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Occupational Risk for Coronary Artery Disease in Shift Workers – A Systematic Review

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Abstract

Background: *Coronary artery disease (CAD) prevention in shift workers (SWs) poses a significant challenge worldwide, as CAD remains a major cause of mortality and disability. In the past, SWs were found at higher risk of CAD than non-s SWs. Nevertheless, the pathogenic mechanism between shift work and CAD to date is unclear. This systematic review aims to enhance understanding of the risk of CAD occurrence in SWs.* **Methods:** *A systematic literature review was conducted from January 2013 to December 2023. MEDLINE/Pubmed databases were used initially, and additional relevant studies were searched from references. Shift work was defined as any schedule outside traditional shifts, including the night shift.* **Results:** *Fifteen pertinent papers were categorized into risk assessment or risk management. Findings demonstrated an increased risk of CAD among SWs compared to non-SWs, with an increased CAD risk observed for both shift work and night shift work.* **Discussion:** *Duration-response associations indicate that greater shift exposure is linked to higher CAD risk. SWs incur an increased risk of CAD through the atherosclerotic process. As shift work duration increases as the risk of atherosclerosis is higher, workers demonstrate a higher prevalence and severity of coronary artery plaques.* **Conclusions:** *The evidence-based results underscore the increased risk of CAD in SWs and are sufficient for proposing guidelines aimed at reducing the risk of CAD in SWs and at managing people with CAD in return to work characterized by disrupted circadian rhythms.*

1. Introduction

Preventing coronary artery disease (CAD) among shift-workers (SWs) presents a significant global challenge for both workers and enterprises worldwide. CAD, a condition where the heart's arteries fail to deliver sufficient oxygen-rich blood, remains a leading cause of disability [1, 2]. To date, CAD persists as a major cause of mortality, responsible for one-third of all deaths in individuals aged ≥ 35, with a global prevalence ranging from 5% to 8% [3, 4]. Low- and middle-income countries bear a disproportionately higher burden of CAD, recording 7 million deaths and 129 million disability-adjusted life years annually. In the United States, CAD affects 16.8 million individuals, resulting in nearly 8 million cases of myocardial infarction (MI) [5, 6].

The World Health Organization (WHO) estimated that CAD will remain one of the top three causes of death worldwide, with nearly 9.3 million

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deaths annually in 2030 [7]. Moreover, the economic impact of CAD is significant, with CAD-associated financial burdens in the U.S. amounting to $188 billion in 2015 and projected to exceed $366 billion by 2035 [8].

A growing body of literature has revealed a relationship between shift work and the disruption of circadian rhythms and alerting cycles, resulting in an increased risk of cardiovascular diseases, including CAD [9-11].

In the past, a prospective cohort study among Japanese workers indicated that rotating SWs had a higher risk of death due to CAD compared to daytime workers [12], aligning with the findings of a British cohort study associating nighttime and early morning work with adverse CAD risk profiles attributable to socio-economic and occupational factors [13]. Moreover, in a systematic review, Bøggild & Knutsson [14] found that SWs had a 40% increase in the risk of cardiovascular diseases, including CAD, and suggested analyzing the risk factors for such diseases, given that the risk is probably multifactorial. Still, the literature was mainly focused on the behavior of SWs and neglected other possible causal connections.

Nevertheless, to date, the pathogenic mechanism between shift work and CAD is unclear. However, circadian rhythm disruption (through changes in the sleep/wake cycle) is known to be associated with an increase in psychosocial stress, a change in eating habits (i.e., eating an overly rich diet at night), and the autonomic nervous system unbalance [15, 16]. In particular, the role of autonomic cardiovascular control in promoting CAD in SWs is complex and only partially understood. Previously, Furlan et al. [17] first described the circadian changes in cardiac autonomic control in shift workers and suggested that the mismatch between the endogenous circadian rhythms and the continuous changes in the time of work and sleep may increase the risk of cardiac diseases. Thus, increasing evidence shows that shift working patterns might be associated with chronic circadian misalignment, resulting in a decrease in leptin and an increase in glucose and insulin. Due to these changes, individuals may experience increased body weight, high blood glucose, impaired glycogenesis, and an increased risk of CAD [18-27].

Interestingly, in a prospective cohort study of retired workers, Li et al. [28] found an association between the duration of past shift work and increased risk of incident CAD, particularly among service or sales workers compared to workers in other job categories. Moreover, being physically active after retirement proved protective in lowering the excess CAD risk associated with past shift work. In such study, incident CAD events were defined as the first occurrence of fatal or nonfatal coronary events as described by the International Classification of Diseases, Tenth Revision, codes I20– I25 [29], following the recommended guidelines for observational research from the American Heart Association [30]. Although several studies in the past proved associations between shift work and CAD, many of such studies suffer from selection bias, which raises the need to study the association between shift work and CAD and to upgrade the understanding of this issue [11]. Moreover, in a recent editorial, Harma et al. [31] highlighted that many studies focusing on SWs have quality problems as they suffer from the "healthy shift worker effect" and, therefore, may not sufficiently add to the knowledge.

Given the current concern with the impact of shift work on workers' health, with increased risk of CAD, a summary of new evidence may help to accelerate or stimulate policymakers to enact guidelines for preventing and screening CAD in SWs. Indeed, shift work is a modifiable risk factor that seems to be associated with an increased risk of cardiac diseases, including CAD, as reported by several previous studies. The present systematic review aimed to search for new additional insights or new occupational interventions produced by the last 10-year period to mitigate the risk of CAD among SWs.

For the purpose of this systematic review, shift work was defined as any work schedule outside traditional shifts, including night shift; CAD was defined as ischemic heart disease (IHD) according to the International Classification of Diseases, 10th revision (ICD-10) codes I20–25, a condition in which there is an inadequate supply of blood and oxygen to the myocardium; it is sometimes called coronary heart disease [2, 29].

2. Materials and Methods

2.1. Search Strategy

We performed a systematic review of the literature starting from January 1, 2013, up to December 31, 2023. Initially, MEDLINE/PubMed databases were used; afterward, the reference sections of the selected publications were scanned for relevant studies satisfying the adopted criteria. Selected keywords were used to identify articles for this systematic review of literature.

The keywords as search MeSH were: "ischemic heart disease," or "coronary heart disease," "coronary artery disease," or "myocardial infarction" and "shift work" or "rotating shift work" or "night shift work" or "irregular work schedule."

We aimed to identify original research articles (i.e., non-reviews) using the above-mentioned keywords with the following inclusion criteria: i) written in English; ii) published after December 31, 2012 and before January 1, 2024; iii) human studies; and iv) full reports.

Eligibility criteria were established using the PICOS reporting system [32]:

- Population: employees from 18 to 70 years old exposed to shift work.
- Intervention: shift work is defined as any work schedule outside traditional shifts, including the night shift.
- Comparator(s): employees working on schedules without shifts.
- Outcome(s): any evaluation of CAD risk in shift workers, with evaluations of occupational interventions aimed at mitigating the risk as a secondary outcome.
- Study type: case-control studies, cross-sectional studies, retrospective and prospective cohort studies, survey studies, case series, and case reports.

2.2. Formulating the Answerable Question

According to the PICO framework, the question of the present study can be summarized as follows: do SWs face an increased risk for CAD than non-SWs?

2.3. Data Extraction

The screening of articles was carried out in two phases. In the first phase, articles were screened based on title and abstract. The abstracts of all the selected titles were sorted for more detailed information. Two independent reviewers (G.d and G.C.) read the abstracts and categorized them as relevant, not relevant, and possibly relevant. In the second phase, the full-text articles were assessed for eligibility. Two reviewers (R.T. and P.P.) independently applied inclusion criteria to potentially eligible papers and both reviewers then independently extracted data from the original articles. Disagreements were discussed and resolved through a consensus session with a third-party researcher (GLT), and a consensus was reached.

2.4. Quality Assessment

The Newcastle–Ottawa scale (NOS) was used to evaluate the quality of the studies [33]. This is a validated, easy-to-use scale of 8 items in three domains: selection, comparability, and exposure/outcome for case-control or cohort studies, respectively. Each item can be given one point, except comparability, which has the potential to score up to two points. Studies are rated from 0-9, with those studies rating 0-3 (poor quality), 4-6 (fair quality), and 7-9 (good/high quality). The NOS scale adapted for cross-sectional studies was used to assess the quality of cross-sectional studies; this scale was a modified version of the NOS scale, as also used by several other studies that have felt the need to adapt the NOS scale to assess the quality of cross-sectional studies appropriately. Through a search of the literature, we found that a NOS score of 7 or more can be considered a "good" study [34]. So, we used this criterion as a cut-off for good quality study.

2.5. Categorization of Selected Articles

Every full-text article that met the inclusion criteria was reviewed and categorized into one or more categories based on its subject matter: risk assessment and risk management. This systematic review was reported in accordance with the PRISMA statement [35].

2.6. Search for Ongoing Clinical Trials

The Clinical Trials.gov website, the European Union Clinical Trials Register, the International Council for Harmonization Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice Clinical Trials Registry, the Australian New Zealand Clinical Trial Registry, the Chinese Clinical Trial Registry, the Thai Clinical Trials Registry, the International Clinical Trials Registry Platform (ICTRP), the Cochrane Central Register of Controlled Trials were consulted online on March 2023 using the selected keywords (last updated on January 31, 2024).

3. Results

Our research of the literature database retrieved 445 publications that matched our inclusion criteria; 421 were removed because they were deemed irrelevant (i.e., non-research conference proceedings or not concerning SWs). Therefore, 15 papers remained in the study (Figure 1). These 15 papers were then categorized according to their subject matter. Fourteen of the checked studies focused on "risk assessment," and only one paper targeted the focus "risk management." The characteristics, outcomes, and main results of the checked studies are reported in Tables 1 and 2.

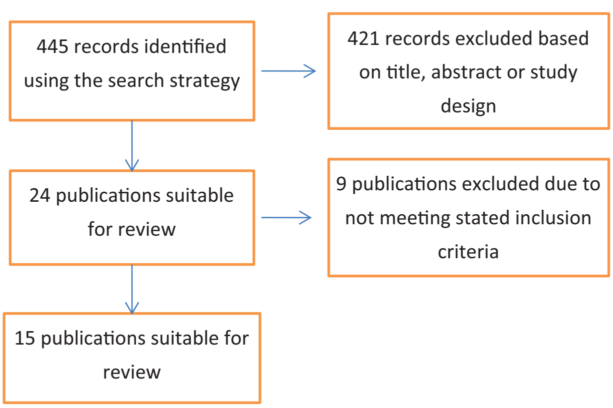

Figure 1. Flow-chart of included studies.

3.1. Best-Evidence Synthesis

The studies were considered good quality if the NOS score was 7 or more. All 14 studies focusing on the risk assessment of CAD reach a good quality level. Eleven had a cohort design, two had a cross-sectional design, and one had a case-control design. The reported odds ratios (ORs), and hazard ratios (HRs) proved moderate evidence for a positive relationship between shift work and CAD; two studies found increased CAD mortality among workers exposed to shift work. The interventional study targeted at risk management of CAD risk reached a level of good quality. It showed the effectiveness of leisure-time physical activity in minimizing the risk of CAD in shift workers (Tables 1, 2).

4. Discussion

The 14 articles focusing on the risk assessment of CAD in shift-workers aimed to identify the relationship between shift work and the occurrence of CAD. In all the reviewed papers, an increased risk of CAD was found among SWs compared to non-SWs after adjusting for covariates, consistent with a meta-analysis of Vyas et al. [23], which previously reported increases in CAD risk of 10%–30% for shift-work and 40% for night shift-work. Moreover, the findings of our search align with those of Torquati et al. [11], who found that shift work was associated with an increased risk of both CAD morbidity and mortality. Interestingly, the cohort study by Jørgensen et al. conducted on the female nurses of the Danish nurse cohort showed an increased rate of CAD mortality (130%) related to night shift work [36]. Studies investigating gender differences in CAD confirmed the slightly higher risk in females than males for either night shifts or shift work in general. In particular, the longitudinal study by Eng et al. [37] found associations between males and females, with higher HRs for CAD observed in females (HR 1.25; 95% CI 1.17 to 1.34) than in males (HR 1.10; 95% CI 1.05 to 1.14). However, despite this evidence, the reviewed studies did not establish the pathway leading to such gender differences in CAD risk.

Table 1. Summary of the articles included in the review.

Reference	Study design	Study location	Sample size	Risk assessment	Risk management	Risk of bias assessment[a)]	Adjustment of covariates	Quality (NOS[b)])
Havakuk et al. (2018) (39)	Cohort	Israel	349	X		Low	Age, gender, hypertension, hyperlipidemia, diabetes mellitus, family history of CAD, smoking status, BMI, physical activity, clinical status	8
Barger et al. (2017) (50)	Cohort	United States	13 026	X		Low	Age, gender, current smoker, race, region, BMI, hypertension, hyperlipidemia, diabetes mellitus, past MI, past percutaneous coronary intervention, index diagnosis (ST-elevation MI versus non-ST-elevation ACS), days from qualifying event, baseline low-density lipoprotein, Lp-PLA2 activity, baseline estimated glomerular filtration rate	8
Mamen et al. (2020) (48)	Interventional	Norway	Intervention = 19 Control group = 37		X	Low	Age, height, BMI, systolic blood pressure, diastolic blood pressure, CRP, total cholesterol, high-density lipoprotein, low-density lipoprotein, glycated hemoglobin, vigorous physical activity, maximal oxygen uptake relative to body mass, maximal oxygen uptake	7
Eng et al. (2022) (37)	Cohort	New Zeland	1.594.677	X		Moderate	Age, gender, ethnicity, smoking status	7
Solymanzadeh et al. (2023) (51)	Cross sectional	Iran	60 shift workers 60 day workers	X		Moderate	Age, gender,BMI, blood pressure, cholesterol	7
Wang et al. (2021) (42)	Cohort	UK	283 657	X		Low	Age, gender, ethnicity, education, socioeconomic status, BMI, smoking status, physical activity, total cholesterol, glycated haemoglobin, blood pressure, sleep duration, chronotype.	7
Carreòn et al. (2014) (52)	Cohort	United States	1874	X		Moderate	Age, gender, smoking status	7

(continued)

Table 1. Summary of the articles included in the review. *(continued)*

Reference	Study design	Study location	Sample size	Risk assessment	Risk management	Risk of bias assessment[a)]	Adjustment of covariates	Quality (NOS[b)])
Kang et al. (2016) (40)	Cross sectional	South Korea	110	X		Moderate	Age, low-density lipoprotein cholesterol, BMI, physical activity, smoking, hypertension, diabetes mellitus	7
Vetter et al. (2016) (45)	Cohort	United States	189.158	X		Low	Medical history, anthropometric data, diet, lifestyle	8
Hermansson et al. (2018) (41)	Case-control	Sweden	Cases 5941 Controls 7252	X		Low	Triglycereds, cholesterol, blood pressure. Diabetes type II, BMI>28, job strain, tobacco smoking	8
Wang et al. (2016) (53)	Cohort	Finland	1891	X		Low	Demographic, biological, behavioural and psychosocial job factors	7
Ho et al. (2021) (38)	Cohort	UK	238.661	X		Low	Sex, age, ethnicity, education level, deprivation index, work h per week, duration of current job, walking/standing at work, heavy manual/physical work, sleep duration, television viewing, smoking, alcohol intake, blood pressure, low-density lipo-protein, cholesterol, lipoprotein(a), glycated haemoglobin, cystatin C and γ-glutamyltransferase	9
Jørgensen et al. (2017) (36)	Cohort	Denmark	18 015 female nurses	X		Low	Age, smoking status, leisure-time physical activity, alcohol consumption,BMI, pre-existing diseases, work stress, marital status.	8
Kader et al. (2022) (44)	Cohort	Sweden	30.300	X		Low	Gender, age, country of birth, education, and profession.	8
Vestergaard et al. (2023) (47)	Cohort	Denmark	100.149 night workers and 153.882 day workers	X		Moderate	Age, gender, diabetes, family history of cardiovascular disease, educational level, BMI, hypercholesterolaemia, hypertension	8

a) Risk of bias due to: shift work exposure definition, exposure assessment,reliability, confounders assessment, analysis methods in the study (research-specific bias), blinding of assessors, attrition, selective reporting, funding, conflict of interest.
b) Newcastle–Ottawa scale (NOS).

Table 2. Characteristics, outcomes and main results of the checked articles.

Reference	**Primary Outcome**	**Methods**	**Main results**
Havakuk et al. (2018) (39)	To assess the prevalence and the degree of CAD among shift workers, as detected by cardiac computed tomography angiography, compared with non-shift workers	Cardiac computed tomography angiography	CAD was present in 74.2% of shift workers and 53.9% of non-shift workers (OR 2.38, CI 1.21-4.96, p = 0.01), stenosis >50% was more prevalent in shift workers (20.2 vs. 11.2%, respectively; p = 0.006), and a coronary calcium score of zero was shown in 46.8% of shift workers and 63.4% non-shift workers (p = 0.034)
Barger et al. (2017) (50)	To assess predictors of major coronary events	Questionnaire	Patients working overnight shifts for at least 1 year had a 15% increased risk of major coronary events (adj HR, 1.15; 95% CI, 1.03–1.29; P=0.01), a 12% increased risk of major adverse cardiovascular (adj HR, 1.12; 95% CI, 1.00–1.27; P=0.06) and a 21% increased risk of myocardial infarction (adj HR, 1.21; 95% CI, 1.04–1.39; P=0.01) than those who did not report working overnight shifts
Mamen et al. (2020) (48)	To study if high-intensity physical activity could modify the risk of early manifestations of CVD in shift-workers	Questionnaire, examination, laboratory tests	Physical activity could counteract the increased risk for CADin shift-workers
Eng et al. (2022) (37)	To examine associations between occupational exposure to noise, long working h, shift work, sedentary work and ischaemic hearth disease.	Survey	Night shift work was associated with ischaemic hearth disease for males (HR 1.10; 95% CI 1.05 to 1.14) and females (HR 1.25; 95% CI 1.17 to 1.34).
Solymanzadeh et al. (2023) (51)	To determine the prediction of risk of CAD based on the Framingham risk score (FRS) in association with shift work among nurses.	CAD risk assessment tools	Shift-work was associated with high prevalence of CAD risk based on the FRS (p = 0.04).
Wang et al. (2021) (42)	To test whether current and past night shift work was associated with incident atrial fibrillation and whether this association was modified by genetic vulnerability. Its associations with coronary heart disease, stroke, and heart failure were measured as a secondary aim.	Questionnaire, consultation of UK Biobank	Usual/permanent current night shifts, ≥10 years and 3-8 nights/month of lifetime night shifts were significantly associated with a higher risk of incident CHD (HR 1.22, 95% CI 1.11-1.35, HR 1.37, 95% CI 1.20-1.58 and HR 1.35, 95% CI 1.18-1.55, respectively).
Carreòn et al. (2014) (52)	To assess association between shift work and coronary artery disease	Occupational database, questionnaire	Increased CAD mortality among workers exposed 90 days or more to both shift work and carbon disulfide (SMR 1.36, 95% CI: 1.03–1.76)
Kang et al. (2016) (40)	To investigate whether shift work is related to elevated risk of coronary artery disease	Cardiac computed tomography angiography	Shift work was associated with increased risk of CAD (OR, 2.92; 95% CI 1.02 to 8.33)
Vetter et al. (2016) (45)	To determine whether rotating night shift work is associated with coronary artery disease risk	Self-administered questionnaire	Longer duration of rotating night shift work was associated with an absolute increase in CAD risk.

(continued)

Table 2. Characteristics, outcomes and main results of the checked articles. *(continued)*

Reference	Primary Outcome	Methods	Main results
Jørgensen et al. (2017) (36)	To examine the association between shift work and all-cause mortality and mortality due to CVD, cancer, diabetes, neurodegenerative and psychiatric diseases	Consultation of the Danish nurse cohort (DNC)	Association between shift work and CAD mortality among shift nurses working night shifts (HR 1.47, 95% CI 0.94–2.32)
Hermansson et al. (2018) (41)	To assess the risk for MI from an interaction between parental cardiovascular mortality or parental premature MI and shift work	Consultation of databases, questionnaire	Paternal mortality from MI or sudden cardiac death and shift work interact to increase the risk of MI in men (OR for both exposures was 2.88 (95% CI 1.75–4.57)
Wang et al. (2016) (53)	To assess ischaemic hearth disease risk/mortality	Consultation of data in the prospective Kuopio Ischemic Heart Disease Risk Factor Study cohort	Travelling work (at least 3 nights per week away from home) was strongly positively associated with acute myocardial infarction among men with ischaemic hearth disease (HR=2.45, 95% CI 1. 08 to 5.59) but not among men without (HR=0.93, 95% CI 0.43 to 2.00
Kader et al. (2022) (44)	To examine the effects of various aspects of night and shift work on the risk of incident ischemic heart disease and atrial fibrillation	Consultation of registry-based exposure data	The risk of CAD was increased among employees who the preceding year had permanent night shifts compared to those with permanent day work [hazard ratio (HR) 1.61, 95% confidence interval (CI) 1.06–2.43] and among employees working night shifts >120 times per year compared to those who never worked night (HR 1.53, 95% CI 1.05–2.21)
Ho et al. (2022) (38)	To assess the associations between shift work and incident and fatal CVD	Consultation of UK Biobank	Increased risk of CAD (HR 1.09, 95% CI 1.03–1.15) and heart failure (HR 1.15, 95% CI 1.03–1.28) in shift-workers compared to non shift-workers
Vestergaard JM et al. (2023) (47)	To examine exposure-response relations between quantitative night work characteristics and coronary heart disease	Consultation of exposure data and health information, including information from the Danish National Patient Register	Incidence rate ratios for female and male night workers were 1.06 (95% CI: 0.97, 1.17) and 1.22 (95% CI 1.07, 1.39). Highest risks were observed in top exposure categories for several night work characteristics. No consistent exposure-response relations by number of monthly night shifts, cumulative night shifts, years with rotating night shifts, years with any night shift and consecutive night shifts were observed among the night workers of either sex

Regarding the relationship between shift work and CAD, Eng et al. [37] hypothesized that night shifts disrupt the circadian rhythm, leading to dysregulation of sleep-wake cycles, body temperature, energy metabolism, cell cycle, and hormone production. Moreover, night shift work was found to have an indirect effect through stress-related factors such as adverse psychosocial working conditions, disruption to work-life balance, insufficient time for recovery outside of work, and promotion of unhealthy lifestyles, which could impact CAD risk. In line with these findings, Ho et al. [38], in a cohort study, demonstrated that current smoking, short sleep duration, poor sleep quality, adiposity, and higher glycated hemoglobin play a pivotal role in the mediation between shift work and CAD, representing the main potentially modifiable mediators. These findings led the authors to suggest the need for workplace interventions targeting such mediators to minimize shift workers' CVD risk.

Interestingly, in the prospective trial conducted by Havakuk et al. [39], cardiac computed tomography angiography (CCTA) showed that in shift workers, coronary artery plaques were not only more prevalent and severe than in non-SWs but, in addition, the positive coronary calcium score (CCS), a measure of the presence of CAD, was also more prevalent in SWs. These findings were obtained in individuals with no differences for risk factors and were not influenced by the clinical status of the participants; nevertheless, in this historical cohort, single-center study, most of the clinical information were collected by a telephonic questionnaire and potentially suffered from bias.

However, in line with these findings, the cross-sectional study of Kang et al. [40] demonstrated that shift work was associated with increased risk of incurring high CCS compared with day work in three different stress models focused on psychosocial, behavioral and physiological stressors that could explain the relationship between shift work and CAD: psychosocial-behavioral model [OR 2.89 (95% CI 1.07 to 7.82)]; physiological model [OR 2.92 (95% CI 1.02 to 8.33)]; psychosocial-behavioral and physiological model [OR 3.35 (95% CI 1.13 to 10.00)]. Additionally, the duration of shift work was positively associated with both the risk of atherosclerosis and the increased likelihood of developing high scores of CCS [OR 1.06 (95% CI 1.01 to 1.12)]. Studies by Havakuk et al. [39] and Kang et al. [40] revealed that shift workers face an increased risk of CAD due to the atherosclerotic process, with a higher risk of atherosclerosis associated with longer durations of shift work.

Consistent with these findings, Hermansson et al. [41], in a case-control study, reported an increased risk of short-term mortality after MI in SWs compared to non-SWs. They hypothesized that if arteries of SWs are more affected by atherosclerosis, the atherosclerotic process may have damaged the intima of blood vessels, leading to an increased risk of rupture and thrombosis when the patient is fragile due to a previous MI. These findings concur with those reported by Wang et al. [42], who proved that shift work among traveling employees was associated with acute MI in men with a previous diagnosis of CAD (HR=2.45, 95% CI 1.08 to 5.59) but not in men without CAD (HR=0.93, 95% CI 0.43 to 2.00). Moreover, the cohort study by Zhao et al. [43] revealed that SWs experiencing acute myocardial infarction face a greater risk of worsened prognosis due to reperfusion injury compared to daytime workers. This underscores the importance of maintaining normal circadian rhythm in the primary prevention of cardiovascular conditions and the clinical significance of work schedule acquisition in patients with MI for stratification and prognostic purposes.

Concerning the duration–response associations with shift work, the cohort study conducted by Kader et al. [44] demonstrated a higher risk of CAD in employees working night shifts more than 120 times per year compared to those who never worked night (HR 1.53, 95% CI 1.05–2.21). Consistent with this finding, Wang et al. [42] showed that usual/permanent current night shifts were associated with a higher risk of CAD (HR 1.22, 95% CI 1.11–1.35) and there were also associations between more than 10 years and 3–8 nights/month of night shift work exposure and the risk of CAD (HR 1.37, 95% CI 1.20–1.58 and HR 1.35, 95% CI 1.18–1.55, respectively). These findings are in line with the US Nurses' Health Study in which the risk of CAD increased with longer duration of rotating shift-work [45]; particularly, after correction for confounders, the authors observed elevated risk for 5 years or more of shift work (multivariable HR for 5-9 years, 1.12 [95% CI, 1.02-1.22]; multivariable HR for ≥10 years, 1.18 [95% CI, 1.10-1.26]; $P<0.001$ for trend). Previously, a meta-analysis conducted by Torquati et al. [11] proved a positive non-linear dose-response relationship that was significant after the first five years of shift work, with a 7.1% (95% CI 1.05–1.10) incremental risk of CAD events for each subsequent 5-year exposure. Interestingly, a meta-analysis performed by Cheng et al. [46] confirmed a dose-response relationship between the prolonged duration of shift work as a continuous variable and the risk of CAD (RR 1.009; 95% CI 1.006–1.012). Furthermore, the study revealed that each 1-year extension of shift work was associated with a 0.9% enhanced risk of CAD compared to daytime workers.

On the contrary, a recent prospective cohort study conducted by Vestergaard et al. [47] found that among employees working on average 1.8 night shifts per month, only females experienced an increased risk of CAD compared to day workers (IRR 1.22 [95% CI 1.07, 1.39]) while male shift-workers didn't exhibit a higher risk compared to daytime workers (IRR 1.06 [95% CI: 0.97, 1.17]. However, no consistent exposure-response relations were observed by number of monthly night shifts, cumulative night shifts, years with rotating night shifts, years with any night shift, and consecutive night shifts among the SWs of either sex. Nevertheless, the authors emphasize that their study involved a population with low exposure to night work. Therefore, they can not conclude that there is no increased risk of CAD in employees working night shifts.

Regarding the relationship between paternal history of cardiovascular disease and CAD in shift workers, Hermansson et al. [41] found an interaction between paternal mortality from MI or sudden cardiac death and shift work on the risk of MI in men. Indeed, forty percent of MIs that occurred in the studied population were attributed to this interaction, demonstrating that paternal mortality from MI or sudden cardiac in shift workers led to a higher risk of MI than in daytime workers. Given this finding, the authors suggest investigating the medical history of paternal mortality from MI or sudden cardiac death when assessing susceptibility to CAD in SWs.

Only one study focused on interventions to minimize the CAD risk among SWs. In this pre-post intervention study, Mamen et al. [48] demonstrated that improvement in physical activity focusing on cardiorespiratory health among rotating shift workers in the industry can modify risk factors associated with CAD; in particular, SWs trained in healthy physical activity showed significant improvement of systolic and diastolic blood pressure, glycated hemoglobin (HbA1c), body mass and cholesterol ($p < 0.05$). These findings led the authors to suggest promoting physical activity as a strategic way to minimize the impact of shift work on workers' health and CAD risk. Nevertheless, Holtermann et al. [49], in the Copenhagen General Population Study, observed that higher leisure time physical activity was associated with reduced risk of major cardiac events and all-cause mortality. In contrast, higher occupational physical activity was associated with increased risks, independent of each other. These findings highlighted the independent association of physical activity with the risk of major cardiac events and all-cause mortality. They supported the physical activity paradox given the contrasting health effect of leisure time physical activity and occupational physical activity.

4.1 Limitations

This study has some limitations. The limited number of manuscripts included in this study does not make it possible to draw strong conclusions; indeed the focus of the present review was limited to CAD and didn't consider all the CVDs, therefore leading to select a small number of articles. The manuscripts included in this study suffer from differences in the criteria adopted for assessing CAD and the analysis of confounders. Two of the fifteen included studies were cross-sectional. Consequently, the nature of these studies limited the assessment of temporality and could not establish a causal relationship between shift work and CAD. The quantification of risk exposure (duration and type of shift work) as a quantitative measure of the occupational risk factor is not well quantified and only by a few studies. Finally, our systematic review did not consider the presence of quantitative measures of risk exposure in the selection of manuscripts.

5. Conclusions

Data on CAD risk among SWs are lacking in the current literature, and international guidelines do not provide subpopulation measures to prevent CAD.

Although the findings of the present systematic review point in the same direction and highlight a relationship between shift work and the occurrence of CAD, more studies are required to clarify better the role of different variables as confounders, mediators, or effect modifiers. Moreover, as most of the selected papers did not quantify exposure to shift work, future studies are needed to fill this major gap.

Several studies have proven modifiable factors at both the individual and organizational levels to be common confounders for exposure-outcome and mediator–outcome relationships. Nevertheless, to date, the data regarding management interventions focused on the risk of CAD among SWs are lacking, and therefore, a special effort is required to detect strategic ways to minimize the likelihood of CAD occurrence in SWs.

Evidence-based guidelines are required to prevent and screen CAD in SWs. These guidelines should focus on understanding and addressing the increased risk of CAD associated with disrupted circadian rhythms and occupational factors.

Supplementary Materials: Supplementary material A: Search strategies.

Institutional Review Board Statement: Not applicable.

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Supplemetary Materials

Supplementary Material A

Pubmed Search Strategy:

(Ischemic Heart Disease [Mesh] OR Coronary Heart Disease [Mesh] OR Coronary Artery Disease [Mesh] OR Myocardial Infarction [Mesh]) AND (Shift Work [Mesh] OR Rotating Shift Work [Mesh] OR Night Shift Work [Mesh] OR Irregular Work Schedule [Mesh])