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10-Minute vs. 4-Hour Post-Gadolinium 3D-FLAIR MRI for Sudden Sensorineural Hearing Loss: A Systematic Review and Meta-analysis

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ABSTRACT

Purpose: The purpose of this study was to perform a meta-analysis comparing the performance of 10-minute and 4-hour delayed-enhanced Three-Dimensional Fluid-Attenuated Inversion Recovery Magnetic Resonance Imaging (3D-FLAIR MRI) for the detection of inner ear abnormalities in sudden sensorineural hearing loss (SSNHL).Methods: A comprehensive literature search was performed independently by two researchers, covering databases including PubMed, Web of Science, Science Direct and CNKI up to June 4, 2025. Original research studies comparing 10-minute and 4-hour delayed-enhanced 3D-FLAIR MRI in evaluating SSNHL were included. The Joanna Briggs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data (JBI) was used for quality assessment. All literature was independently screened and data were extracted, followed by meta-analysis and subgroup analysis using RevMan 5.4 to compare the performance of 10-minute and 4-hour delayed-enhanced 3D-FLAIR MRI.Results: Four studies including 211 affected ears in 210 SSNHL patients met inclusion criteria for the systematic review. All patients underwent 10-minute and 4-hour delayed-enhanced 3D-FLAIR MRI scanning. The meta-analysis showed a statistically significant difference in detection rates between the 10-minute and 4-hour delays (risk difference [RD], -0.24; 95% CI, -0.38 to -0.10; $I^2 = 63\%$; $p = 0.0006$). Subgroup analyses indicated that study type, region and Gd dose may be the sources of heterogeneity.Conclusion: A 4-hour delay reveals 24% more abnormal findings than a 10-minute delay in Gd-enhanced 3D-FLAIR MRI. Therefore, we recommend a 4-hour delay for the clinical evaluation of SSNHL patients.

KEYWORDS

Sudden Sensorineural Hearing Loss, Fluid-Attenuated Inversion Recovery, Magnetic Resonance Imaging, Meta-analysis.

1 Introduction

As a sensorineural subset of sudden hearing loss (SHL), SSNHL is defined by an acute onset within 72 hours and fulfillment of predetermined audiometric standards. It affects 5 to 27 per 100,000 people (Chandrasekhar et al., 2019). The most widely accepted hypotheses regarding the pathophysiology of SSNHL include vascular compromise, cochlear membrane rupture, and viral infection (Kuhn et al., 2011). In addition, manifestations such as tinnitus or vertigo may co-occur in patients with SSNHL (Tian et al., 2018).

3D-FLAIR MRI, compared with traditional MRI, has the ability to restrict free-water signals. In SSNHL patients who undergo gadolinium (Gd)-enhanced 3D-FLAIR MRI, abnormal enhancement is observed in the affected side, indicating pathological changes. Previous studies also suggested that high signals in the inner ear on 3D-FLAIR MRI are associated with more severe initial hearing loss (Gao and Chi, 2014), and correlate with poor hearing prognosis (Zhu et al., 2015). Nowadays, detection rates of abnormal enhancement have increased up to 69.05% (Lee et al., 2012; Kim et al., 2015; Wang et al., 2019; Bossy et al., 2022), making 3D-FLAIR MRI an ideal way to visualize inner ear changes and evaluate SSNHL in clinical practice (Conte et al., 2019; Wang et al., 2019). However, there is ongoing debate regarding the optimal imaging window (10-minute vs. 4-hour) following Gd-based contrast administration (Kim et al., 2015; Byun et al., 2019).

This study conducted a meta-analysis to synthesize clinical research data, investigating differences in detection rates of 3D-FLAIR MRI examinations across varying temporal windows post-Gd enhancement. The ultimate aim was to identify evidence-based optimal time points for clinical decision and protocol optimization.

2 Methods

This study has been registered in PROSPERO (ID: CRD420251056906).

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2.1 Search Strategy

A systematic search strategy was employed to retrieve studies from multiple databases including PubMed, Embase, and Web of Science. Combinations of keywords such as "sudden hearing loss", "SSNHL", "3D-FLAIR MRI" and "gadolinium-based contrast agents" were used, with the time range set from database inception to June 4, 2025.

2.2 Study Selection

This review included studies that fulfilled the following criteria: (1) included >30 patients with SSNHL, (2) were retrospective or prospective studies on SSNHL, (3) include patients diagnosed with SSNHL via pure -tone audiometry (PTA), (4) included patients who had not received any primary treatment before attending the research institution, (5) reported data on the detection rates of 3D-FLAIR at 10-minute and 4-hour delayed time points, and (6) defined positive cases as those in which the affected ear demonstrated higher signals than the contralateral unaffected ear at any time point(10-minute or 4-hour) assessed. Studies were excluded with the following traits: (1) The data is vague, incomplete or non-extractable, (2) used non-comparable metrics, (3) were case reports, review articles, or non-human studies, or (4) pertained to progressive hearing loss, congenital hearing loss, or conductive/mixed hearing loss. Screening of articles by title, abstract, and full text was independently conducted by two authors, and any conflicts were resolved by a third author.

2.3 Data Management and Quality Assessment

Two authors extracted and cross-checked the following data from each study: study characteristics, patient demographic characteristics, definition of SSNHL, initial hearing threshold, scanner settings, contrast agents, areas of labyrinthine abnormality, and detection rates. The Joanna Briggs Institute (JBI) Critical Appraisal Checklist (Whiting et al., 2011; Campbell et al., 2015) was used to assess the risk of bias. Two authors independently reviewed the articles using the checklists, rating each item as “yes,” “no,” “unclear,” or “not applicable.” All disagreements were resolved by a third author.

2.4 Statistical Analysis

For dichotomous variables, the risk difference (RD) and 95% confidence interval (CI) were used for description. Heterogeneity was assessed based on I^2 values and P-values: results with $I^2 \geq 50\%$ were considered to exhibit substantial heterogeneity, for which the Mantel-Haenszel random-effects model (REM) was employed to pool effect sizes. When $I^2 < 50\%$, a fixed-effects model (FEM) was applied. In cases of significant heterogeneity, plausible causes were systematically analyzed through subgroup analyses. If substantial heterogeneity persisted within subgroups after stratification, potential sources of heterogeneity were thoroughly investigated and rationally interpreted. The significance level for the meta-analysis was set at $\alpha=0.05$, with statistical significance defined as a two-tailed P-value<0.05. Possible publication bias was assessed by inspecting the funnel plot and conducting Egger's regression tests (Egger et al., 1997). The results of the tests suggested the presence of possible publication bias if the P-value in Egger's test was <0.05. If evidence of publication bias was noted, the trim-and-fill method was applied (Duval and Tweedie, 2000).

3 Results

3.1 Study screening and selection

A total of 1308 studies were retrieved. After removing duplicates, 1075 studies remained. These studies were screened by reviewing titles and abstracts, and those that did not meet the predefined criteria were excluded. Ultimately, 4 studies (Zhu et al., 2015; Min et al., 2018; Byun et al., 2019; Compagnone et al., 2022) were incorporated into meta-analysis (Fig. 1). The detection rate was defined as the proportion of patients showing asymmetric enhancement in the affected inner ear compared to the total number of patients detected. It is to be noted that in Min et al. (2018)’s study, three criteria (no abnormality, mild elevation, obvious elevation) were adopted to evaluate inner ear signal changes. Only obvious elevation cases were considered in the calculation of detection rates. Table 1 summarizes the baseline characteristics of the included studies.

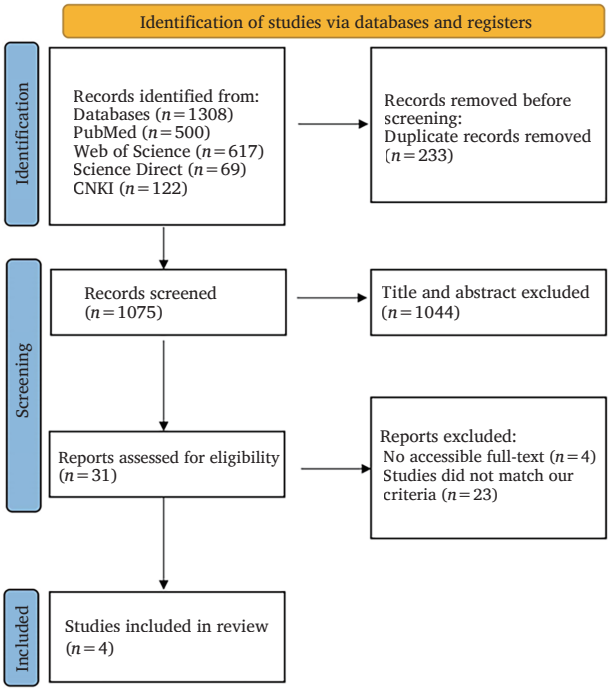


Figure 1 PRISMA flow diagram: details on the review filtering process

3.2 Quality Assessment

The results of quality assessment of the 4 included studies can be seen in Table 2.

3.3 Patient Characteristics

The relationship between patient characteristics (age (Zhu et al., 2015; Min et al., 2018; Byun et al., 2019; Compagnone et al., 2022), initial hearing threshold (Zhu et al., 2015; Byun et al., 2019; Compagnone et al., 2022) and detection rates (10-minute, 4-hour) was compared. In Min et al. (2018)'s study, age was presented as the median, which we converted to mean ± SD using a validated conversion formula (Wan et al., 2014; Luo et al., 2018). No obvious relationship was observed between age and detection rates (R^2=0.14 in 10-minute, R^2=0.34 in 4-hour), while detection rates showed an inverse study level association with the initial hearing threshold (R^2=0.88 in 10-minute, R^2=0.64 in 4-hour). Results can

Table 1 Basic characteristics of included studies

Study (Year)	Region	Research Type	Subjects Numbers	Age (Mean ± SD)	SSNHL Definition	Initial Hearing Threshold (dB)	Scanner Settings	Gd Dose	Detection Rates	
									10 min	4 h
Byun 2019	Korea	Prospective	87	50.44 ± 13.71	Definition 1[a]	62.17 ± 30.01	3T	Double	20.10%	59.70%
Compa-gnone 2022	France	Prospective	36	54.5 ± 16.3	Definition 1[a]	92.28 ± 10.88	3T	Standard	0%	27.78%
Min 2018	China	Unclear	42	51.9 ± 12.6	Definition 2[b]	Unclear	3T	Standard	26.19%	40.48%
Zhu 2014	China	Unclear	46	58.4 ± 8.1	Definition 2[b]	61.03 ± 27.18	1.5T	Standard	32.60%	41.30%

a. Acutely-developed sensorineural-type hearing loss with an increased pure-tone threshold of > 30dB affecting at least three consecutive frequencies within a 72-hour period (Chandrasekhar et al., 2019).

b. Acutely-developed sensorineural-type hearing loss with an increased pure-tone threshold of ≥ 20dB affecting at least two consecutive frequencies within a 72-hour period (Editorial Board of Chinese Journal of ORL-HNS, 2015).

Table 2 Results of quality assessment

Study	Criteria									
	1	2	3	4	5	6	7	8	9	10
Byun et al., 2019	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Compagnone et al., 2022	No	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Min et al., 2018	Unclear	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	No	Yes
Zhu et al., 2015	Unclear	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes

be seen in Fig. 2.

3.4 *Meta-analysis*

All the four studies (Zhu et al., 2015; Min et al., 2018; Byun et al., 2019; Compagnone et al., 2022) reported the detection rates of SSNHL at 10-minute and 4-hour time points. We conducted a meta-analysis of these data (Fig. 3), which showed substantial statistical heterogeneity with I^2=63%. The REM was used for analysis. The pooled detection rate was 44/211 (20.85%) for a 10-minute delay and 98/211 (46.45%) for a 4-hour delay. The aggregated data indicated a statistically significant difference in detection rates between the 10-minute and 4-hour delays (risk difference [RD], −0.24; 95% CI, −0.38 to −0.10; p=0.0006). Therefore, we have reason to believe that a 4-hour delay yields higher detection rates for SSNHL.

Given the high statistical heterogeneity, subgroup analyses were performed based on region, Gd dose, scanner settings, research type, and SSNHL definition to identify

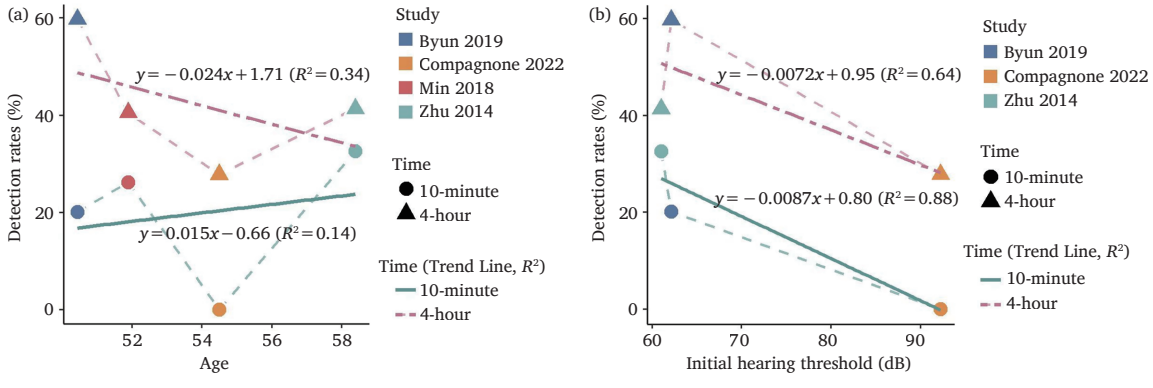


Figure 2 Forest plot: detection rates comparison of 10 min and 4 h

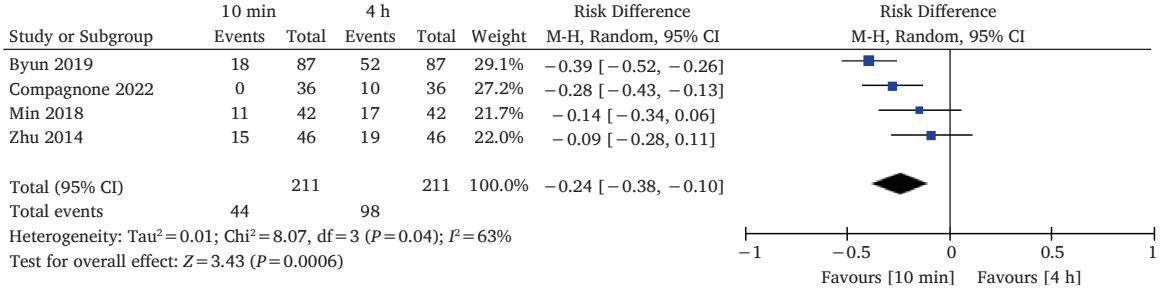


Figure 3 The relation of patient characteristics and detection rates: A, Patients' age. B, Patients' initial hearing threshold

potential sources of heterogeneity (Fig. 4 and Fig. 5).

3.4.1 Research Type

Included studies were divided into two subgroups: prospective (Byun et al., 2019; Compagnone et al., 2022) and unclear (Zhu et al., 2015; Min et al., 2018). Statistical heterogeneity in subgroup: prospective (56.3%) was 25%; unclear (43.7%) was 0%, and different in total (I^2=63%), with P-value of subgroup difference was 0.02. Therefore, we have reason to believe there are differences between subgroups, and research type may be one of the sources of heterogeneity (Fig. 4, A).

3.4.2 Region

Included studies were divided into three subgroups: China (Zhu et al., 2015; Min et al., 2018), Korea (Byun et al., 2019), and France (Compagnone et al., 2022). Statistical heterogeneity in subgroup: China (43.7%) was 0% but high in total (I^2=63%), with P-value of subgroup difference was 0.02. Therefore, we have reason to believe there are differences among subgroups, and region may be one of the sources of heterogeneity (Fig. 4, B).

3.4.3 Gd Dose

Included studies were divided into two subgroups: standard dose (Zhu et al., 2015; Min et al., 2018; Compagnone et al., 2022) and double dose (Byun et al., 2019). Statistical heterogeneity in subgroup: Standard dose (70.9%) was 31% while increased in total (I^2=63%), with P-value of subgroup difference was 0.03. Therefore, we have reason to believe there are differences between subgroups, and Gd dose may be one of the sources of heterogeneity (Fig. 4, C).

3.4.4 Scanner Settings

Included studies were divided into two subgroups: 1.5 T (Zhu et al., 2015) and 3T (Min et al., 2018; Byun et al., 2019; Compagnone et al., 2022). Statistical heterogeneity in subgroup: 3T (78.0%) was 53% while different in total (I^2=63%). with P-value of subgroup difference was 0.10. Therefore, we have no reason to believe there are differences between subgroups, and scanner settings may not be one of the sources of heterogeneity (Fig. 5, A).

3.4.5 SSNHL Definition

Included studies were divided into two subgroups: definition 1[a] (Min et al., 2018; Byun et al., 2019; Compagnone et al., 2022) and definition 2[b] (Zhu et al., 2015). Statistical heterogeneity in subgroup: definition 1[a] (78.3%) was 68%, while different in total (I^2=63%), with P-value of subgroup difference was 0.35. Therefore, we have no reason to believe there are differences between subgroups, and SSNHL definition may not be one of the sources of heterogeneity (Fig. 5, B).

3.5 Publication Bias

Cochran's Q test for heterogeneity revealed significant study variance between the 10-minute and 4-hour groups (Q = 7.99, τ^2 = 0.0118, I^2 = 62.5%, p = 0.0461). Additionally, Egger's test for funnel plot asymmetry indicated no obvious potential publication bias (p = 0.361) (Fig. 6). Trim and-fill analysis was, therefore, not carried out (Duval and Tweedie, 2000). Cochran's Q test suggests substantial heterogeneity while Egger's test suggests the opposite. Therefore, we have reason to believe that publication bias may not be the source of heterogeneity.

4 Discussion

Previous studies evaluating the application of post-gadolinium (Gd) 3D-FLAIR MRI in sudden sensorineural hearing loss (SSNHL) have yielded conflicting diagnostic detection rates, ranging widely across different imaging time windows. To provide a unified synthesis of current evidence, our meta-analysis comparing 10-minute and 4-hour post-Gd 3D-FLAIR MRI in 211 ears demonstrated that a 4-hour delayed scan yields a significantly higher detection rate of inner ear signal abnormalities than a 10-minute scan (46.45% vs. 20.85%; pooled RD, −0.24; 95% CI, −0.38 to −0.10; p = 0.0006). Additionally, analysis of demographic factors revealed no significant study-level association between patient age and detection rates (R^2=0.14 in 10-minute, R^2=0.34 in 4-hour). Given that the age distribution across the four included studies was highly concentrated (p=0.008 in ANOVA test), there is a possibility that our conclusion is biased.

The mean age of patients in the included studies was 53.16±13.27, which could be the peak incidence of SSNHL. This finding is consistent with previous studies (Byl, 1984; Kitoh et al., 2017). For initial hearing thresholds, an inverse study-level association with MRI detection rates was observed (R^2=0.88 for 10-min and R^2=0.64 for 4-h imaging). However, previous studies demonstrated worse hearing in patients with MRI-positive endolymphatic hydrops (Naganawa et al., 2016; Song et al., 2021; Conte et al., 2022). Moreover, the analysis included only three studies and therefore represents an ecological association rather than an individual-level relationship. Above all, this finding should be interpreted cautiously.

Our meta-analysis compared detection rates of SSNHL between the 10-minute and 4-hour delayed imaging windows. Results showed that the 4-hour delay identified 24% more abnormal findings than the 10-minute delay on 3D-FLAIR MRI. Therefore, we recommend a 4-hour delay in clinical practice. Among the included studies, the findings by Byun et al. (2019) and Compagnone et al. (2022) support our conclusion, while Min et al. (2018) and Zhu et al. (2015) reported no statistically significant differences. Due to the observed heterogeneity, we conducted subgroup analyses to explore potential sources. It is found that study type, region and Gd dose may explain our heterogeneity. Further research is needed to fully explain these sources of heterogeneity.

The pathogenesis of SSNHL remains unclear. Previous studies have shown that the majority of SSNHL cases are idiopathic (Chandrasekhar et al., 2019) and require comprehensive evaluation. Several major hypotheses derived from imaging findings include minor hemorrhage, acute inflammatory process and blood-labyrinth barrier (BLB) disruption (Berrettini et al., 2013; Conte et al., 2019). In pre-contrast 3D-FLAIR MRI, high signals were observed while, in T1- or T2-weighted MRI, such signals were not detected. This indicates an increased concentration of protein in the inner ear, which might be a sign of minor hemorrhage or acute inflammation. Normally, Gd-enhancement can only be observed in perilymphatic fluid due to the presence of the BLB. Therefore, contrast enhancement observed in endolymphatic fluid indicates BLB breakdown (Lee et al., 2012; Berrettini et al., 2013).

In addition, some studies have reported that endolymphatic hydrops (EH) is observed in several SSNHL patients (Chen et al., 2012; Zheng et al., 2019), which may also be a cause of SSNHL. EH is indirectly measured by the area of the narrowed contrast-enhanced perilymph space (Suárez et al., 2020). These factors above may irreversibly damage hair cells or other cochlear struc-

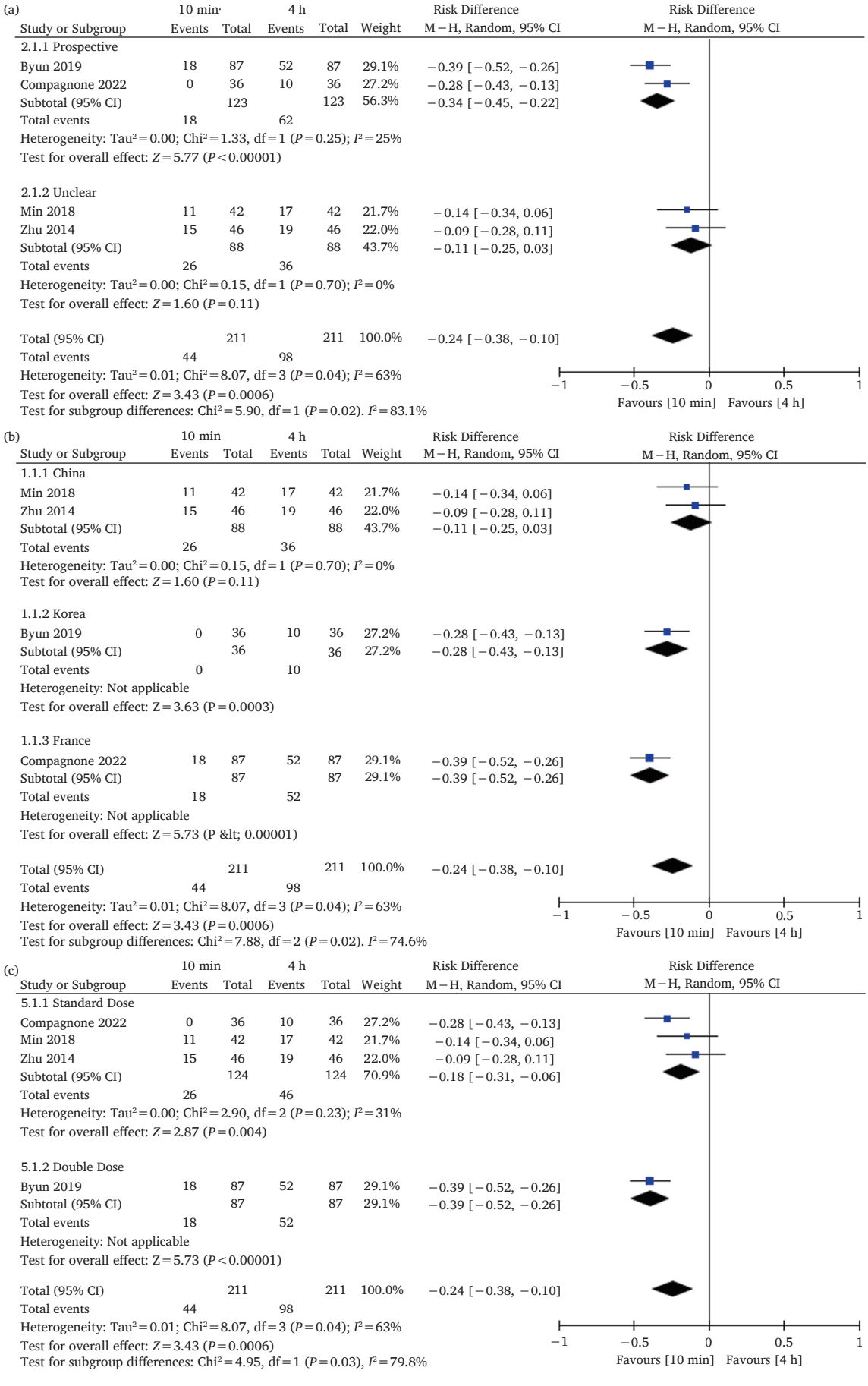


Figure 4 Subgroup analysis forest plot: A, Study type; B, Region; C, Gd dose

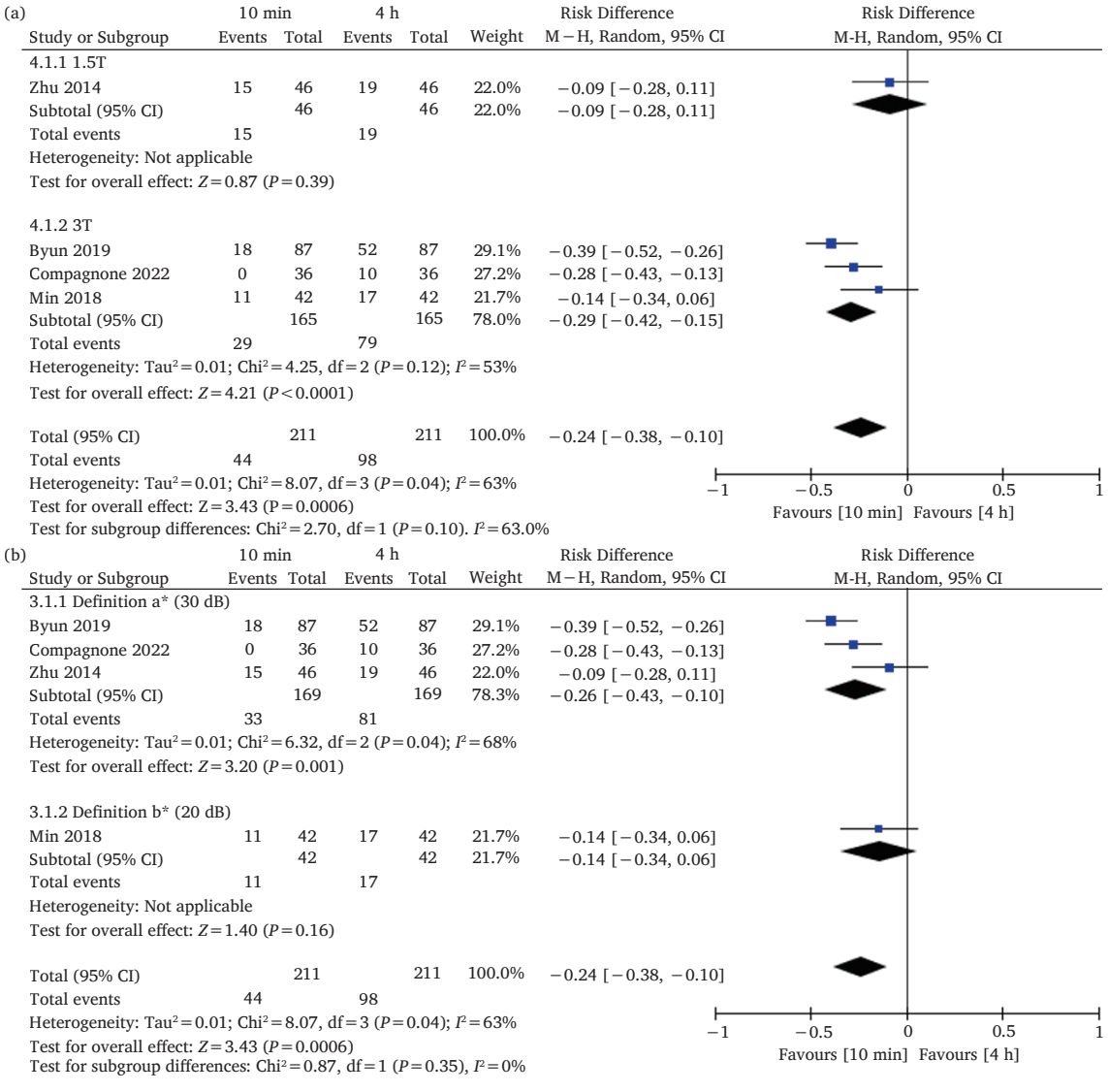


Figure 5 Subgroup analysis forest plot: A, Scanner settings; B, SSNHL definition

tures, leading to hearing loss (Kuhn et al., 2011). Previous studies also indicated that vascular embolism may account for a small percentage in the mechanism of SSNHL (Sato and Kawagishi, 2014; Wang et al., 2019). In fact, there is no published evidence that supports the idea that viral or vascular etiologies are common causes of ISSHL (Merchant et al., 2008). Given that a specific cause for SSNHL is identified in only 10-15% (Cadoni et al., 2006) of cases, the diagnostic process heavily relies on excluding known retrocochlear pathologies such as vestibular schwannoma (Metrailer and Babu, 2016; Tsuzuki and Wasano, 2024), which can be effectively identified through MRI (Kabashi et al., 2020). Consequently, clinical guidelines recommend conducting diagnostic imaging, preferably contrast-enhanced MRI of the brain, for all SSNHL patients (Chandrasekhar et al., 2019). While rare, other retrocochlear lesions such as arachnoid cysts in the cranial posterior fossa have also been occasionally associated with unilateral SSNHL, further underscoring the critical role of comprehensive imaging in the diagnostic workup (Merchant et al., 2008). These imaging findings in SSNHL frequently manifest with characteristic complications including vertigo, tinnitus and ear fullness. SSNHL patients with vertigo exhibit abnormal vestibular function (Li et al., 2021), which leads to a worse prognosis than those without vertigo (Hong et al., 2023). Wang et al. (2019) demonstrated through quantitative analysis that the degree of signal enhancement in inner ear structures (measured by the corrected asymmetry ratio on post-contrast 3D-FLAIR) correlates significantly with the degree of initial hearing loss and hearing recovery rates following steroid therapy, suggesting that greater permeability of the blood-labyrinth barrier may relate to a poor recovery.

However, implementing a routine 4-hour delayed scanning protocol presents noticeable operational challenges with increased patient non-compliance. To improve clinical applicability, future optimization of the scanning sequence is suggested to decrease the overall examination time. Clinicians must weigh the cost-effectiveness and resource utilization of extended patient waiting times against the enhanced diagnostic benefit of delayed imaging.

Several limitations of our meta-analysis should be noticed: (1) The included studies were generally small and single-centered. (2) Only two of the included studies were prospective; the remaining two had unclear study designs. This may introduce selection and misclassification bias in subgroup analyses. Therefore, larger-scale prospective studies are needed. (3) Due to the nature of SSNHL, no gold standard can be proposed, making it impossible to verify the accuracy of imaging findings. (4) None of the included studies

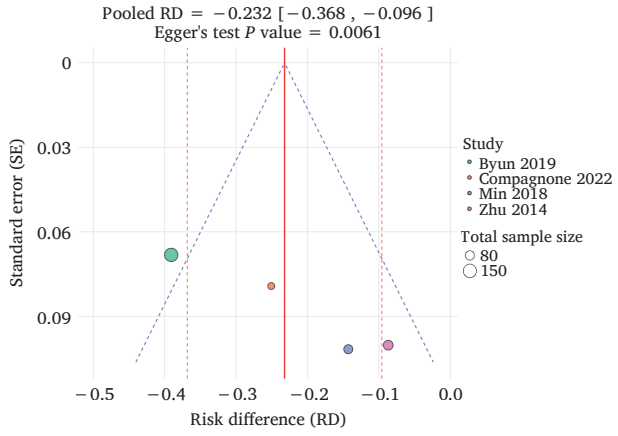


Figure 6 Funnel plot: with pseudo 95% confidence limits

incorporated healthy control groups. As highlighted by Berrettini et al. (2013), understanding the physiological baseline of 3D-FLAIR signal intensity in unaffected or healthy ears is essential for establishing normal thresholds; the absence of control cohorts prevents the precise calculation of diagnostic specificity, false-positive rates, and true sensitivity, and thus prevents us from performing conventional diagnostic test meta-analysis.

5 Conclusion

Our meta-analysis demonstrates that a 4-hour delay reveals 24% more abnormal findings than a 10-minute delay in Gd-enhanced 3D-FLAIR MRI. Therefore, we recommend a 4-hour delay for the clinical evaluation of SSNHL patients. However, given the limitations of this study, these findings should be interpreted with caution.

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Data availability statement

All data generated or analyzed during this study are included in the published article.

Informed consent statement

Not applicable.

Conflicts of interest

The authors have no competing interests to declare that are relevant to the content of this article.

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