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ORIGINAL ARTICLE

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Sensitivity and specificity of meningeal signs in patients with meningitis

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Abstract

Background: Several types of physical examinations are used in the diagnosis of meningitis, including nuchal rigidity, jolt accentuation, Kernig's sign, and Brudzinski's sign. Jolt accentuation was reported to have sensitivity of nearly 100% and to be highly efficient for excluding meningitis, but more recent studies showed that a number of patients with meningitis may present negative in this test.

Methods: We systematically reviewed studies on the above-mentioned physical examination tests and performed meta-analysis of their diagnostic characteristics to evaluate the clinical usefulness. Nine studies, comprising a total of 599 patients with pleocytosis in the cerebrospinal fluid (CSF) and 1216 patients without CSF pleocytosis, were enrolled in the analysis.

Results: Jolt accentuation showed a decent level of odds ratio (3.62; 99% confidence interval (CI): 1.13-11.60, P = 0.004) comparable to that in nuchal rigidity (2.52; 1.21-5.27, P = 0.001) for the correct prediction of CSF pleocytosis among subjects with suspected meningitis. The estimated sensitivity was relatively high (40%-60%) in nuchal rigidity or jolt accentuation tests. On the other hand, Kernig's and Brudzinski's signs exhibited relatively low sensitivity (20%-30%). The estimated specificity was higher in Kernig's and Brudzinski's signs (85%-95%) than in nuchal rigidity or jolt accentuation tests (65%-75%).

Conclusion: Approximately half of the patients with meningitis may not present typical meningeal signs upon physical examination. Combining several examinations for the detection of meningeal signs may decrease the risk of misdiagnosis.

KEYWORDS
jolt accentuation, Kernig's sign, meningitis, meta-analysis, nuchal rigidity

1 | INTRODUCTION

Correct diagnosis of meningitis based on physical examinations is one of the most difficult and important topics in the field of clinical neurology. Most cases of viral meningitis are usually self-remitting and not fatal, but severe cases, such as bacterial, tuberculous, and fungal meningitis, can be fatal if the proper antibiotics are not timely administered.[1,2] Therefore, whether the clinicians in the primary care setting can correctly diagnose meningitis with CSF pleocytosis by performing diagnostic physical examination or not is very important.

At present, physical examination tests for meningitis mainly comprise the following four maneuvers: nuchal rigidity (neck stiffness), jolt accentuation, Kernig's sign, and Brudzinski's sign.[3] Though the nuchal rigidity test is the most famous and prevailing physical examination, correctly assessing the rigidity can be quite difficult in the clinical scene, even by well-trained clinicians. As an alternative diagnostic maneuver with relatively high sensitivity, jolt accentuation was introduced in the late 20th century.[4] The maneuver of jolt accentuation involves head rotation at a frequency of 2-3 times per second and examining whether the headache exacerbates or not. Due to its simplicity, jolt accentuation became popular and prevailed in Asian and Middle East countries, but not in Western countries. Besides, most of the follow-up studies for the validation of the original data showed that the sensitivity of jolt accentuation was much lower than originally reported.[5–9] As a result, the usefulness of jolt accentuation for diagnosing meningitis in the primary care setting has been doubted and unsettled. However, the easiness in the performance and interpretation of jolt accentuation, even by physicians other than neurologists, is attractive and desired to be reconsidered. Therefore, the objective assessment of the usefulness of jolt accentuation based on previous clinical studies worldwide is required.

In this report, after systematically reviewing articles studying the diagnostic characteristics (ie, sensitivity and specificity) of physical examination tests applied for the detection of meningeal signs, including jolt accentuation, we evaluated and compared the clinical usefulness of each test by performing a meta-analysis of the eligible studies.

2 | MATERIALS AND METHODS

2.1 | Search method

We searched MEDLINE, PubMed, Cochrane Library, Embase, and Google Scholar in December 2018. Search terms were as follows: "meningitis," "physical examination," "jolt accentuation," "nuchal rigidity," "Kernig," "Brudzinski," "sensitivity," "odds ratio," and "review." These search terms were suitably combined in repeated searches not to overlook eligible studies; for example, the following combination was used in PubMed: ("meningitis"[MeSH Terms]) AND ("nuchal rigidity"[All Fields] OR "neck stiffness[All Fields]") AND ("Jolt accentuation"[All Fields] OR "Kernig"[All Fields]) AND ("sensitivity"[All Fields] OR "specificity"[All Fields]) NOT ("Case"[TITLE] OR "review"[TITLE]). Reviews or letters to the editor that did not contain original data were manually excluded after

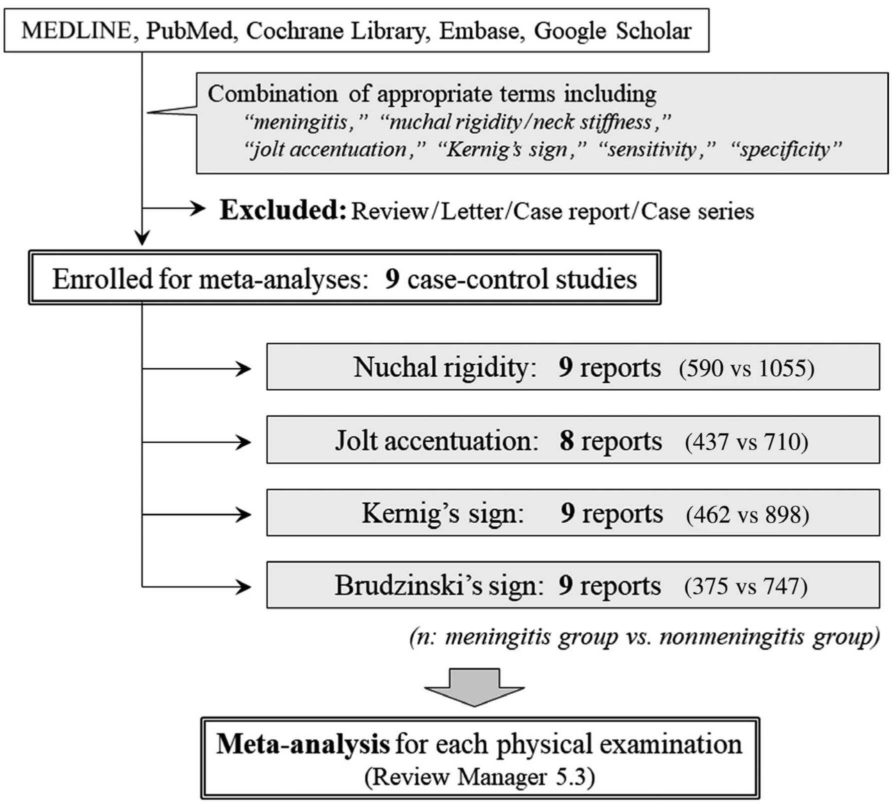

FIGURE 1 Overview of the study design. After the initial search, reviews and letters without original datasets were excluded from the following meta-analysis. As a result, a total of nine case-control studies were enrolled in the subsequent meta-analysis

the initial search. As a result, a total of nine studies were considered as eligible for the subsequent meta-analysis.[4–12] Moreover, we confirmed that there was no report of meta-analysis that assessed or compared the usefulness of nuchal rigidity and jolt accentuation tests. The overview of the above-described study design is illustrated in Figure 1. Details of the enrolled nine case-control studies are summarized in Table 1.

2.2 | Statistical analyses and software

We performed a systematic review of the nine selected studies regarding their eligibility for being enrolled in the meta-analysis with observational studies.[13,14] To perform the meta-analysis of the eligible nine case-control studies with respect to the accuracy of the tests in meningitis diagnosis, the Review Manager 5.3 software was used.[15,16] Since a considerable heterogeneity among the enrolled studies was suspected in advance, the random-effects model was applied. Heterogeneity among the enrolled studies for each of the studied variables was assessed with the Higgins I^2 (heterogeneity statistic) and τ^2 (between-study heterogeneity variance), both of which are parameters of between-study dispersion.[17,18] The PRISMA checklist was referenced in the process of meta-analysis.[19] Statistical analyses in other parts of this study were performed using the SPSS Statistics Base 22 software (IBM) and MATLAB R2015a. Because of the simultaneous comparisons, we considered a P-value lower than 0.01 to be significant in this study.

3 | RESULTS

3.1 | Results of the meta-analysis with forest plots

The results of the meta-analysis (forest plots) for each physical examination are presented in Figure 2. The heterogeneities in nuchal rigidity test, jolt accentuation, and Kernig's sign were high for unknown reasons. As causes of these heterogeneities, ethnicity or meningitis subtypes were unlikely. Differences in the thresholds to judge positivity in these physical examinations among the clinicians might be one of the candidate causes, but not conclusive.

Though there was high heterogeneity in 3 out of the 4 physical examinations, nuchal rigidity test (2.52; 99% confidence interval (CI): 1.21-5.27, P = 0.001), jolt accentuation (3.62; 1.13-11.60, P = 0.004), and Brudzinski's sign (2.91; 1.23-6.87, P = 0.001) were suggested to have significant odds ratio to differentiate meningitis patients with CSF pleocytosis from other nonmeningitis patients without CSF pleocytosis. On the other hand, Kernig's sign method did not reach statistical significance with odds ratio of 2.37 (99% CI: 0.76-7.36, P = 0.05).

The calculated scores for the heterogeneity of the enrolled studies and the calculated odds ratios with their 99% CIs are summarized in Table 2. The calculated positive likelihood ratio was best for Kernig's sign (2.61; 1.83-3.71), and the negative likelihood ratio was best for jolt accentuation (0.67; 0.58-0.77).

3.2 | Estimated sensitivity and specificity for each physical examination test

The provisional overall sensitivity, by simply summing up the cases from the enrolled nine studies, was 46.1% (242/525) for nuchal rigidity, 52.4% (229/437) for jolt accentuation, 22.9% (106/462) for Kernig's sign, and 27.5% (103/375) for Brudzinski's sign. The estimated 99% CI of the summed provisional sensitivity was 40.5%-51.7% for nuchal rigidity, 46.2%-58.6% for jolt accentuation, 17.9%-28.0% for Kernig's sign, and 21.5%-33.4% for Brudzinski's sign. Regarding the specificity of the physical examination tests, the provisional overall specificity was 71.3% (727/1020) for nuchal rigidity, 71.1% (505/710) for jolt accentuation, 91.2% (819/898) for Kernig's sign, and 88.8% (663/747) for Brudzinski's sign. As a conclusion, nuchal rigidity and jolt accentuation tests

TABLE 1 Overview of the enrolled data for the meta-analysis

Author	Published year	Location	Pleocytosis: pos./neg. (n)	NR	JA	KS	BS
Afhami[5]	2017	Iran	64/163	(+)	(+)	(+)	(+)
Ala[10]	2018	Iran	45/75	(+)	(+)	(+)	(+)
Mofidi[6]	2017	Iran	33/15	(+)	(+)	(+)	(+)
Nakao[7]	2013	U.S.A.	47/183	(+)	(+)	(+)	(+)
Sato[11]	2017	Japan	58/60	(+)	(+)	(+)	(−)
Tamune[8]	2013	Japan	139/392	(+)	(+)	(+)	(+)
Thomas[12]	2002	U.S.A.	80/217	(+)	(−)	(+)	(+)
Uchihara[4]	1991	Japan	34/20	(+)	(+)	(+)	(−)
Waghdhare[9]	2010	India	99/91	(+)	(+)	(+)	(+)

Note: Superscripts on the upper right of author names correspond to the numbers in the reference list.

Abbreviations: BS, Brudzinski's sign; JA, jolt accentuation; KS, Kernig's sign; NR, nuchal rigidity; (+), evaluated; (−), not evaluated.

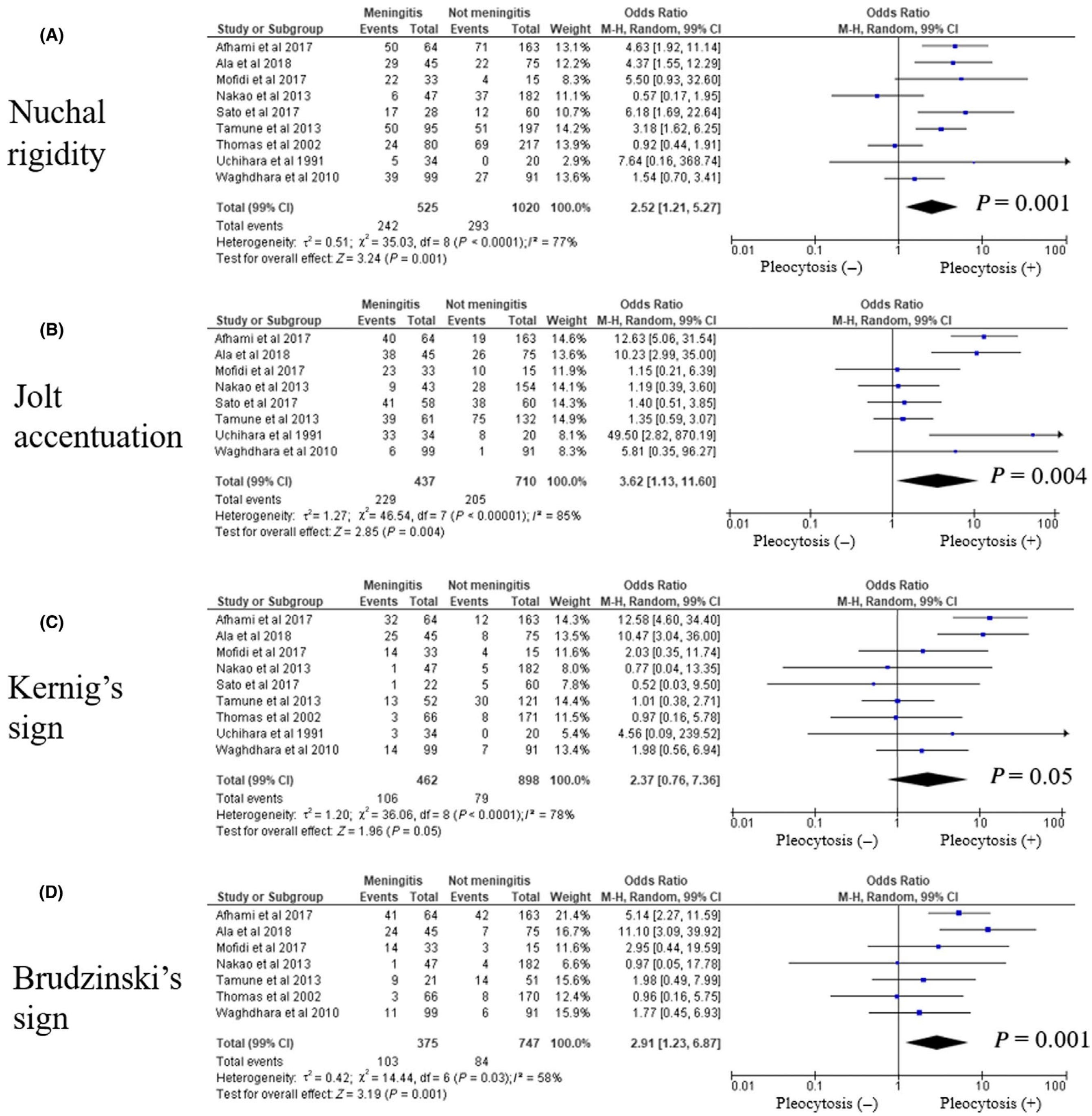

FIGURE 2 Forest plots of physical examination tests in meningitis. Examinations other than Kernig's sign showed a significant odds ratio for the prediction of pleocytosis in the cerebrospinal fluid

showed higher sensitivity and lower specificity than Kernig's and Brudzinski's signs.

4 | DISCUSSION

In this meta-analysis, we compared the clinical significance and reliability of nuchal rigidity test, jolt accentuation, Kernig's sign, and Brudzinski's sign in the prediction of CSF pleocytosis. Our results suggested that jolt accentuation has similar levels of sensitivity, specificity, and odds ratio with the nuchal rigidity test in differentiating patients with CSF pleocytosis from the others.

The protocol of jolt accentuation (ie, head rotation, 2-3 times per second) is simple, and the results are much more consistent among clinicians than those of the nuchal rigidity test. Undoubtedly, the most popular and prevailing physical examination is nuchal rigidity. In contrast to jolt accentuation, nuchal rigidity can be applied even in the patients with disturbed consciousness. Neck stiffness can be evaluated in obtunded or comatose patients, because it is a subjective finding, exclusively judged by the examiner. Thus, if a clinician

TABLE 2 Calculated effect sizes for each of the studied diagnostic examinations

	Datasets (n)	τ^2	I^2 [%]	Sensitivity (99% CI)	Specificity (99% CI)	LR+ (99% CI)	LR− (99% CI)	Odds ratio (99% CI)	*P*-values
Nuchal rigidity	9	0.51	77	46.1% (40.5-51.7)	71.3% (67.6-74.9)	1.60 (1.35-1.91)	0.76 (0.67-0.85)	2.52 (1.21-5.27)	0.001
Jolt accentuation	8	1.27	85	52.4% (46.2-58.6)	71.1% (66.7-75.5)	1.81 (1.50-2.20)	0.67 (0.58-0.77)	3.62 (1.13-11.60)	0.004
Kernig's sign	9	1.20	78	22.9% (17.9-28.0)	91.2% (88.8-93.6)	2.61 (1.83-3.71)	0.84 (0.79-0.91)	2.37 (0.76-7.36)	0.05
Brudzinski's sign	7	0.42	58	27.5% (21.5-33.4)	88.8% (85.8-91.7)	2.44 (1.74-3.44)	0.82 (0.75-0.89)	2.91 (1.23-6.87)	0.001

Abbreviations: CI, confidence interval; LR+, positive likelihood ratio; LR−, negative likelihood ratio.

can correctly assess the nuchal rigidity, this would be the most useful physical examination to diagnose meningitis. Meanwhile, correctly assessing the nuchal rigidity in cases with only weak neck stiffness is not always easy and the diagnosis could vary between examiners. Considering the above, together with the fact that the suggested sensitivity and odds ratio of jolt accentuation were as high as those of nuchal rigidity, jolt accentuation would be another useful and reliable diagnostic physical examination test to predict CSF pleocytosis.

At this point, we should acknowledge that the sensitivity of jolt accentuation in meningitis diagnosis is much lower than originally reported.[4] In the clinic, several patients with meningitis are negative in jolt accentuation. Based on the present study, the suggested sensitivity of jolt accentuation in meningitis diagnosis would be around 40%-60%, far lower than originally reported. Jolt accentuation is, undoubtedly, a useful and reliable diagnostic physical examination test for meningitis, but it must be performed and interpreted together with other meningeal signs, accompanying symptoms, and clinical history. Otherwise, patients with meningitis could be misdiagnosed.

As a perspective for future research, it would be useful to assess the characteristics of each diagnostic physical examination test after classifying the patients based on the detected meningitis-causing microorganisms, that is, viruses or bacteria. Because bacterial meningitis is usually more urgent and fatal than viral meningitis,[20,21] knowing the sensitivity and specificity of each physical examination for each type of the causative microorganism may help clinicians to estimate the risk for bacterial meningitis in the primary care setting. Likewise, subgroup analyses for the characteristics of each physical examination test with variables other than the microorganism, such as disease severity or the level of CSF pleocytosis, would be also important. Another perspective for future research would be to evaluate the overlapping pattern of the four physical examination tests in the detection of meningeal signs. If the meningeal signs are independently detected in each of the four tests, performing all four physical examinations in combination would lower the risk of misdiagnosing cases with meningitis. On the other hand, if there are overlaps in the detection of meningeal signs among the four tests, their combination would not significantly decrease the risk of misdiagnosis.

There are some limitations in this study. First, most of the previous studies that assessed the usefulness of jolt accentuation were reported mainly from groups in Japan and Iran. Further data from Western countries are needed to conclude the usefulness of jolt accentuation in the diagnosis of meningitis. Another limitation is that the heterogeneity among the enrolled studies was high in nuchal rigidity, jolt accentuation, and Kernig's sign due to unknown causes. The threshold of positivity in each of the four physical examination tests could have varied among the clinicians and affected the results. Further accumulation of clinical data, followed by systematic review and meta-analysis of the new datasets, will be necessary to conclude the superiority among the four physical examinations.

In conclusion, odds ratio, sensitivity, and specificity in predicting CSF pleocytosis are almost similar between jolt accentuation and nuchal rigidity tests. Because the correct assessment of nuchal rigidity is not always easy for the clinicians, jolt accentuation would be a helpful supplementary physical examination to avoid misdiagnosing meningitis. However, sensitivities in both nuchal rigidity and jolt accentuation tests are lower than 40%-60%. Thus, the clinicians need to remember that a number of patients with meningitis may not present with meningeal signs. A careful review of clinical history and symptoms, together with the meningeal signs, is necessary to decrease the risk of misdiagnosis.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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