Original Article

# Systematic review and meta-analysis of psychological intervention on patients with coronary heart disease

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**Background:** Coronary heart disease is both a physical and mental disease, so psychological intervention can be used as part of a general cardiac rehabilitation plan. This study aimed to evaluate the effect of psychological intervention on the negative psychology of patients with coronary heart disease.

**Methods:** Multiple databases like PubMed, Embase, Web of Science, and Cochrane Library were used to search for the relevant studies, and full-text articles involved in the evaluation of psychological intervention versus usual care for patients with coronary heart disease. Review Manager 5.4 (The Cochrane Collaboration, Software Update, Oxford, 2020) was adopted to estimate the effects of the results among selected articles. Forest plots, sensitivity analysis, and bias analysis were also performed on the included articles.

**Results:** There were 17 studies that eventually met the final inclusion criteria. There were significant differences in anxiety level [mean difference (MD) –4.53; 95% confidence interval (CI), –6.36 to –2.7; P<0.00001; $I^2$=96%], depression level (MD–3.43; 95% CI, –4.85 to –2.01; P<0.00001; $I^2$=96%), and stress level (MD –4.19; 95% CI, –6.86 to –1.52; P<0.00001; $I^2$=94%), but no difference was found for total mortality (P=0.50).

**Conclusions:** This study indicated that psychological intervention has important health benefits for patients with coronary heart disease and can effectively reduce negative psychological effects such as depression, anxiety, and stress. However, the results need to be further confirmed due to the limitations.

**Keywords:** Psychological intervention; usual care; coronary heart disease; meta-analysis

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## Introduction

Coronary heart disease is a cardiovascular disease with a high incidence rate in clinic. The prevalence of coronary heart disease continues to rise, especially in the elderly, the prevalence over 60 years old is more than 30%. The symptoms of coronary heart disease mainly depend on the degree of ischemia involving the heart (1). Plaque composed of cholesterol and other deposits accumulate in the coronary artery wall, which can lead to coronary artery stenosis or occlusion, and then lead to coronary heart disease. Generally, when the diameter of coronary artery stenosis is more than 75%, angina pectoris, arrhythmia, and even sudden death can occur (2). It seriously threatens the physical and mental health of patients, and reduces their quality of life (3).

At present, coronary heart disease is recognized as a psychosomatic disease, bad emotional stimulation can cause anxiety, tension, fear and other emotional changes in patients, thus affecting the conduction velocity of the

heart, and then lead to coronary heart disease, social and psychological factors play an important role in its occurrence, development, rehabilitation, and prognosis (4,5). It has been reported that 55.3% of patients with coronary heart disease have different degrees of negative psychology. For example, anxiety and depression are important factors affecting the occurrence, development, treatment, and rehabilitation of coronary heart disease (6). Therefore, in addition to physical therapy, psychological intervention should be given to eliminate negative psychology and to help patients increase confidence to overcome the disease, so they can recover as soon as possible (7,8).

From Menninger's research on the relationship between mental state and physiology to Friedman's attempt to identify the individual characteristics of diseases by analyzing the relationship between psychological attributes and physical diseases, the relationship between psychology and physiology is a field that scientists throughout the 20th century have been trying to better understand (9-11). Huffman et al. proposed that positive psychological intervention exercises may have a positive impact on the prognosis of patients with coronary heart disease (12).

Randomized controlled trials of psychological intervention for patients with coronary heart disease have been conducted all over the world (13-15). However, due to the limitations of sample size, region, and research object, the conclusions of single studies require verification and cannot be used to form the basis of evidence for guiding clinical practice. In short, the effect of psychological intervention on improving anxiety and depression in patients with coronary heart disease remains unclear.

In order to clarify the negative emotional impact of psychological interventions on patients with coronary heart disease, we collected relevant research reports and conducted meta-analysis for the purpose of increasing the sample size, improving test efficiency, and providing evidence-based guidance for clinical practice. We present the following article in accordance with the PRISMA reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1623).

## Methods

### *Literature search strategy*

Electronic databases including PubMed, Embase, Web of Science, and Cochrane Library were systematically searched for eligible studies from January 2000 to April 2021. The following keywords were used: (I) *psychological intervention*, (II) *usual care*, (III) *coronary heart disease*. These keywords were used in combination with the Boolean operator "AND" to search the literature. No restrictions on the publication language were set in the literature retrieval. In order to maximize the specificity and sensitivity of the search, the references of retrieved articles were also searched.

### *Study selection*

Potentially relevant articles were reviewed in full to ensure that all of the following inclusion criteria were satisfied:

(I) Research compared patients receiving psychological intervention and usual care;
(II) Patients had coronary heart disease or coronary artery disease;
(III) Articles contained indicators evaluating psychologically relevant effects between psychological intervention and usual care;
(IV) Psychological intervention had at least two core components: psychological and social support. Psychological factors included cognitive behavioral therapy, psychotherapy, counseling, supportive therapy or motivational interviewing, and social support factors included social skills training to develop social networks or minimize social isolation or conflict (family/work).
(V) Full text of articles was available in English.

Studies were excluded based on the following exclusion criteria:

(I) Research focused on other diseases;
(II) Comparisons were made between other interventions;
(III) Available data were lacking, and;
(IV) Articles were classified as a review, abstract, or duplicate publication.

### *Data extraction and quality assessment*

Teams of 2 reviewers independently screened all titles and abstracts identified by the literature search, obtained full-text articles of all potentially eligible studies, and evaluated them for eligibility. The following data from each eligible study were extracted: first author's name, patient's age and gender, country of origin, year of publication, sample size, study duration, time of follow-up, and primary outcome. The overall methodological quality was evaluated as moderate by the Cochrane bias risk assessment tool.

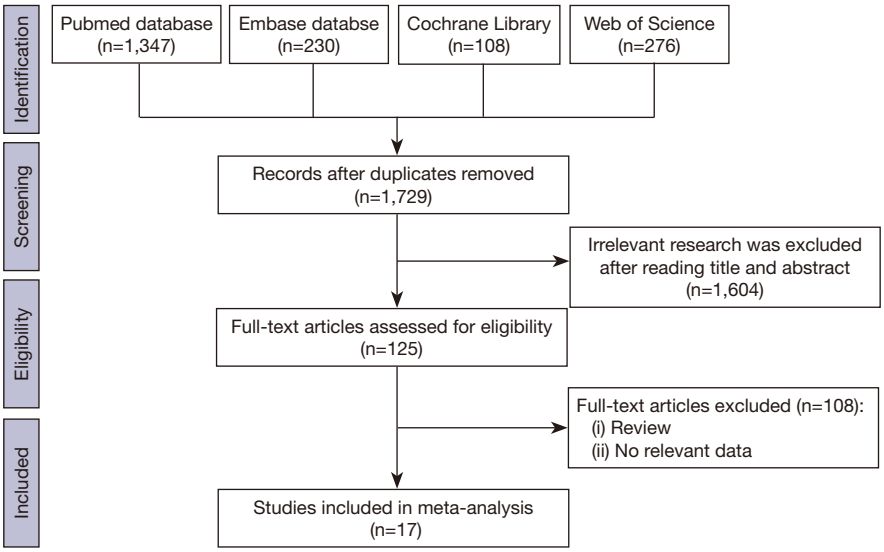


**Figure 1** Flow chart of the study selection process.

### *Statistical analysis*

Meta-analysis was performed with Review Manager 5.4 (The Cochrane Collaboration, Software Update, Oxford, 2020). Mean difference (MD) was used for measurement data, risk ratio (RR) was used for classification data, and 95% confidence interval (CI) was used for both types of indicators. Chi-square tests and $I^2$ statistics were used to test the heterogeneity. If $I^2$<50% and P<0.05, the homogeneity of the included literature was considered to be good, and the fixed effect model would be used; if $I^2$>50% or P≥0.05, heterogeneity was considered to exist between the studies, a random effects model would be used, with sensitivity analysis being conducted to evaluate the robustness of the results. Funnel plot and Egger rank correlation were used to identify any publication bias.

## Results

### *Search process*

The electronic searches provided a total of 1,729 citations after the removal of 232 duplicate records. After a careful reading of these articles, 1,604 studies were excluded because they did not meet the inclusion criteria. With consideration to the study design and insufficient data presented, 108 articles were rejected. Finally, 17 papers were selected for analysis (16-32). The literature search process, the inclusion and exclusion criteria, and the final sample size are illustrated in *Figure 1*.

### *Characteristics of included studies*

*Table 1* summarizes the characteristics of the 17 studies included in the meta-analysis. The years of publication were between 2003 and 2017. These studies contained a total of 4,198 patients (2,107 of whom received psychological intervention and 2,091 of whom received usual care). The primary outcomes consisted of the rate of total mortality, and scores for anxiety, depression, and stress.

### *Results of quality assessment*

Risk of bias assessment was performed at the study level, and a methodological quality assessment was performed using the Cochrane bias risk assessment tool. Only 2 studies showed selection bias, 2 studies showed performance bias, and 2 showed reporting bias. In terms of the bias summary, there was no high risk in detection bias, attrition bias, or other biases (*Figure 2*). *Figure 3* presents a summary of the risk of bias for each included study.

### *Results of heterogeneity test*

A total of 10 studies, comprising 379 intervention groups and 376 control groups, were found that reported anxiety scores. To analyze the differences in anxiety scores between these 2 groups, a meta-analysis was performed to calculate the overall MD using a random effects model in patients with coronary heart disease based on heterogeneity analysis.

**Table 1** Description of included studies

| Study | Country | No. patients | | Gender (M/F) | | Age | | Duration | Follow-up | Primary outcome* |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Intervention | Control | Intervention | Control | Intervention | Control | | | |
| Berkman 2003 | USA | 1,238 | 1,243 | 706/532 | 691/552 | 61±12.6 | 61±12.5 | October 1996 to April 2001 | 6 months | 2,4 |
| Barth 2005 | Germany | 27 | 32 | 22/5 | 23/9 | 60.81±11.06 | 50.62±10.05 | September 2002 to December 2003 | 4 weeks | 1,2 |
| McLaughlin 2005 | USA | 45 | 34 | – | – | 59.9±10.2 | 60.7±9.8 | September 2001 to August 2003 | 6 months | 1,2 |
| Michalsen 2005 | Germany | 48 | 53 | 38/10 | 40/13 | 59.0±8.7 | 59.8±8.6 | July 2001 to December 2001 | 12 months | 1,2,3 |
| Francois 2007 | Canada | 142 | 142 | 98/44 | 116/26 | 59.0±9.81 | 57.3±8.35 | May 2002 to March 2006 | 4 weeks | 2 |
| Koertge 2007 | Sweden | 119 | 128 | 0/119 | 0/128 | 61.36±9.10 | 62.73±8.72 | August 1996 and January 2000 | 1–2 years | 2,3,4 |
| Freedland 2009 | USA | 41 | 40 | 18/23 | 23/17 | 62±11 | 61±9 | December 2001 to August 2005 | 9 months | 1,2,3 |
| Neves 2009 | Portugal | 40 | 41 | 34/7 | 35/7 | 59.5±10.8 | 59.6±10.8 | – | 2 years | 3,4 |
| Merswolken 2011 | Sweden | 25 | 27 | 19/6 | 19/8 | 62.5±8.3 | 59.8±7.5 | May 2008 to December 2008 | 6 months | 1,2 |
| Schneider 2012 | USA | 99 | 102 | 58/41 | 57/45 | 59.9±10.7 | 58.4±10.5 | March 2004 to July 2007 | 5.4 years | 2,4 |
| Turner 2012 | Australia | 25 | 32 | 19/6 | 23/9 | 61±11 | 62±9 | June 2006 and May 2008 | 12 months | 1,2 |
| Roncella 2013 | Italy | 49 | 45 | 45/4 | 39/6 | 55±9 | 55±8 | June 2005 to January 2011 | 12 months | 2,3,4 |
| Mahdavi 2015 | Iran | 15 | 15 | – | – | – | – | October to November in 2015 | 8 weeks | 1,2,3 |
| Zhang 2015 | China | 50 | 50 | – | – | – | – | December 2012 to July 2014 | 6 months | 1,2 |
| Lv 2016 | China | 38 | 37 | 26/12 | 27/10 | 52.4±6.3 | 52.0±6.2 | January 2014 to May 2014 | 8 weeks | 1,2 |
| Nikrahan 2016 | Iran | 41 | 14 | 33/8 | 9/5 | 56.4±7.2 | 56.9±6.7 | – | 15 weeks | 2 |
| Fernandes 2017 | Portugal | 65 | 56 | 44/21 | 40/16 | 61.77±12.11 | 66.11±12.61 | – | 2 months | 1,2 |

*1: anxiety; 2: depression; 3: stress; 4: total mortality.

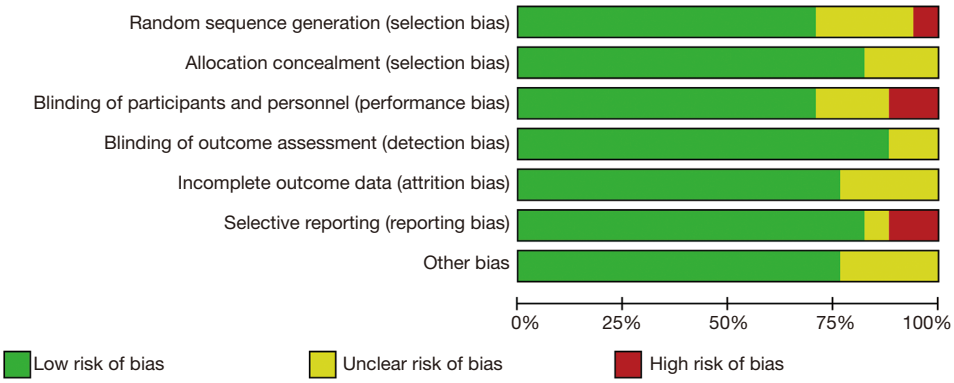


**Figure 2** Assessment of the quality of the included studies: low risk of bias (green), unclear risk of bias (yellow), and high risk of bias (red).

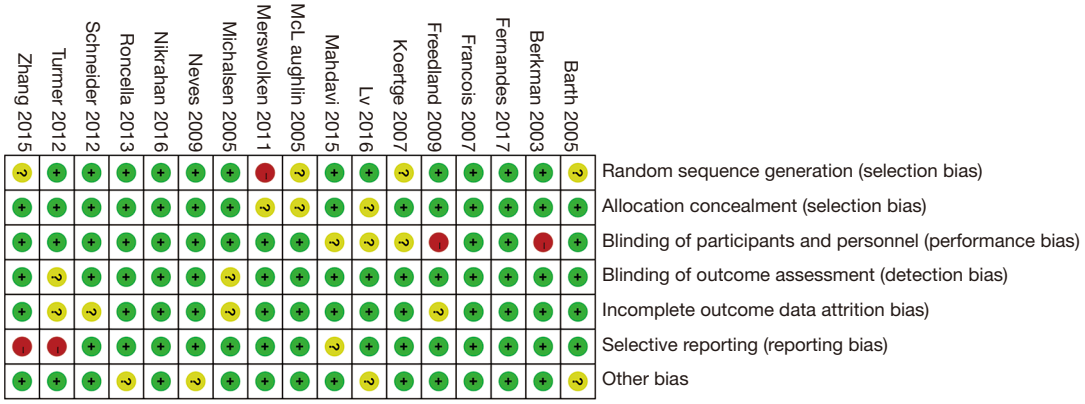


**Figure 3** Risk of bias summary of each included study.

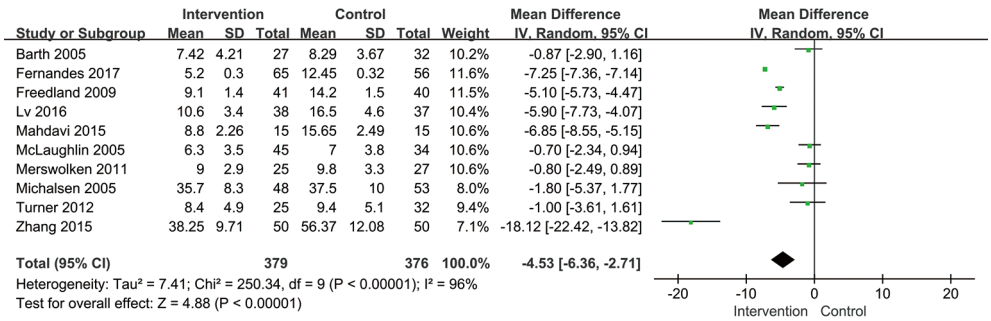


**Figure 4** Forest plot showing the mean difference of anxiety scores between psychological intervention versus usual care.

The MD was –4.53 (95% CI, –6.36 to –2.71; P<0.00001), and there was significant heterogeneity (P<0.00001; $I^2$=96%; *Figure 4*).

All but 1 included study reported a depression score. A random effects model was used to evaluate the heterogeneity of the depression scores, as there was significant heterogeneity among the included studies (P<0.00001, $I^2$=94%) (*Figure 5*). The results showed that the intervention group had a significantly lower level of depression than did the control group (MD =–3.43; 95% CI, –4.85 to –2.01; P<0.00001).

In the evaluation of differences in stress scores between

 

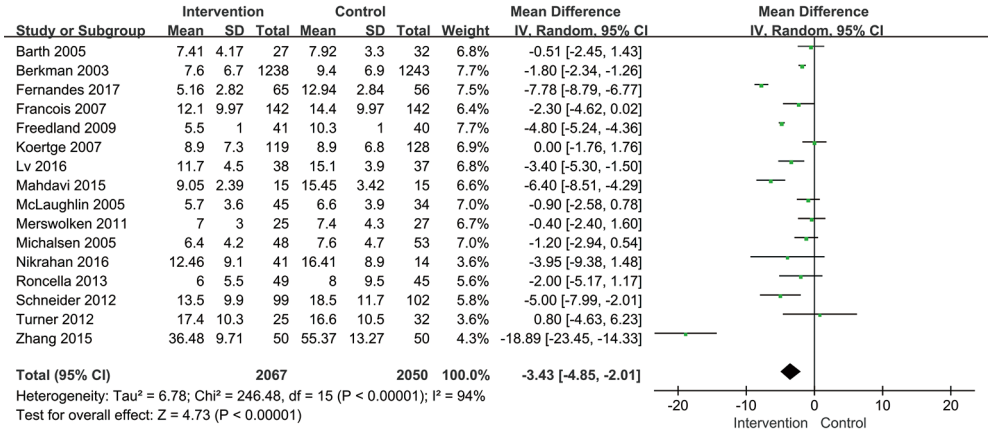


**Figure 5** Forest plot showing the mean difference of depression scores between psychological intervention versus usual care.

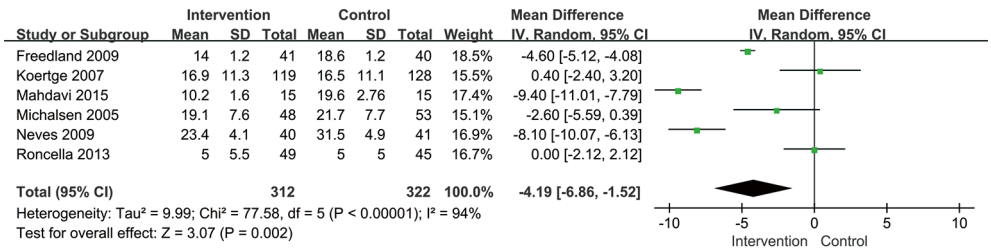


**Figure 6** Forest plot showing the mean difference of stress scores between psychological intervention versus usual care.

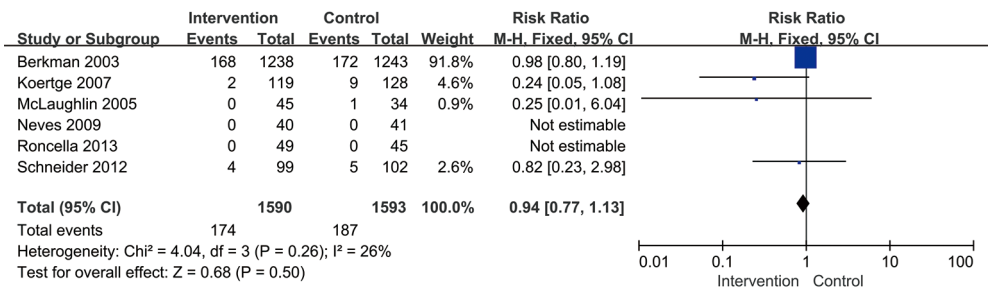


**Figure 7** Forest plot showing the risk ratio of total mortality between psychological intervention versus usual care.

the intervention group and the control group, 6 articles involving 634 patients were included. Meta-analysis showed that compared to the control group, the intervention group had a lower level of stress (MD = –4.19; 95% CI, –6.86 to –1.52; P=0.002, random effects model), with significant heterogeneity (P<0.00001; $I^2$=94%; *Figure 6*).

A total of 6 studies reported the rate of total mortality. The forest plot showed no significant differences between the intervention group and the control group (RR 0.94; 95% CI, 0.77–1.13; P=0.50, fixed effects model) and no significant heterogeneity among studies (P=0.26; $I^2$=26%; *Figure 7*).

### *Results of sensitivity analysis and publication bias*

A sensitivity analysis was carried out to evaluate the stability of the outcomes. The results of excluding a relative outlier showed that, for heterogeneity, $I^2$ for anxiety changed from 96% to 93% when the 2017 Fernandes study was removed (P=0.001), $I^2$ for depression changed from 94% to 92%

 

when the 2003 Berkman study was removed (P<0.001), and $I^2$ for stress changed from 94% to 91% when the 2105 Mahdavi study was removed (P=0.02). These results were not changed after sensitivity analysis, which indicated that the heterogeneity of these studies was relatively stable.

A funnel plot was performed to qualitatively evaluate the publication bias for 4 indexes. While the shape of the funnel plot showed some evidence of asymmetry, the Egger test was nonsignificant (anxiety P=0.72, depression P=0.79, stress P=0.45, total mortality P=0.28).

## Discussion

The rehabilitation of the heart requires multifaceted intervention, and aims to improve the health and quality of life for patients with coronary heart disease. The rehabilitation of the heart includes 3 core modes: education, exercise training, and psychological support (33,34). Related studies have proved that anxiety and depression are important factors that contribute to coronary heart disease (35,36). Under the influence of negative emotions such as anxiety, depression, and tension, the body's sympathetic excitability increases. This leads to increased adrenaline and adrenocortical hormone secretion, an accelerated heart rate, and even the inducement of arrhythmia (37). An excessive release of norepinephrine leads to vasoconstriction, increased blood pressure, increased myocardial oxygen consumption, angina pectoris, and even myocardial infarction (38).

With the transformation from a "biomedical model" to a "biological-psychological-social-medical model", it has been discovered that the occurrence of cardiovascular disease is closely related to psychosocial factors. Thus, the application of psychological intervention is an important measure in improving the quality of medical care. This is especially true for elderly patients who often have negative emotions, such as pessimism. Appropriate psychological intervention can achieve good results for those who are lonely with no dependence, and those with other basic diseases (39). Oranta's study evaluated the interpersonal counselling (IPC) implemented by a registered nurse on outcomes for depressive symptoms and distress in myocardial infarction patients. The results showed that in the IPC intervention group, depressive symptoms decreased from 37.3% to 20.4% at 6 months, and to 16.7% at 18 months, while distress decreased from 37.3% to 26.5% during the 6-month follow-up, and to 20.8% at 18 months (40).

A systematic review on the evaluation of clinical outcomes (such as death from myocardial infarction and heart failure) showed that there was a significant correlation between anxiety and health indicators of patients with heart disease in 5 studies, mild correlation in 3 studies, and no correlation in 4 studies (41). Roest *et al.* studied the relationship between anxiety and risk factors of coronary artery disease in a meta-analysis and found that anxiety was an independent risk factor of coronary heart disease and cardiac death (42). However, the association between anxiety and coronary heart disease was slightly lower than that found between depression and coronary heart disease, but this association was stronger than that found between irritable personality and coronary heart disease (4,43). A survey on the physiological and psychological symptoms of patients with anxiety disorder and coronary heart disease showed that anxiety was related to physical factors. Patients with anxiety disorder can have palpitations, facial anger and redness, abnormal heartbeat, muscle tension, and other physical symptoms when not performing any physical activity, increasing the risk of coronary heart disease (44). It has been suggested that positive psychological intervention may play an important role in the treatment of heart disease with anxiety (45). However, due to the differences in social and cultural background, the effect of positive psychological intervention varies across different countries or regions (46,47).

This study showed that compared with usual care, psychological intervention on patients with coronary heart disease can significantly improve patients' anxiety (P<0.00001), depression (P<0.00001), and stress scores (P=0.002). Although there was no strong evidence that psychological intervention can reduce total mortality in patients with coronary heart disease (P=0.50), a decrease in cardiac death (RR =0.94) in patients receiving intervention was observed. While this is not statistically significant, it may still have clinical importance. Specifically, scientific and rationally based psychological intervention can help patients with coronary heart disease have a positive and optimistic mood. This makes the endocrine system, autonomic nervous system, and immune system function optimally, enhancing the disease resistance ability of patients.

A number of limitations must be acknowledged here. The details of the intervention group and the control group were not well reported, which made it difficult to classify and compare the psychological intervention investigated in different studies. Researchers should pay more attention to the report of the test results and the description of the interventions provided. When the information is insufficient, the scalability and implementation of the positive results are affected. In addition, due to the lack of

 

results of psychological intervention on clinical efficacy, the meta-analysis did not examine the efficacy of psychological intervention on clinical results, which will be an important objective of future analysis.

In conclusion, psychological intervention has important health benefits for patients with coronary heart disease and can effectively reduce negative psychological effects such as depression, anxiety, and stress. However, due to the influence of bias and limitations, large-sample and multicenter randomized control trials are still needed in the future. Researchers must provide clearer reports on their methods and interventions. Moreover, further analysis of this subject using more or different research indicators should be carried out to verify the conclusions.

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## Footnote

*Reporting Checklist:* The authors have completed the PRISMA reporting checklist. Available at https://dx.doi.org/10.21037/apm-21-1623

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-1623). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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