Protocol

Fatigue in Coronary Artery Disease: Protocol for a Theory of Unpleasant Symptoms–Guided Scoping Review

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Abstract

Background: Fatigue is a complex and multifactorial symptom that affects 40%-48% of patients with coronary artery disease (CAD), significantly impairing quality of life and clinical outcomes. Despite its distinct characteristics, CAD-related fatigue lacks conceptual clarity and validated, population-specific assessment tools. Grounded in the Theory of Unpleasant Symptoms (TOUS), this scoping review addresses this gap by mapping definitions, manifestations, influencing factors, consequences, and measurement instruments.

Objective: This scoping review aims to (1) map the definitions of fatigue used in studies specifically involving patients with CAD; (2) map the manifestations and influencing factors of fatigue, as well as its influence on the performance of CAD-related fatigue; (3) map and characterize the methods and instruments used to assess fatigue; and (4) propose a conceptual framework and formulate an initial definition of CAD-related fatigue.

Methods: This protocol follows JBI methodology and adheres to PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) reporting guidelines. A comprehensive 3-phase search will be conducted across MEDLINE (PubMed), CINAHL, Embase, Web of Science, PsycINFO, and Scopus; ProQuest Dissertations & Theses Global; and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) Theses and Dissertations Catalog, with no language or publication date restrictions. Eligible studies will include adults aged 18 years or older with diagnosed CAD. Screening and selection will be performed by 2 independent reviewers in Rayyan (Qatar Computing Research Institute). Duplicate records will be removed, and any discrepancies will be resolved through discussion, with a third reviewer consulted when necessary. Data extraction will be conducted using Covidence (Future Evidence Foundation), with iterative piloting to ensure consistency. Extracted data will include study characteristics, definitions of fatigue, manifestations, influencing factors, consequences, and assessment of fatigue. A hybrid deductive-inductive qualitative content analysis will be adopted, guided by the TOUS.

Results: This unfunded project initiated database searches in July 2024, retrieving 6958 records. After removing 3161 duplicates, 3797 titles/abstracts were screened. Of these, 281 full-text articles were assessed for eligibility, and 146 met the inclusion criteria. Four additional studies were identified through reference list searching, resulting in 150 (3.9% of screened records) studies being included for data extraction. Data collection (extraction) began in February 2025 and was completed in August 2026, alongside data analysis and synthesis. Submission is scheduled for early 2027, with publication expected by mid-2027.

Conclusions: This will be the first scoping review guided by the TOUS to map CAD-related fatigue. Its findings will enhance the conceptual clarity of fatigue in CAD, support the development of validated assessment instruments, and inform clinical practice and policy by enabling early recognition and appropriate management of this symptom. Ultimately, this review will provide a foundation for future research and contribute to improving patient outcomes and quality of life.

Trial Registration: OSF Registries osf.io/geqm6; https://osf.io/geqm6

International Registered Report Identifier (IRRID): DERR1-10.2196/90173

JMIR Res Protoc 2026;15:e90173; doi: 10.2196/90173

Keywords: coronary artery disease; fatigue; scoping review; Theory of Unpleasant Symptoms; measurement instruments; nursing

Introduction

Coronary artery disease (CAD), characterized by myocardial ischemia secondary to atherosclerosis, remains a leading cause of global morbidity and mortality [1-4]. Between 1990 and 2019, CAD was considered the leading cause of death [1] until the COVID-19 pandemic altered this landscape [1,2,5]. Nevertheless, CAD accounts for approximately 17.8 million deaths annually [1,2,5]. A changing demographic profile, marked by an aging population and increasing rates of hypertension, obesity, and diabetes, contributes significantly to the global burden of CAD [1-3,5]. In the United States, CAD affects over 20 million adults, whereas in Brazil, the age-standardized mortality rate remains high, estimated at 67.1 per 100,000 population in 2021 [1,2].

Individuals with CAD often present with a variety of symptoms, such as angina, shortness of breath, and fatigue [4,6,7]. Fatigue is reported by approximately 50% of patients with CAD [7-9], often co-occurring with other debilitating conditions, such as depression and sleep disorders [8-10]. Fatigue is characterized by an overwhelming and sustained sense of exhaustion that impairs physical and psychosocial functioning, resulting in poorer control of CAD [7-9,11,12]. Furthermore, fatigue can have substantial economic and social consequences, including decreased productivity, increased health care use, and long-term disability [7,13,14].

Fatigue is not unique to CAD but is also commonly observed in other chronic diseases, such as heart failure, multiple sclerosis, rheumatoid arthritis, chronic kidney disease, cancer, chronic obstructive pulmonary disease, and COVID-19 [13-16]. While fatigue shares certain characteristics across these conditions, it often exhibits disease-specific features. For instance, pruritus is commonly linked to fatigue in chronic kidney disease, early satiety in chronic obstructive pulmonary disease, and pain in rheumatoid arthritis [14].

Additionally, the influencing factors of fatigue vary significantly across different chronic diseases [15,17,18]. For instance, influencing factors of fatigue in heart failure may include low cardiac output and, consequently, impaired tissue perfusion; muscle metabolic abnormalities; abnormalities in the autonomic nervous system; effects of deconditioning; and endothelial dysfunction [15]. In cancer, fatigue can be attributed to alterations originating in the central nervous system (inflammatory processes and alterations in the hypothalamic-pituitary-adrenal axis) and/or in the peripheral nervous system (eg, reduced energy mechanisms) and/or to chemotherapy treatment [15,17]. In CAD, fatigue has been associated with inflammatory processes, thyroid hormone deficiencies, cortisol imbalances, and treatment with statins, coronary artery bypass grafting, and percutaneous coronary intervention [17-21]. Consequently, the characteristics of fatigue, such as its manifestation, influencing factors, and performance, may vary depending on the specific context and study population.

Theories provide structured conceptual frameworks that can assist in clarifying the concept of fatigue, guiding the review, interpreting findings, and developing interventions [22-24]. How the reviewer approaches a clinical problem helps determine which theory is most appropriate [24]. By integrating nursing theories into the scoping review, researchers can advance the understanding of the complex phenomenon of CAD-related fatigue, overcome existing methodological limitations, and ultimately improve the care and quality of life for these patients [22-25]. The Theory of Unpleasant Symptoms (TOUS) is a theoretical framework that has been widely used in the study of symptoms, including fatigue [9,26,27]. It asserts that a symptom experience can impact an individual's capacity to function and perform in physical, cognitive, and socially defined roles [28]. According to the TOUS, symptoms are a multidimensional experience consisting of 4 dimensions: intensity (strength or severity), timing (duration and frequency), distress (the degree of unpleasantness or disturbance experienced by the individual as a result of the symptom), and quality (the vocabulary used to describe how the symptom is felt) [25,28]. Symptoms are interconnected with physiological, psychological, and situational influencing factors that give rise to or affect the nature of the symptom experience, as well as with the functional and cognitive consequences (or performance) of the symptom experience [25].

The current gap in the literature is that there is still no consensus regarding a clear and specific definition of CAD-related fatigue. This conceptual gap hinders both the advancement of CAD-related fatigue research and the clinical recognition. By identifying knowledge gaps, this review will provide an essential foundation for guiding future research, supporting clinical decision-making, and strengthening nursing and health care practice. Moreover, aligning the findings with the TOUS will enhance the conceptual clarity of CAD-related fatigue, as the theory offers a structured framework for analyzing symptom manifestations, influencing factors, and consequences. The purpose of this scoping review is (1) to map the definitions of fatigue used in studies specifically involving patients with CAD; (2) to map the manifestations and influencing factors of fatigue, as well as its influence on the performance of CAD-related fatigue; (3) to map and characterize the methods and instruments used to assess fatigue; and (4) to propose a conceptual framework and formulate a definition of CAD-related fatigue.

In addition, the guiding questions for this scoping review were as follows: What definitions of CAD-related fatigue are reported in the literature? What are the manifestations, influencing factors, and consequences of CAD-related fatigue? What methods and measurement instruments have been used to assess CAD-related fatigue?

Methods

Study Design

This protocol follows guidance from the JBI Manual for Evidence Synthesis [29] and is reported in accordance with the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) statement [30], adapted for scoping reviews. The completed PRISMA-P checklist is provided in Checklist 1. This protocol was preregistered on the Open Science Framework (OSF) [31]. It is worth noting that the forthcoming scoping review arising from this protocol will be conducted in accordance with the JBI methodology for scoping reviews and reported in line with the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) guidelines [29,32]. The TOUS [25] will guide all stages of planning for this scoping review, from the selection and extraction of data sources to the interpretation and presentation of results.

Study Selection (Eligibility/Inclusion Criteria)

Participants

This review will consider studies that include adults aged 18 years or older with a confirmed diagnosis of CAD. To ensure the broad coverage appropriate for a scoping review, studies using any diagnostic confirmation method documented in the literature will be included, such as coronary angiography revealing stenosis of 50% or greater in at least one major epicardial vessel, documented myocardial infarction by electrocardiographic and enzymatic criteria, positive stress testing with imaging, and a documented history of coronary revascularization, among other clinical criteria [4,33]. No restrictions will be applied regarding sex or gender. Clinical presentations of fatigue duration/timing will be classified into 3 distinct phases: acute (0 to 30 d postevent), subacute/recovery (30 d to 6 mo), and chronic (more than 6 mo). All clinical phases will be included; however, they will be extracted and documented separately during data extraction to enable phase-specific analyses. Comorbidities (eg, arterial hypertension, diabetes, and depression) will be extracted as variables rather than used as exclusion criteria.

Concept

The concept of interest is fatigue in patients with CAD. Specifically, we aim to identify definitions, manifestations, influencing factors, consequences (outcomes), and measurement instruments used to assess fatigue, as well as other methods for evaluating fatigue in this population. This review will consider all definitions of fatigue provided by the authors. Manifestations of fatigue are the characteristics of the symptom, for example, its intensity or severity; time (frequency, duration, and the relationship between symptom onset and precipitating events). Causes will be understood as the factors that influence or lead to the manifestation of fatigue. Consequences or outcomes (performance) will be understood as events or incidents that result from fatigue. Measurement instruments will be defined as those that are standardized and validated or other forms of measurement used in studies to assess the characteristics of fatigue, including narratives and statements from study participants. Studies that have addressed any dimension of fatigue in people with CAD, including but not limited to physical fatigue, mental fatigue, cognitive fatigue, general fatigue, and exertion fatigue, will be considered. Articles that analyzed fatigue as part of a symptom cluster will be excluded. This decision was made to focus exclusively on factors associated with fatigue, thereby allowing the consolidation of a specific core concept and facilitating comparison with similar studies.

Context

This review will not be limited by any context, setting, discipline, or field. There is no geographic restriction; studies from low-, middle-, and high-income countries will be included. This approach is essential given that health care infrastructure, access to cardiac rehabilitation, cultural conceptualizations of fatigue, and diagnostic resources vary substantially across settings. To account for geographic and socioeconomic variation, the country where each study was conducted will be recorded, and its income classification will be contextualized using World Bank criteria corresponding to the publication period [34]. Regarding clinical environments, eligible settings will encompass hospital inpatient units (including intensive care units and cardiology wards), outpatient clinics, cardiac rehabilitation programs, community settings, and home-based care. The specific setting type will be documented for each included study. Additionally, the health care system context (public, private, or mixed) will be extracted whenever reported. Contextual heterogeneity across studies (eg, public, private, or mixed health care systems) is anticipated and will be addressed through narrative synthesis rather than through study exclusion or context-based restrictions.

Types of Sources

This scoping review will consider experimental and quasi-experimental studies, including randomized controlled trials, nonrandomized controlled trials, before-and-after studies, and interrupted time series studies. Additionally, this review will include analytical observational studies (eg, cohort, case-control, and cross-sectional studies) and descriptive observational studies (eg, case series and case reports). Qualitative studies, including but not limited to designs such as phenomenology, grounded theory, ethnography, qualitative description, action research, and feminist research, will also be considered. Additionally, systematic reviews that meet the inclusion criteria will be included. However, systematic reviews will be analyzed with caution, and their results will be included if they provide additional information not described in the primary studies considered in this scoping review. Mixed

methods and psychometric studies, guidelines, and gray literature will also be considered. Conference proceedings and opinion pieces will be excluded.

Search Strategy

The search strategy will be designed to identify both published and unpublished studies. A 3-step literature search will be conducted as recommended by the JBI [29]. The search strategy will be reported in accordance with the applicable elements of the PRISMA-S (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Reporting Literature Searches in Systematic Reviews) checklist [35], adapted for the scoping review context (Checklist 2). In the first step, a preliminary limited search was conducted in MEDLINE (PubMed) to identify relevant studies and map keywords and controlled vocabulary (eg, MeSH). Initial descriptors included terms such as "fatigue," "coronary artery disease," "coronary disease," "myocardial infarction," and "acute coronary syndrome."

In the second stage, all identified keywords and descriptors will be adapted and refined to formulate search strategies for each database and information source. The development of these search strategies will be supported by 2 researchers with specialized knowledge in cardiology and fatigue and validated by a librarian specializing in nursing with experience in systematic and scoping reviews, who will advise on appropriate terminology, databases, and review strategies. Published studies will be searched in MEDLINE (PubMed), CINAHL (EBSCO), Embase (Elsevier), Web of Science (Clarivate), PsycINFO (APA), and Scopus (Elsevier). Sources of gray literature to be searched will include the Thesis and Dissertations Catalog from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and ProQuest Dissertations & Theses Global (PQDT). These databases were selected based on their comprehensive coverage of the literature on fatigue in patients with CAD within the health sciences domain.

A full search strategy was developed for PubMed and adapted for each database, combining controlled vocabulary and free-text terms. The search terms were organized around two central concepts: (1) CAD terms (eg, "myocardial infarction," "cardiovascular stroke," "coronary artery disease," and related terms), which were combined using the Boolean operator OR; and (2) fatigue-related terms. The 2 concepts will subsequently be combined using the Boolean operator AND. Double quotation marks will be consistently applied around multiword phrases to enforce exact phrase matching. Broadly, no publication date or language restrictions were applied during database retrieval to ensure maximum retrieval comprehensiveness. However, database-specific structural filters (eg, excluding book chapters, letters, conference proceedings, and nonhealth domains in Scopus and CAPES) were applied as needed to align retrieval with the study's predefined eligibility criteria and to exclude nonprimary literature types. Full, unedited search strings and step-by-step translation strategies for all selected databases are provided in Multimedia Appendix 1.

In the third step, the reference lists of all sources selected for full-text review will be examined for additional papers to identify any additional studies that may not have been retrieved through database searches. Documents published in any year and in any language will be considered. Translations of articles in languages other than Portuguese will be performed with the assistance of the following resources: Gemini (online version; Google LLC), Google Lens (mobile app), and DeepL Pro.

Study/Source of Evidence Selection

Following the search, all identified records will be collated and uploaded to Zotero (version 6; Corporation for Digital Scholarship), where duplicate documents will be manually removed by merging them. Subsequently, the data will be uploaded to Rayyan (Qatar Computing Research Institute), where titles and abstracts will be assessed and selected by 2 independent reviewers, blinded to each other, according to the inclusion and exclusion criteria established for this review. Subsequently, the selected studies will undergo full-text screening. To ensure accuracy in identifying relevant articles, reviewers will conduct a pilot test with 20 documents during all screening phases (titles, abstracts, and full text). The full text of selected citations will be assessed in detail against the inclusion criteria by 2 independent reviewers. Reasons for exclusion of full-text papers that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion or with an additional reviewer with expertise in cardiology and fatigue. If the full text of an article cannot be obtained, the authors will be contacted. An email will be sent to the corresponding author or to the author who has provided a contact email address. If no response is received within a week, a follow-up email will be sent. Studies for which the full text cannot be obtained after contact attempts will be excluded.

Data Extraction

The selected citations for data extraction will be exported from Rayyan and imported into the online software, Covidence 2024 (Future Evidence Foundation). A pilot test will then be conducted on 10 articles using the data extraction instrument (Multimedia Appendix 2) to ensure that all relevant findings were adequately and consistently extracted by the 2 reviewers involved at this stage.

Data will be extracted from the included evidence sources using a standardized data extraction instrument (Multimedia Appendix 2). Given the large number of included studies (n=150), a primary extraction with a cross-verification strategy was adopted in accordance with JBI methodological guidance [36]. The included documents will be divided equally between 2 reviewers for primary extraction using the Covidence platform: reviewer A will extract data from 75 documents, and reviewer B will extract data from the remaining 75. To minimize errors and bias, the extracted data will then be exported to a standardized Microsoft Excel spreadsheet for cross-verification, wherein reviewer A will independently verify all data extracted by reviewer B,

and vice versa. Any discrepancies will be resolved through discussion or, if necessary, through adjudication by a third, senior reviewer.

The extracted data will encompass specific details regarding participants, concept, context, study methods, and key findings relevant to the review questions. Table 1 outlines the primary categories to be extracted from the included studies. A comprehensive data extraction instrument containing all operational definitions of the variables to be extracted is provided in Multimedia Appendix 2.

Table 1. Primary data extraction categories from the included studies.

Category	Data items
Source identification	Record the unique study identifier, full title, first author, publication year, publication type (journal article, thesis, and dissertation), country of origin, language, database source, and study objective verbatim.
Study design and setting	Record study design using a standardized classification (quantitative observational: cross-sectional, cohort, and case-control; quantitative experimental: randomized trial and quasi-experimental; qualitative; mixed methods), clinical setting (inpatient, outpatient, rehabilitation, community, and mixed), clinical phase studied (acute, recovery, chronic, mixed, and not specified), and total sample size.
Population characteristics	Record mean age with SD or age range, sex distribution as the percentage of female participants, CAD[a] diagnosis confirmation method, specific CAD condition (myocardial infarction, unstable angina, stable CAD, postrevascularization, and mixed), and major comorbidities listed, if reported.
Fatigue definition	Record whether fatigue is explicitly defined, the verbatim definition if provided, the source of the definition if adapted from prior literature, synonyms used, and how fatigue was operationally defined for measurement purposes.
Fatigue manifestations	For each TOUS[b] dimension (intensity, timing, distress, and quality), record descriptions as they appear in the source. Include a free-text field for manifestations not captured by these dimensions.
Influencing factors	Separately record physiological, psychological, and situational factors as identified in each study. Document both statistical associations (for quantitative studies) and emergent themes (for qualitative studies). Include explanations of mechanisms when provided.
Functional consequences	Record impacts on activities of daily living, occupational function, social participation, quality of life, and any other domains.
Measurement instruments	For each instrument used, record instrument name, developers and year, number of items, dimensions assessed, response format, score range and interpretation, reported psychometric properties in CAD populations, administration time, mode of administration, language and translation status, and any reported cutoff scores.
Reviewer assessment and quality control	Include reviewer identification, extraction date, verification date, any disagreements and their resolution, and an overall assessment of the study's contribution to the review objectives.

[a]CAD: coronary artery disease.
[b]TOUS: Theory of Unpleasant Symptoms.

These tools will be modified and revised as necessary during the data extraction process from each included evidence source. Modifications will be detailed in the full scoping review. Additionally, if necessary, the authors of the articles will be contacted twice by email to request any missing or additional data.

Data Analysis and Presentation

Data analysis will aim to map the available evidence on CAD-related fatigue through an iterative process comprising 4 main stages: data reduction, data description, data comparison, and conclusion drawing/verification [37]. In accordance with JBI guidelines for scoping reviews, a hybrid deductive-inductive qualitative content analysis will be adopted, using structured Microsoft Excel spreadsheets for data management, coding, and audit trails.

Deductive coding will apply the TOUS framework dimensions, including symptom characteristics (intensity, timing/duration, distress, and quality), influencing factors (physiological, psychological, and situational factors), patient performance among individuals with CAD, and fatigue assessment tools. Inductive coding will capture emerging subcategories and themes not anticipated by the theoretical framework.

To ensure analytical rigor and reproducibility, 2 analysts will independently code 15% (23/150) to 20% (30/150) of the included studies to develop and refine the codebook, with disagreements resolved through discussion and consensus. The remaining studies will be coded by 1 analyst, with regular verification by the second. Quantitative data will be tabulated as descriptive frequencies (eg, the number of studies identifying each TOUS dimension and the most-used assessment instruments). At the same time, qualitative findings will be organized thematically, with supporting quotations. Furthermore, 20% (30/150) of all coded material will be independently audited by a third independent reviewer to confirm data accuracy and consistency. Finally, after grouping and synthesizing all results into their respective categories, an integrated definition and conceptual framework of CAD-related fatigue will be developed.

The results of this scoping review will be presented through a 4-component presentation plan.

The first component will be the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram, which will visually summarize the search, study selection, and inclusion processes [38] detailing the exact numbers at each stage (identification, screening, eligibility, and inclusion).

The second component will describe the characteristics of the included studies through a descriptive synthesis and structured tables organized by primary author, publication year, geographic origin, language, study design, population characteristics, and clinical setting.

The third component will present the findings according to the three guiding research questions. Definitions of fatigue will be presented thematically and supported by representative quotations from definitions formulated by the authors, described by study participants, or extracted from secondary references, along with the specific references used by the authors to define fatigue in their studies. Definitions will be extracted from any section of the study (including the *Introduction, Methods, Results, and Discussion*). Manifestations, influencing factors, and performance will be summarized in structured tables and complemented by narrative descriptions of the main findings according to the TOUS categories, accompanied by supporting evidence counts. Fatigue assessment will be presented in summary tables, graphs, and narrative descriptions detailing all assessment methods (including standardized measurement instruments, semistructured interviews, and instruments developed by the study authors), along with their dimensional coverage, target populations, and frequency of use across the included studies.

The fourth component will be a conceptual map developed from the synthesis to visually integrate the identified definitions, dimensions, influencing factors, and functional consequences into a proposed framework for fatigue in CAD. Conceptual validation of the definition of CAD-related fatigue and the conceptual map will be conducted in a subsequent study.

Findings from gray literature will be integrated throughout the review where they contribute unique insights, with their specific source types clearly identified.

Ethical Considerations

Ethics approval was not required for this study, as it is a scoping review protocol based on published literature and does not involve human subjects or primary data collection.

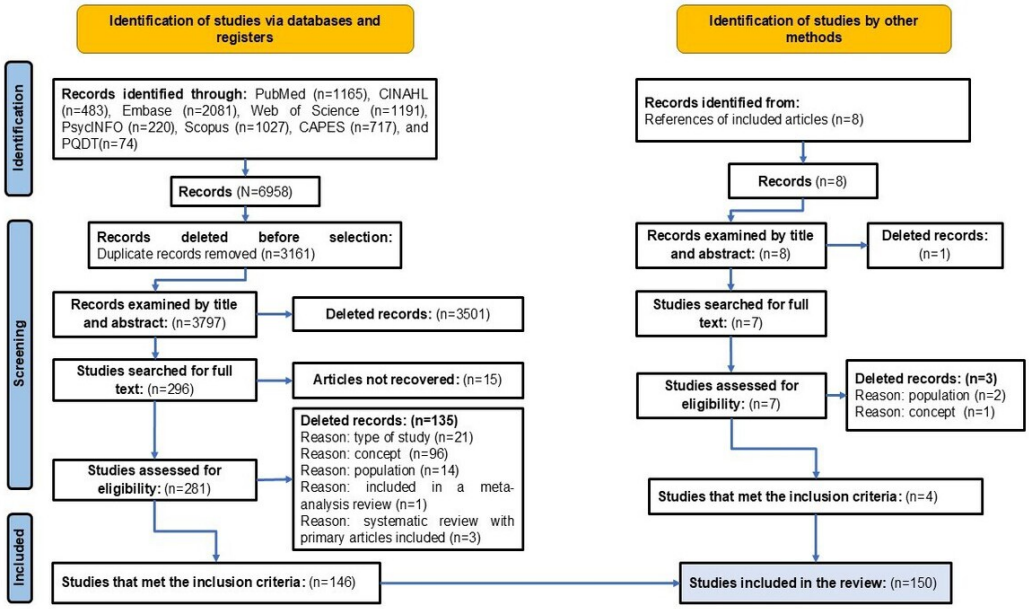
Results

The search strategy was developed with the support of 2 researchers with specialized knowledge in cardiology and fatigue, in collaboration with an expert nursing librarian with extensive experience in systematic and scoping reviews. This study received no external funding. Preliminary database searches were initiated in July 2024 and adapted for multiple electronic databases. A total of 6958 records were identified across 8 sources of information (PubMed, CINAHL, Embase, Web of Science, PsycINFO, Scopus, the Thesis and Dissertations Catalog from CAPES, and PQDT) and uploaded into Zotero. After removing 45.4% (3161/6958) duplicates, 3797 titles and abstracts were imported into Rayyan for screening.

Of these 3797 titles and abstracts, 296 were selected for full-text assessment; however, 15 could not be retrieved. The remaining 281 (7.4%) full-text articles were assessed for eligibility, and 146 (3.8%) met the inclusion criteria. In addition to the studies identified through the primary search, 4 additional studies were included after manual screening of reference lists. In total, 150 (3.9%) studies met all predefined inclusion criteria and were retained for data extraction.

The study selection process took place between July 2024 and February 2025. Data collection (extraction) began in February 2025 and was completed in August 2026, alongside data analysis, and data synthesis. The findings of this review will be presented in a final manuscript aligned with the study objectives, with journal submission anticipated by early 2027 and expected publication in mid-2027. The study selection and inclusion process is illustrated in the PRISMA flow diagram (Figure 1).

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of the scoping review process, including search results and study selection and inclusion.



The results will address each of our research questions by presenting specific findings organized into descriptive statistics and a detailed narrative synthesis. We developed a comprehensive search strategy to identify studies that present definitions of CAD-related fatigue, its manifestations, influencing factors, performance of individuals with CAD-related fatigue, and methods used to assess it. Furthermore, these results may contribute to the development of a new concept, referred to as CAD-related fatigue. This new definition will support future investigations and guide clinical strategies for assessing and managing fatigue in patients with CAD. The analysis may also highlight gaps in current knowledge and clinical practice. Finally, our study will be presented as a scoping review that provides detailed and aggregated information, summarizing the data in tables, figures, and graphs, as well as a conceptual framework of CAD-related fatigue.

Discussion

Anticipated Findings

A preliminary search of OSF, MEDLINE, the Cochrane Database of Systematic Reviews, and the JBI Database of Systematic Reviews and Implementation Reports was conducted. During this search, a systematic review exploring factors contributing to fatigue in acute coronary syndrome was identified [12]. However, this scoping review aims to go beyond the scope of that study by systematically mapping definitions, manifestations, influencing factors, and consequences of fatigue in patients with CAD, as well as identifying how authors have evaluated fatigue in this population. To address the limitations of the previous review [12], this scoping review adopted broader inclusion criteria by including a wider population, encompassing both acute and chronic patients with CAD; expanding the scope of the search to 8 databases to increase the diversity of data sources; incorporating gray literature, randomized controlled trials, and studies published in languages other than English; and including more recent data, as the systematic review was conducted in 2018 [12]. Additionally, to the authors' knowledge, this will be the first scoping review to investigate the definitions, manifestations, influencing factors, consequences, and methods of assessing CAD-related fatigue, guided by the TOUS.

The results of this study will be of interest to all health care professionals and policymakers involved in the care of patients with CAD. This review aims to map the definitions of fatigue used in studies involving patients with CAD, contributing to a deeper understanding of this phenomenon among health professionals, researchers, and patients. These findings will support the development of a new, more comprehensive definition of CAD-related fatigue. Furthermore, identifying the conceptual descriptions currently used in the literature will make a significant contribution to existing knowledge. Such insights may inform improvements in clinical assessment, the planning of individualized care, and the development of targeted intervention strategies for effective fatigue management.

The findings will enable health care professionals to recognize CAD-related fatigue as a persistent and limiting symptom that requires specialized attention, moving beyond a unidimensional measure and emphasizing the importance of evaluating its manifestations across the 4 dimensions proposed by the TOUS: intensity, duration, distress, and quality. Consequently, this knowledge informs more individualized and effective interventions aimed at symptom relief, preventing adverse outcomes, and promoting early recovery following CAD treatment [39-42]. Furthermore, identifying physiological (eg, age and sex), psychological (eg, depression and anxiety), and situational (eg, educational level and cardiac rehabilitation) influencing factors enables the early recognition of patients at risk of developing

CAD-related fatigue, guiding health professionals to manage these factors whenever possible. Finally, understanding the impact of fatigue (performance) on these patients, such as on quality of life and restrictions on daily, physical, and social activities, will facilitate the development of care strategies that consider the interaction between personal, psychological, and social factors in an integrated and personalized manner, ultimately promoting patient well-being.

Finally, the findings of this scoping review will provide a comprehensive overview of the methods and measurement instruments used to assess CAD-related fatigue. This overview will offer diverse options for evaluating this phenomenon and assist in identifying the intensity of fatigue. These results may guide the selection or refinement of assessment tools in future research and clinical practice, promoting greater standardization in the evaluation of CAD-related fatigue [12]. Furthermore, they will support the development of more accurate and meaningful assessments that reflect the lived experience of individuals with CAD.

Another benefit arising from the findings of this research is its potential to inform public health guidelines and services to recommend the routine assessment of fatigue in patients with CAD. This is crucial to ensure that the symptom is recognized as early as possible and that appropriate treatment measures can be implemented. Such an approach may help prevent adverse outcomes for these patients and facilitate timely recovery after CAD treatment.

Ultimately, the final findings of this scoping review will guide the development of a preliminary definition for CAD-related fatigue and a proposed conceptual framework. Moreover, the results of this research may guide the development of new investigations by identifying knowledge gaps related to the underlying pathophysiological mechanisms of fatigue, associated factors, and the performance of individuals with CAD. They may also highlight the need to develop and validate specific instruments for the assessment of CAD-related fatigue, such as the creation of an item bank to enable the use of computerized adaptive testing [43], thereby ensuring more precise and individualized measurements of the symptom.

Strengths and Limitations

This scoping review has several strengths. The protocol was preregistered prior to title and abstract screening, which reduces the risk of bias and ensures transparency in the research process [29]. Additionally, the methodological framework of the JBI and the PRISMA guidelines will be applied throughout all stages of the review, including the reporting of results, thereby reinforcing the methodological rigor of this study [29,32,36]. Furthermore, a comprehensive search strategy was carried out across 8 databases to identify both published and unpublished studies, supported by an experienced librarian. The broad scope of inclusion criteria was intentionally chosen to capture the widest possible range of information related to CAD-related fatigue. Finally, no restrictions on publication dates or language were applied, ensuring the inclusion of the maximum number of relevant documents.

Nevertheless, this review may present some limitations. Although a broad and systematic search was conducted across multiple scientific databases and complemented by gray literature, some relevant studies may still have been missed. This limitation could be associated with nonindexed publications or the use of nonstandardized descriptors by authors. To reduce this bias, measures such as the use of different Boolean operators, the combination of search strategies across databases, and manual reference list screening were adopted.

Another limitation of this review is the expected methodological heterogeneity among the included studies. Variations may occur in study design, population characteristics, instruments used to assess fatigue, CAD diagnostic criteria, and timing of assessment. This diversity may hinder direct comparisons of results. To minimize this impact, a structured categorization and narrative synthesis approach, aligned with the study's qualitative content analysis framework, will be used [29,36]. Lastly, the inclusion of studies published in different languages may also represent a limitation, as there is a risk of imprecise interpretation during data extraction and analysis. To address this issue, reliable automated translation tools were used in combination with dual verification of extracted information, ensuring greater accuracy and consistency in the analysis.

Future Directions and Stakeholder Consultation Plan

Ultimately, the final findings of this scoping review will guide the development of a preliminary definition for CAD-related fatigue and a proposed conceptual framework. The content validation of this preliminary definition and conceptual map will be conducted in a subsequent study.

This future consultation will involve four distinct stakeholder groups: (1) cardiologists with at least 5 years of CAD clinical experience; (2) nurses specializing in cardiac rehabilitation; (3) researchers with published literature on symptom assessment in cardiovascular populations; and (4) patients with CAD who self-identify as experiencing fatigue.

The consultation method in the subsequent study will use semistructured interviews (involving 8 to 12 participants across stakeholder groups). The process will specifically address: (1) the clarity and comprehensiveness of the proposed preliminary definition; (2) the completeness of the identified dimensions, manifestations, and influencing factors; (3) the practical clinical utility of the recommended assessment instruments; and (4) the identification of potential gaps or omissions in the synthesized framework. All consultation findings will be reported transparently in the follow-up study, explicitly documenting which stakeholder suggestions were incorporated and the rationale behind those revisions.

Acknowledgments

This scoping review aims to support the doctoral research of AGM, a PhD candidate at the School of Nursing, University of São Paulo (USP), São Paulo, Brazil. The authors would like to express their gratitude to librarian Fabiana Gulin Longhi, a member of the Brazilian Centre for Evidence-Based Health Care: a JBI Centre of Excellence (JBI Brazil), for validating the search strategies across various databases.

Generative AI Use

The authors declare the use of generative AI (GenAI) in the research and writing process. According to the Generative AI Delegation Taxonomy (GAIDeT), the following tasks were delegated to GenAI tools under full human supervision: text summarization, adapting and adjusting the emotional tone, translation, and reformatting. The GenAI tools used were ChatGPT (OpenAI; GPT-4o), Gemini (Google LLC), and Grammarly. The authors retain full responsibility for the final manuscript. GenAI tools are not listed as authors and do not bear responsibility for the final outcomes.

Funding

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Brazil (Finance Code 001). The author, AGM, received a scholarship from the above-mentioned agency for the completion of a PhD in Science at the School of Nursing, University of São Paulo (EEUSP), São Paulo, Brazil. The funder was not involved in the development of the scoping review's content.

Data Availability

Data sharing is not applicable to this protocol article because no datasets were generated or analyzed during the current study. The data extraction forms and search strategies planned for the scoping review are available in the supplementary files. Upon completion of the scoping review, the full dataset of extracted variables will be made available from the corresponding author upon reasonable request.

Authors' Contributions

AGM, RdCGeSB, and LJRD contributed to conceptualization, methodology, original draft preparation, and editing. RdCGeSB and LJRD contributed to supervision. AGM and GAPJ contributed to the final methodology and designed the search strategy. All authors participated in the study selection, data extraction, analysis, and synthesis phases of the scoping review. All authors reviewed and edited the manuscript, approved the final draft, and read and agreed to the published version of the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Detailed search strategy.
[DOCX File (Microsoft Word File), 23 KB-Multimedia Appendix 1]

Multimedia Appendix 2

Data extraction table.
[DOCX File (Microsoft Word File), 42 KB-Multimedia Appendix 2]

Checklist 1

PRISMA-P checklist.
[DOCX File (Microsoft Word File), 27 KB-Checklist 1]

Checklist 2

PRISMA-S checklist.
[DOCX File (Microsoft Word File), 18 KB-Checklist 2]

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Abbreviations

CAD: coronary artery disease
CAPES: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior
OSF: Open Science Framework
PQDT: ProQuest Dissertations & Theses Global
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRISMA P: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols

PRISMA-S: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Reporting Literature Searches in Systematic Reviews
PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews
TOUS: Theory of Unpleasant Symptoms

Edited by Amy Schwartz; peer-reviewed by Emerson Roberto dos Santos; submitted 22.Dec.2025; initial comments to author 10.Jun.2026; final revised version received 11.Aug.2026; accepted 21.Aug.2026; published 26.Nov.2026

Please cite as:
Muller AG, Jaimes GAP, Díaz LJR, Butcher RdCGeS
Fatigue in Coronary Artery Disease: Protocol for a Theory of Unpleasant Symptoms–Guided Scoping Review
JMIR Res Protoc 2026;15:e90173
URL: https://www.researchprotocols.org/2026/1/e90173
doi: 10.2196/90173

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