Upregulated miR-328-3p and its high risk in atrial fibrillation
A systematic review and meta-analysis with meta-regression

Haitao Huang, MDa, Hao Chen, MDb, Xiao Liang, MDc, Xiuting Chen, MDa, Xiaoxin Chen, MDb, Can Chen, PhDa,*

Abstract
Background: Several studies have shown miR-328-3p increased in atrial fibrillation (AF), but some researches indicated no difference or even decreased. This inconsistent result confuses researchers, and it is urgent to know the truth. This study is to assess the association between miR-328-3p levels in plasma/atrial tissue and patients with AF.

Methods: PubMed, EMBASE, Scopus, Web of Science, and ProQuest were searched from inception to February 1, 2021. The standardized mean differences (SMD) with their 95% confidence interval (CI) were calculated to evaluate the association between miR-328-3p levels and AF.

Results: Twelve studies met the inclusion criteria and were used for our meta-analysis. Overall, the levels of miR-328-3p were higher in patients with AF than in the control group (SMD = 0.69, 95% CI [0.10, 1.28], P = .022). After adjustment, the overall SMD was 0.82 (95% CI [0.22, 1.42], P = .007). Sensitivity analysis indicated that the results were stable, and the trim-fill analysis showed that the results were credible. Subgroup analyses showed that AF patients, n ≥ 30, various of comorbidity, articles published earlier, and Asia groups had higher levels of expression of miR-328-3p.

Conclusions: High levels of miR-328-3p are significantly associated with an increased risk of AF. It implies that miR-328-3p played an important role in diagnosis and may serve as a potential momentous, and useful biomarker to identify AF.

Abbreviations: 95% CI = 95% confidence interval, AF = atrial fibrillation, NOS = The Newcastle-Ottawa Quality Assessment scale, SD = standard deviation, SMD = standardized mean differences.

Keywords: atrial fibrillation, meta-analysis, meta-regression, miRNA-328-3p, systematic review

1. Introduction

Atrial fibrillation (AF) is the most common persistent arrhythmias in adults, globally, 46.3 million individuals in 2016.[1] It can lead to stroke, heart failure, dementia, and even death, with a high rate of disability and fatality, thus exerts a great deal of burden in the world at large.[2] The pathogenesis and maintaining mechanism of AF is the result of many aspects,[3] atrial electrical remodeling, structural remodeling, autonomic nerve remodeling, calcium ion homeostasis disorders, etc. Interestingly, binge drinking is associated with the occurrence of AF.[4] Previous studies have confirmed that multiple miRNAs are involved in the regulation of atrial remodeling and changes in mRNA expression can increase the risk of AF.[5]

MicroRNAs (miRNAs) are a class of short non-coding endogenous RNAs that regulate gene expression post-transcriptionally in major cardiac physiological and pathological processes, for instance, myocardial infarction, atrial remodeling, arrhythmia, contractility, hypertrophy,[1,6–9] and relevant to the development and maintenance of AF. However, the full spectrum of miRNA function remains elusive. Recently, some studies have proved that miR-328-3p has a potential role as a disease biomarker and therapeutic target. Lu et al.[10] found that miR-328-3p increased in patients with AF. But it is strongly conflicted, with some papers reporting that it has a weak correlation even irrelevance with AF patients.[11–13]

Considering these contradictory findings, we performed a meta-analysis of case-control studies between miR-328-3p with AF. This study synthesized data from existing literatures to evaluate the expressions of miR-328-3p in patients with AF. Meanwhile, we explored the difference between circulation and atrial tissue concerning AF, as well as the study region and sample size.
2. Methods

This meta-analysis was performed according to the Cochrane systematic review guidelines and the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) statement. The study protocol has been published previously in PROSPERO (CRD42021225803). All analyses were based on previous published studies; thus, no ethical approval and patient consent are required.

2.1. Search strategy

For this systematic review and meta-analysis, we searched articles in 4 electronic databases including PubMed (https://pubmed.ncbi.nlm.nih.gov/), EMBASE (https://www.embase.com), Scopus (https://www.scopus.com/home.uri), Web of Science (www.webofknowledge.com/), and ProQuest (https://www.proquest.com/). “Atrial fibrillation” and (“microRNA-328” or “miRNA-328” or “miR-328”) were selected as the subject headings for searching literature, recorded between the inception of each database and February 1, 2021. All the English publications were searched without any restriction of countries or article type. The reference list of all selected articles will independently be screened to identify additional studies left out in the initial search.

2.2. Inclusion and exclusion criteria

Studies were included if case-control studies evaluated the association between the miR-328-3p expression level and AF risk, patients diagnosed with AF in the case group and healthy people or patients without AF in the control group, detailed miRNA expression level data were extracted for the calculation of standardized mean difference (SMD) and 95% confidence interval (CI), applied miRNA expression analysis including miRNA sequencing experiments or quantitative real-time polymerase chain reaction (RT-qPCR) technologies, if serial studies from the same group of people were reported, included the latest study, and the search was limited to the language or date publication.

The following types of articles were excluded: studies unrelated to miR-328-3p expression level and atrial fibrillation risk; case studies, case series, intervention studies, qualitative studies, systematic reviews, expert comments, abstracts, conference papers, meta-analysis, and repetition of previous publications; the same article of previous publications; the information provided in the original literature is not enough to calculate the statistical index SMD value.

2.3. Data extraction

Studies will be identified by 2 reviewers independently. Disagreements will be resolved by discussion or consensus with a third investigator. If the detailed data of miRNA expression level was not reported directly, only statistical graphs without specifying the specific values of mean and standard deviation (SD), data were extracted from the statistical graph by utilizing Adobe Photoshop 2020 (Adobe Inc., San Jose, CA). When the literature merely provided median and interquartile range, the mean and the SD were calculated by the formula given by Hozo et al. Data was extracted from included studies as follows: name of the first author, year of publication, study country, characteristics of case and control groups, sample size, age, gender, specimen type, detection method, the mean and SD of miR-328-3p in each group, etc.

2.4. Quality assessment

The Newcastle-Ottawa Quality Assessment scale (NOS) was used to assess the quality of studies incorporated in this meta-analysis. Each study was evaluated based on the following 3 aspects: the selection of participants, comparability of the groups, and ascertainment of exposure. The lowest score was 0 and the highest was 9, and a NOS score ≥5 indicated that the study was reliable. Any studies with <7 stars in NOS were defined as high risk of bias and those with ≥7 stars were regarded as low risk of bias. Any discrepancies between reviewers were resolved by mutual consensus.

2.5. Data analysis

Analyses were performed in STATA version 12.0 (StataCorp., College Station, TX). All reported probabilities were 2-sided, and statistical significance was regarded as P < .05. A forest plot with SMD and corresponding 95% CI was used to assess the strength of association between miR-328-3p expression levels and AF risk for continuous outcomes. Statistical heterogeneity was investigated by Q test and I² statistics and according to the statistical value of consistency checking, a meta-analysis model was chosen. When P < .1 or I² > 50%, which indicated that there is heterogeneity among the research results, the DerSimonian–Laird random-effects model was utilized. Otherwise, the inverse-variance fixed-effect model was applied.

2.6. Meta-regression and subgroup analysis

To explore the sources of heterogeneity, the meta-regression and subgroup analyses were performed according to the year of publication, the variance of comorbidity between AF and control groups, specimen type (peripheral blood plasma and atrial tissue), study region (Asia, America, and Europe) and sample size of AF group (n < 30, n ≥30).

2.7. Sensitivity and publication bias

Sensitivity analysis 1 study at a time was removed and the rest were analyzed, was used to explore the extent to which our results and conclusions alter as a result of changes in data or analytical methods. Egger linear regression test was used to evaluate the symmetry of funnel plots to explore the latent publication bias. Duval trim and fill method was used to assess the potential impact of small sample studies, and visualized the outcome through funnel plots.

3. Results

3.1. Search results and study characteristics

A total of 255 citations were identified from PubMed, Embase, Scopus, Web of Science, and ProQuest during the initial search. According to the titles and abstracts, 84 duplicate records were removed and 151 studies were excluded. Of the 37 remaining literatures, 12 were eventually included in the meta-analysis after satisfying the study criteria (Fig. 1). These eligible studies included a total of 3084 subjects with 555 AF patients and 2529 controls. In the study of Soeki et al., specimens were isolated from the blood of periphery and left atrial appendage, respectively. Consequently, we served this study as 2 independent studies. Overall, 7 studies explored plasma, 5 studies explored atrial tissue, and 1 explored whole blood. The study characteristics of the included studies were shown in Table 1.

2
3.2. Quality evaluation

As presented in Table 1 and Table 2, a total of 12 articles were included, all of which were case-control designs. According to the NOS quality scale, all documents were reliable, 4 studies had a high risk of bias and 8 studies had a low risk of bias.

3.3. Meta-analysis

As shown in Fig. 2, miRNA expression was found to be significantly higher in patients with AF than the controls, and the overall SMD of the randomized effect model was 0.69 (95% CI [0.10–1.28], P = .022; Heterogeneity: $I^2 = 94.8\%$, $P < .001$). The

| Table 1 |
|--------|
| Characteristics of the included studies. |
| **First Author** | **Year** | **Country** | **Sample type** | **Sample size** | **Age** | **P-value** | **Gender (male/female)** | **Methods** | **NOS** |
| Liu et al[12] | 2014 | China | LAA | 6 | 6 | 47.5 ± 8.4 | 49.4 ± 11.9 | .79 | 3/3 | 2/4 | Microarray |
| da Silva et al[43] | 2018 | Brazil | Plasma | 15 | 21 | 55.0 ± 12 | 57.7 ± 10.5 | .8 | 7/8 | 15/6 | RT-qPCR |
| Liu et al[13] | 2016 | China | Plasma | 40 | 40 | 52.3 ± 11 | 53.9 ± 13.4 | .56 | 29/11 | 29/11 | RT-qPCR |
| Lu et al[11] | 2010 | China | RAA | 10 | 12 | 38.8 ± 11.3 | 56.6 ± 7.4 | .00 | 5/5 | 4/8 | RT-qPCR |
| McManus et al[14] | 2014 | American | whole blood | 2185 | 153 | 65.6 ± 8.7 | 72.7 ± 6.2 | .00 | 932/1253 | 93/60 | RT-qPCR |
| Soekki et al[27] | 2016 | Japan | Plasma | 10 | 30 | 65 ± 3 | 63 ± 2 | .02 | 6/4 | 22/8 | RT-qPCR |
| Zholankin et al[45] | 2020 | Russian | Plasma | 30 | 30 | 47.3 ± 5.6 | 67.6 ± 10 | < .01 | 15/15 | 15/15 | RT-qPCR |
| Ma et al[60] | 2019 | Italy | RAA | 21 | 9 | 74.1 ± 10.1 | 74.4 ± 4.4 | .98 | 18/3 | 6/3 | RT-qPCR |
| Biczki et al[47] | 2019 | Germany | Atrial tissue | 8 | 14 | 55 ± 11 | 70 ± 9 | .00 | 5/3 | 9/5 | RT-qPCR |
| Xu et al[28] | 2021 | China | Plasma | 96 | 109 | 60.3 ± 5.1 | 62.6 ± 7.7 | .01 | 39/57 | 40/69 | RT-qPCR |
| Sieweke et al[46] | 2020 | Germany | Plasma | 60 | 21 | 58.2 ± 19 | 71.8 ± 11.3 | .00 | 42/18 | 14/7 | RT-qPCR |
| Galenko et al[48] | 2019 | American | Plasma | 48 | 110 | 57.8 ± 11.5 | 63.3 ± 10.5 | .00 | 21/27 | 66/44 | RT-qPCR |

AF = atrial fibrillation, LAA = left atrial appendage, NOS = The Newcastle-Ottawa Quality Assessment Scale score, RAA = right atrial appendage, RT-qPCR = quantitative real-time polymerase chain reaction, SR = sinus rhythm.
result showed the miR-328-3p expression level may be predictive and serve as a diagnostic tool for AF.

3.4. Evaluation of heterogeneity

Significant heterogeneity between studies was found using the chi-square test, and McManus et al.,[13] Soeki et al.,[26] Lu et al.,[10] Xu et al.[27] were the potential source of heterogeneity by visual inspection of the Galbraith plot (Fig. 3A). McManus’ study was a community-based cohort contained numerous subjects from the Framingham Offspring Study. However, the difference in age, current smoking, medication history, and comorbidity (for instance, myocardial infarction, heart failure, and diabetes mellitus) between the AF group and controls were statistically significant. Moreover, 107 new-onset AF patients were omitted, which leads to considerable selection bias. And most importantly, the whole blood was chosen to isolate miR-328-3p, neither plasma nor atrial tissue. The composition of human peripheral blood was complexed in which there were blood cells, serum, exosomes, and so on. Each type of blood cell contains a unique miRNA profile.[28] Considering the above 3 defects, we excluded this study in the next subgroup analysis. Analyzing the other

| Study                  | Selection | Comparability | Outcome | Total score | Quality |
|------------------------|-----------|---------------|---------|-------------|---------|
| Liu et al, 2014        | ☀️☀️      | ☀️            | ☀️      | 7           | High    |
| da Silva et al, 2018   | ☀️☀️      | ☀️            | ☀️      | 8           | High    |
| Liu et al, 2016        | ☀️☀️      | ☀️            | ☀️      | 8           | High    |
| Lu et al, 2010         | ☀️        | -             | ☀️      | 5           | Low     |
| McManus et al, 2014    | ☀️        | -             | ☀️☀️    | 6           | Low     |
| Soeki et al, 2016      | ☀️        | ☀️            | ☀️      | 7           | High    |
| Zhelankin et al, 2020  | ☀️☀️      | ☀️            | ☀️      | 6           | Low     |
| Maeki et al, 2019      | ☀️        | ☀️            | ☀️      | 6           | Low     |
| Biliczki et al, 2019   | ☀️☀️      | ☀️            | ☀️      | 8           | High    |
| Xu et al, 2021         | ☀️        | ☀️            | ☀️      | 7           | High    |
| Sieweke et al, 2020    | ☀️☀️      | ☀️            | ☀️      | 7           | High    |
| Galenko et al, 2019    | ☀️☀️      | ☀️            | ☀️      | 7           | High    |

Selection, representativeness of studies (score 0–4); Comparability, comparability of studies (score 0–2); Outcome, assessment of outcome and follow up (score 0–3). Low, high risk of bias (total score 0–6); High, low risk of bias (total score 7–9).

Figure 2. Forest plot of standardized mean difference with corresponding 95% CI of studies on the association between miR-328-3p level and atrial fibrillation. 95% CI = 95% confidence interval.
3 pieces of literature repeatedly, we did not find any shortcoming which results in clinical heterogeneity. In short, except for McManus et al.[13] there was only statistical heterogeneity, but no clinical heterogeneity.

3.5. Meta-regression and subgroup analysis

Since the heterogeneity was still very high after the deletion of McManus et al.[13] meta-regression and subgroup analyses were performed to investigate potential sources of between-study variability in terms of year of publication, comorbidity, specimen type, study region, and sample size. To avoid data dredging and get better goodness of fit, there was only a single covariate incorporated into the meta-regression model that used the restricted maximum of likelihood (REML) method at every turn. The adjusted $R^2$ (the value meant that the current covariate can explain the size of heterogeneity, CI=confidence interval, Coef. = regression coefficients, SE=standard error of regression coefficients). Table 3 shows the results of meta-regression analysis.

3.6. Sensitivity analyses and publication bias

From the results of the sensitivity analysis, the combined results did not significantly change the overall results, indicating the results were relatively stable (Fig. 3B). Visual inspection of the funnel plot found the graph is seemingly asymmetrical (Fig. 3C), which suggested that there may be some publication bias among the results. 

Figure 3. The results of sensitivity analysis and publication bias. (A) Heterogeneity analysis with a Galbraith plot. (B) Sensitivity analyses of miR-328-3p level difference between AF and control group by excluding one study at a time. (C) The funnel plot of miR-328-3p level difference between AF and controls. The SMD effect size was estimated using random-effects model. (D) Egger test to detect publication bias. AF=atrial fibrillation, SMD=standardized mean difference.

| Covariates           | Coef. | S.E. | 95% CI      | $t^2$ | Adjusted $R^2$ | $P$-value |
|----------------------|-------|------|-------------|-------|----------------|-----------|
| Comorbidity          | 2.53  | 1.11 | (0.05, 5.01)| 3.082 | 30.13%         | .047      |
| Year of publication  | -0.37 | 0.2  | (-0.82, -0.08) | 3.577 | 18.93%        | .096      |
| Region               | 0.88  | 0.71 | (-0.12, 2.60) | 4.195 | 4.92%          | .243      |
| Specimen type        | 0.76  | 0.65 | (-0.70, 2.22) | 4.289 | 2.77%          | .274      |
| Sample size          | 0.3   | 0.68 | (-1.22, 1.81) | 4.823 | -9.32%        | .672      |
| Detection method     | 0.38  | 1.61 | (-3.21, 3.96) | 4.94  | -11.98%       | .818      |

REML estimate of between-study variance. $t^2$=study between the component of variation size, adjusted $R^2$=the current covariate can explain the size of heterogeneity, CI=confidence interval, Coef. = regression coefficients, SE=standard error of regression coefficients.
the included studies. However, as shown in Fig. 3D, the Egger test results ($t = 1.44, P = .179$) was inconsistent with the funnel plot. And then, we evaluated the effect of publication bias on the results through trim and fill analysis. The trim and fill analysis showed data unchanged, which suggested that there was no publication bias and the results were relatively robust.

4. Discussion

AF is the leading cause of stroke and atrial appendage thrombus formation worldwide results in a major public health-care burden. In the United States, the annual incremental cost of AF was an estimated $26.0$ billion, and arising from an estimated 0.7 million additional cardiovascular-specific inpatient admissions and 3.2 million additional hospital days.

Ambulatory electrocardiographic (ECG) monitoring is the most widely used method to detect cardiac arrhythmias in the outpatient ambulatory setting, but it often fails. Previous studies have reported contradictory results on the subclinical arrhythmias is often missed by evidence that a large amount of morbidity and mortality. The increased expression of miR-328-3p may contribute to the prognosis assessment of clinical AF. It has also been reported that miR-328-3p takes inhibitory effect in AF by regulating the expression of lncRNA and circRNA. TCONS_00075467, a novel lncRNA, mediates the anti-tumor effect in osteosarcoma. Interestingly, miR-328-3p plays an oncogenic role and can promote tumor cell migration and invasion in glioma.

It is worth noting that miR-328-3p has been implicated in many other pathological conditions. Several studies have demonstrated that miR-328-3p has antitumor activity. In human cervical cancer tissues and cells, miR-328-3p was significantly downregulated. Further research found that miR-328-3p repressed cell proliferation and colony formation of cervical cancer cells in vitro and inhibited the growth of cervical cancer xenografts in vivo.

Circulating microRNAs are easily detectable, generally stable, and tissue-specific. Hsa-miR-328-3p (5′-CUGGCCUCUC-GGCCGUUCGCU-3′) belongs to the miRNA-328 family, which is located on chromosome chr16:67202327-67202348. miR-328-3p plays an important role in the occurrence and maintenance of AF and is expected to become a marker for the diagnosis and prognosis of AF. It reported that miR-328-3p targets the genes encoding L-type Ca$^{2+}$ channel proteins to reduce $I_Ca_l$ density and increased AF vulnerability by shortening atrial action potential duration, which served as a mechanism underlying the atrial arrhythmogenic potential. Furthermore, through translational inhibition of SERCA2a, miR-328-3p enhances the level of intracellular Ca$^{2+}$, activates the calcineurin/NFATc3 signaling pathway, and promotes cardiac hypertrophy. After cardiac surgery, the expression of miR-328-3p is significantly higher in postoperative AF patients (POAF), compared with non-POAF patients.

It is worth noting that miR-328-3p has been implicated in many other pathological conditions. Several studies have demonstrated that miR-328-3p has antitumor activity. In human cervical cancer tissues and cells, miR-328-3p was significantly downregulated. Further research found that miR-328-3p repressed cell proliferation and colony formation of cervical cancer cells in vitro and inhibited the growth of cervical cancer xenografts in vivo. Han et al. showed that miR-328-3p suppresses the survival of esophageal cancer cells and Shi et al. showed that miR-328-3p mediates the anti-tumor effect in osteosarcoma. Interestingly, miR-328-3p plays on oncogenic role and can promote tumor cell migration and invasion in glioma.

Previous studies have reported contradictory results on the levels of miR-328-3p in patients with AF. In this study, meta-
miR-328-3p (plasma of periphery blood atrial tissue group showed higher miR-328-3p levels. Interestingly, the levels of miR-328-3p may be a risk factor for AF. The NOS scale was used to analyze the quality of the included literature, and the results showed that all the studies had high scores, indicating the high quality of the included literature. The funnel plot looks asymmetrical, while Egger test and trim-fill analysis showed the outcome was stable and credible.

Bearing in mind the high heterogeneity observed in the meta-analysis, we conducted meta-regression and subgroup analyses. The results of meta-regression indicated that various comorbidity may lead to differences between studies. Five studies were partly variance in comorbidity included rheumatic heart disease, Wolff–Parkinson–White syndrome, valvular disease, and stroke. Additionally, we also noticed that the relative quantitative detection of RT-qPCR may not applicable for merging, the selection of internal reference is related to the authenticity and reliability of the relative quantitative results, which may lead to some deviation. When stratified by year of publication, miR-328-3p levels were significantly higher in articles published between 2010 and 2019 than 2019 to 2021. It indicated that the risk of miR-328-3p in AF is higher in the earlier researches than the latest, but the total sample from 2010 to 2018 is only 40% of the sample from 2019 to 2021 which may cause some bias. When stratified by sample size, AF patients from the n ≥ 30 group manifested higher miR-328-3p levels and the merging result was more stable. This shows that small sample studies are sometimes unstable. When stratified by specimen type, AF patients from the atrial tissue group showed higher miR-328-3p levels. Interestingly, the closer to the myocardium, the higher expression levels of miR-328-3p (plasma of periphery blood < plasma of left atrial appendage blood < atrial tissue). The regional distribution of miR-328-3p illustrated that the potential mechanism of changing the profile of circulating plasma miRNAs in AF is the secretion of exosomes by atrial cardiomyocytes. These exosomes contain a specific miRNA signature altered in AF. When stratified by study region, AF patients from the Asia group showed higher miR-328-3p levels, however, the heterogeneity is relatively high, and the confidence interval of the results is wider, suggesting that the quality of research in Asia needs to be further strengthened. To conclude, sample size, specimen type, and study region were associated with miR-328-3p levels in AF patients.

Patients were divided into new-onset AF and well-controlled AF in da Silva et al. and they found that expression of miR-328-3p is higher in patients with acute new-onset AF compared with patients with well-controlled AF (P < .05), whereas the expression levels of well-controlled AF is like healthy controls. This discovery has been a great inspiration for future research. However, the reliability of the results is worthy of further demonstration by large sample sizes and multi-region studies.

5. Limitations

Nevertheless, this study has several disadvantages. Firstly, heterogeneity was substantial among studies although we performed subgroup analyses to explore the source of it. Secondly, we did not study the difference of the expression of miR-328-3p between paroxysmal and persistent AF. Thirdly, we pooled Soeki et al as 2 independent studies and omitted McManus et al. which may lead to a certain bias. Lastly, the studied population presented inhomogeneities in comorbidities, for example, valvular disease and rheumatic heart disease, which may have acted as confounding factors, contributing to the variability of miRNA expression.

6. Conclusions

In summary, our study reveals that a higher level of miR-328-3p is a potential risk factor for AF. In addition, the levels of miR-328-3p in atrial tissue are higher than in peripheral blood plasma. These results may pave the way for future experimental studies and are expected to become an important target for the diagnosis of AF. Furthermore, more large sample studies that applied absolute quantitative detection methods are needed to better clarify the effect of miR-328-3p in AF.

Acknowledgments

The authors thank Dr Wei Lei and Dr Yuan He of the Affiliated Hospital of Guangdong Medical University for providing technical assistance.

Author contributions

Haitao Huang and Can Chen contributed to the conception or design of the work. Haitao Huang, Hao Chen, and Xiao Liang conducted the literature search. Haitao Huang, Xiaoxin Chen, and Xiuting Chen conducted screening and extraction of data. Haitao Huang and Hao Chen conducted statistical analyses, Haitao Huang, Can Chen, and Xiao Liang wrote the draft. All authors reviewed the manuscript, gave their final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

Conceptualization: Haitao Huang, Can Chen.
Data curation: Haitao Huang, Hao Chen, Xiao Liang, Xiuting Chen, Xiaoxin Chen.
Formal analysis: Haitao Huang, Hao Chen, Xiao Liang, Xiaoxin Chen.
Investigation: Haitao Huang.
Methodology: Haitao Huang.
Project administration: Haitao Huang.
Software: Haitao Huang.
Supervision: Haitao Huang.
Validation: Haitao Huang.
Visualization: Haitao Huang.
Writing – original draft: Haitao Huang, Xiao Liang.
Writing – review & editing: Haitao Huang, Can Chen.

References

[1] Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. Circulation 2019;139:e56–68.
[2] Michaud GF, Stevenson WG. Atrial fibrillation. N Engl J Med 2021;384:353–61.
[3] Andrade J, Khairy P, Dobrev D, Nattel S. The clinical profile and pathophysiology of atrial fibrillation: relationships among clinical features, epidemiology, and mechanisms. Circ Res 2014;114:1453–68.
Soeki T, Matsuura T, Bando S, et al. Relationship between local paroxysmal atrial fibrillation and the risk of stroke. Int J Cardiol 2020;310:137.

Liu H, Wu H, Yao C, Chen Y, Tao L. Advanced methods of data extraction for continuous outcomes in meta-analysis. Chin J Evid Based Clin Med 2017;17:117–21.

Huang et al. Medicine (2022) 101:9

Voskoboinik A, McDonald C, Cheng D, et al. Acute electrical, autonomic and structural effects of binge drinking: insights into the ‘holiday heart syndrome’. Int J Cardiol 2021;331:100–5.

van den Berg NW, Kawasaki M, Berger WR, et al. MicroRNAs in atrial fibrillation: from expression signatures to functional implications. Cardiovasc Drugs Ther 2017;31:345–65.

Liu Y, Mao S, Luo X, Wang Y. Circulating miR-1/UCA1 is a novel biomarker for the diagnosis and prognosis of acute myocardial infarction. Int J Cardiol 2020;310:137.

Belmonte T, Mangas A, Calderon-Dominguez M, et al. Peripheral microRNA panels to guide the diagnosis of familial cardiomyopathy. Transl Res 2020;218:1–15.

Zhang M, Cheng K, Chen H, et al. MicroRNA-27 attenuates pressure overload-induced cardiac hypertrophy and dysfunction by targeting galecinin-3. Arch Biochem Biophys 2020;689:108405.

Scalori FL, Faganello LS, Garbin HI, Piva E, Mattos B, Biolo A. A systematic review of microRNAs in patients with hypertrophic cardiomyopathy. Int J Cardiol 2021;327:146–54.

Lu Y, Zhang Y, Wang N, et al. MicroRNA-328 contributes to adverse electrical remodeling in atrial fibrillation. Circulation 2010;122:2378–87.

Liu H, Chen GX, Liang MY, et al. Atrial fibrillation alters the microRNA expression profiles of the left atria of patients with mitral stenosis. Circ Cardiovasc Disord 2014;14:10.

Liu T, Zhong S, Rao F, Xue Y, Qi Z, Wu S. Catheter ablation restores decreased plasma miR-409-3p and miR-432 in atrial fibrillation patients. Europace 2016;18:92–9.

McManus DD, Lin H, Tanriverdi K, et al. Relations between circulating microRNAs and atrial fibrillation: data from the Framingham Offspring Study. Heart Rhythm 2014;11:663–9.

Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA GroupPreferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097.

Liu H, Wu H, Yao C, Chen Y, Taotao L. Advanced methods of data extraction for continuous outcomes in meta-analysis. Chin J Evid Based Med 2017;17:117–21.

Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMJ Med Res Methodol 2005;5:13.

Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 2010;25:603–5.

Higgins JP, Thompson SG, Spiegelhalter DJ. A re-evaluation of random-effects meta-analysis. J R Stat Soc A Stat Soc 2009;172:137–59.

DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.

Honey EP. I shrunk the pooled SMD! Guide to critical appraisal of systematic reviews and meta-analyses using the Cochrane review on exercise for depression as example. Mental Health Phys Activ 2015;8:21–36.

Harbord RM, Higgins JPT. Meta-regression in stata. Stata J 2018;8:493–519.

Baker WL, White CM, Cappelleri JC, et al. Understanding heterogeneity in meta-analysis: the role of meta-regression. Int J Clin Pract 2009;63:1426–34.

Alexander PE, Bonner AJ, Agarwal A, et al. Sensitivity subgroup analysis based on single-center vs. multi-center trial status when interpreting meta-analyses pooled estimates: the logical way forward. J Clin Epidemiol 2016;74:80–92.

Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis: the role of meta-regression. Int J Clin Pract 2009;63:1426–34.

Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of assessing and adjusting for publication bias in meta-analysis. Biometrics 2000;56:453–63.

Sooki T, Matsui T, Bando S, et al. Relationship between local production of microRNA-328 and atrial substrate remodeling in atrial fibrillation. J Cardiol 2016;68:472–7.