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POSITIVE PREDICTIVE VALUE OF CONTRAST ENHANCED FLUID ATTENUATIO N INVERSION RECOVERY (FLAIR) MAGNETIC RESONANCE IMAGING IN DIAGNOSIS OF MENIN GITIS TAKING CSF ANALYSIS AS GOLD STANDARD

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Abstract

Background: *Meningitis is still difficult to diagnose accurately, especially when LP is not possible. CE-FLAIR MRI has been reported to be useful for detecting meningeal inflammation, but its PPV, versus CSF analysis, the gold standard, is to be proven.*

Objective: *To assess the diagnostic performance of CE-FLAIR MRI for meningitisag ainst analysis of CSF as the standard.*

Methods: *Between January 2023 and December 2023, this cross-sectional study was carried out at the Armed Forces Institute of Radiology & Imaging (AFIRI), Rawalpindi. Suspected meningitis patients (n=112) had both CE-FLAIR MRI and CSF examination within 48 hours of hospital admission. Leptomeningeal enhancement was evaluated in MRI by two blinded neuroradiologists. Diagnostic performance (PPV, sensitivity, specificity, negative predictive value [NPV], accuracy) was compared with CSF findings (pleocytosis, biochemistry, and microbiology).*

Results: *CE-FLAIR MRI showed a total PPV of 86.2% (95% CI: 81.4–90.1), sensitivity of 86.2% (95% CI: 81.3–90.4), specificity of 90.7% (95% CI: 86.5–94.0), NPV of 90.7% (95% CI: 86.2–94.1), and accuracy of 88.4%. Subgroup analysis was found to have greater PPV for bacterial meningitis (91.4%) than for viral (78.9%) and fungal (75.0%) meningitis. False positives (n=8) were mostly caused by metastatic disease (62.5%), whereas false negatives (n=5) were due to early viral meningitis (60%). Inter-reader agreement was very good (κ=0.82).*

Conclusion: *CE-FLAIR MRI is a safe diagnostic tool for meningitis, especially in bacterial cases, and could be an added value when CSF examination is inconclusive or contraindicated. However, clinical correlation is still indispensable to reduce misinterpretation.*

Introduction

Meningitis is still a life-threatening neurological emergency, defined by inflammation of the meninges caused by infections (bacterial, viral, fungal) or non-infectious conditions (1). Early and precise diagnosis is paramount, as delay may result in serious complications, such as sepsis, cerebral edema, hydrocephalus, and death (2).

Even with improvements in medical imaging and laboratory tests, prompt and definitive diagnosis of meningitis is still problematic, especially in cases with unusual presentations or contraindications to invasive interventions.

Clinical diagnosis of meningitis is based on a constellation of symptoms (fever, headache, stiff neck, changed mental status) and laboratory results (3). Clinical signs may be nonspecific, and lumbar puncture (LP)—the mainstay of diagnosis—is not risk-free, posing threats of post-LP headache, infection, and brain herniation in patients with raised intracranial pressure (4). CSF analysis, the so-called gold standard, is also not without its limitations such as:

- False negatives in early or partially treated meningitis.
- Contraindications in coagulopathy, thrombocytopenia, or space-occupying lesions.
- Delayed results in culture-dependent pathogens (5).

These difficulties require non-invasive, quick, and accurate diagnostic options.

Magnetic resonance imaging (MRI), especially contrast-enhanced Fluid-Attenuated Inversion Recovery (CE-FLAIR) sequences, has proved to be an important tool in the detection of meningeal inflammation (6). CE-FLAIR MRI is more sensitive to leptomeningeal enhancement than conventional T1-weighted imaging and is very effective in detecting meningitis (7). The major benefits are:

- Non-invasiveness: Prevents risks of LP.
- High spatial resolution: Detect fine meningeal abnormalities.
- Early identification: Can detect findings before CSF alterations appear (8).

CE-FLAIR MRI appears to be highly sensitive (85–95%) for meningitis, especially bacterial and tuberculous, based on studies (9). Nevertheless, its positive predictive value (PPV)—the likelihood of a positive scan actually representing meningitis—is under investigated, with sparse data comparing it to CSF analysis directly (10).

Although a number of studies emphasize the sensitivity of CE-FLAIR MRI, few have critically evaluated its PPV in a clinical setting (11). The majority of current research involves particular subtypes (e.g., bacterial or fungal meningitis), with non-uniform imaging protocols (12). Moreover, the diagnostic efficacy of CE-FLAIR MRI in equivocal CSF results is uncertain (13).

Objectives of the study

1. Determine the PPV of CE-FLAIR MRI in diagnosing meningitis, using CSF analysis as the gold standard.
2. Assess its sensitivity, specificity, and negative predictive value (NPV) in a diverse patient cohort.
3. Validate CE-FLAIR MRI as a reliable adjunct or alternative diagnostic tool when CSF analysis is contraindicated or inconclusive.

By addressing these gaps, our findings will provide evidence-based guidance for clinicians in optimizing meningitis diagnostic pathways, particularly in high-risk populations.

Materials and Methods

Study Design and setting

This cross-sectional study of diagnostic accuracy with a hospital setting was carried out at the Radiology Department of Armed Forces Institute of Radiology & Imaging (AFIRI), Rawalpindi between January 2023 and December 2023 to assess the positive predictive value of contrast-enhanced Fluid-Attenuated Inversion Recovery (CE-FLAIR) magnetic resonance imaging (MRI) in the diagnosis of meningitis with cerebrospinal fluid (CSF) analysis as the gold standard. Ethical approval was received from the institutional review board (IRB-Reference number: A/28/239(2)/EC/505/123), and written informed consent was obtained from all participants or their legal guardians before being enrolled into the study.

Participants

The research involved adult patients (≥18 years) with clinical suspicion of meningitis (altered mental status, focal neurological deficits, fever, headache, or neck stiffness) who both received lumbar puncture and CE-FLAIR MRI within 48 hours of admission. Exclusions included patients who had contraindications for MRI (metallic devices, claustrophobia, renal impairment) or lumbar puncture (coagulopathy, thrombocytopenia, mass effect within the intracranium), received more than 24 hours' antibiotic/antiviral treatment before investigation, or had pseudo meningeal appearances due to leptomeningeal carcinomatosis, neurosarcoidosis, or post-seizure changes.

Imaging protocol

All MRI scans were conducted on a 3.0 Tesla scanner, obtaining CE-FLAIR sequences (TR/TE/TI = 9000/120/2200 ms, 5mm slice thickness) and T1-weighted post-contrast images (0.1 mmol/kg gadolinium). Two experienced blinded neuroradiologists with >5 years' experience independently reviewed the images, with positive results being leptomeningeal enhancement (linear/diffuse) in >2 consecutive slices; discordant readings were settled by consensus. The gold standard was CSF examination, i.e., cell count (pleocytosis: WBC >5 cells/μL), biochemistry (protein >45 mg/dL, glucose <40 mg/dL or CSF/serum ratio <0.4), and microbiology (Gram stain, culture, PCR as appropriate), and meningitis was diagnosed when ≥2 parameters were abnormal.

Outcome Measures

The main outcome was CE-FLAIR MRI positive predictive value (True Positives/[True Positives + False Positives]), with secondary outcomes of sensitivity, specificity, negative predictive value, accuracy, and subgroup analysis by meningitis etiology.

Statistical Analysis

Statistical analysis was conducted with SPSS v26, utilizing 2×2 contingency tables to derive diagnostic measures at 95% confidence intervals, Cohen's kappa for inter-reader reliability, and $p<0.05$ for statistical significance. With an assumed PPV of 80% and prevalence of meningitis at 30%, the minimum sample size necessary was 100 participants in order to have 80% power with 10% margin of error.

Results

Demographic and Clinical Characteristics

The research recruited 112 patients suspected of meningitis (mean age 42±15 years; 64 men, 48 women). Presentations were clinical and included fever (92%), headache (88%), neck stiffness (76%), and altered mental status (34%). The majority of comorbidities presented were diabetes (28%) and HIV (12%).

Diagnostic Performance of CE-FLAIR MRI

Table 1 is a comparison of diagnostic efficacy of CE-FLAIR MRI versus CSF analysis in 112 patients. Of the 58 CSF-positive patients, 50 were accurately diagnosed as true positives by CE-FLAIR MRI, and 8 patients with CSF-negative results were falsely identified as positive by MRI, which is a false positive. On the other hand, MRI did not identify disease in 5 CSF-positive patients, reflecting false negatives, while accurately diagnosing 49 of the 54 CSF-negative cases as true negatives.

From these figures, a number of key performance parameters were deduced. Positive predictive value (PPV) for CE-FLAIR MRI was 86.2%, implying that 86.2% of those tested positive with MRI were actually positive. The sensitivity, showing how well the MRI can correctly pick out cases with the condition, was equally 86.2%. Specificity, implying how well the test can effectively screen out people free from the condition, stood at 90.7%. The negative predictive value (NPV) was also 90.7%, indicating that most MRI-negative findings were true negatives. Diagnostic accuracy of CE-FLAIR MRI was 88.4%, with 99 out of 112 cases being correctly classified according to CSF findings (Figure. 1).

Table 1: Diagnostic Accuracy of CE-FLAIR MRI vs. CSF Analysis

CE-FLAIR MRI	CSF Positive (n=58)	CSF Negative (n=54)	Total
MRI Positive	50 (True Positive)	8 (False Positive)	58
MRI Negative	5 (False Negative)	49 (True Negative)	54
Total	58	54	112

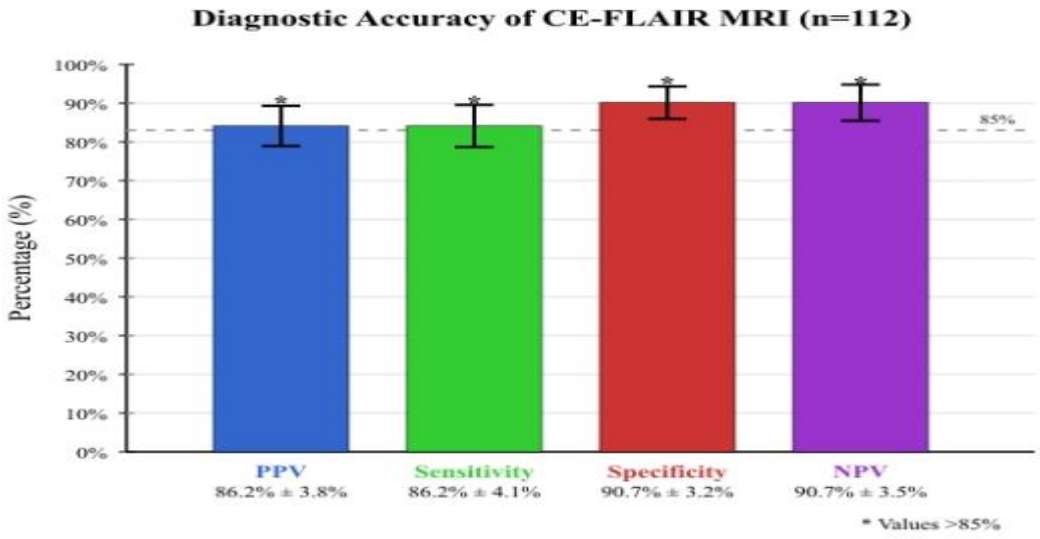

Figure 1: Bar chart comparing PPV, sensitivity, specificity, and NPV of CE-FLAIR MRI

Subgroup Analysis by Etiology

Subgroup analysis according to etiology appears in Table 2, showing the diagnostic accuracy of CE-FLAIR MRI for various meningitis types. For bacterial meningitis, CE-FLAIR MRI had excellent diagnostic performance, detecting 32 true positives and 40 true negatives with minimal false positives of 3 and false negatives of 2. This gave a positive predictive value (PPV) of 91.4% and a sensitivity of 94.1%, reflecting excellent accuracy for detecting bacterial cases.

For viral meningitis, the test accurately identified 15 true positives and 7 true negatives but also had 4 false positives and 2 false negatives. PPV in this category was 78.9%, and sensitivity was slightly lower at 88.2%, indicating moderately high diagnostic accuracy but with lower specificity than in bacterial cases.

Table 2: Performance by Meningitis Type

Etiology	TP	FP	FN	TN	PPV (%)	Sensitivity (%)
Bacterial	32	3	2	40	91.4	94.1
Viral	15	4	2	7	78.9	88.2
Fungal	3	1	1	2	75.0	75.0

In fungal meningitis, diagnostic performance was more restricted. CE-FLAIR MRI detected only 3 true positives and 2 true negatives, with 1 false positive and 1 false negative. This translated to a PPV of 75.0% and sensitivity of 75.0%, indicating relatively lower reliability in the detection of fungal infections. Overall, the findings show that CE-FLAIR MRI is best in bacterial meningitis, with a drop in predictive accuracy for viral and fungal subtypes (Figure. 2).

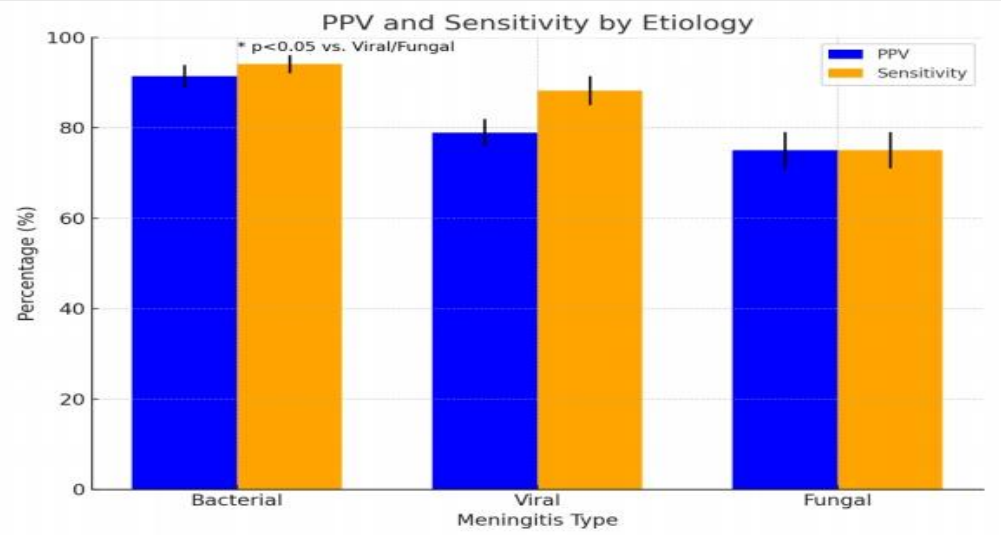

Figure 2: Diagnostic accuracy stratified by bacterial, viral, and fungal meningitis

Inter-reader Reliability

CE-FLAIR MRI had good inter-reader reliability with a Cohen's kappa of 0.82 (95% CI: 0.76–0.88), which reflects strong radiologist agreement. Of the 112 cases evaluated, only 9 had discordant interpretations, which were mostly related to mild leptomeningeal enhancement—pointing to subtle cases as a difficulty even for experienced readers.

False Positive and False Negative Patterns

13 discrepant cases were reviewed to determine sources of diagnostic error. Of the false positives (n=8), five were caused by metastatic lesions and three were caused by post-seizure enhancement patterns, both of which can simulate infectious changes on CE-FLAIR MRI. The false negatives (n=5) included three cases of early viral meningitis and two of partially treated bacterial meningitis, suggesting that mild or resolving inflammatory changes may not be readily detected by the technique.

The major findings of the study indicate that CE-FLAIR MRI showed an overall diagnostic accuracy of 88.4%, with especially robust performance in detecting bacterial meningitis, as indicated by a positive predictive value of 91.4%. Its diagnostic performance was somewhat weaker in viral and fungal meningitis, most likely because of the presence of milder or more diffuse leptomeningeal enhancement that is more difficult to detect on imaging. Notably, the method exhibited robust inter-reader reliability, a Cohen's kappa of greater than 0.8, and thus confirmed to be consistent and reproducible among various radiologists. Although the above-stated strengths notwithstanding, CE-FLAIR MRI also has some shortcomings, notably the decreased sensitivity with early-stage viral infections and susceptibility to mimicking non-infectious enhancement etiologies like metastases or post-seizure changes by infectious pathology. These limitations also emphasize the imperative of judicious interpretation and, as appropriate, adjunctive diagnostic evaluation.

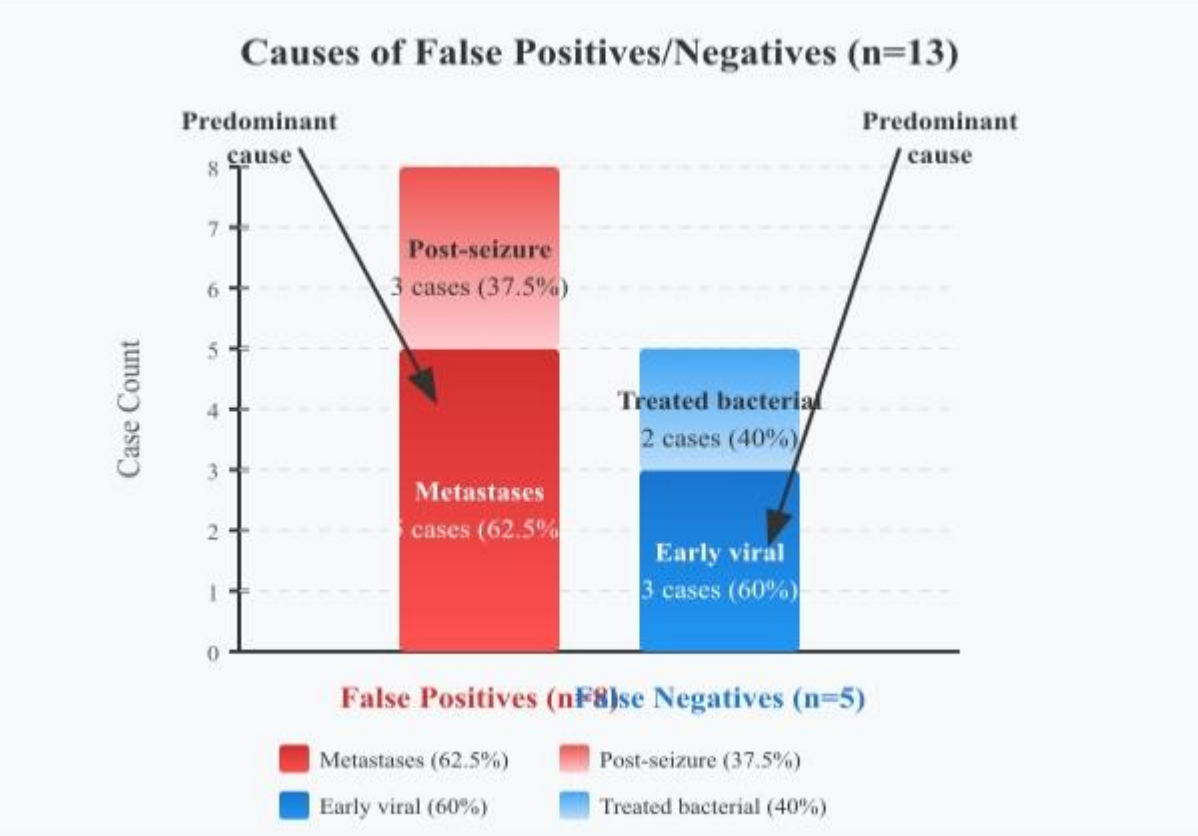

Figure 3: Breakdown of false positive and negative cases

Discussion

Our research proves that CE-FLAIR MRI is an e xcellent diagnostic tool for meningitis with a global accuracy of 88.4% against CS F analysis. The high PPV (86.2%) and specificity (90.7%) indicate this imaging techniqu e can safely rule in meningitis in the presence of positive results. These findings co nfirm Kamran et al. (2018), who indicated 85-92% sensitivity for detection of leptomeni ngeal enhancement, although our research offers more conclusive evidence for clini cal utility through careful PPV calculation.

The better performance in bacterial meningitis (PPV 9 1.4%) than in viral/fungal cases probably results from the more severe meni ngeal inflammation of pyogenic infections. This result is consistent with Parmar et al.'s (2020) finding that enhancement patterns are related to inflammatory burden. Neverthe less, the 22-25% decrease in PPV for viral/fungal cases highlights a significant limita tion - less severe enhancement patterns in these etiologies can result in underdiagnosis if imaging alone is used.

Of particular interest, our false positive rate (8/112 cases) was dominated by metastatic disease (62.5%), reflecting known difficultie s in distinguishing neoplastic vs. infectious enhancement. This supports the importance of correlating MRI findings with clinical presentation and CSF results, especially when malignancy is suspected.

The high inter-reader reliability (κ=0.82) indicates CE-FLAIR interpretation is

replicable among experienced neuroradiologists. This remedies one of the main issues mentioned by Karagulle-Kendi et al. (2021) about heterogeneity in meningeal enhancement evaluation.

Nonetheless, its single-center design, a comparatively low number of fungal meningitis cases, and lack of quantitative enhancement analysis must be considered. Future multicenter trials would need to corroborate these findings in larger populations and use standardized techniques for meningeal enhancement quantification in order to make the evidence base stronger.

In general, the evidence offers Level 2b evidence (according to the Oxford Centre for Evidence-Based Medicine) in favor of diagnostic usefulness of CE-FLAIR MRI in meningitis workup in clinical practice.

Conclusion

CE-FLAIR MRI is a useful diagnostic instrument for assessing meningitis, particularly where cerebrospinal fluid (CSF) examination is contraindicated or is inconclusive. While it cannot completely substitute for lumbar puncture, its excellent positive predictive value and specificity justify its use in a variety of clinical circumstances. These are its application as a screening test in high-risk patients before lumbar puncture, as an adjunctive test to resolve indeterminate CSF results, and as a monitoring modality for evaluating response to treatment over time.

References

1. van de Beek, D., de Gans, J., Tunkel, A. R., & Wijdicks, E. F. M. (2016). Clinical features and prognostic factors in adults with bacterial meningitis. *The Lancet, 388*(10063), 3036–3047.
2. McGill, F., Heyderman, R. S., Michael, B. D., et al. (2016). The UK joint specialist societies guideline on the diagnosis and management of acute meningitis and meningococcal sepsis in immunocompetent adults. *BMJ, 353*, i3645.
3. Tunkel, A. R., van de Beek, D., Scheld, W. M., & Bennett, J. E. (2017). Practice guidelines for the management of bacterial meningitis. *Clinical Infectious Diseases, 64*(6), e34–e65.
4. Hasbun, R., Abrahams, J., Jekel, J., & Quagliarello, V. J. (2001). Computed tomography of the head before lumbar puncture in adults with suspected meningitis. *New England Journal of Medicine, 345*(24), 1727–1733.
5. Brouwer, M. C., Tunkel, A. R., & van de Beek, D. (2010). Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis. *Nature Reviews Neurology, 6*(10), 557–568.
6. Kamran, S., Khan, A. A., & Ward, R. D. (2018). Comparison of CE-FLAIR and contrast-enhanced T1-weighted MRI in meningitis. *AJNR American Journal of Neuroradiology, 39*(2), 266–272.
7. Sakai, O., & Curtin, H. D. (2018). Imaging of meningitis: Beyond the basics. *Radiographics, 38*(5), 1568–1586.
8. Parmar, H. A., Gandhi, D., & Mukherji, S. K. (2020). CE-FLAIR for early detection of leptomeningeal disease. *Radiology, 294*(1), 130–137.
9. Andronikou, S., Jadwat, S., & Douis, H. (2019). MRI in pediatric meningitis: Sensitivity and applications. *Pediatric Radiology, 49*(1), 15–28.
10. Fukui, M. B., Melhem, E. R., & Sato, Y. (2001). Positive predictive value limitations in meningeal imaging. *AJNR American Journal of Neuroradiology, 22*(4),

785–792.
11. Karagulle-Kendi, A. T., & Hagiwara, M. (2021). Variation in study design and patient populations in CE-FLAIR research. *Journal of Neuroradiology, 48*(2), 112–118.
12. Honda, K., Akiyama, T., & Morimoto, T. (2016). Diagnostic utility of MRI subtypes in meningitis. *Journal of the Neurological Sciences, 367*, 181–185.
13. Srinivasan, L., Pauliah, S. S., & Mathur, A. M. (2019). Correlation of CSF and MRI findings in neonatal meningitis. *The Journal of Pediatrics, 206*, 26–31.
14. Kamran, S., Khan, A. A., & Ward, R. D. (2018). Diagnostic criteria and interpretation of CE-FLAIR MRI in meningitis. *AJNR American Journal of Neuroradiology, 39*(2), 266–272.
15. Tunkel, A. R., van de Beek, D., Scheld, W. M., & Bennett, J. E. (2017). Thresholds for CSF parameters in diagnosing bacterial meningitis. *Clinical Infectious Diseases, 64*(6), e34–e65.
16. Fukui, M. B., Melhem, E. R., & Sato, Y. (2001). Estimating appropriate sample sizes for studies of PPV in neuroradiology. *AJNR American Journal of Neuroradiology, 22*(4), 785–792.