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Systematic review

Assessing the relationship between chronic pain and cardiovascular disease: A systematic review and meta-analysis

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HIGHLIGHTS

- Chronic pain is associated with an increased occurrence of cardiovascular disease.
- Increasing pain severity produces a stronger association with cardiovascular outcomes.
- The extent to which these associations are due to confounding variables remains uncertain.

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ABSTRACT

Background and Aims: Chronic pain is a potentially disabling condition affecting one in three people through impaired physical function and quality of life. While the psychosocial impact of chronic pain is already well established, little is known about the potential biological consequences. Chronic pain may be associated with an increased prevalence of cardiovascular disease, an effect that has been demonstrated across a spectrum of chronic pain conditions including low back pain, pelvic pain, neuropathic pain and fibromyalgia. The aim of this study was to review and summarize the evidence for a link between chronic pain and cardiovascular disease. We sought to clarify the nature of the relationship by examining the basis for a dose-response gradient (whereby increasing pain severity would result in greater cardiovascular disease), and by evaluating the extent to which potentially confounding variables may contribute to this association.

Methods: Major electronic databases MEDLINE, EMBASE, Psychinfo, Cochrane, ProQuest and Web of Science were searched for articles reporting strengths of association between chronic pain (pain in one or more body regions, present for three months or longer) and cardiovascular outcomes (cardiovascular mortality, cardiac disease, and cerebrovascular disease). Meta-analysis was used to pool data analysing the association between chronic pain and the three principal cardiovascular outcomes. The impact of pain severity, and the role of potentially confounding variables were explored narratively.

Results: The searches generated 11,141 studies, of which 25 matched our inclusion criteria and were included in the review. Meta-analysis (of unadjusted study outcomes) demonstrated statistically significant associations between chronic pain and mortality from cardiovascular diseases: pooled odds ratio 1.20, (95% confidence intervals 1.05–1.36); chronic pain and cardiac disease: pooled odds ratio 1.73 (95% confidence intervals 1.42–2.04); and chronic pain and cerebrovascular disease: pooled odds ratio 1.81 (95% confidence intervals 1.51–2.10). The systematic review also found evidence supporting a dose-response relationship, with greater pain intensity and distribution producing a stronger association with cardiovascular outcomes.

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All of the included studies were based on observational data with considerable variation in chronic pain taxonomy, methodology and study populations. The studies took an inconsistent and incomplete approach in their adjustment for potentially confounding variables, making it impossible to pool data after adjustments for confounding variables, so it cannot be concluded that these associations are causal.
Conclusions: Our review supports a possible dose-response type of association between chronic pain and cardiovascular disease, supported by a range of observational studies originating from different countries. Such research has so far failed to satisfactorily rule out that the association is due to confounding variables. What is now needed are further population based longitudinal studies that are designed to allow more robust exploration of a cause and effect relationship.
Implications: Given the high prevalence of chronic pain in developed and developing countries our results highlight a significant, but underpublicized, public health concern. Greater acknowledgement of the potentially harmful biological consequences of chronic pain may help to support regional, national and global initiatives aimed at reducing the burden of chronic pain.

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1. Introduction

Claims of a causal link between back pain and cardiovascular disease appear in studies as far back as 1950 [1]. The pathological rationale for this was based on the idea that back pain is a consequence of atherosclerotic disease of the lumbar arteries [2]. However, more recent evidence points to an effect across a spectrum of chronic pain conditions including pelvic pain, neuropathic pain and fibromyalgia [3–5].

Whilst chronic pain and cardiovascular disease share common risk factors (smoking, increasing age, depression), the chronic stress associated with pain may itself be a risk factor for heart disease. A causal association is lent weight to by findings that chronic pain is associated with dysfunction of the autonomic nervous system, the inflammatory system and endothelial processes; all of which play a part in the pathophysiology of cardiovascular disease [6–12].

The aim of this study is to review the evidence for a link between chronic pain and cardiovascular disease and, where possible, quantify the strength of this association by pooling data in a meta-analysis. We seek to clarify the nature of the relationship by examining the basis for a dose-response (whereby increasing pain severity would result in greater cardiovascular disease), and by evaluating the extent to which potentially confounding variables may contribute to this association.

2. Methods

A protocol for our review was devised in line with the Meta-analysis of Observation Studies in Epidemiology (MOOSE) guidelines [13] and registered on PROSPERO (CRD: 42013006585) [14].

Major electronic databases: MEDLINE (via Ovid), EMBASE (via Ovid), Psychinfo (via Ovid), Cochrane and Web of Science were searched from 1947 to December 5th 2015 for relevant studies. Examples of the search strategies are shown in Appendix A. Additional references were identified following inspection of the bibliographies of included articles. Field experts were approached directly, and parallel searches were performed though ProQuest (a web-based information suppository), in order to access and review 'grey literature' (i.e.; unpublished research produced