lncRNAs are potential prognostic markers in patients with nasopharyngeal carcinoma in China: A systematic review and meta-analysis

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Abstract. The present study aimed to investigate the association between the expression profiles of long non-coding RNAs (lncRNAs) and the clinical characteristics or prognosis of patients with nasopharyngeal carcinoma (NPC). The findings presented in the present review may provide novel strategies for the prevention and treatment of NPC. For the analyses, medical databases, including PubMed, Web of Science and Cochrane library were searched using specific search terms, search strategies and screening strategies. Endnote X9 document management software was then employed to extract documents from January, 2010 to May, 2023. Data were extracted following the prescribed standards. Review Manager 5.4 and STATA 12.0 data analysis software were used for data analysis. A total of 490 publications were analyzed for inclusion. In total, 29 publications, composed of 24 studies with upregulated lncRNAs and 5 studies with downregulated lncRNAs, were included in the final analysis. The analysis revealed that the upregulation of lncRNAs was significantly associated with T stage, N stage and clinical stage, as well as with the overall survival (OS) and disease-free survival (DFS) of patients with NPC (P<0.05). However, there was no significant association between the upregulated lncRNAs and sex, M stage or relapse-free survival (RFS) (P>0.05). On the other hand, the suppression of lncRNA expression was significantly associated with N stage, M stage, clinical stage and the OS of patients with NPC (P<0.05), but not with T stage and RFS (P>0.05). Taken together, the present review demonstrates that the up- and downregulation of different lncRNAs was associated with an advanced clinical stage and a shorter OS of patients with NPC. Therefore, lncRNAs may serve as potential prognostic factors in NPC.

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Abbreviations: lncRNAs, long non-coding RNAs; NPC, nasopharyngeal carcinoma; OS, overall survival; DFS, disease-free survival; RFS, relapse-free survival; HR, hazard ratio; CI, confidence interval

Key words: NPC, lncRNA, clinical feature, prognosis, meta-analysis

Introduction

Nasopharyngeal carcinoma (NPC), a common malignant head and neck human tumor, is an epithelial cell carcinoma originating from the nasopharynx mucosa lining. There are three pathological subtypes of NPC, keratinizing squamous, non-keratinizing and basaloid squamous cell carcinoma (1). Non-keratinizing squamous cell carcinoma is classified as differentiated and undifferentiated tumors, and >95% of NPC cases in endemic areas are of the non-keratinizing subtype (2). To date, the pathogenesis of NPC remains unclear. The main influencing factors may involve genetic factors, environmental factors and Epstein-Barr virus (EBV) infection. Luo (3) synthesized Darwin's theory of biological evolution with the mechanisms underlying the occurrence and development of NPC and conducted a comprehensive analysis of the biological behaviors associated with NPC, including its occurrence, metastasis and recurrence, from a multidimensional perspective. As a result, the author proposed a novel perspective, positing NPC as an ecological disease characterized by a unified pathological ecosystem that integrates ecological and evolutionary processes (3). It is encouraging to observe a general decline in the global incidence of NPC over the past few decades (4). Nevertheless, patients with NPC are typically diagnosed during the advanced stages of the disease, when symptoms become more pronounced, significantly affecting their quality of life and thereby reducing the survival rate (5). Moreover, NPC has the propensity to metastasize to various organs, such

as the bone, brain and liver (6). Although radiotherapy and chemotherapy are frequently employed in the clinical management of patients with NPC, their efficacy is limited in cases of locally advanced disease or distant metastasis. In recent years, there has been a gradual emergence of immunotherapy as a promising strategy in combatting the recurrence and metastasis of NPC. However, emerging immunotherapies, including PD-1 inhibition, have exhibited restricted efficacy in a subset of clinical cases (1). Consequently, it is imperative to identify more effective prognostic markers for the assessment of prognosis and efficacy in patients with NPC.

Long non-coding RNAs (lncRNAs) are a form of RNA sequence, which do not encode proteins and have been considered as non-functional genes in the genome. With advancements being made in research, lncRNAs have been shown to be major regulators of gene expression in a number of cases, playing a key role in various biological functions and disease processes, including cancer (7). lncRNAs have been shown to promote or inhibit cancer and participate in cell proliferation, metastasis and other biological functions (8). Previous studies have reported that FAM225A, PVT1, LINC00312, TINCR, HOTAIR and other lncRNAs play regulatory roles in NPC (9-13). In addition, Liang *et al* (14) conducted a microarray analysis to identify a nine-lncRNA signature associated with the immune system. The predictive capability of this signature in determining distant metastasis of locoregionally advanced NPC was further validated through experimental verification (14). The upregulated expression of lncRNA ZEB1-AS1, DLX6-AS1 and SNHG7 in a variety of tumors has been demonstrated to be significantly associated with overall survival (OS), tumor stage, lymph node metastasis and other indicators, and to have the ability to indicate the prognosis of patients with tumors (15-17).

These findings suggest the potential use of lncRNAs as predictive biomarkers for the prognosis of patients with NPC. Thus, the present study integrated relevant studies into the meta-analysis to determine the prognostic value of lncRNA expression in NPC, and to investigate the potential use of lncRNAs as novel biomarkers and therapeutic targets for NPC. A similar study of meta-analysis (18), that has been published in 2018, retrieved a total of 219 articles and included 14 articles ultimately in the analysis. As a result of the limited number of articles extracted, Guo *et al* (18) did not conduct subgroup analysis. Thus, the authors updated the literatures to May 2023 and verified their conclusions through subgroup analysis.

Materials and methods

Search strategy. The present meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement (19). A comprehensive search was conducted using the PubMed (https://pubmed.ncbi.nlm.nih.gov/), Web of Science (https://www.webofknowledge.com/), Cochrane Library (https://www.cochranelibrary.com/) databases for studies on the association between lncRNA biomarkers and prognosis or clinical features in NPC, published from January 2010 to May 2023. A combination of key words and free words were used: ('nasopharyngeal cancer OR nasopharyngeal neoplasm OR nasopharyngeal tumor OR NPC') AND ('long non-coding RNAs, OR long non-coding RNA OR lncRNA OR lnRNA') AND ('prognosis OR survival'). Manual retrieval was also performed in order to improve the integrity and accuracy of the retrieval.

Inclusion and exclusion criteria. The inclusion criteria were as follows: The inclusion criteria for articles encompassed data pertaining to the association between the expression of lncRNAs and the prognosis of NPC, as well as other pertinent information. In instances where multiple articles presented identical data, preference was given to the most recent publication or the one with the most comprehensive dataset. Furthermore, the selected articles provided information on various patient characteristics, including age, sex, TNM stage, lymph node metastasis, OS, disease-free survival (DFS), relapse-free survival (RFS), 95% confidence interval (95% CI) and other relevant indicators. The literature encompassed a dataset comprising more than three items, with flexibility in accommodating cases where the number of documents was inadequate.

The following exclusion criteria were used: i) Articles without complete data; ii) animal experiments, cell experiments, reviews, case reports, letters or meeting records.

Data extraction. Relevant data were extracted from the included literature according to standard protocols. Differences were discussed and solved by the members of the group, independently. The extracted information included the author's name, publication year, research population, research period, sample size, type and number and lncRNA types. Endpoints (OS/RFS/DFS), sex, clinical stage, tumor size, lymph node metastasis, distant metastasis were also extracted from the literature. In the case that the hazard ratio (HR) and 95% CI values could not be obtained from the articles, Engauge digitizer 11.1 (http://markummitchell.github.io/engauge-digitizer/) was used to extract the data from Kaplan-Meier survival curves, and then converted into HR or 95% CI values. Of note, three members collected data from each report, independently. The detailed information included in the literature is presented in Tables SI-SXI. The included studies were strictly assessed following the Newcastle Ottawa Scale, with a full score of 9 and not <6 points adopted for the meta-analysis.

Statistical analysis. Review Manager 5.4 (Cochrane Collaboration) was used to calculate the odds ratio (OR) or HR and 95% CI to evaluate the statistical association between the lncRNAs and clinical features (sex, T stage, N stage, M stage or overall stage) and the prognosis (OS, DFS, RFS) of patients with NPC, and generate a forest map. $P<0.05$ was considered to indicate a statistically significant difference. The Cochrane Q test and Chi-squared test were used to evaluate the heterogeneity of the included studies. As recommended by the Cochrane Handbook for Systematic Reviews of Interventions (https://training.cochrane.org/handbook/current/chapter-10#section-10-10-4-1), the random effects model was used to calculate the pooled HRs or ORs. To analyze the association between the lncRNAs and clinical characteristics or prognosis of patients with NPC and to test the stability of the results, exclusive sensitivity analysis and combined effect analysis were performed using Review Manager 5.4. In addition, a funnel plot was generated by Review Manager 5.4, and the Begg and Egger's tests were performed using Stata 12.0 (StataCorp LP) software to evaluate presence

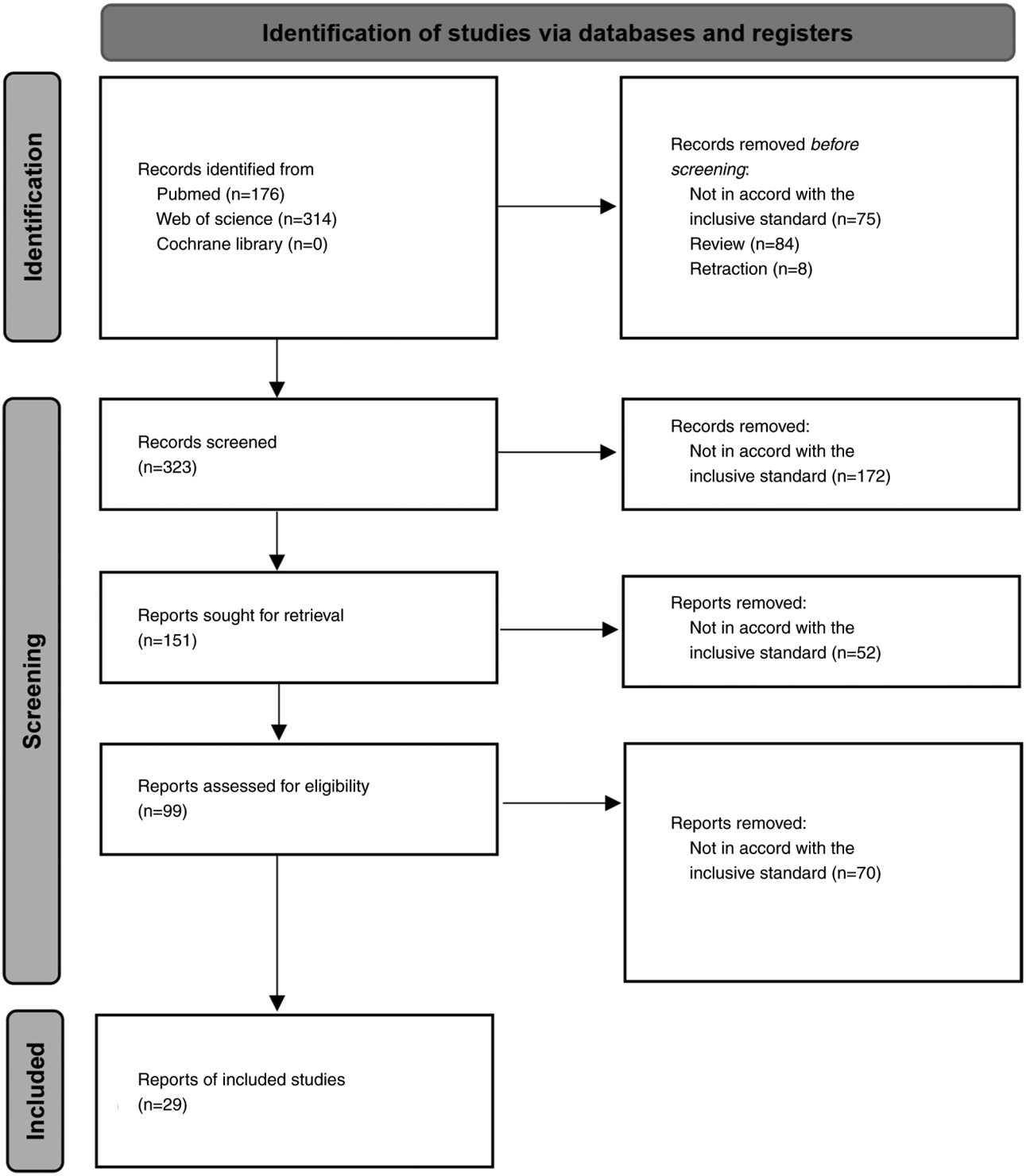

Figure 1. Flowchart of the screening process for relevant literature used in the present study.

of publication bias. There was no publication bias if the P≥0.05. The Egger's test has a higher sensitivity compared with the Begg test. If the two test results were inconsistent, the Egger's test results were used as a reference.

Screening results. A total of 490 relevant studies were retrieved from the PubMed, Web of Science and Cochrane Library databases. After screening the literature twice, 29 studies were finally included in the analysis. Among these, 24 studies included data on the upregulation of lncRNAs, while the remaining 5 studies included data on the suppressed expression of lncRNAs (Fig. 1).

Results

Association between the upregulated expression of lncRNAs and clinical characteristics of patients with NPC. A total of 24 studies which examined the association between a high

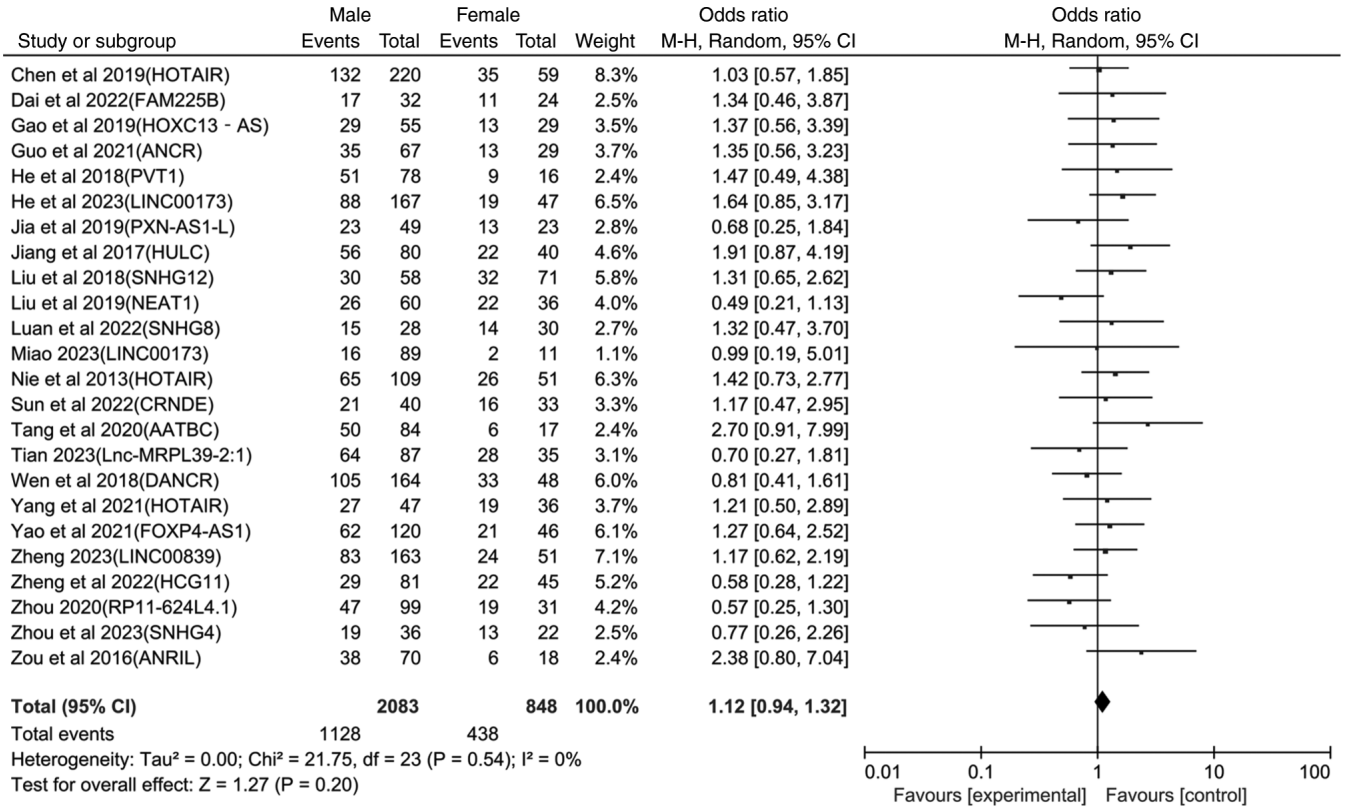

Figure 2. Forest map illustrating the association between the upregulated expression of long non-coding RNAs and the sex of patients with nasopharyngeal carcinoma. CI, confidence interval.

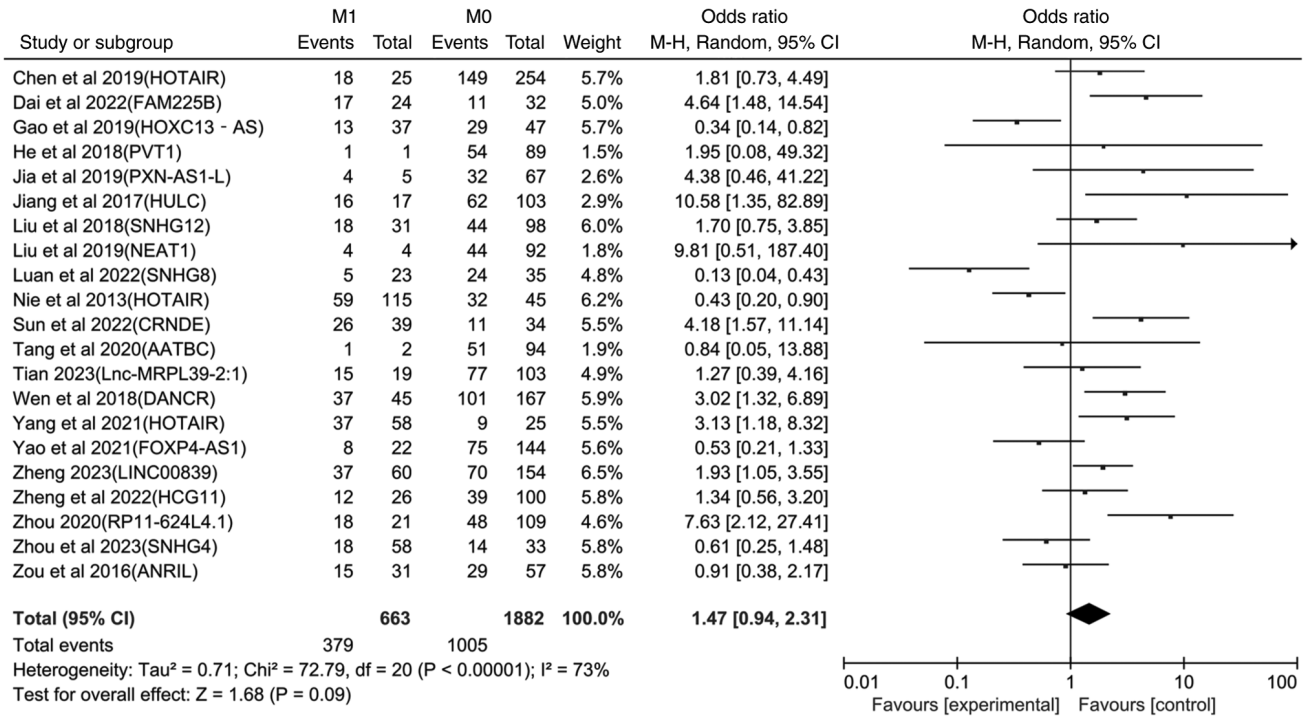

Figure 3. Forest map illustrating the association between the upregulated expression of long non-coding RNAs and tumor distant metastasis (M) stage. CI, confidence interval.

lncRNA expression and the clinical characteristics of patients with NPC were included in the present analysis (13,20-42). The analysis demonstrated that the high expression of lncRNAs was not significantly associated with the sex (HR, 1.12; 95% CI, 0.94-1.32; P=0.20; Fig. 2) and tumor M stage (HR, 1.47; 95% CI, 0.94-2.31; P=0.09; Fig. 3) of the patients; however,

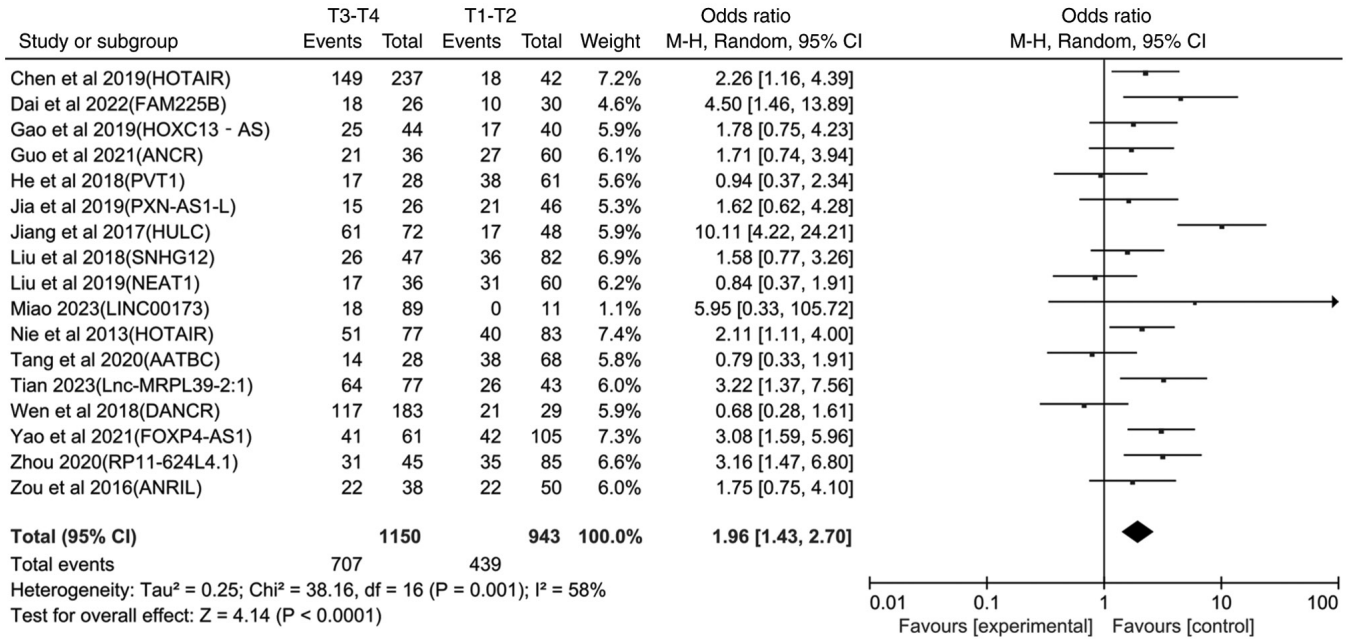

Figure 4. Forest map illustrating the association between the upregulated expression of long non-coding RNAs and primary tumors (T) stage. CI, confidence interval.

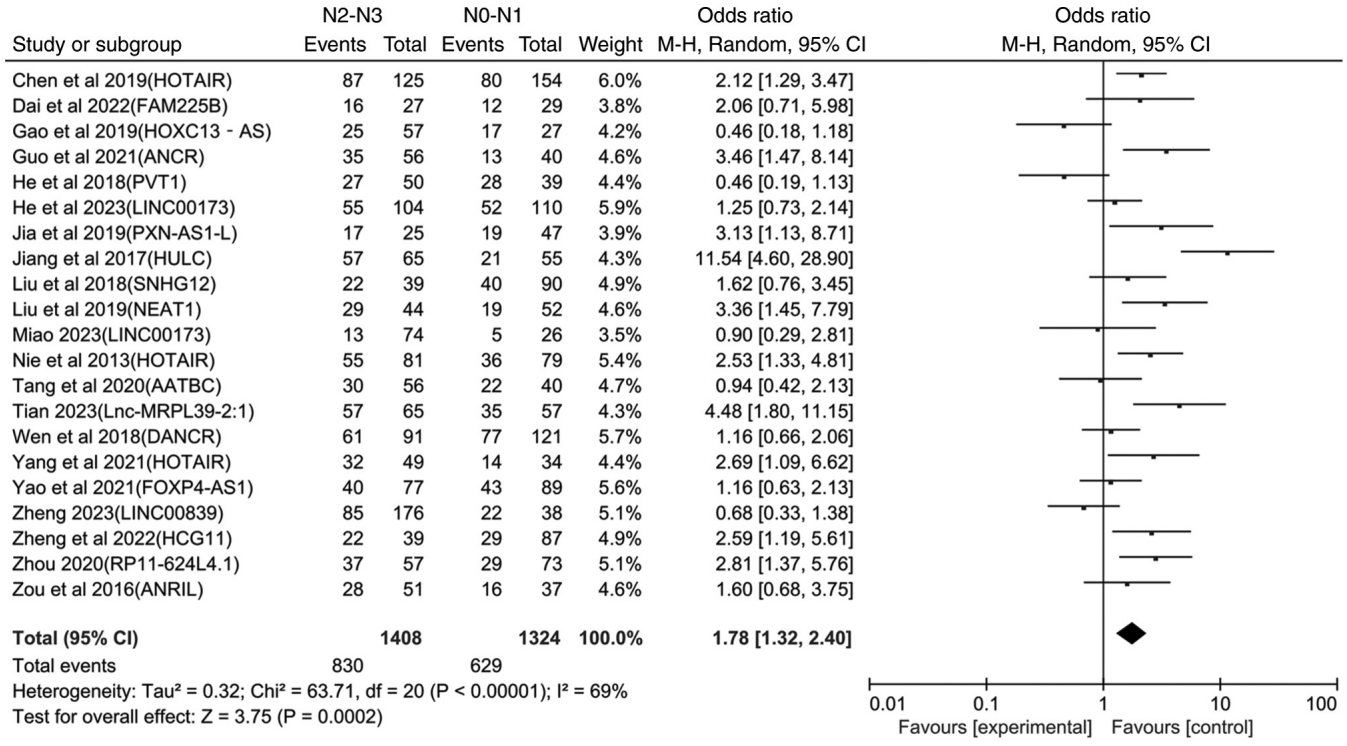

Figure 5. Forest map illustrating the association between the upregulated expression of long non-coding RNAs and regional lymph node (N) stage. CI, confidence interval.

it exhibited a significant association with primary tumors (T) stage, regional lymph node (N) stage and tumor clinical stage. These data demonstrated that the expression of lncRNAs was significantly higher in patients with T3-T4 stage disease compared with those with T1-T2 stage disease (HR, 1.96; 95% CI, 1.43-2.70; P<0.0001; Fig. 4). Furthermore, the expression of lncRNAs was significantly higher in patients with N2-N3 stage disease than in those with N0-N1 stage disease (HR, 1.78; 95% CI, 1.32-2.40; P=0.0002; Fig. 5). In addition, the upregulation of lncRNA expression was significantly higher in patients with III-IV stage disease than in those with I-II stage disease (HR, 3.21; 95% CI, 1.91-5.38; P<0.00001; Fig. 6).

Association between the upregulated expression of lncRNAs and the prognosis of patients with NPC. A total of 23 studies were included to evaluate the association between the high

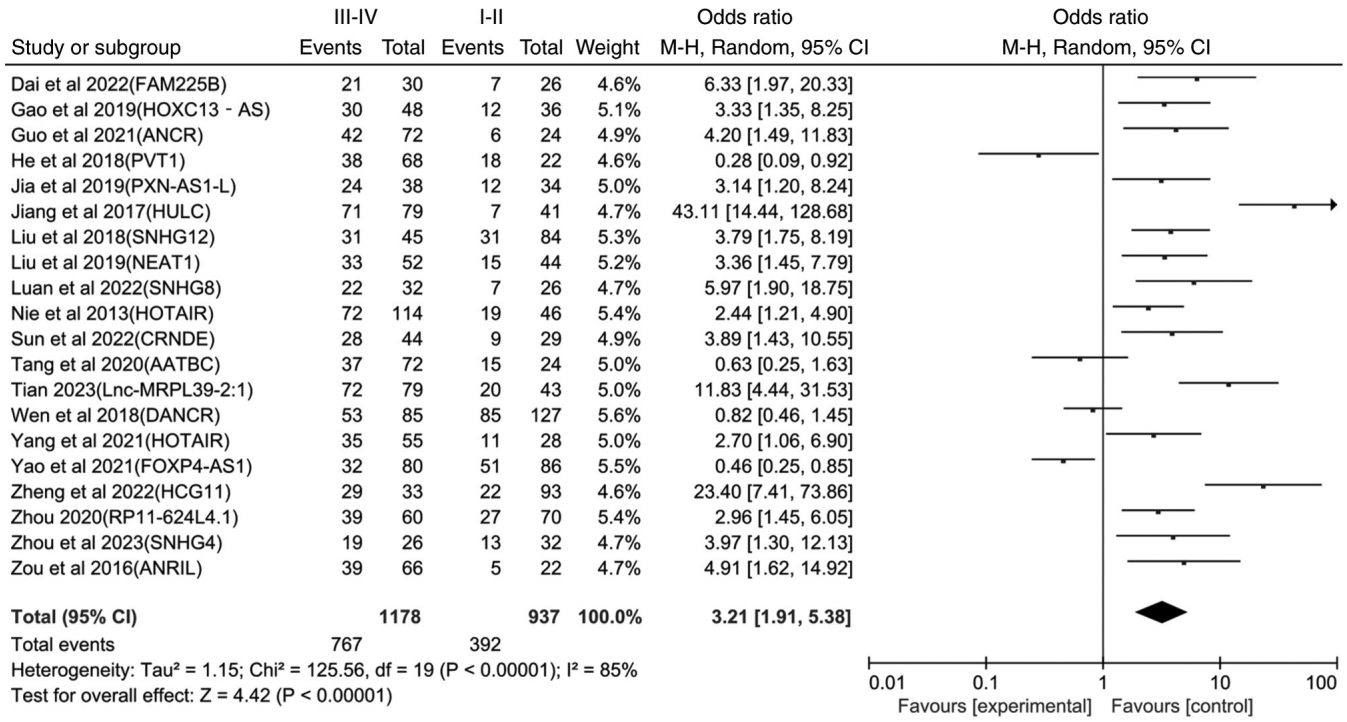

Figure 6. Forest map illustrating the association between the upregulated expression of long non-coding RNAs and tumor clinical stage. CI, confidence interval.

expression of lncRNAs and the prognosis of patients with NPC. The results demonstrated that the high expression of lncRNAs was significantly associated with the OS and DFS of patients. Patients exhibiting an overexpression of lncRNAs had a shorter OS and DFS compared with those with a low expression of lncRNAs (HR, 2.01; 95% CI, 1.71-2.36; P<0.00001; Fig. 7A; HR, 1.63; 95% CI, 1.32-2.00; P<0.00001; Fig. 7B). However, the upregulated expression of lncRNAs was not significantly associated with RFS (HR, 1.46; 95% CI, 0.94-2.27; P=0.09; Fig. 7C).

Association between the downregulated expression of lncRNAs and the clinical characteristics of patients with NPC. A total of five studies were included for the analysis of the association between the low expression of lncRNAs and the clinical characteristics of patients with NPC (43-47). The analysis demonstrated that there was no significant association between the sex of the patients, primary tumors (T) stage and lncRNA expression, (HR, 0.83; 95% CI, 0.55-1.24; P=0.36; Fig. 8A; HR, 2.00; 95% CI, 0.93-4.30; P=0.08; Fig. 8B). However, there was a significant association between lncRNA expression and regional lymph node (N) stage, tumor distant metastasis (M) stage and tumor clinical stage. These data demonstrated that the downregulated expression of lncRNAs in N2-N3 stage primary tumors was more significant than that in N0-N1 stage primary tumors (HR, 2.88; 95% CI, 1.67-4.96; P=0.0001; Fig. 8C). In addition, the downregulated expression of lncRNAs was significantly more prominent in the M1 stage compared with the M0 stage (HR, 2.06; 95% CI, 1.23-3.45; P=0.006; Fig. 8D). Furthermore, the expression of lncRNAs in patients with III-IV stage NPC was significantly lower than that in patients with I-II stage NPC (HR, 3.23; 95% CI, 2.17-4.83; P<0.00001; Fig. 8E).

Association between the downregulated expression of lncRNAs and the prognosis of patients with NPC. A total of five studies were included in the analysis of the association between the low expression of lncRNAs and the prognosis of patients with NPC. The results revealed that the suppression of lncRNAs was significantly associated with OS (HR, 1.64; 95% CI, 1.07-2.51; P=0.02; Fig. 9A), but not with RFS (HR, 1.22; 95% CI, 0.56-2.67; P=0.62; Fig. 9B).

Heterogeneity, sensitivity analysis and publication bias

Association between the upregulated expression of lncRNAs and the prognosis of patients with NPC (subgroup analysis). The association between 24 upregulated lncRNA genes and the prognosis of patients with NPC was then analyzed (Table SII). Patients who had a high expression of HOTAIR (HR, 1.95; 95% CI, 1.02-3.73; P=0.04), LINC00173 (HR, 2.18; 95% CI, 1.31-3.63; P=0.003), SNHG12 (HR, 3.00; 95% CI, 1.51-5.97; P=0.002), NEAT1 (HR, 2.53; 95% CI: 1.35-4.75; P=0.004), Lnc-MRPL39-2:1 (HR, 3.25; 95% CI, 1.77-5.98; P=0.0001), FOXP4-AS1 (HR, 3.22; 95% CI, 1.72-6.03; P=0.0003), HCG11 (HR, 3.71; 95% CI, 1.21-11.33; P=0.02), LINC00839 (HR, 1.90; 95% CI, 1.21-2.98; P=0.005), RP11-624L4.1 (HR, 3.74; 95% CI, 1.40-9.97; P=0.008) and ANRIL (HR, 4.35; 95% CI, 1.37-13.82; P=0.01) had a significantly shorter OS compared with those with a low expression of these lncRNAs (P<0.05). There was no evident association between the expression of other lncRNAs and the prognosis of patients with NPC (P>0.05). LINC00839 (HR, 2.10; 95% CI, 1.34-3.29; P=0.001) and ANRIL (HR, 2.05; 95% CI, 1.21-3.49; P=0.008) were associated with a shorter DFS compared with other lncRNAs with a low expression (P<0.05).

Sensitivity analysis of the upregulated lncRNAs. The present study demonstrated that the high expression of lncRNAs was

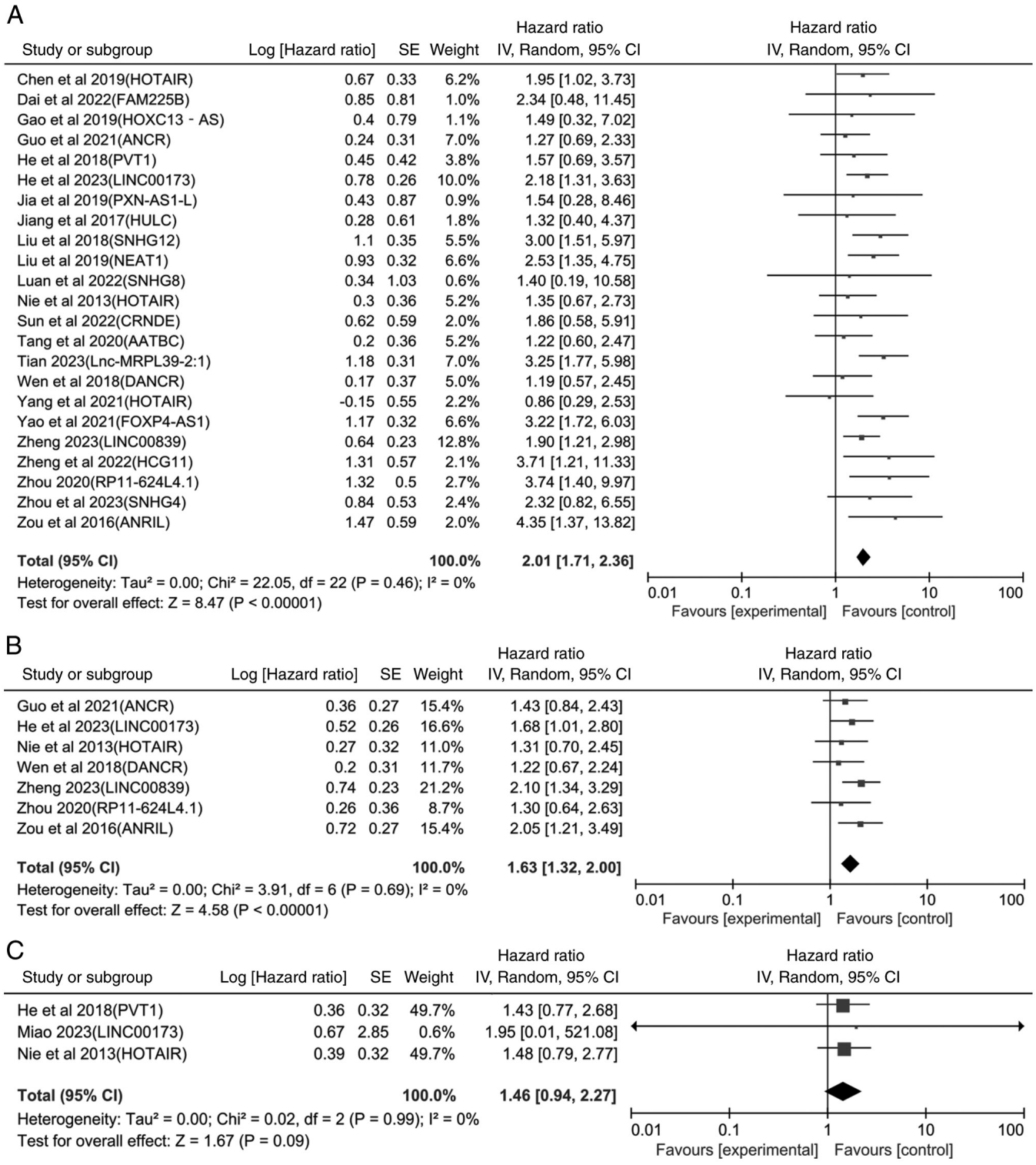

Figure 7. Forest maps illustrating the association between the upregulated expression of lncRNAs and the prognosis of patients with nasopharyngeal carcinoma. (A) Forest map illustrating the association between the upregulated expression of lncRNAs and overall survival. (B) Forest map illustrating the association between the upregulated expression of lncRNAs and disease-free survival. (C) Forest map illustrating the association between the upregulated expression of lncRNAs and relapse-free survival. lncRNAs, long non-coding RNAs; CI, confidence interval.

associated with T stage, N stage, M stage and clinical stage in patients with NPC. Exclusion sensitivity analysis was used for four studies (Tables SIII-SVI). Compared with the results from the combined analysis before and after exclusion, there was no significant change in the association between the high expression of lncRNAs and the T stage, N stage and clinical stage of patients with NPC. The association between the high expression of lncRNAs and the M stage of patients with NPC was affected by the data from the studies by Gao *et al* 2019 (22), Luan *et al* 2022 (37) and Nie *et al* 2013 (29); when these studies were excluded, the I^2 was reduced from 73 to 67%. The data demonstrated that the expression of lncRNAs in

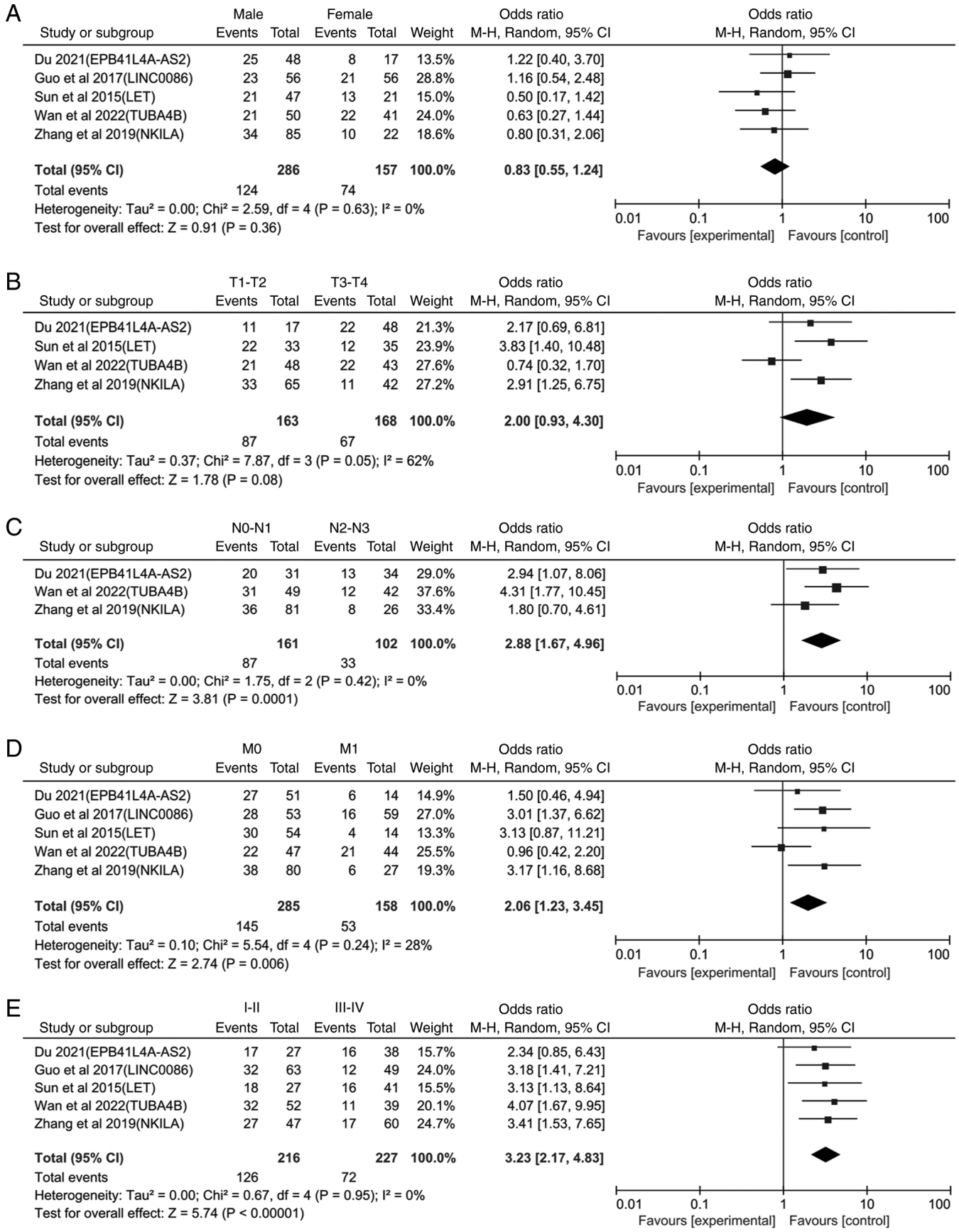

Figure 8. Forest maps illustrating the association between the downregulated expression of lncRNAs and characteristics of patients with NPC. (A) Forest map illustrating the association between the downregulated expression of lncRNAs and the sex of patients with NPC. (B) Forest map illustrating the association between the downregulated expression of lncRNAs and primary tumors (T) stage. (C) Forest map illustrating the association between the downregulated expression of lncRNAs and regional lymph node (N) stage. (D) Forest map illustrating the association between the downregulated expression of lncRNAs and tumor distant metastasis (M) stage. (E) Forest map illustrating the association between the downregulated expression of lncRNAs and tumor clinical stage. lncRNAs, long non-coding RNAs; NPC, nasopharyngeal carcinoma; CI, confidence interval.

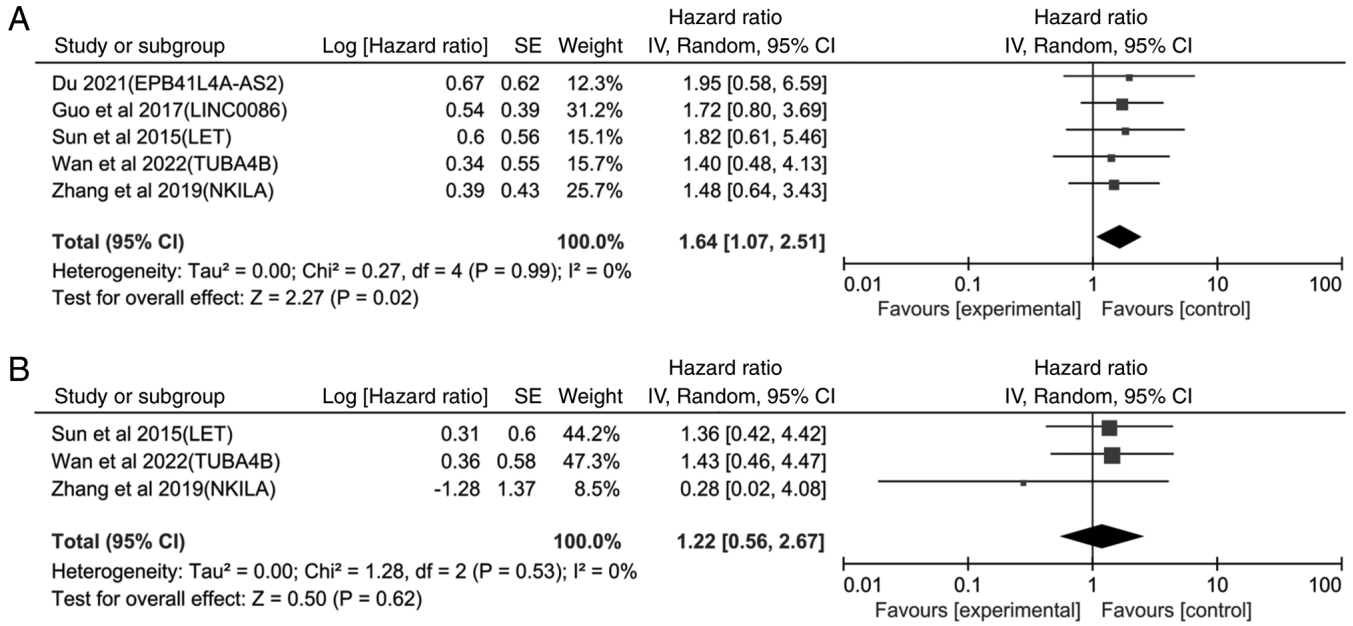

Figure 9. Forest maps illustrating the association between the downregulated expression of lncRNAs and the prognosis of patients with nasopharyngeal carcinoma. (A) Forest map illustrating the association between the downregulated expression of lncRNAs and overall survival. (B) Forest map illustrating the association between the downregulated expression of lncRNAs and relapse-free survival. lncRNAs, long non-coding RNAs; CI, confidence interval.

the M1 stage was significantly higher than that in the M0 stage (P<0.05) in patients with NPC. As there was a very limited number of articles on the downregulation of lncRNA expression in NPC (only five articles), further sensitivity analysis could not be conducted.

Analysis of publication bias. The funnel plot revealed a symmetrical association between the expression of lncRNAs and the sex, T stage, N stage, M stage, clinical stage or OS of patients with NPC (Fig. 10). The data indicated that the meta-analysis results were less affected by publication bias. Subsquently, the Begg and Egger's methods were used to further quantitatively verify the results. The results revealed that there was a publication bias in the association analysis between the upregulated LncRNAs and the clinical stage of tumors (P<0.05, Table SVII), which was caused by multiple factors, such as search bias, screening bias and data extraction bias. Publication bias could be avoided by expanding the search scope, screening literature with high quality and optimizing data extraction methods. The Egger's and Begg tests for each of the other studies yielded a value of P>0.05 (Table SVII), indicating that there was no publication bias in the included studies.

Discussion

Recent research has elucidated the advancements in the early diagnosis and prolonged survival rates of patients with NPC. However, the primary causes of mortality continue to be recurrence and metastasis subsequent to treatment. Consequently, it is imperative to urgently identify pertinent biomarkers capable of predicting the outcomes of patients with NPC. In the previous years, the prognostic marker function of lncRNAs has emerged as a prominent area of research. For example, the assessment of plasma lncRNA XLOC_1014172 and LOC149086 levels enables the differentiation between metastatic and non-metastatic liver cancer, and this approach demonstrates a specificity of 90%, a sensitivity of 91% and an AUC of 0.934 (combination) (48). HOTAIR has been identified as a negative prognostic indicator for colorectal cancer, with a sensitivity of 92.5%, a specificity of 67% and an AUC of 0.8742 (49). Furthermore, the abnormal expression of HOTAIR and GAS5 has been revealed to be associated with an unfavorable DFS, RFS and disease-specific survival of patients with bladder cancer (50). Permuth *et al* (51) demonstrated that a two-lncRNA marker was able to effectively discriminate between inert (benign) intraductal papillary mucinous neoplasm (IPMN) and invasive (malignant) IPMN, surpassing the accuracy of conventional clinical and radiological characteristics (51). These findings underscore the viability of lncRNAs as potential prognostic indicators for diverse malignancies.

In the present study, the meta-analysis revealed that the up- and downregulated expression of different lncRNAs was markedly associated with tumor T stage, N stage and overall clinical stage. Pooled HRs for OS indicated a critical role played by lncRNAs in NPC. Furthermore, the data revealed that patients with a high expression of HOTAIR, SNHG12, NEAT1, FOXP4-AS1 and ANRIL had a significantly shorter OS compared with those with a low expression of these lncRNAs. Dysregulated lncRNAs have been reported to play a vital role in NPC tumor cell apoptosis, invasion, metastasis and angiogenesis through transcriptional regulation, epithelial and mesenchymal transformation, and the expression and release of angiogenesis factors (52). Previous research has indicated that lncRNA LINC00930 promotes the expression of glycolysis regulator phosphofructo-2-kinase/fructose-2,6-biphosphatase 3, thereby promoting glycolysis and the proliferation of tumor cells, thus promoting the development of NPC. Similarly, targeted therapy with LINC00930 has been shown to achieve significant results (53). LncRNA DLX6-AS1 has been revealed to promote the proliferation, migration and invasion of NPC cells (54).

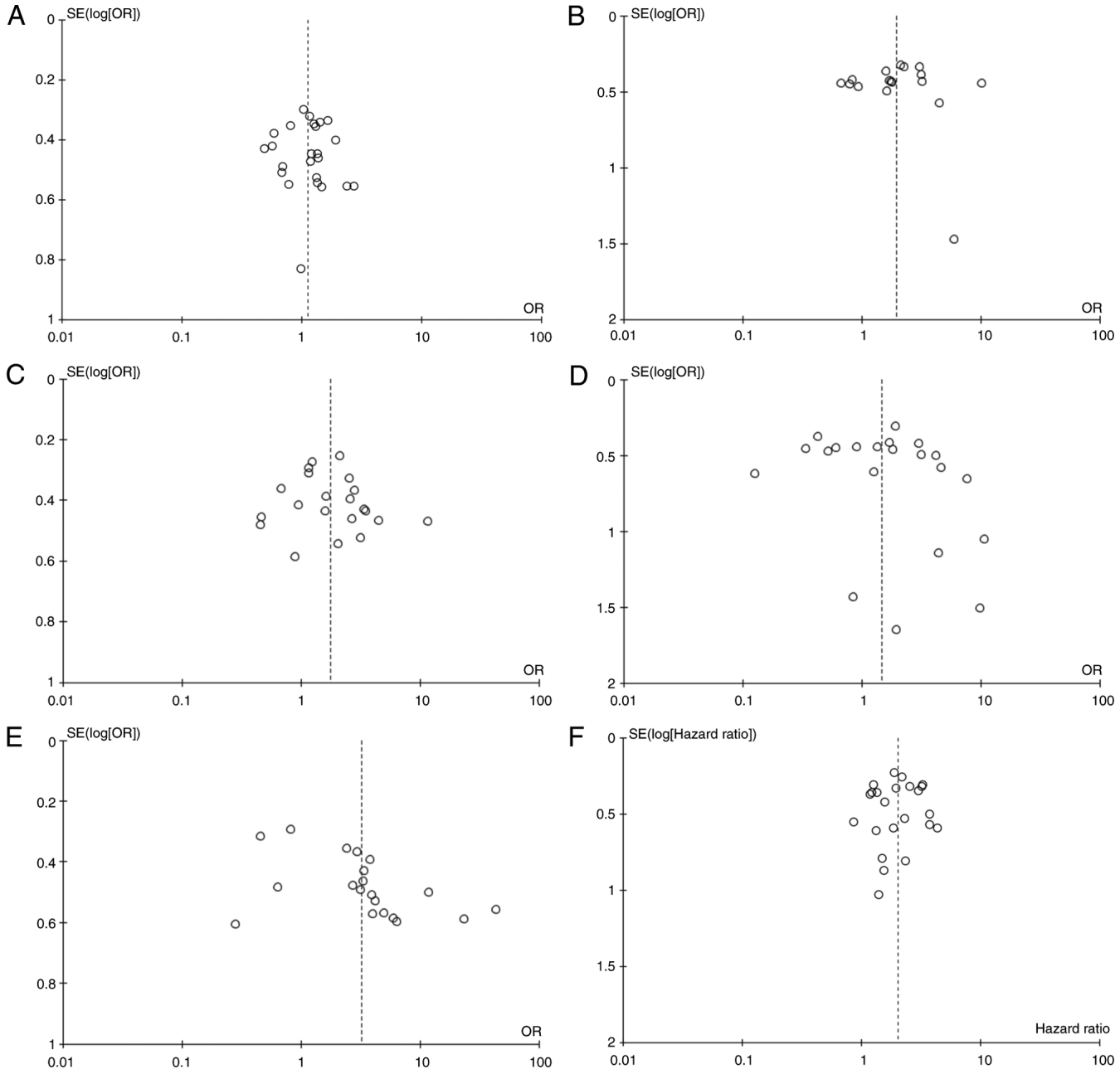

Figure 10. Funnel plot illustrating the association between the upregulated lncRNAs and characteristics of patients with NPC. (A) Upregulation of lncRNAs and sex of patients with NPC. (B) Funnel plot of the association between the upregulation of lncRNAs and T stage of the primary tumors. (C) Funnel plot of the association between the upregulation of lncRNAs and N stage of regional lymph node metastasis. (D) Funnel plot of the association between the upregulation of lncRNAs and M stage of distant metastasis. (E) Funnel plot of the association between the upregulation of lncRNAs and clinical stage of tumors. (F) Funnel plot of the association between the upregulation of lncRNAs and overall survival of patients with NPC. lncRNAs, long non-coding RNAs; NPC, nasopharyngeal carcinoma.

Furthermore, cell transfection experiments have demonstrated that miR-199a-5p can inhibit the invasion and migration of NPC cells. At the same time, studies have demonstrated that miR-199a-5p regulates the expression of hypoxia inducible factor 1α (HIF-1α). In addition, other studies have demonstrated that HIF-1α is expressed in the majority of tumor cells. HIF-1α mediates the adaptation of tumor cells to a hypoxic environment, improves the energy utilization of tumor cells, enhances the resistance of tumor cells to radiotherapy and chemotherapy, and improves the ability of DNA repair (55). The miR-199a-5p binding site on DLX6-AS1 negatively regulates miR-199a-5p expression, thereby indirectly regulating the HIF-1 content in the tumor microenvironment and promoting the development of NPC (54). It has been reported that lncRNA MALAT1 and ANRIL are highly expressed in NPC cell lines, and their knockout leads to the enhanced radiosensitivity of cancer cells. MALAT1 regulates tumor stem cell activity and radiation resistance by regulating the miR-1/slug axis. It has been found that the high expression of ANRIL in NPC inhibits apoptosis and decreases radiosensitivity by downregulating miR-125a. Therefore, lncRNA can be used as a target for gene therapy in NPC (56,57). On the other hand, studies have demonstrated that

lncRNA AFAP1-AS1 is a prognostic risk factor in a variety of cancers. AFAP1-AS1 functions as a bridge between proteins that regulate the integrity of actin and participates in formation of pseudopodia. The deletion of AFAP1-AS1 leads to a decrease in stress fiber content, demonstrating that AFAP1-AS1 can mediate metastasis by changing cell adhesion and migration (58). Therefore, further exploration of the association between lncRNAs and NPC will define tumor pathogenesis and improve the diagnosis and treatment of patients with NPC.

Due to the limited number of articles containing RFS of NPC, the present meta-analysis did not find any significant association between lncRNA expression and the RFS of patients with NPC. Multiple studies have identified lncRNAs, such as ZEB1-AS1, lncRNA ATB, SNHG12 and SNHG20, as potential prognostic markers for RFS in various tumors (15,59-61). Furthermore, the neutrophil-to-lymphocyte ratio, O blood group, EBV DNA and serum LDH have been proposed as potential biomarkers for RFS in patients with NPC (62-65). Badowski *et al* (66) suggested that integrating different analytical methods, such as circulating lncRNAs, miRNAs and clinical data can enhance the accuracy of diagnosis or prognostic evaluation. Therefore, conducting further comprehensive investigations on lncRNAs may contribute to validating the efficacy of combining lncRNAs with other indicators in the diagnosis or prognosis of patients with NPC.

The present study has provided significant findings. However, it is important to acknowledge that the inclusion of data without textual research may introduce errors that could potentially influence the results. Additionally, the scale of the included studies, the selection criteria for subjects and healthy controls, and the grouping of the subjects may have an impact on the analysis. Furthermore, the present study examined certain factors related to patient clinical characteristics and prognosis indicators, such as age, which could not be included due to the absence of a standardized classification system. Furthermore, the accuracy of using the Engauge digitizer 11. 1 to extract the data from the survival curve was limited. Lastly, most of relevant studies have been conducted in China since NPC is epidemic in the population of Southern China. A few non-Chinese studies that were searched were retrieved but did not meet the authors' inclusion criteria and were not included in further analysis.

In conclusion, the present study demonstrated that lncRNAs are associated with the T stage, N stage, clinical stage and OS, suggesting that they may serve as potential prognostic factors for patients with NPC. With the deepening of the functional elaboration of lncRNAs, they are expected to become a new choice of clinical prognostic biomarkers and drug treatment targets for NPC, providing further opportunities for early diagnosis and treatment.

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Availability of data and materials

The datasets generated during and analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

PY, JY and SZ performed retrieval of studies and formulation of clear inclusion and exclusion criteria, literature screening, data extraction, result analysis and manuscript writing. YC contributed to the guidance and revision of the paper. Data authentication is not applicable. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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