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PROTOCOL

Prostate Cancer Incidence and Mortality Linked to Metalworking Fluid Exposure: A Systematic Review and Meta-Analysis

Zahra Moradpour[1], Amin Barik[2], Goljamal Jorjani[3], Mohammad Reza Taherian[4], Sepideh Tousizadeh[5], Aram Halimi[3], Yaser Soleimani[6], Mobina Karimian[7], Tina Khavari[1], Fateme Azizi Kalankari[1], Fatemeh Asadipour[1], Mojtaba Azari[8], Niloofar Yousefzadeh Shakouri[6], Saeideh Karamian[6], Nasser Bahari[6], Alireza Mosavi Jarrahi[9]

[1]Department of Occupational Health Engineering and Safety, School of Public Health and Safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [2]Department of Health, Safety and Environment, School of Public Health and Safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [3]Department of Epidemiology, School of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [4]Student Research Committee, School of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [5]Student Research Committee, Shahrekord University of Medical Sciences, Shahrekord, Iran. [6]Medical School, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [7]Department of Occupational Health Engineering, Student Research Committee, Sabzevar University of Medical Sciences, Sabzevar, Iran. [8]Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran. [9]Department of Social Medicine, School of Public Health and Safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract

Introduction: Prostate cancer is a significant health concern, and occupational exposures, including metalworking fluid (MWF) exposure, have been implicated as potential risk factors. This protocol outlines a systematic review and meta-analysis methodology to investigate the association between MWF exposure and prostate cancer risk among male workers. **Methods:** Eligible studies include cohort, case-control, and cross-sectional studies published until between 1990 and 2023 focusing on MWF exposure and prostate cancer risk in male workers. Two independent reviewers will screen studies, extract data using a standardized form, conduct a meta-analysis using random-effects models, and assess study quality using the Newcastle-Ottawa Scale. Heterogeneity will be assessed, and sensitivity analyses will be conducted to explore sources of bias. **Results:** Anticipated outcomes include a comprehensive list of eligible studies, a synthesized analysis using random-effects meta-analysis models to estimate the association between MWF exposure and prostate cancer risk, and a quality assessment report of included studies. Subgroup analyses based on MWF type, exposure duration, and study design will be performed to explore heterogeneity. **Conclusion:** This systematic review and meta-analysis protocol aim to provide robust evidence on the association between MWF exposure and prostate cancer risk among male workers. The anticipated findings will have implications for occupational health practices and may guide future research and intervention strategies.

Keywords: Prostate Cancer- Fluid Exposure- Systematic Review

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Introduction

Prostate cancer stands as a formidable health challenge globally, particularly impacting men, with a multifaceted etiology involving genetic [1] predispositions [2], environmental factors [3], and lifestyle [4] influences. Among these environmental factors, occupational exposures have gained significant attention, particularly the exposure to metalworking fluids (MWFs) used extensively in machining processes [5]. MWFs, complex

Corresponding Author:
Dr. Alireza Mosavi Jarrahi
Department of Social Medicine, School of Public Health and Safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
Email: rmosavi@yahoo.com

mixtures comprising oils, water, emulsifiers, and additives, play a crucial role in cooling and lubricating metal surfaces during manufacturing operations [6]. Industries such as automotive, aerospace, and manufacturing heavily rely on MWFs, potentially exposing workers to health risks through various routes such as inhalation, dermal contact, and ingestion.

The association between occupational exposure to MWFs and prostate cancer risk has been extensively studied, albeit yielding conflicting results. While some studies suggest a positive correlation between MWF exposure and prostate cancer incidence or mortality, others have reported inconclusive or even contradictory findings. These discrepancies could stem from methodological differences, including variations in study designs, exposure assessment techniques, participant demographics, and the types of MWFs used across different industries. Consequently, a systematic review and meta-analysis are crucial to consolidate existing evidence, elucidate the potential association between MWF exposure and prostate cancer risk, and identify factors contributing to the observed heterogeneity in study outcomes.

This protocol delineates a systematic methodology aimed at comprehensively assessing the potential link between MWF exposure and prostate cancer risk, contributing to the existing body of knowledge and informing occupational health practices and policies.

Methods

Eligibility Criteria

The review will consider cohort studies, case-control studies, and cross-sectional studies published between 1990 and 2023 that examine the association between MWF exposure and prostate cancer risk. The population of interest includes male workers with documented occupational exposure to MWFs. Studies must provide clear documentation of exposure to any type of MWFs, and the primary outcomes of interest are the incidence and mortality of prostate cancer.

Information Sources

A comprehensive search strategy will be developed to include electronic databases such as PubMed, Scopus, Web of Science, Embase, and the Cochrane Library. Additionally, supplementary sources including reference lists of relevant studies and grey literature databases will be explored to ensure comprehensive coverage of the literature.

Search Strategy

The search strategy will be developed iteratively, incorporating relevant keywords and MeSH terms such as "Prostate Cancer," "Metalworking Fluids," "Occupational Exposure," and related terms. Pilot searches and consultation with subject matter experts will be undertaken to refine the search strategy for each database.

Study Selection

Two independent reviewers will initially screen titles and abstracts to identify potentially eligible studies, followed by a full-text review of selected articles. Disagreements will be resolved through consensus or consultation with a third reviewer.

Data Extraction

A standardized data extraction form will be used to capture pertinent information from included studies, including study characteristics, participant demographics, exposure assessment methods, outcome measures, and statistical findings. Data extraction will be conducted independently by two reviewers to ensure accuracy and reliability.

Quality Assessment

The quality of included studies will be evaluated using established tools such as the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies, with modifications for cross-sectional studies. Quality assessment will focus on domains such as selection bias, comparability of groups, exposure/outcome ascertainment, and statistical analysis.

Data Synthesis

The synthesis of data will involve both qualitative and quantitative approaches. A narrative synthesis will provide a descriptive overview of study characteristics, exposure assessment methods, and reported associations. Additionally, a meta-analysis using random-effects models will be conducted to pool effect sizes and estimate the overall association between MWF exposure and prostate cancer risk.

Statistical Analysis

Heterogeneity among studies will be assessed using the I^2 statistic and Cochran's Q test. Subgroup analyses will explore potential sources of heterogeneity based on MWF type, duration of exposure, geographic region, and study design. Sensitivity analyses will assess the robustness of the findings by excluding studies with a high risk of bias, ensuring the reliability of the meta-analysis results.

Results

As this is a protocol for a systematic review and meta-analysis, the Results section will provide an outline of the anticipated outcomes and steps to be taken during the data collection, analysis, and synthesis stages. The actual data and findings will be reported in the final manuscript upon completion of the study. Below are the expected outcomes and processes:

Study Identification and Inclusion

The anticipated results of the study identification and inclusion process involve the screening of databases and supplementary sources to identify relevant studies. The expected outcome is a comprehensive list of eligible studies, including cohort studies, case-control studies, and cross-sectional studies published between 1990 and 2023. These studies will focus on examining the association

between metalworking fluid (MWF) exposure and prostate cancer risk among male workers.

Study Selection Process

During the study selection process, two independent reviewers will screen titles, abstracts, and full texts of potential studies to determine eligibility. The anticipated outcome is a final selection of studies meeting the inclusion criteria, with disagreements resolved through consensus or consultation with a third reviewer.

Data Extraction and Synthesis

The data extraction process will involve using a standardized form to capture relevant information from each included study. This information will include study characteristics, participant demographics, exposure assessment methods, outcome measures, and statistical findings. The anticipated outcome is a comprehensive dataset ready for synthesis.

The data synthesis will encompass both qualitative and quantitative approaches. A narrative synthesis will provide a descriptive overview of study characteristics and reported associations. Additionally, a meta-analysis using random-effects models will be conducted to pool effect sizes and estimate the overall association between MWF exposure and prostate cancer risk. The anticipated outcome is a synthesized analysis providing insights into the collective evidence from the included studies.

Statistical Analysis and Quality Assessment

Heterogeneity among studies will be assessed using the I^2 statistic and Cochran's Q test during the data analysis phase. Subgroup analyses will explore potential sources of heterogeneity based on MWF type, duration of exposure, geographic region, and study design. Sensitivity analyses will be conducted to assess the robustness of the findings by excluding studies with a high risk of bias publications. The anticipated outcome is a thorough statistical analysis providing insights into the variability and reliability of the findings.

The quality assessment of included studies will be conducted using established tools such as the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies. The anticipated outcome is a quality assessment report detailing the strengths and limitations of the included studies.

Reporting and Dissemination

The anticipated results of this systematic review and meta-analysis protocol will be reported following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The final manuscript will include a detailed synthesis of findings, statistical analysis results, quality assessment report, and interpretations of the evidence. The findings will be disseminated through peer-reviewed publications, conference presentations, stakeholder meetings, and public access repositories to ensure wide accessibility and impact.

Discussion

Given that this is a protocol outlining the methodology for a systematic review and meta-analysis, the Discussion section will not include actual data or findings. It will instead discuss the anticipated implications of the study, potential challenges, and areas for further research based on the outlined methodology.

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