderen KG, Brush A, Dreyer RP. Psychosocial factors and recovery after acute myocardial infarction in younger women. Curr Cardiol Rep 2019;21:50.

- **36.** Chandrasekhar J, Gill A, Mehran R. Acute myocardial infarction in young women: current perspectives. Int J Womens Health 2018;10: 267-84.
- 37. Streed CG, Beach LB, Caceres BA, et al. Assessing and addressing cardiovascular health in people who are transgender and gender diverse: a scientific statement from the American Heart Association. Circulation 2021;144:e136-48.
- Mahendran M, Lizotte D, Bauer GR. Quantitative methods for descriptive intersectional analysis with binary health outcomes. SSM Popul Health 2022;17:101032.
- Martinez RAM, Andrabi N, Goodwin AN, et al. Conceptualization, operationalization, and utilization of race and ethnicity in major epidemiology journals, 1995–2018: a systematic review. Am J Epidemiol 2023;192:483-96.
- Dreyer RP, Arakaki A, Raparelli V, et al. Young women with acute myocardial infarction: risk prediction model for 1-year hospital readmission. CJC Open 2023;5:335-44.
- Beckman AL, Bucholz EM, Zhang W, et al. Sex differences in financial barriers and the relationship to recovery after acute myocardial infarction. J Am Heart Assoc 2016;5:e003923.
- Pelletier R, Humphries KH, Shimony A, et al. Sex-related differences in access to care among patients with premature acute coronary syndrome. CMAJ 2014;186:497-504.
- 43. Leung Yinko SSL, Pelletier R, Behlouli H, et al. Health-related quality of life in premature acute coronary syndrome: Does patient sex or gender really matter? J Am Heart Assoc 2014;3:e000901.
- 44. Zimmermann-Viehoff F, Wang HX, Kirkeeide R, et al. Women's exhaustion and coronary artery atherosclerosis progression: the Stockholm Female Coronary Angiography Study. Psychosom Med 2013;75: 478.
- Lichtman JH, Lorenze NP, D'Onofrio G, et al. Variation in recovery: role of gender on outcomes of young AMI patients (VIRGO) study design. Circ Cardiovasc Qual Outcomes 2010;3:684-93.
- 46. Pilote L, Karp I. GENESIS-PRAXY (GENdEr and Sex determInantS of cardiovascular disease: From bench to beyond-Premature Acute Coronary SYndrome). Am Heart J 2012;163:741-746.e2.
- [47]. Stephenson E. "Mental disorders and access to mental health care". Insights on Canadian Society. Statistics Canada Catalogue no. 75-006-X. Available at: https://www150.statcan.gc.ca/n1/pub/75-006-x/ 2023001/article/00011-eng.htm. Accessed August 15, 2023.
- Chhabra S, Eagles D, Kwok ESH, Perry JJ. Interventions to reduce emergency department door-to- electrocardiogram times: a systematic review. CJEM 2019;21:607-17.
- **49.** Jin X, Chandramouli C, Allocco B, et al. Women's participation in cardiovascular clinical trials from 2010 to 2017. Circulation 2020;141: 540-8.

Supplementary Material

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