Influential Determinants on Health-Related Quality of Life in Intensive Care Unit Survivors: A Meta-Analysis

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ABSTRACT

This study aimed to identify the factors influencing the health-related quality of life (HRQoL) in ICU survivors. The electronic search period was established until April 2023, using CNKI, Wanfang, VIP, CBM, PubMed, Embase, and Cochrane databases. Meta-analysis of data was performed using RevMan 5.4 and STATA 15.0 software. Of the 183 references screened, 12 studies with a total sample size of 19,517 were eventually included. The results showed that duration of mechanical ventilation (OR = 2.24), length of stay in ICU, and length of hospital stay were risk factors for lower quality of life in ICU survivors. Gender was not associated with the quality of life of ICU survivors. The relationship between age, complication count, and quality of life of ICU survivors was not clear. Depression score had a significant effect on the mental health score (MCS) of ICU survivors.

Key Words: *Intensive care unit (ICU), Survivors, Health-related quality of life (HRQoL), Risk factors, Meta-analysis, Systematic review*.

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INTRODUCTION

In recent years, the hospital mortality rate of critically ill patients has significantly decreased as a result of advancements in intensive care medicine, improvements in the quality of intensive care, and the development of long-term multi-organ support technology.[1] However, the long-term outcomes for survivors of intensive care unit (ICU) stays have become a prominent concern. It is common for ICU survivors to experience physical, psychological, and cognitive impairments that persist for months or even years after being discharged,[2,3] ultimately leading to a substantial reduction in their overall quality of life (QoL).

Numerous studies have investigated the determinants of health-related quality of life (HRQoL) among survivors of ICU, yet the findings of these studies remain incongruous. In a cohort study, the duration of mechanical ventilation was identified as a potential influencing factor of HRQoL.[4] Conversely, another study found no substantial correlation between the duration of mechanical ventilation and HRQoL.[5] The aim of this meta-analysis was to examine the influencing factors of HRQoL among ICU survivors, with the goal to establish a foundation of evidence-based support for early interventions.

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METHODOLOGY

The databases of the Cochrane Library, PubMed, Embase, Wanfang, CNKI, China Biology Medicine Disc, and VIP were searched. Search terms and keywords were employed, and the included studies' references were located. The thematic terms "intensive care unit," "survivor," "quality of life," and "risk factors" were used. The database's creation date was limited to April 2023 for searches.

The inclusion criteria were cohort studies, case-control studies, and cross-sectional studies published in Chinese and English languages, where the research objects were adult patients (age ≥18 years) who survived ICU admission, and the research content was risk factors related to the QoL of ICU survivors. Outcome measures were HRQoL of ICU survivors. The following contents were excluded from the analysis: Studies that did not meet the above conditions, those with incomplete research data or data that could not be extracted, repeated publications, conference papers, studies for which full text could not be obtained, and literature review.

Using NoteExpress, two researchers separately sorted and extracted the literature. Duplicate, irrelevant, and unqualified literature was removed. The first-loosening, then-tightening approach was used to ensure that the literature was as thorough as possible, and secondary screening was carried out where needed. Group discussion was used to decide inclusion in the event of a disagreement. The authors of the included studies, the publication date, the publication nation, the kind of included studies, the study participants, the sample size, the follow-up period, the QoL assessment instruments, and the influencing factors were among the content collected.

Two researchers independently evaluated the quality of the literature according to the type of study. Cohort studies and case-control studies were evaluated by the Newcastle-Ottawa Scale (NOS).[6] The NOS included 3 parts, including study population selection, comparability between groups, and exposure factors, with 8 items in total. The item comparability was assigned two points, and the other seven items were assigned one point, respectively. A total score ≥6 was considered to be of high quality.

The cross-sectional study used the evaluation criteria for cross-sectional studies recommended by the Agency for Healthcare Research and Quality (AHRQ),[7] with a total of 11 items. Each item was rated as yes, no, or unclear. Yes, was assigned one point, no or unclear were scored 0, with 0-3 as low quality, 4-7 as medium quality, and 8-11 as high quality. Differences of opinion during the evaluation process were resolved by mutual discussion or consultation with the third researcher.

The combined data were analysed using RevMan 5.3 software to determine the OR and RR, and STATA 15.0 was utilised to determine the regression and correlation coefficients. When the studies were homogeneous ($p > 0.05$ and $I^2 < 50\%$), the fixed effect model was employed for the meta-analysis. There was a variability among the studies if $p \leq 0.05$ and $I^2 \geq 50\%$. After excluding studies that contributed to heterogeneity, the combined effect was computed using subgroup analysis to examine the source of heterogeneity. Descriptive evaluation was utilised since there were few studies on affecting factors or because the data could not be integrated. Statistics were deemed significant if $p < 0.05$.

RESULTS

A total of 583 studies were retrieved, comprising 561 in English and 22 in Chinese; 33 duplicates and 369 other literature were eliminated following a review of the title and abstract. Out of the 181 literature, 2 literature were located through reference tracking, and 12 literature were eventually included following a review of the entire text.[5,8-18] The procedure for screening literature is displayed in Figure 1.

There were eight cohort studies,[5,8-14] one case-control study,[15] and three cross-sectional observational studies[16-18] among the 12 included papers. Six ICU survivors were among the illness categories that were examined,[5,10,11,16,17] with a total sample size of 2,171 cases. A total of 225 cases comprised the sample, of which, two trauma victims were included.[8,18] Two individuals had sepsis,[9,15] making a total of 12,266 instances in the sample. The coronavirus disease 2019 (COVID-19) study included 403 cases as its sample size.[13] Acute respiratory distress syndrome (ARDS) was one of them, with 4,452 instances in the sample size.[14] Out of these, five articles provided the QoL drop rate, which ranged from 34 to 92.1%.[9,10,13,14,16] Table I displays the fundamental attributes and methodological quality assessment of the incorporated literature.

The impact of the length of mechanical ventilation on the HRQoL of ICU survivors was shown in five studies.[9,10,12,15,17] The same data type was used in three research studies,[9,10,15] meta-analysis was done, and the study results varied ($I^2 = 95\%$, $p < 0.001$). Following subgroup analysis, one heterogeneous article was eliminated,[10] and the two publications that remained[9,15] had negligible heterogeneity ($I^2 = 0\%$, $p = 0.33$). A fixed effect model was used for analysis. The results showed that the duration of mechanical ventilation was an influencing factor for the HRQoL of ICU survivors, and the difference was statistically significant [OR = 2.24, 95% CI (1.78, 2.82), $p < 0.001$] (Figure 2A, B).

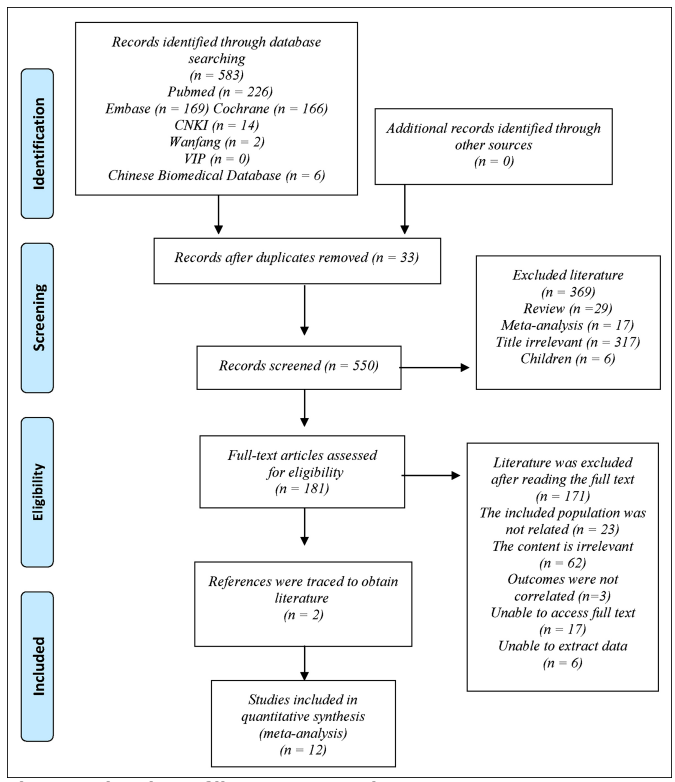

Figure 1: Flowchart of literature screening.

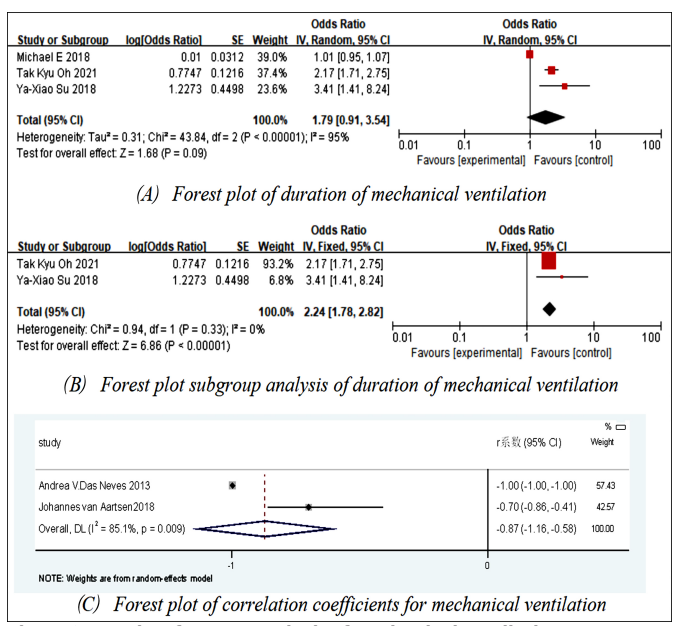

Figure 2: Results of a meta-analysis of mechanical ventilation.

Table I: Basic characteristics of included literature (n = 12).

Study included	Nation	Type study	Population sample size	Sample size (T/C)	Follow-up (m)	Assessment tool	QOL decline incidence	Effect factor	NOS/ AHRQ score
Abraham *et al.*[8] 2014	US	Cohort study	Trauma	115	12	SF-36	-	1, 3, 7, 8	8
Oh and Song[9] 2021	Korean	Cohort study	Sepsis	11960	12	SF-36	77%	1, 9, 10, 11	9
Detsky *et al.*[10] 2018	US Canadian	Cohort study	ICU Survivors	162	6	Patient self-report	34%	1, 6, 12, 13, 14	6
Orwelius *et al.*[11] 2008	Swedish	Cohort study	ICU Survivors	1625 (911)	6, 12	SF-36	-	15	8
Kang *et al.*[16] 2022	Korean	Cross-sectional study	ICU Survivors	534	1~12	EQ-5D-5L	92.1%	2, 3, 4, 14, 16	5
Van Aartsen and Van Aswegen[17] 2018	South African	Observational longitudinal study	ICU Survivors	24	1, 6	SF-36 EQ-5D	100%	1, 4, 5, 7	4
Griffith *et al.*[5] 2018	UK	Nested cohort	ICU Survivors	240	3, 6, 12	SF 12 v2	100%	2, 6, 17	5
Das Neves *et al.*[12] 2015	Argentina	Cohort study	ICU Survivors	112	1, 3, 6, 12	EQ-5D	-	1, 16, 24	6
Goixart *et al.*[18] 2014	Spain	Prospective, observational study	Sepsis	110	6, 12	SF-3 6EQ-5D-5L	-	2, 18, 19	6
Su *et al.*[15] 2018	China	Case-control study	Sepsis	306/306	Discharge, 3, 12, 24	SF-36 EQ-5D	-	1, 2, 3, 6	7
Likhvantsev *et al.*[13] 2022	Italy	Prospective cohort	COVID-19	403	6	SF-36	68% PCS 48% MCS	2, 3, 20, 21, 22	7
Choi *et al.*[14] 2022	Korean	Cohort study	ARDS	4452	12	SF-36	37.4%	2, 3, 14, 23, 25	7

T refers to the experimental group or exposure group; C, the control group or non-exposed group; QoL stands for the quality of life; Newcastle-Ottawa scale for NOS; AHRQ Agency for Healthcare Research and Quality; SF-36 is a health survey scale; EQ-5D and EQ-5D-5L are European 5-dimensional health scales.
Effect factor: 1. Duration of mechanical ventilation; 2. Age; 3. Gender; 4. Length of ICU stay; 5. Length of hospital stay; 6. Count of comorbidities and complications; 7. Depression score; 8. Post-traumatic stress disorder, PTSD; 9. Tracheal intubation; 10. CRRT; 11. Use of vasopressin; 12. Capacity for action; 13. Cognition; 14. Places of residence; 15. Sleep status; 16. Unemployment or return to work; 17. Social deprivation; 18. Trauma score, TRISS ≥10; 19. Visual analogue scale, EVA ≤85; 20. Low molecular heparin; 21. Weight index; 22. Cerebrovascular accident; 23. Hospitalisation expenses; 24. Weak; 25. Follow-up.

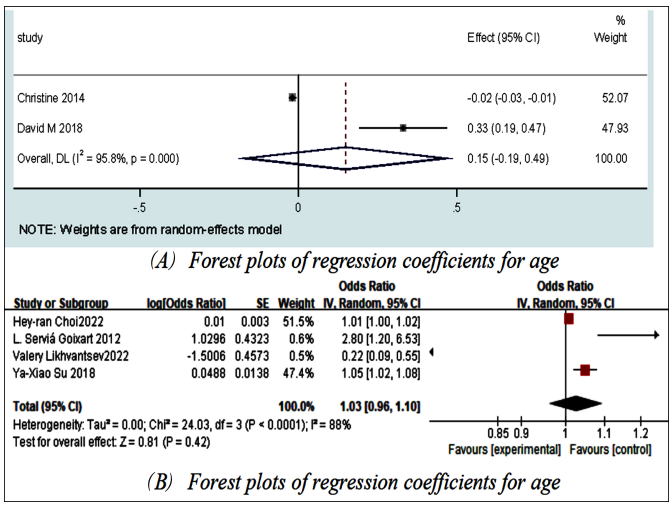

Figure 3: Results of meta-analysis of age.

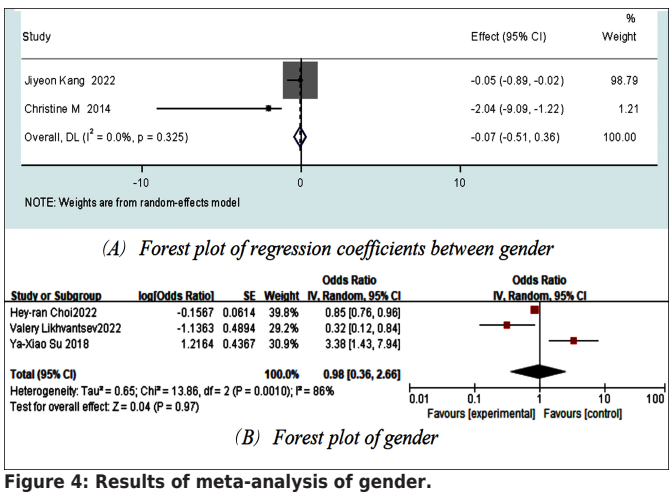

Figure 4: Results of meta-analysis of gender.

Two studies had similar data types and were converted to the same study data.[12,17] Stata 15.0 was used for meta-analysis, and a random-effects model was used for analysis. The difference was statistically significant [r (95% CI) = -0.87 (-1.16, -0.58), p = 0.009], as shown in Figure 2C. However, there was heterogeneity between the results of the two studies (I^2 = 85.1%, p = 0.009). First, the sources of heterogeneity were different from those of the other studies. Second, van Aartsen *et al*. suggested that mechanical ventilation mainly affects the mental component scale (MCS) score of the SF-36.[17]

Seven studies reported the effect of age on HRQoL in ICU survivors.[5,8,13-16,18] After analysing the same research results, a regression coefficient meta-analysis of three studies showed that there was heterogeneity among the studies (I^2 = 95.8%, p <0.001).[5,8,16] Because one of the regression coefficients was -0.00, Stata 15.0 was used for the meta-analysis, and the results showed that only two studies were combined. A random effects model analysis showed that age was an influencing factor in the HRQoL of ICU survivors, and the difference was statistically significant [β (95% CI) = 0.15 (-0.19, 0.49), p <0.001, Figure 3A]. However, the heterogeneity of these two studies was too high, the combination of the two studies was considered meaningless, and a systematic review was used. After analysing the two studies, it was considered that the inconsistency of the study subjects was the reason for the great heterogeneity of the two studies.

The other four studies obtained the same OR, and the OR was converted to the same dependent variable,[13-15,18] that is, the QoL of older patients was lower. The pooled results were analysed by Review Manager 5.4, and the results showed that there was a high heterogeneity among the results of the four studies (I^2 = 88%, p <0.05, p = 0.0003). The random effects model showed that age was not an influencing factor in ICU survivors' QoL, and the difference was not statistically significant [OR = 1.03, 95% CI = 0.96, 1.10); p = 0.42, Figure 3B]. Analysis of these four studies showed that one of the study subjects was inconsistent, and the four studies involved trauma patients,[18] sepsis patients,[15] COVID-19

patients,[13] and ARDS survivors.[14] Second, the types of studies were inconsistent, four studies were observational,[18] case-control,[15] and cohort.[13,14] Third, the age ranges used in each study were not consistent. The ages included in the four studies were more than 45 years,[18] not mentioned,[15] more than 52 years,[13] and more than 66 years;[14] therefore, this merger was not of research significance. Taken together, these findings led to the conclusion that there is insufficient evidence that age has an effect on HRQoL and is an influencing factor for the QoL of ICU survivors.

Gender effects on the HRQoL of ICU survivors were documented in five research studies,[8,13-16] and two studies yielded identical findings.[8,16] The dependent variable was the same for the transformation regression coefficient B value. The data from a meta-analysis of men's and women's QoL were obtained using Stata 15.0 ($I^2 = 0.0\%$). There was no heterogeneity among the included trials ($p = 0.325$). Gender did not influence the HRQoL of ICU survivors, according to fixed-effect model analysis results; the difference was not statistically significant [β (95% CI) = -0.07 (-0.51, 0.36), $p = 0.325$], as shown in Figure 4A.

Both of the studies were examined. The two types of investigations, cross-sectional and observational, were incongruous with one another. Second, the populations covered in the two articles were not consistent; they were ICU trauma survivors and patients, respectively. Consequently, there is no scientific significance to this merger. The identical OR value was achieved by the other three investigations,[13-15] and the OR value was then translated to the same dependent variable. Review Manager 5.4 was utilised to conduct a meta-analysis based on the QoL of men and women. The findings indicated a significant degree of heterogeneity between the three studies' findings ($I^2 = 86\%$, $p = 0.001$). As seen in Figure 4B, the random effect model was used to determine that age was not a significant factor influencing the QoL of ICU survivors. The difference was not statistically significant [OR = 0.98, 95% CI (0.36, 2.66), $p = 0.97$]. Consequently, this study found that among ICU survivors, gender had no bearing on QoL.

The impact of ICU duration of stay on the HRQoL of ICU survivors was examined in two studies,[16,17] the results of which could not be merged due to inconsistencies in the data. The length of an ICU stay was found to be inversely connected with the HRQoL of ICU survivors, according to both publications. The length of hospital stays and HRQoL of ICU survivors were the subject of three investigations.[4,17,19] The study data were inconsistent and could not be pooled, but all three studies found a negative correlation between the two variables.

The effect of the comorbidity index on the HRQoL of ICU survivors was the subject of three studies,[4-5,15] the results of which could not be merged due to inconsistencies in the data. According to two studies,[4,5] there was a negative correlation between the HRQoL of ICU survivors and the comorbidity index. According to one research,[15] there was no relationship between the index of comorbidities and the ICU survivors' HRQoL.

The effect of depression scores on HRQoL in intensive care unit survivors was the subject of two studies,[8,17] the results of which could not be merged due to inconsistencies in the data. Research from two different studies revealed a negative correlation between the depression score and the mental health score (MCS) of ICU survivors' HRQoL.

It was discovered in this study that there were several requirements for descriptive analysis because there were only a few literature reports or hard-to-combine data.

Self-related factors reported by patients were pain,[4] weakness,[12] mobility,[10] and sleep.[11] Place of residence,[10,16] social deprivations,[5] return to work,[12,16] and other variables were examples of socially relevant characteristics. Research has demonstrated a relationship between the HRQoL and all of the aforementioned characteristics of ICU survivors.

DISCUSSION

This study included 12 publications in all, with a middling overall quality. Data could not be collected from various literature, and the included research results were dispersed. The effect sizes needed to be merged even after the data were retrieved because they varied. In addition, even though they had identical data, the kinds of research, the diseases that the individuals had, or the dependent variables were inconsistent and must be integrated after conversion. After merging, the outcomes of several investigations were incredibly inconsistent. As a result, it is important to proceed cautiously with the study's findings, and additional excellent clinical research is anticipated in the future. A publication bias test could not be conducted since each contributing factor had fewer than 10 included studies.

According to this study, ICU survivors who had been on mechanical breathing for a longer period had a worse QoL overall. This could be connected to long-term ventilator usage, the use of sedatives or analgesics during mechanical breathing, a further deterioration in respiratory muscle strength, muscle weakness, and lung damage brought on by the ventilator. This aligns with the findings of the Caamano *et al*.'s report.[20] Six months following ICU release, inspiratory muscle strength consistently reduced in COVID-19 survivors receiving invasive ventilation.[21]

This study indicates that among ICU survivors, age does not appear to be a significant factor in HRQoL. Elderly patients have a decreased basic QoL as a result of an increase in fundamental diseases and a decline in their capacity for self-care as they age. There may be bias because the majority of the studies included in this analysis did not assess patients' baseline QoL. Second, the age ranges that the research insti-

tutes set[13-15,18] are not the same; they range from 45 to 66 years. Thirdly, even though every participant in this research was an ICU survivor, the illnesses that brought them there were diverse. Consequently, there is a great deal of heterogeneity in the combined studies' results, and further research involving large samples and multiple centres is required to provide clarification.

In this study, it is not possible to conclude whether men or women have lower HRQoL due to the inconsistency of study types and disease types studied. Despite this, the results of the pooled analysis were unable to corroborate the association between gender and QoL associated with ICU survivors. Nevertheless, a combination of research has shown that men are more likely than women to perform poorly in the role-physical domain as well as the mental health aspects of social functioning and role-emotional, which will result in worse QoL ratings.[8] However, after a serious illness, women are more susceptible than men, and this can also lower some women's QoL.[22] In the future, these theories must be verified by extensive prospective research.

Extended stays in the intensive care unit and hospital might result in the onset of physical symptoms such as fatigue, disturbed sleep patterns, and appetite loss, which are frequently linked to mental health issues.[17] It consequently results in a lower QoL following discharge.

Even though four research studies[4,5,10,15] examined the connection between complication counts and HRQoL in ICU survivors, the studies' inconsistent reporting of their findings and the inability to combine data prevented a conclusive finding. As a result, the nature of the relationship was unclear.

Depression is classified as a mood disorder, and individuals with depression have longer-term distress than is typically acknowledged in terms of psychological distress and HRQoL. Conversely, research has demonstrated a consistent correlation between longer-term reductions in physical functioning and elevated negative mood levels.[22] Consequently, people with lower depression ratings typically have lower QoL, and mental health scores are more affected by depression than by physical functioning.

The limitations of these results need also be considered. The inclusion and exclusion criteria, age distribution, gender ratio, and underlying diseases of patients varied widely amongst studies due to differences in sample size, assessment tools, observation frequency, and duration. As a result, the results of the surveys that are included are dispersed and exhibit significant heterogeneity. The literature reviewed for this paper contained a wide range of reported affecting factors. A limited number of studies were available on certain influencing factors, and some could only be subjected to descriptive analysis rather than meta-analysis. The majority of the included literature was from the American and European nations; very few were from the Asian nations, particularly China. As a result, it is important to proceed cautiously with the study's findings, and additional excellent clinical research is anticipated in the future.

CONCLUSION

The length of hospital stays, the length of ICU stays, and the duration of mechanical breathing were all associated with a lower QoL for ICU survivors. Among ICU survivors, gender did not correlate with QoL. It is unclear how the age, number of complications, and QoL of ICU survivors relate to one another. Depression scores had a significant impact on ICU survivors' MCS of quality of life. The findings of this study can be used by clinical nursing staff to enhance patient outcomes by facilitating early and effective intervention, screening for low QoL in ICU survivors, and strengthening assessment and screening processes. Nevertheless, it is advised to do large sample multi-centre research in the future to further investigate strategies and tactics to enhance the QoL for severe survivors, given the short sample size and suboptimal calibre of pertinent research.

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COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

LF, YN: Conceived and designed the study.
LF, YN, YL: Collected the data.
YD, JD: Re-examined the data.
LF, YB: Analysed the data.
LF: Wrote the first draft of the manuscript.
YN, YL: Wrote sections of the manuscript.
YD: Reviewed and revised the manuscript.
All authors approved the final version of the manuscript to be published.

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