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REVIEW ARTICLE

Prevalence of Moderate to Severe Anxiety Symptoms among Patients with Myocardial Infarction: a Meta-Analysis

Yajun Lian[1] · Jingsha Xiang[2,3] · Xiaoyan Wang[4] · Atipatsa C. Kaminga[2,3,5] · Wenhang Chen[6] · Zhiwei Lai[7] · Wenjie Dai[2,3] · Jianzhou Yang[8]

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Abstract

This study attempted to synthesize the evidence on the prevalence of moderate to severe anxiety symptoms among myocardial infarction (MI) patients to offer a reliable and accurate estimate on the number of MI patients suffering from moderate to severe anxiety symptoms. Comprehensive electronic searches (PubMed, Embase and Web of Science) were performed from their inception to February 2021. Between-study heterogeneity was analyzed using the Cochran's Q test and I^2 statistic, and if it was high across the eligible studies, meta-regression and subgroup analyses were conducted to examine the source of heterogeneity. Publication bias and the robustness of the pooled results were also examined. A total of 18 eligible studies covering 8,532 MI patients were included, of which 3,443 were identified with moderate to severe anxiety symptoms. Between-study heterogeneity was high (I^2=98.8%) with the reported prevalence ranging from 9.6% to 69.17%, and the pooled prevalence was 38.08% (95% confidence interval: 28.82–47.81%) by a random-effects model. Meta-regression analyses indicated that publication year ($\beta=-0.014$) was significant moderators contributing 16.11% to the heterogeneity. Subgroup analyses indicated that studies using the anxiety subscale of Brief Symptom Inventory to assess anxiety were homogenous (I^2=0.0). Furthermore, the pooled prevalence of moderate to severe anxiety symptoms varied significantly by geographic region, instrument used to assess anxiety, methodological quality, sex, education level, a history of previous MI and hypercholesterolemia. Additionally, the results of Egger's linear test ($t=-0.630$) and Begg's rank test ($z=-0.190$) indicated no evidence of publication bias, and the sensitivity of the pooled results was low. Nearly two fifth of MI patients suffered from moderate to severe anxiety symptoms, which emphasizes the importance of early identification of anxiety symptoms after MI, as well as the need of implementing psychological interventions for those with elevated anxiety symptoms.

Keywords Prevalence · Anxiety · Symptom · Myocardial infarction · Meta-analysis

Yajun Lian and Jingsha Xiang contributed equally to this work.

✉ Jianzhou Yang
jzyang@aliyun.com

Extended author information available on the last page of the article

Background

Myocardial infarction (MI), defined as myocardial cell death due to significant and sustained ischemia, affects people without regard to geographic area and is one of the leading causes of death and disability both in developed and developing countries [1, 2]. MI could lead to reduced quality of life, severe long-term functional impairment, and adverse health outcomes including recurrent MI, ventricular arrhythmias, heart failure, and sudden cardiac death [3, 4]. Therefore, individuals who experienced MI are usually at heightened risk for psychological distress, of which anxiety is a major manifestation [5, 6].

Anxiety, characterized by excessive worry, fear, tension or panic, is common among MI patients [6]. Accumulating evidence have convergently suggested that in addition to the negative effects on quality of life, elevated anxiety symptoms in MI were associated with a wide range of subsequent poor prognosis, including increased in-hospital arrhythmic and ischemic complications, poor attendance at cardiac rehabilitation, lower adherence to many important risk-reducing recommendations after MI, higher rates of future coronary events and cardiac rehospitalization, as well as increased risk for cardiac and all-cause mortality [7–11]. A prior meta-analysis in 2010 of 12 prospective studies covering 5,750 MI patients indicated that increased anxiety symptoms following MI could put individuals at 71%, 23% and 47% higher risk for new cardiac events, cardiac mortality and all-cause mortality, respectively [12]. Therefore, early identification of anxiety symptoms, as well as timely and effective psychological interventions for those with increased anxiety symptoms is crucial among MI patients, which could be facilitated by offering an accurate and reliable estimate on the prevalence of moderate to high anxiety symptoms among MI patients given its contribution to allocating psychological resources properly.

There has been an increasing number of publications examining the prevalence of moderate to high anxiety symptoms among MI patients over the last two decades. However, their reported prevalence varied markedly from 18 to 57% [13–18]. Several possible reasons may contribute to the disparate findings seen, including socio-demographic characteristics such as sex, living status and education level, cardiovascular risk factors such as smoking status, hypertension, diabetes and hypercholesterolemia, characteristics of the index MI, the instrument used to assess anxiety, timing of anxiety assessment, and a history of previous psychiatric disorder [9, 13, 19–23]. Another reason may be the varying methodological quality across these studies. In this regard, a pooled estimate combing all relevant findings of the individual studies is warranted. Accordingly, this study sought to synthesize the evidence on the prevalence of moderate to high anxiety symptoms among MI patients using meta-analytic methods.

Methods

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Search Strategy

Comprehensive electronic searches of the PubMed, Embase and Web of Science databases were performed from their inception to February 2021. The search strategy included a

combination of subject headings and free-text regarding anxiety and MI, and the specific search terms were customized across databases (Additional file 1). The reference lists of two relevant reviews [12, 24] and full-text articles were extracted and further screened to obtain more potentially eligible studies.

Eligibility Criteria

The inclusion criteria for this meta-analysis were: (1) the study design was cross-sectional, case-control, baseline data from longitudinal studies, or baseline data from randomized control trials before allocating the groups; (2) the primary target population was MI patients and the diagnosis of MI was affirmed by medical records; (3) the study identified moderate to high anxiety symptoms by validated self-report questionnaires with appropriate psychometric quality and established threshold information; (4) the study provided sufficient information to calculate the prevalence of moderate to high anxiety symptoms among MI patients and the corresponding sample size; (5) the sample size of subjects with MI was at least 200; and (6) the study was published in English in a peer-reviewed journal. Case reports, comments, letters to the editor, or conference abstracts were excluded. Additionally, if data overlapped among multiple publications, the earliest publication was included in this meta-analysis. Two raters independently screened and assessed the eligibility of the individual studies using the preceding established criteria and any disagreement between them was resolved by discussing with the third rater.

Data Extraction

The outcome of this meta-analysis was the prevalence of moderate to high anxiety symptoms among MI patients identified by either above the established cut-off values or above the norm-referenced values of the self-report questionnaires, and for the purpose of this study, data extracted from the eligible studies were: (1) study-level characteristics including the first author, publication year, study country, study design, sample source, number of subjects with anxiety, sample size of subjects with MI, the prevalence of anxiety among MI patients, and the methodological quality; (2) sample socio-demographic characteristics including age, sex, living status, and education level; (3) sample MI- and anxiety- related characteristics including a history of previous MI, the instrument used to assess anxiety, type of anxiety, and timing of anxiety assessment; and (4) sample characteristics on cardiovascular risk factors including smoking status, hypertension, diabetes and hypercholesterolemia, and a history of previous psychiatric disorder. Two raters independently extracted the preceding data and any disagreement between them was resolved by discussing with the third rater.

Quality Assessment

The methodological quality of the eligible studies was assessed using the Loney scale [25]. This scale has been widely used to appraise the methodological quality of observational studies which examine the prevalence of health-related outcomes. It consists of 8 questions comprehensively assessing the representativeness of sample, the validity of methods, and the interpretation of the results. Each question is answered by "Yes", "No" or "Unclear", with 1 point assigned for each answer of "Yes" and 0 point assigned

for each answer of "No" or "Unclear". Accordingly, the maximum score of this scale is 8 points, with more points indicating higher methodology quality. A total score of 0 to 3, 4 to 6, and 7 to 8 points suggests low, moderate and high quality, respectively.

Statistical Analyses

All statistical analyses were conducted using the "meta" and "metafor" packages of R software-version 3.6.0. Between-study heterogeneity was analyzed using the Cochran's Q test and I^2 statistic [26]. Specifically, a P value of < 0.05 of the Cochran's Q test indicated significant heterogeneity, and a value of $\geq 25\%$, $\geq 50\%$, and $\geq 75\%$ of the I^2 statistic suggested low, moderate, and high heterogeneity, respectively [27]. If between-study heterogeneity was not significant, data on the reported prevalence of moderate to severe anxiety symptoms among the individual studies were combined by a fixed effects model using Freeman-Tukey double arcsine method. Otherwise, a random effects model was applied [28].

If between-study heterogeneity was high across the eligible studies, meta-regression analyses and subgroup analyses were conducted to examine the contribution of possible moderators to the heterogeneity. Specifically, meta-regression analyses were performed using the restricted maximum-likelihood estimator method according to some continuous moderators such as publication year, mean age of subjects, proportion of male subjects, proportion of subjects with first-time MI, and quality assessment score, whereas subgroup analyses were performed according to some categorical moderators such as sex, living status, educational level, a history of previous MI, hypertension, diabetes, and hypercholesterolemia. For moderators tested in the meta-regression analyses, the included studies should be at least 10, while for moderators tested in subgroup analyses, the included studies should be at least 2. Furthermore, the disparity in each subgroup was tested by chi-square test, and a P value of < 0.05 was considered as significant [29].

Publication bias was examined not only visually by funnel plot but also objectively by the Egger's linear test and Begg's rank test [30–32]. Sensitivity analyses were performed to explore the robustness of the pooled results both by removing each eligible study serially and removing the eligible studies with low methodological quality [29].

Results

Search Results

A total of 4,875 studies were initially retrieved through the systematic search described above, and 846 of which were duplicates. After reviewing abstracts, 85 full-text articles were shortlisted for the eligibility assessment. Among the 85 full-text articles, 23 were excluded for not reporting the prevalence of moderate to severe anxiety symptoms in MI, 21 were excluded for neither using a validated self-report questionnaire to assess moderate to high anxiety symptoms nor diagnosing by clinicians, 8 were excluded for a sample size of less than 200 and 15 were excluded for repeated data. Finally, 18 eligible articles were included in this meta-analysis (Fig. 1).

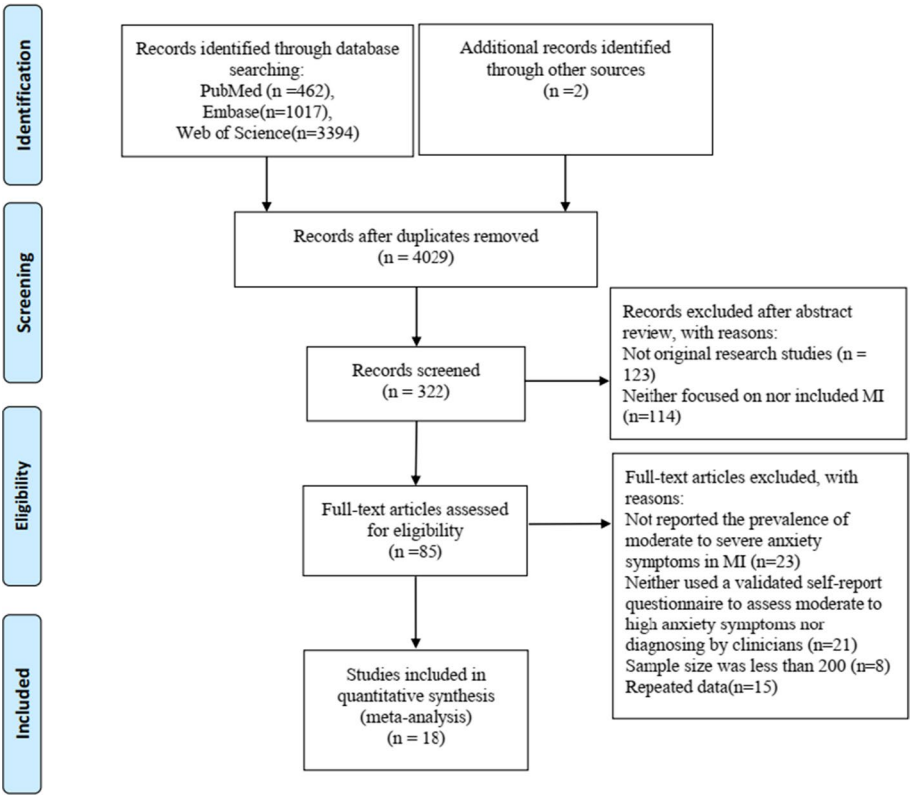

Fig. 1 PRISMA flow chart of study selection

Study Characteristics

The characteristics of the 18 eligible studies were shown in Table 1, and the reference list of the 18 eligible studies was shown in the Additional file 2. They were published from 1996 to 2020 and conducted in 14 countries including Canada, United Kingdom (UK), Netherlands, Australia, Japan, South Korea, United States of America (USA), Norway, Sweden, Pakistan, Iran, Denmark, German, and China. Fifteen of the 18 eligible studies were longitudinal studies, 2 were cross-sectional studies, and 1 was a case-control study. Furthermore, 17 were hospital-based, and 1 was population-based.

In terms of the instrument used to assess anxiety, 4 identified moderate to severe anxiety symptoms using the Spielberger's State-Trait Anxiety Inventory (STAI), 4 using the anxiety subscale of Hospital Anxiety and Depression Scale (HADS), 2 using the anxiety subscale of Brief Symptom Inventory (BSI), 1 using the Hamilton Anxiety Rating Scale (HARS), 1 using the anxiety subscale of 90-item Symptom Check List (SCL-90), 1 using the of the phobic anxiety subscale of Middlesex Hospital Questionnaire (MHQ), 1 using Beck Anxiety Inventory (BAI), 1 using the anxiety subscale of Multiple Affect Adjective Checklist (MAACL), 1 using the Generalized Anxiety Disorder scale (GAD-7), 1 using used the Spielberg state anxiety questionnaire, and 1 using the Zung Self-Rating Anxiety Scale (SAS).

Table 1 Characteristics of the 18 eligible studies

First author	Publication year	Country	Study design	Sample source	Mean age (SD)	Male proportion (%)	Proportion of first-time MI (%)	Instrument and cutoff	**Type of anxiety**	Timing of anxiety assessment	Subjects with anxiety	Sample size	Prevalence
Crowe	1996	Canada	Longitudinal	Hospital-based	61	87	84	STAI-trait anxiety subscale > 41 or state anxiety subscale > 42	NR	Average 3 days (range:2–14 days) after MI	543	785	69.17
Mayou	2000	UK	Longitudinal	Hospital-based	63.16	73	NR	HADS-A subscale ≥ 8	NR	within the first 3 days after admission	130	346	37.6
Lane	2001	UK	Longitudinal	Hospital-based CCU	62.7 (11.5)	74.7	78.4	STAI- state anxiety subscale ≥ 40	State anxiety	Average 6 days (range:2–15 days) after MI	75	288	26.0
Strik	2003	Netherlands	Longitudinal	Hospital-based	58(11)	100	100	SCL-90-anxiety subscale ≥ 2	NR	one month after MI at home or during the first post-MI visit	185	318	58.2
De Jong	2004	Australia,UK, Japan, South Korea and USA	Longitudinal	Hospital-based	61(13)	72.1	78.9	BSI-anxiety subscale ≥ 0.35	Compare with healthy adults	Mean53 (within 72 h of hospital admission)	421	912	46.2

Table 1 (continued)

First author	Publication year	Country	Study design	Sample source	Mean age (SD)	Male proportion (%)	Proportion of first-time MI (%)	Instrument and cutoff	**Type of anxiety**	Timing of anxiety assessment	Subjects with anxiety	Sample size	Prevalence
Grace	2004	Canada	Longitudinal	Hospital-based CCU	61.9 (12.0)	64.8	NR	MHQ-phobic anxiety subscale ≥ 4	Phobic anxiety	2–5 days of hospitalization	157	479	32.8
Moser	2007	USA and Australia	Longitudinal	Hospital-based CCU	62 (14)	66	73	BSI-anxiety subscale ≥ 0.35	State anxiety Compare with healthy adults	Within 72 h in hospital	262	536	48.9
Hanssen	2009	Norway	Longitudinal	Hospital-based	60.2 (12.0)	80.9	88.5	HADS-A subscale ≥ 8	NR	1 week after discharge	48	244	19.7
Kuhl	2009	USA	Longitudinal	Hospital-based	NR	57	60.0	BAI ≥ 10	NR	3–5 days after MI	119	278	42.8
Johansson	2010	Sweden	Longitudinal	Hospital-based CCU	64 (10)	70	76.6	HADS-A Subscale ≥ 8	NR	During the first week in hospital	51	204	25.0
Khan	2010	Pakistan	Case-control	Hospital-based CCU	59	69	100	HADS-A Subscale ≥ 18	NR	2–4 days after MI	115	200	57.5
Moser	2010	USA	Cross-sectional	Hospital-based	65.8 (7.2)	86.6	NR	MAACL-anxiety subscale ≥ 7	State anxiety	≥ 3 months after hospitalization	128	298	43.0
Hosseini	2011	Iran	Longitudinal	Hospital-based CCU	58 (12.2)	69.0	86.9	STAI-state anxiety subscale ≥ 40	State anxiety	Within 15 days after MI	556	806	69.0

Table 1 (continued)

First author	Publication year	Country	Study design	Sample source	Mean age (SD)	Male proportion (%)	Proportion of first-time MI (%)	Instrument and cutoff	**Type of anxiety**	Timing of anxiety assessment	Subjects with anxiety	Sample size	Prevalence
Roest	2014	Netherlands	Longitudinal	Hospital-based	59 (11.4)	81.1	84.4	HARS ≥ 18	Psychological (i.e., Items 1–6, and 14) and somatic (i.e., Items 7–13) anxiety	2 months after MI	40	418	9.6
Hosseini	2014	Iran	Longitudinal	Hospital-based CCU	59.1 (12.03)	69.1	86.3	STAI-state anxiety subscale anxiety ≥ 40	State anxiety	Average 6 days (range:2–15 days) after MI	145	285	50.9
Larsen	2014	Denmark	Longitudinal	Population-based	67.0 (11.6)	69.2	100	HADS-A Subscale ≥ 8	NR	12–14 weeks after discharge	211	896	23.6
Fang	2018	German	Cross-sectional	Hospital-based CCU	62.50 (12.15)	73.83	NR	GAD-7 ≥ 10	Generalized anxiety disorder	NR	71	619	11.5

Table 1 (continued)

First author	Publication year	Country	Study design	Sample source	Mean age (SD)	Male proportion (%)	Proportion of first-time MI (%)	Instrument and cutoff	**Type of anxiety**	Timing of anxiety assessment	Subjects with anxiety	Sample size	Prevalence
He	2020	China	Longitudinal	Hospital-based	63.7(12.9)	41.9	NR	Zung Self-Rating Anxiety Scale (SAS), Scores ≥ 50	NR	Within 7 days of coronary angiography	186	620	30.0

SD standard deviation, *NR* not reported, *MI* myocardial infarction, *STAI* Spielberger's State-Trait Anxiety Inventory, *HADS* Hospital Anxiety and Depression Scale, *SCL-90* 90-item Symptom Check List, *BSI* Brief Symptom Inventory, *BAI* Beck Anxiety Inventory, *MAACL* Multiple Affect Adjective Checklist, *HARS* Hamilton Anxiety Rating Scale, *SAS* Zung Self-Rating Anxiety Scale, *GAD-7* Generalized; Anxiety Disorder scale, *MHQ* Middlesex Hospital Questionnaire

For most eligible studies, anxiety was assessed during their hospitalization. The sample mean age varied from 58 to 67 years, the sample proportion of male subjects varied from 41.9% to 100%, and the sample proportion of subjects with first-time MI varied from 60% to 100% across the 18 eligible studies.

Regarding the methodological quality assessment, the total score ranged from 3 to 7 points across the 18 eligible studies, with 1 scoring 7 points, 10 scoring 5 points, 5 scoring 4 points and 2 scoring 3 points, respectively. Only one eligible study was population-based and the study subjects was regarded as a whole population with an unbiased sampling frame. For all eligible studies, anxiety was assessed by standard instruments, and 11 recruited a sample size of more than 300 (Table 2).

Pooled Prevalence of Moderate to Severe Anxiety Symptoms among MI Patients

The 18 eligible studies covered a total of 8,532 MI patients and 3,443 of them were identified with moderate to severe anxiety symptoms. Between-study heterogeneity was significant and high (I^2=98.8%, $P<0.05$) across the 18 eligible studies with the reported prevalence ranging from 9.6% to 69.17%. The lowest prevalence was reported in a hospital-based study in Netherlands in 2014 [33], and the highest prevalence was reported in a hospital-based study in Canada in 1996 which used the STAI to assess anxiety [6]. The

Table 2 Methodological quality assessment of the 18 eligible studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Total score
Crowe 1996	0	0	1	1	0	1	1	1	5
Mayou 2000	0	0	1	1	0	1	1	1	5
Lane 2001	0	0	0	1	1	0	1	1	4
Strik 2003	0	0	1	1	0	1	1	1	5
De Jong 2004	0	0	1	1	1	0	1	1	5
Grace 2004	0	0	1	1	0	1	1	1	5
Moser 2007	0	0	1	1	0	1	1	1	5
Hanssen 2009	0	0	0	1	0	1	1	1	4
Kuhl 2009	0	0	0	1	0	1	1	1	4
Johansson 2010	0	0	0	1	0	1	1	1	4
Khan 2010	0	0	0	1	0	0	1	1	3
Moser 2010	0	0	0	1	0	0	1	1	3
Hosseini 2011	0	0	1	1	0	1	1	1	5
Roest 2014	0	0	1	1	0	1	1	1	5
Hosseini 2014	0	0	0	1	0	1	1	1	4
Larsen 2014	1	1	1	1	0	1	1	1	7
Fang 2018	0	0	1	1	0	1	1	1	5
He 2020	0	0	1	1	0	1	1	1	5

Q1: Random sample or whole population; Q2: Unbiased sampling frame (i.e., census data); Q3: Adequate sample size (>300 subjects); Q4: Measures were the standard; Q5: Outcomes measured by unbiased assessors; Q6: Adequate response rate (70%), refusers described; Q7: Confidence intervals, subgroup analysis; Q8: Study subjects described

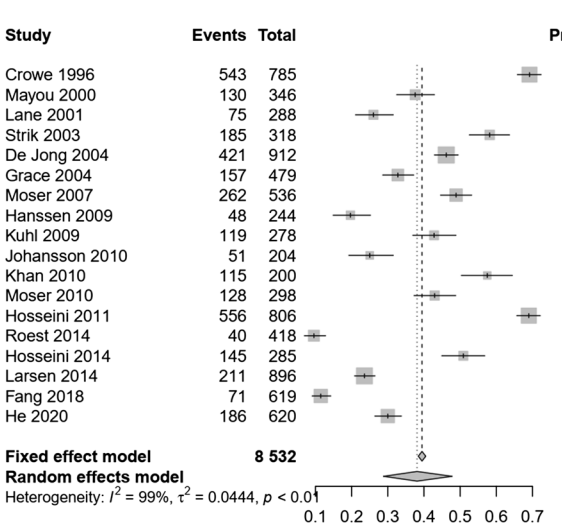

Fig. 2 Forest plot presenting the pooled prevalence of moderate to severe anxiety symptoms among MI patients

pooled prevalence of moderate to severe anxiety symptoms among MI patients was 38.08% (95% confidence interval [CI]: 28.82–47.81%) by a random-effects model (Fig. 2).

Meta-Regression Analyses

The results of meta-regression analyses were shown in Table 3. Mean age of subjects ($\beta = -0.030$, $P = 0.101$), proportion of male subjects ($\beta = 0.214$, $P = 0.584$), proportion of subjects with first-time MI ($\beta = 0.170$, $P = 0.755$), quality assessment score ($\beta = -0.036$, $P = 0.500$), study design ($\beta = -0.046$, $P = 0.525$), and sample source ($\beta = -0.168$, $P = 0.409$) were not moderators contributing significantly to the

Table 3 Meta-regression analyses of the contribution of possible moderators to the overall heterogeneity

	Number of included studies	β	Standard error	Z value	P value	tau^2
Publication year	18	−0.014	0.007	−2.041	0.041	0.032
Mean age of subjects, years	18	−0.030	0.018	−1.641	0.101	0.036
Proportion of male subjects	18	0.214	0.390	0.548	0.584	0.040
Proportion of subjects with first-time MI	13	0.170	0.545	0.312	0.755	0.047
Quality assessment score	18	−0.036	0.053	−0.674	0.500	0.039
Study design	18	-0.046	0.073	-0.636	0.525	0.039
Sample source	18	−0.168	0.203	−0.825	0.409	0.039

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heterogeneity, while publication year ($\beta = -0.014$, $P = 0.041$) was significant moderators which contributed 16.11% to the heterogeneity, respectively.

Subgroup Analyses

The results of subgroup analyses were shown in Table 4. The pooled prevalence of moderate to severe anxiety symptoms among studies from Europe/UK, North America/Australia, and Asia was 25.23% (95CI%: 15.70–36.14%), 47.40% (95%CI: 33.50-61.52%), and 51.81% (95CI%: 31.75–71.57%), respectively. The pooled prevalence among studies that used STAI, the anxiety subscale of HADS, and the anxiety subscale of BSI to assess anxiety was 53.90% (95CI%: 35.87–71.43%), 26.25% (95CI%: 19.36–33.78%), and 47.17% (95CI%: 4.46–49.74%), respectively. The pooled prevalence among female and male subjects was 47.02% (95CI%: 26.68–67.89%) and 40.71% (95CI%: 24.49–58.03%), respectively. Furthermore, the pooled prevalence among subjects with and without a history of previous MI was 62.33% (95CI%: 37.57–84.15%) and 54.96% (95CI%: 32.31–76.58%), respectively. Between-study heterogeneity was high among studies included in most of the subgroups. Nonetheless, studies using the anxiety subscale of BSI to assess anxiety were homogenous (I^2=0.0, $P = 0.317$).

The pooled prevalence of moderate to severe anxiety symptoms varied significantly in terms of geographic region, instrument used to assess anxiety, methodological quality, sex, education level, a history of previous MI and hypercholesterolemia ($P < 0.05$). In particular, the pooled prevalence was significantly higher among studies from North America/Australia and Asia (vs. studies from Europe/UK), among studies with low methodological quality (vs. studies with moderate to high methodological quality, among studies using STAI to assess anxiety (vs. studies using the anxiety subscale of HADS, and studies using the anxiety subscale of BSI, respectively), among female subjects (vs. male subjects), among subjects with education level of below secondary school (vs. subjects with education level of secondary school or above), among subjects with a history of previous MI (vs. subjects without a history of previous MI), and among subjects with hypercholesterolemia (vs. subjects without hypercholesterolemia).

Publication Bias and Sensitivity Analysis

Publication bias was not observed in this meta-analysis based on the findings of Egger's linear test ($t = -0.630$, $P = 0.538$) and Begg's rank test ($z = -0.190$, $P = 0.850$) and the funnel plot was symmetrical (Fig. 3).

By removing the 18 eligible studies one-by-one, the pooled results varied from 36.26% (95CI%: 27.51–45.49%) to 40.10% (95CI%: 30.99–49.56%), and the I^2 statistic values varied from 98.6% to 98.9%. In particular, by removing the only one population-based study, the pooled result was 39.00% (95CI%: 29.28–49.17%) and the I^2 statistic value was 98.8%, and by removing the only one study which included exclusively male subjects, the pooled result was 36.93% (95CI%: 27.45–46.95%) and the I^2 statistic value was 98.8%. Furthermore, by excluding 2 eligible studies with low methodological quality, the pooled prevalence decreased from 38.08% (95% CI: 28.82–47.81%) to 36.62% (95%CI: 26.71–47.14%), and the I^2 statistic value was 98.9%.

Table 4 Subgroup analyses on the prevalence of anxiety among patients with myocardial infarction

Subgroup	Category	Number of included studies	Number of subjects with anxiety	Sample size	Pooled prevalence (95% CI) (%)	Heterogeneity test		χ^2test	
						I^2value (%)	*P* value	χ^2value	*P* value
Geographic region[a]	Europe/UK	8	811	3333	25.23 (15.70–36.14)	97.9	< 0.001		
	North America/Australia	5	1209	2376	47.40 (33.50–61.52)	97.9	< 0.001	436.23	< 0.001
	Asia	4	1002	1911	51.81 (31.75–71.57)	98.7	< 0.001	422.77	< 0.001
Methodological quality	Low	2	243	498	50.08 (35.97–64.19)	90.1	0.002	15.286	< 0.001
	Moderate to high	16	3200	8034	36.62 (26.71–47.14)	98.9	< 0.001		
Instrument used to assess anxiety[b]	STAI	4	1319	2164	53.90(35.87–71.43)	98.5	< 0.001		
	HADS	4	440	1690	26.25 (19.36–33.78)	90.0	< 0.001	464.89	< 0.001
	BSI	2	683	1448	47.17 (4.46–49.74)	0.0	0.317	66.154	< 0.001
Sex	Female	6	543	1160	47.02(26.68–67.89)	98.1	< 0.001	5.242	0.022
	Male	7	981	2300	40.71 (24.49–58.03)	98.6	< 0.001		
Living alone	Yes	2	55	243	28.68 (4.62–62.23)	95.5	< 0.001	0.421	0.516
	No	2	135	654	24.07 (1.82–60.08)	98.8	< 0.001		
Education level	≥ Secondary school and above	3	226	589	37.83 (5.38–78.47)	99.0	< 0.001	15.430	< 0.001
	< Secondary school	3	529	1094	44.19 (9.75–82.28)	99.4	< 0.001		
A history of previous MI	Yes	3	182	299	62.33 (37.57–84.15)	94.1	< 0.001	12.695	< 0.001
	No	7	1407	2812	54.96 (32.31–76.58)	99.3	< 0.001		
Current smoking	Yes	5	364	689	50.54 (37.98–63.07)	90.8	0.011	0.374	0.541
	No	5	827	1611	49.75 (31.59–67.95)	98.1	< 0.001		
Diabetes	Yes	6	339	625	55.39 (40.81–69.52)	92.1	< 0.001	2.746	0.097
	No	5	1114	2211	48.91 (36.16–61.72)	97.3	< 0.001		
Hypertension	Yes	6	665	1262	55.07 (38.95–70.67)	97.0	< 0.001	1.836	0.175
	No	6	788	1574	46.26 (34.15–58.58)	95.7	< 0.001		
Hypercholesterolemia	Yes	4	394	677	56.23 (32.32–78.72)	97.4	< 0.001	16.019	< 0.001
	No	4	651	1338	46.74 (28.54–65.39)	97.8	< 0.001		

CI Confidence Interval; *MI* Myocardial Infarction

[a] Europe/UK was the reference group, [b] STAI was the reference group

Discussion

Main Findings

This meta-analysis synthesized the evidence on the prevalence of moderate to severe anxiety symptoms among MI patients. Eighteen eligible studies conducted in 14 countries with a total of 8,532 MI patients were included, of which 3,443 were identified with moderate to severe anxiety symptoms. The reported prevalence ranged markedly from 9.6% to 69.17% across the 18 eligible studies, and the pooled prevalence of moderate to severe anxiety symptoms among MI patients was 38.08% (95%CI: 28.82–47.81%) by a random-effects model. To the best of our knowledge, this is the first meta-analysis to explore the pooled prevalence of moderate to severe anxiety symptoms among MI patients.

This study suggested that the pooled prevalence of moderate to severe anxiety symptoms among MI patients (38.08%, 95%CI: 28.82–47.81%) was lower than that among patients with heart failure (55.5%, 95% CI: 48.08–62.83%) [34], but higher than that among patients with many other somatic diseases such as osteoarthritis (21.3%, 95%CI: 15.5–28.5%) [35], prostate cancer (27.04%, 95%CI: 24.26–30.01%) [36], and multiple sclerosis (34.2%, 95%CI: 23.2–47.1%) [37]. Based on the high pooled prevalence of moderate to severe anxiety symptoms in MI and the potential role of increased anxiety symptoms in subsequent adverse outcomes among MI patients, it is highly recommended for researchers, clinicians and policy-makers to take effective measures to screen anxiety symptoms at an early stage after MI and implement psychological interventions for those with elevated anxiety symptoms accordingly.

When examining the study-level characteristics, subgroup analyses suggested that the pooled prevalence of moderate to severe anxiety symptoms in MI differed significantly by geographic region and methodological quality, which were in line with many previous meta-analyses with similar topic [37–39]. For example, Boeschoten et al. [37] conducted a meta-analysis exploring the pooled prevalence of depression among patients with multiple sclerosis and found that it was lower among studies from Europe. The varying socioeconomic level and sociocultural background may contribute largely to the regional disparity in anxiety prevalence. Additionally, it has been well established that methodological quality of the individual studies plays an important role in the stability of the pooled results [40]. In particular, studies with low methodological quality often employ biased sampling strategies with limited sample sizes, thus inducing various types of selection bias and ultimately overestimate the pooled effect size [41]. Therefore, it is recommended for future studies to employ unbiased sampling strategies with large sample sizes (e.g., recruiting subjects from the whole population with a sample size of >300).

Consistent with previous meta-analyses exploring the pooled prevalence of anxiety [38, 42], this study showed that the pooled prevalence of moderate to severe anxiety symptoms in MI differed significantly by sample socio-demographic characteristics including sex and education level, which could be explained by the sex differences in psychosocial, personalistic and behavioral factors, such as coping strategies, social support, personality traits, and resilience, as well as the sex differences in hormone levels and the varying utilization of neural resources in response to stress between males and females [43–45]. Therefore, when allocating psychological resources targeting anxiety following MI, sex and education level should be taken into consideration. In particular, female subjects or those with education level of below secondary school should be given special attention.

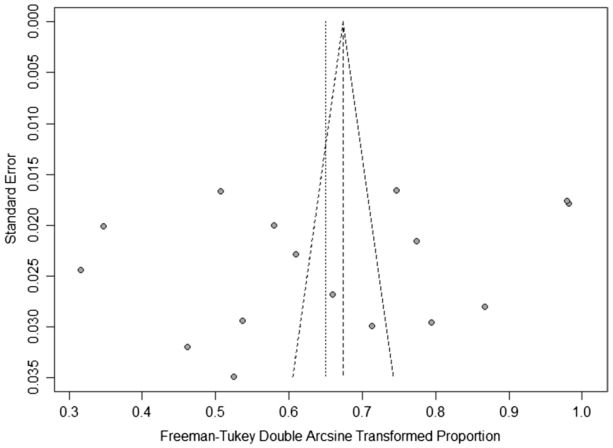

Fig. 3 Funnel plot of the 18 eligible studies in these meta-analyses

Additionally, this study showed that the pooled prevalence of moderate to severe anxiety symptoms varied significantly in terms of the instrument used to assess anxiety. Similar findings were observed in previous meta-analyses exploring the pooled prevalence of anxiety among patients with systemic lupus erythematosus and adults with traumatic brain injury [46, 47]. The varying psychometric quality and cut-off values, as well as the different conceptual and operational definitions of anxiety across the self-repot instruments used to assess anxiety could account for the disparate findings seen, suggesting the need for standardizing the measurement of moderate to severe anxiety symptoms among MI patients.

With regard to MI-related factors and cardiovascular risk factors, this study found that those with a history of previous MI and hypercholesterolemia exhibited higher pooled prevalence of moderate to severe anxiety symptoms than their counterparts. Similar findings were observed in a prior meta-analysis exploring the pooled prevalence of depression among MI patients [39]. MI is a serious disease with poor health-related outcomes such as heart failure and sudden cardiac death, and those with recurrent MI or comorbid with other diseases may exhibit higher risk for adverse cardiac events [48, 49], as a consequence of which, adverse psychological outcomes including depression and anxiety are more likely to occur. These findings significantly stressed the need for researchers, clinicians and policymakers to pay special attention to those with a history of previous MI and hypercholesterolemia when allocating psychological resources targeting anxiety following MI.

In terms of the source of heterogeneity, meta-regression analyses showed that publication year was a significant moderator contributing 16.11% to the heterogeneity, and subgroup analyses showed that studies using the anxiety subscale of BSI to assess anxiety were homogenous. These findings suggested that when evaluating and comparing the prevalence of moderate to severe anxiety symptoms in MI across multiple publications, the differences in publication year, instrument used to assess anxiety should be considered.

Strengths and Limitations

Some limitations should be noted. Firstly, the overall heterogeneity was high across the 18 eligible studies. However, the absence of publication bias and low sensitivity of the pooled results, as well as the identified role of publication year and instrument used to

assess anxiety, could add great reliability when interpreting the findings of this meta-analysis. Secondly, though some individual studies showed that the timing of anxiety assessment and a history of previous psychiatric disorder were associated with the prevalence of anxiety in MI [20, 21, 23], relevant data were unable to be synthesized either due to the varying indicators or due to the limited number of studies reporting such data. Therefore, future studies should find more factors which may contribute to the anxiety prevalence among MI patients and measuring such data using consistently standardized indicators. Thirdly, it should be stressed here that regarding the sample source, all but one eligible study was hospital-based. Therefore, whether the findings of this study could be generalized into population-based studies should be further explored on the condition of the presence of an adequate number of population-based studies. Nonetheless, in a prior meta-analysis exploring the pooled prevalence of anxiety following spinal cord injury, it was found that sample source did not affect the pooled results significantly [50]. Furthermore, since the disparities in all subgroups was tested univariately without controlling potential confounders, relevant findings should be interpreted with caution.

Conclusions

Anxiety is common among MI patients with nearly two fifth suffering from moderate to severe anxiety symptoms. The reported prevalence of moderate to severe anxiety symptoms is highly heterogenous across the eligible studies, which could be partially explained by publication year and the instrument used to assess anxiety. Additionally, the pooled prevalence of moderate to severe anxiety symptoms varied significantly by geographic region, instrument used to assess anxiety, methodological quality, sex, education level, a history of previous MI and hypercholesterolemia, stressing the need for researchers, clinicians and policy-makers to take the preceding factors into account when comparing the prevalence of moderate to severe anxiety symptoms in MI across multiple publications and allocating psychological resources targeting anxiety among MI patients. Future efforts should work towards exploring more factors affecting anxiety and standardizing the measurement of moderate to severe anxiety symptoms among MI patients. Furthermore, more population-based studies with high methodological quality are warranted.

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Data Availability All data generated or analyzed during this study are included in this article.

Declarations

Ethics Approval and Consent to Participate Not applicable.

Consent for Publication Not applicable.

Conflict of Interest The authors declare that they have no conflict of interest.

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Yajun Lian, MD is a general practitioner in Heping Hospital Affiliated to Changzhi Medical College, Changzhi, Shanxi, China.

Jingsha Xiang, MM is a master student in Xiangya School of Public Health, Central South University, Changsha, Hunan, China.

Xiaoyan Wang, MD is a sonographer in Heping Hospital Affiliated to Changzhi Medical College, Changzhi, Shanxi, China.

Atipatsa C Kaminga, MD is a PhD student in Xiangya School of Public Health, Central South University, Changsha, Hunan, China.

Wenhang Chen, MD is a nephrophysician in Xiangya Hospital, Central South University, Changsha, China.

Zhiwei Lai, MM is a Public health practitioner in Hunan Provincial Center for Disease Control and Prevention, Changsha, Hunan, China.

Wenjie Dai, MD is a lecturer in Xiangya School of Public Health, Central South University, Changsha, Hunan, China.

Jianzhou Yang, MD is a professor in Changzhi Medical College, Changzhi, Shanxi, China.

Authors and Affiliations

Yajun Lian[1] · Jingsha Xiang[2,3] · Xiaoyan Wang[4] · Atipatsa C. Kaminga[2,3,5] · Wenhang Chen[6] · Zhiwei Lai[7] · Wenjie Dai[2,3] · Jianzhou Yang[8]

1 Department of General Practice, Heping Hospital Affiliated to Changzhi Medical College, Changzhi, Shanxi, China

2 Department of Epidemiology and Health Statistics, Xiangya School of Public Health, Central South University, Changsha, Hunan, China

3 Hunan Provincial Key Laboratory of Clinical Epidemiology, Changsha, Hunan, China

4 Department of Ultrasound, Heping Hospital Affiliated to Changzhi Medical College, Changzhi, Shanxi, China

5 Department of Mathematics and Statistics, Mzuzu University, Mzuzu, Malawi

6 Department of Nephrology, Xiangya Hospital, Central South University, Changsha, China

7 Immune Planning Division, Hunan Provincial Center for Disease Control and Prevention, Changsha, Hunan, China

8 Department of Preventive Medicine, Changzhi Medical College, Changzhi, Shanxi, China