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The association of depression following percutanous coronary intervention with adverse cardiovascular events
Protocol for a systematic review and meta-analysis

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Abstract

Introduction: Percutanous coronary intervention (PCI) has been increasingly used for patients suffered from severe coronary artery disease. However, physical trauma and potential adverse events related to the procedure often result in detrimental psychological stress. Accumulating evidences have shown that depression is closely related to coronary artery disease. However, the association of depression following percutanous coronary intervention with adverse cardiovascular events is still unknown.

Objective: This review is designed to assess the prognostic association of depression following PCI with adverse cardiac events.

Methods and analysis: The following databases will be searched, PubMed, the EMBASE, CINAHL and Web of Science of English-language publications from inception to 30 October 2018. Cross-referencing from retrieved studies will be conducted additionally, and observational studies were included. Two independent review authors will do the study selection on the basis of the study eligibility criteria. Extracted data will be used for quantitative and qualitative evidence synthesis as well as to assess methodological quality of studies using the Newcastle-Ottawa checklist. The primary objective of this review is adverse cardiac events, presented as a composition of myocardial infarction, repeat coronary revascularization, cardiac readmission, and cardiac death. The accumulated evidence is evaluated and graded according to Grading of Recommendations, Assessment, Development and Evaluation (GRADE).

Results and conclusions: This review will explain the association of depression following percutanous coronary intervention with adverse cardiovascular events, and provide physicians with scientific evidence for psychological intervention in patients after PCI.

Prospero registration number: CRD42018112486.

Abbreviations: CHD = coronary heart disease, GRADE = Grading of Recommendations, Assessment, Development and Evaluation, OR = odds ratio, PCI = percutanous coronary intervention, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

Keywords: adverse cardiovascular events, depression, percutanous coronary intervention, systematic review

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1. Introduction

It is well known age, gender, diabetes, and hypertension are greatly contributing to cardiac events such as myocardial infarction, repeat revisualization procedure, cardiac death, and cardiac readmission.[1–3] The morbidity and mortality of Cardiac events are increasing worldwide.[4] Percutaneous coronary intervention (PCI), which is a safe and effective treatment, has been increasingly used for patients with significant coronary artery disease.[5,6] However, physical trauma and potential adverse events related to the procedure often result in significant psychological stress.

It has been shown that depression as negative emotion is related to development of coronary heart disease (CHD).[7,8] Whereas coronary artery intervention aggravate patients' depression.[9] There is a high prevalence of depression among patients who suffered from an acute cardiac event or underwent PCI.[10] While observational studies assessed relationship of depression with adverse cardiovascular events following percutanous coronary intervention have reached diverse conclusions. Several studies concluded that depression is predictive of mortality or adverse cardiac events in patient post-PCI.[11,12] While other studies showed that there were no association between depression and mortality after myocardial infarction.[13–15] The previous meta analysis has reported that post-MI depression is associated with an increased risk of adverse cardiovascular outcomes.[16,17] However, the association between depression following PCI and adverse cardiovascular events was not mentioned in the 2 earlier meta-analyses. The association of depression following PCI with adverse cardiovascular events is still unknown. Thus, it is of importance to reassess association of depression following PCI with adverse cardiovascular events. The present analysis focuses on the prognostic association of depression following PCI with adverse cardiac events.

2. Outcomes

The primary outcome of this review is adverse cardiac events, presented as a composition of myocardial infarction, repeat coronary revascularization, cardiac readmission and cardiac death. Mortality was the secondary endpoint.

3. Methods

3.1. Standards

The protocol was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statements and the guidelines in Cochrane Handbook for systematic Reviews of interventions.[18] A PRISMA-P checklist is attached (supplementary file1, http://links.lww.com/MD/C741)

3.2. Protocol and registration

This systematic review protocol has been registered with the PROSPERO (CRD42018112486).

3.3. Eligibility criteria

The studies were considered to be eligible if they met the following inclusion criteria:

1. Observational study;
2. adults ≥ 18 years of age;
3. contained patients diagnosed with depression within 6 months after PCI (including during hospitalization), using reliable and validated instruments[19–21] to assess depression;
4. studies included adverse cardiac events (including recurrent myocardial infarction (MI), repeat coronary revascularization, cardiac readmission and cardiac death) and/or mortality as outcomes.
5. All patients were followed up for more than 1 year after PCI.
6. Published in English up to 30 October 2018.

3.4. Information sources

The following databases will be searched, PubMed, the EMBASE, CINAHL and Web of Science of English-language publications from inception to 30 October 2018. Cross-referencing from retrieved studies will be conducted additionally.

3.5. Search strategy

A preliminary search strategy for PubMed is demonstrated in Table 1. Search term will be adapted to other databases based on the specific requirements for each database. We also manually checked reference lists to identify other potential studies.

3.6. Data management

All the literature search results will be combined and uploaded to one single EndNote (X.8) library. Duplicates will be removed.

3.7. Selection process

Two independent review authors will do the study selection on the basis of the study eligibility criteria. The study selection will

Table 1	
Preliminary search strategy: PubMed format.	
Search	Query
1	("Percutaneous Coronary Intervention"[Mesh] OR "Coronary Intervention, Percutaneous" OR "Coronary Interventions, Percutaneous" OR "Intervention, Percutaneous Coronary" OR "Interventions, Percutaneous Coronary" OR "Percutaneous Coronary Intervention'" OR "Percutaneous Coronary Revascularization" OR "Coronary Revascularization, Percutaneous" OR "Coronary Revascularizations, Percutaneous" OR "Percutaneous Coronary Revascularizations" OR "Revascularization, Percutaneous Coronary" OR "Revascularizations, Percutaneous Coronary" OR "Angioplasty, Balloon, Coronary"[Mesh] OR "Transluminal Coronary Balloon Dilation" OR "Balloon Dilation, Coronary Artery" OR "Angioplasty, Coronary Balloon" OR "Angioplasties, Coronary Balloon" OR "Balloon Angioplasties, Coronary" OR "Balloon Angioplasty, Coronary" OR "Coronary Balloon Angioplasties" OR "Coronary Balloon Angioplasty" OR "Coronary Angioplasty, Transluminal Balloon" OR "Angioplasty, Transluminal, Percutaneous Coronary" OR "Percutaneous Transluminal Coronary Angioplasty"
2	("Depression[Mesh]" OR "Depressive Symptoms" OR "Depressive Symptom" OR "Symptom, Depressive" OR "Symptoms, Depressive" OR "Emotional Depression" OR "Depression, Emotional" OR "Depressions, Emotional" OR "Emotional Depressions")
3	#1 AND #2
4	Restrict #3 to English language

be accomplished via 2 stages. Firstly, all the titles and abstracts will be screened by 2 researchers independently, to obtained which appear to meet the inclusion criteria or there is any uncertainty. Any discrepancies will be resolved by discussion. Reviews, letters or editorial, guidelines or clinical experience were excluded. Next, both authors will then obtain the full-text articles to further identified these meet the inclusion criteria. Reasons for exclusion of articles in the full-text screening session will be documented as follows, inappropriate population, inappropriate outcome, insufficient information for effect estimation, others. Discrepancies will be discussed by 2 authors. Further consultation with a 3rd review will be carried out if consensus cannot be reached. A proposed flow chart shown in Figure 1, illustrates the whole search process.

3.8. Data extraction

All the required data will be double extracted by 2 authors using a standardized data extraction form. Data in detail was extracted from each individual study that ultimately was included in the present study, including the following:

1. the 1st author's name and publication year;
2. study design;
3. patient selection;

4. participants' age;
5. percentage of females;
6. instrument prevalence;
7. assessment timing;
8. clinical outcomes;
9. mean follow-up time
10. risk factor adjustment.

Attempt was made to contact authors who published their studies only with abstract, but, failing to obtain original data, these studies were excluded from the present study.

3.9. Quality appraisal for included studies

The methodological quality of studies was assess using the Newcastle–Ottawa checklist,[22] with the highest score (the score meaning better quality) being 9. We defined the high quality as ≥ 7 scores, medium quality as 4 to 6 scores, and low quality as < 4 scores. Newcastle-Ottawa checklist is attached (supplementary file 2, http://links.lww.com/MD/C741).

The 2 authors extracted data independently. Upon completion, they will then review the results of assessment. Any disagreement was resolved by consulting with the 3rd investigator. Summary risk of bias table will be produced.
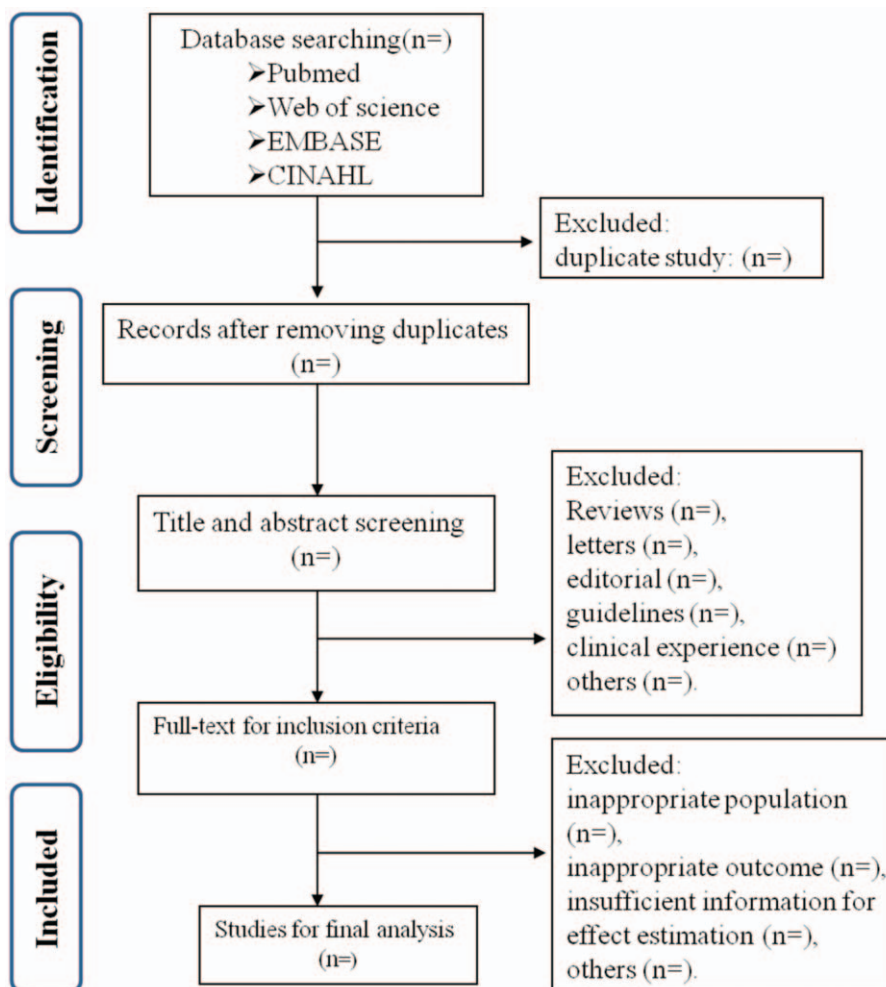

Figure 1. Flow chart of literature screening process.

3.10. Statistical analysis

If there is sufficient evidence, we will consider conducting a meta-analysis to estimate the pooled effect. All statistical analysis was performed using STATA software. Odds ratio (OR) and 95% confidence intervals (CI) were used as summary statistics. Heterogeneity across studies was analyzed using I^2 [I^2=Q-df/Q; where Q is the Chi-square statistic and df is the degree of freedom]. There were no statistical heterogeneity if $P \geq .1$ and $I^2 \leq 50\%$, and fix-effect model was used for meta-analysis. $I^2 > 50$ indicates the possibility of heterogeneity among the studies, and random-effects model was used. Sources of heterogeneity were explored by sensitivity analysis. If I^2 was larger than 75%, which means there was obviously statistical heterogeneity among studies, only results from each single study were present respectively rather than pooling analysis. Begger's plot analysis was used to detect publication bias. If these are not possible we will discuss possible sources of bias across studies.

If we find selected studies bearing sufficiently homogenous, our narrative synthesis will also described subgroup analyses, including: type of depression instrument; population characteristics, such as age strata and gender; number of subjects per study (dichotomized smaller number vs. larger number).

3.11. Confidence in cumulative evidence

The strength of evidence will be assessed by the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach for the relating domains, such as risk of bias, the methodological flaws, the consistency of results, precision and publication bias.[23] Studies will be rated as high (future evidence is unlikely to change the conclusion obtained from our research), moderate (further studies might alter our conclusion), low (further evidence is needed to answer the involved research question with increased confidence), very low quality (the estimate of effects is very uncertain).

3.12. Ethics and dissemination

Ethical review is not required as this protocol is for a systematic review. The result will be published in a peer-review journal. This review will the explain relationship between depression following PCI and cardiovascular events, and provide physicians with scientific evidence for psychological intervention in patients after PCI.

4. Discussion

The previous meta analysis has reported that post-MI depression is associated with an increased risk of adverse cardiovascular outcomes.[16,17] However, the association of depression following PCI with cardiovascular events is still unknown. Currently, although not all the mechanisms have been recognized, several reasons for the prognostic value of depression in patients undergoing PCI were established. First, depression is closely related to unhealthy lifestyles[24] and compromised adherence to medication for coronary heart disease,[25] which, consequently, contributes to the adverse cardiac events following PCI. Second, from pathophysiological perspective, depression is associated with neuroendocrine dysfunction, inflammation, impaired endothelial function, and nutritional deficiencies.[26] The compromised left ventricular function resulted from disorder of the autonomic nervous system and serious myocardial remodeling after depressed lead to the poor prognosis after PCI.[27] Reid G J et al[28] reported that experimentally induced mental stress induced platelet activation in patients with coronary artery disease. Third, depression and adverse cardiac events post-PCI share common risk factors, such as current smoking,[29] central obesity, hypercholesterolemia and diabetes.[30,31] It has been shown that depressed patients also suffer from glucose and lipid metabolism disorder, common risks factor for adverse cardiac events post PCI.

According to Milani, R V et al[32] depressed patients who completed rehabilitation had a 73% lower mortality (8% vs 30%; $P = .0005$) compared with control depressed subjects who did not complete rehabilitation. Evidences have shown that cardiac rehabilitation[33] and pre-discharged counseling have the ability to improve the prognosis of cardiovascular disease. Janey C. Petersona et al first reported that a threshold in physical activity in CAD patients with depressive is associated with a reduction in cardiovascular morbidity and mortality via enhancing parasympathetic tone and decreasing inflammation.[34] Accumulating evidences have shown that depression is closely related to coronary artery disease. However, the association between adverse cardiovascular events after PCI and depression is still unknown. Thus, it is of importance to reassess relationship of depression with adverse cardiovascular events following PCI. The present analysis focuses on the prognostic association of depression with adverse cardiac events following PCI.

Author contributions

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