ORIGINAL ARTICLE

The Diagnostic Utility of Cerebrospinal Fluid Procalcitonin for Acute Bacterial Meningitis and Ventriculitis in Children: A Multicenter Prospective Study

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ABSTRACT

Background and Objective. Accurately diagnosing bacterial meningitis and ventriculitis in children is challenging due to nonspecific symptoms and the lack of specificity in conventional CSF parameters. Cerebrospinal fluid (CSF) procalcitonin (PCT) is a promising diagnostic marker but studies on its utility in children are lacking. We aimed to assess the diagnostic value of CSF procalcitonin for bacterial meningitis and ventriculitis in children and establish a clinically relevant cut-off level.

Methods. A total of 131 patients were included in the study, and the CSF PCT levels were measured in two groups. Group 1 comprised of patients with bacterial meningitis and ventriculitis (n=21), while Group 2 consisted of patients with tuberculous meningitis, fungal meningitis, viral encephalitis, autoimmune encephalitis, central nervous system (CNS) leukemia, and non-infectious or inflammatory CNS conditions (n=110).

Results. CSF PCT demonstrated an area under the curve of 96.57% in the receiver operating characteristic analysis. With a cut-off of 0.19 ng/mL, it achieved high sensitivity (90.48%) and specificity (91.82%), making it an excellent test for distinguishing between bacterial meningitis and ventriculitis from control diseases.

Conclusion. CSF procalcitonin is highly effective in distinguishing pediatric bacterial meningitis and ventriculitis. Especially in clinical scenarios where the conventional laboratory tests are inconclusive, it can complement clinical assessment to diagnose CNS infections accurately and guide prudent antibiotic use.

Keywords: cerebrospinal fluid procalcitonin, bacterial meningitis, ventriculitis, diagnostic utility

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INTRODUCTION

Bacterial meningitis and ventriculitis are serious and potentially life-threatening infections that can be acquired in the community or develop post-neurosurgery.[1] Accurately diagnosing these infections is challenging due to subtle or nonspecific symptoms that can mimic those of other central nervous system (CNS) infections caused by viruses, fungi, and mycobacteria, or those of inflammatory diseases.[2]

Conventional laboratory parameters used to make the diagnosis including cerebrospinal fluid (CSF) total protein (TP), leukocyte count, neutrophils, and serum/CSF glucose ratio, suffer from a lack of specificity.[3] Studies have also shown that these parameters may be altered with neurosurgery

and are hence rendered unreliable in distinguishing intracranial infection from inflammation.[4] Microbiological CSF culture remains the most specific diagnostic tool. However, yield is usually low, with slow turn-around times and false negative results especially following prior antibiotic treatment. To address this dilemma of finding a quick but dependable diagnostic indicator of infection, the potential of other biomarkers has been extensively studied, including CSF heparin-binding protein (HBP), interleukin-6, interleukin-10[3], lactate[5,6], C-reactive protein (CRP), ferritin, and procalcitonin (PCT)[7,8], both alone and in different permutations of combinational markers. Among them, procalcitonin has emerged as the promising diagnostic and prognostic marker for bacterial infection.[9]

Procalcitonin is a protein synthesized by the C cells of the thyroid gland and released from leukocytes of the peripheral blood.[10] It is produced in large quantities by several organ systems as part of a systemic inflammatory response, specifically during bacterial infections. Compared to other acute phase reactants like CRP and erythrocyte sedimentation rate (ESR), PCT levels typically rise faster, allowing for earlier diagnosis. It is also quickly cleared upon effective treatment of infection, making it useful in monitoring response to treatment or an indication of inadequacy of treatment if persistent elevation is present.[11]

Multiple studies have explored the utility of serum and CSF PCT as viable markers of bacterial meningitis in adult, pediatric, and post-neurosurgery cohorts in the past decades.[12] The evidence in adults is mixed but generally supports PCT's utility. A meta-analysis demonstrated a pooled sensitivity of 95% and specificity of 98%, concluding that serum PCT was a highly accurate test for distinguishing between bacterial meningitis and viral and other non-infective differential diagnoses of meningitis.[13] Some studies have shown lower specificity of CSF PCT values in adults compared to children, possibly due to more complex comorbidities.

A recently published systematic review and meta-analysis showed that CSF PCT is a robust marker for infection with a slightly higher pooled sensitivity, specificity, and likelihood ratio compared to serum procalcitonin. Although this systematic review included 23 studies on both community- and hospital-acquired meningitis, the total number of studies focusing on CSF PCT involving children was only three, and two were done in neonates.[1] Furthermore, a recent study in India had contradictory results wherein CSF and plasma PCT were found to be insufficient in discriminating between the presence or absence of bacterial meningitis in neonates.[14] Lastly, the optimal cut-off values for CSF PCT in different age groups and clinical scenarios are not yet firmly established. Despite the generally supportive evidence, available data is lacking to establish guidelines on the use of procalcitonin. This emphasizes the need for more well-designed and adequately powered studies to solidify the evidence on the usefulness of CSF PCT in diagnosing CNS infections.

OBJECTIVES

We aimed to determine the diagnostic utility of CSF PCT for bacterial meningitis and ventriculitis in children in a prospective multicenter cohort study. The basic objectives of the study were: 1) to determine the mean CSF PCT values of patients with bacterial meningitis and ventriculitis (Group 1) and those without bacterial meningitis – non-infectious or inflammatory CNS conditions, tuberculous meningitis (TBM), fungal meningitis, viral encephalitis, autoimmune encephalitis, CNS leukemia (Group 2); 2) to compare the mean CSF PCT levels between patients in Group 1 and Group 2; 3) to determine the diagnostic accuracy of CSF and compare it with serum PCT; 4) to identify a mean cut-off level of CSF PCT as threshold for diagnosing bacterial meningitis and ventriculitis, and to evaluate the diagnostic utility of the determined cut-off level in terms of its sensitivity, specificity, positive predictive and negative predictive values.

MATERIALS AND METHODS

Study Structure and Patient Population

This was a prospective, observational, and multicenter study conducted in the Pediatric Emergency Room, Pediatric Wards, and Intensive Care Unit (ICU) of the University of the Philippines - Philippine General Hospital (UP-PGH) and the National Children's Hospital (NCH) from the period of January 2021 to April 2024.

The study prospectively enrolled a total of 131 patients consecutively, and were divided into the following groups:

1. Group 1 with Bacterial Meningitis and Ventriculitis
2. Group 2 without Bacterial Meningitis and Ventriculitis

Bacterial meningitis and ventriculitis – both community-acquired and post-neurosurgical were diagnosed in patients presenting with clinical signs and symptoms such as headache, altered consciousness, vomiting, fever, neck stiffness, focal neurological deficits, or seizures. This was confirmed by CSF culture or rapid antigen detection tests, which are considered the gold standard.[15] In the absence of a positive culture or antigen detection test, patients were diagnosed if CSF testing showed pleocytosis (WBC >100/mm^3); CSF neutrophil percentage (80%); elevated protein (>1 g/L); low glucose (<2.2 mmol/L); and CSF/plasma glucose ratio <0.3.[15–17] Partially treated bacterial meningitis or ventriculitis was diagnosed in cases where there is a history of previous antibiotic use and the clinical presentation still indicates bacterial etiology, but the CSF parameters show milder pleocytosis (WBC <100/mm^3), decreased neutrophil percentage, elevated protein, and normal or decreased glucose levels (<2.8 mmol/L).[18–20] These patients were included in Group 1.

A study on the diagnostic accuracy of CSF PCT for bacterial meningitis also found that the CSF PCT level was significantly higher in bacterial meningitis (median, 0.22 ng/mL) than in those with TBM (median, 0.12 ng/mL),

viral meningitis (median, 0.09 ng/mL), and autoimmune encephalitis (median, 0.05 ng/mL).[21] Hence, TBM was categorized under Group 2 to ensure that the CSF values in the population of interest (bacterial meningitis and ventriculitis) were not falsely decreased.

Tuberculous meningitis was diagnosed by the presence of CSF acid-fast bacilli (AFB) and/or positive TB polymerase chain reaction (PCR) / GeneXpert MTB/ RIF studies. In cases where bacteriologic confirmation could not be made, the diagnosis was based on a consistent history, clinical and neuroradiologic characteristics, and documentation of pulmonary and extrapulmonary disease.[22] Likewise, viral encephalitis was diagnosed in patients with the pertinent history and clinical findings, and confirmed by positive CSF IgM or PCR studies for specific viruses such as Enteroviruses and Herpes Simplex Viruses (HSV) 1 and 2, Japanese Encephalitis Virus (JEV), West Nile Virus, or Cytomegalovirus (CMV). When viral studies cannot be performed or yield negative results, a high index of suspicion along with mild CSF lymphocytic pleocytosis, slightly elevated protein, and normal glucose were used to diagnose viral encephalitis.[10] Diagnosis of fungal meningitis was made based on a positive CSF fungal culture, a positive cryptococcal antigen latex agglutination (CALAS), or a positive India Ink testing. Autoimmune encephalitis was confirmed with a positive anti–N—methyl–D–aspartate receptor (NMDAr) antibody in CSF studies, while CNS leukemia was diagnosed when evidence of leukemic blasts was found on CSF cytology studies.

Sample Size

The sample size of 120 patients was computed based on the study of Zhang et al.[16] Fifty-three percent (53%) were diagnosed with bacterial and viral meningitis. A procalcitonin level cut-off of 0.085 ng/mL had a 55.17% sensitivity and 95.83% specificity in the diagnosis of bacterial meningitis. Using the formula of Fleiss, the sample size was computed with OpenEpi, Version 3, Open Source Calculator, assuming a 95% confidence interval and power of 85%. A minimum sample size of 106 was obtained, with outcomes present in 53% of the exposed. An adjustment to a minimum of 120 patients was made to achieve a 95% level of confidence, precision of 5%, and to accommodate the expected 20% dropouts.

Sample Collection and Laboratory Methods

The samples of CSF were obtained via initial lumbar puncture. They were submitted to the respective laboratories of UP-PGH and NCH for the following routine tests: 1) Microbiology section for Gram stain, AFB smear, Culture, and Sensitivity; 2) Hematology section for cell counts; and 3) Chemistry section for sugar and protein.

Additional CSF samples were collected as deemed necessary by the clinical working impression and processed accordingly. These tests included the following: HSV 1 and 2, JEV, Enterovirus, CMV, SARS-CoV-2, anti-NMDAR antibody testing, CALAS, India Ink Testing, and cell cytology. In NCH, additional studies included Biofire Meningoencephalitis panel.

The procalcitonin determination was done using the Enzyme-Linked Fluorescent Assay (ELFA) by VIDAS® B·R·A·H·M·S PCT™ at the UP–PGH Department of Laboratories. CSF for procalcitonin determination from the NCH was delivered to the PGH laboratory strictly following a cold-chain transport system and was processed within four hours of collection. A single procalcitonin determination was done for each patient and any subsequent determinations were not included in the study.

Data Collection

The data collected was recorded in a Microsoft Excel File using the alphanumeric code as an identifier. The data recorded include CSF cell counts, CSF glucose (mmol/L) and protein (g/L), CSF procalcitonin level (ng/mL), culture and sensitivity results, Gram stain results, AFB results, viral studies results, India Ink, CALAS, anti-NMDAR antibody titer, and cell cytology. Whenever available, the serum procalcitonin level taken at the same time with the CSF procalcitonin level was also recorded.

In cases wherein specific laboratory tests were not done owing to the clinical working impression and/or non-availability of the test, the data were not imputed, and the cases were excluded from the final analysis of each specific variable.

Statistical Analysis

Descriptive statistics were used to summarize the clinical characteristics of the patients. Frequency and proportion were used for categorical variables, and median and inter-quartile range were used for non-normally distributed continuous variables. Mann-Whitney U test and Fisher's Exact/Chi-square test were used to determine the difference in rank and frequency, respectively, between patients with and without bacterial meningitis and ventriculitis. The area under the receiver operating characteristics (AUROC) curve and its diagnostic parameters were used to determine the diagnostic accuracy of CSF procalcitonin in discriminating against bacterial meningitis and ventriculitis. The odds ratio and corresponding 95% confidence intervals from binary logistic regression were computed to determine if CSF PCT was a significant predictor for bacterial meningitis and ventriculitis. All statistical tests were two-tailed tests. Shapiro-Wilk test was used to test the normality of the continuous variables. Missing values were neither replaced nor estimated. Null hypotheses were rejected at 0.05α-level of significance. Microsoft Excel and STATA 13.1 were used for data management and analysis, respectively.

Ethical Considerations

The study ensured adherence to the 2017 National Ethical Guidelines of Health and Health-related Research.

The protocol was approved by the UP Manila Research Ethics Board (UPMREB 2020-0084-01) and the National Children's Hospital Institutional Review Board. Written informed consent was obtained from the legal guardians of all patients enrolled.

RESULTS

A total of 131 patients were recruited for this study, and their CSF laboratory findings, Total (n=131), Group 1 with Bacterial Meningitis and Ventriculitis (n=21), and Group 2 without bacterial meningitis or ventriculitis (n=110) are presented and compared in Table 1. The causative bacteria in the two subjects who had positive growth in CSF culture

Table 1. CSF Laboratory Findings

	Bacterial Meningitis and Ventriculitis			*P*-value
	Total (n=131)	Group 1 (n=21, 16%)	Group 2 (n=110, 84%)	
	Frequency (%); Median (IQR)			
CSF PCT, ng/mL	0.06 (0.05 to 0.16)	0.63 (0.4 to 1.48)	0.05 (0.05 to 0.1)	<0.001
Serum PCT, ng/mL (n=66)	0.14 (0.05 to 1.36)	2.23 (0.08 to 7.11)	0.13 (0.05 to 0.75)	0.018
CSF Color				0.003
Colorless	105 (80.15)	11 (52.38)	94 (85.45)	
Straw	11 (8.4)	3 (14.29)	8 (7.27)	
Light yellow	5 (3.82)	2 (9.52)	3 (2.73)	
Other colors	10 (7.63)	5 (23.81)	5 (4.55)	
CSF Transparency				0.014
Clear	102 (77.86)	14 (66.67)	88 (80)	
Slightly hazy	18 (13.74)	2 (9.52)	16 (14.55)	
Hazy	9 (6.87)	3 (14.29)	6 (5.45)	
Turbid	2 (1.53)	2 (9.52)	0	
CSF RBC (n=117)	30 (0 to 340)	20 (0 to 910)	30 (0 to 240)	0.564
CSF WBC	4 (0 to 49)	40 (4 to 76)	2 (0 to 33)	0.006
CSF Neutrophil	0 (0 to 4)	4 (0 to 33)	0 (0 to 4)	0.002
CSF Lymphocyte	4 (0 to 38)	14 (2 to 92)	2 (0 to 31)	0.037
CSF Protein, g/L	0.5 (0.36 to 1.91)	3.55 (1.28 to 6.85)	0.49 (0.36 to 1.19)	<0.001
CSF Glucose, mmol/L	3.1 (2.4 to 3.6)	2.1 (1.1 to 3.2)	3.2 (2.6 to 3.7)	0.002
Bacterial culture				0.025
No growth	129 (98.47)	19 (90.48)	110 (100)	
With growth	2 (1.53)	2 (9.52)	0	
TB PCR/GeneXpert (n=9)				1.000
Negative	1 (11.11)	1 (100)	0	
Positive	8 (88.89)	0	8 (100)	
Bactigen (n=120)				0.027
Negative	118 (98.33)	18 (90)	100 (100)	
Positive	2 (1.67)	2 (10)	0	
HSV 1 (n=13)				1.000
Negative	10 (76.92)	1 (100)	9 (75)	
Positive	3 (23.08)	0	3 (25)	
HSV 2 (n=13)				1.000
Negative	12 (92.31)	1 (100)	11 (91.67)	
Positive	1 (7.69)	0	1 (8.33)	
CSF anti-NMDAr (n=23)				-
Negative	16 (69.57)	-	16 (69.57)	
Positive	7 (30.43)	-	7 (30.43)	
CSF Blasts (n=3)				-
Negative	2 (66.67)	-	2 (66.67)	
Positive	1 (33.33)	-	1 (33.33)	
Other tests				0.592
Without	99 (75.57)	15 (71.43)	84 (76.36)	
With	32 (24.43)	6 (28.57)	26 (23.64)	

PCT – procalcitonin, CSF – cerebrospinal fluid, RBC – red blood cell, WBC – white blood cell, HSV – Herpes simplex virus, anti-NMDAr – anti-N-methyl-D-aspartate receptor

Table 2. CSF Procalcitonin Value in Bacterial Meningitis vs Tuberculous Meningitis

	Bacterial Meningitis and Ventriculitis			*P*-value
	Total (n=35)	Group 1 (n=21)	Tuberculous Meningitis (n=14)	
	Median (IQR)			
CSF PCT, ng/mL	0.21 (0.07 to 0.77)	0.63 (0.4 to 1.48)	0.095 (0.05 to 0.175)	<0.001

Table 3. Diagnostic Accuracy of CSF Procalcitonin to Discriminate Bacterial Meningitis and Ventriculitis

		Bacterial Meningitis and Ventriculitis		Total
		Group 1	Group 2	
CSF Procalcitonin	≥0.19	19	9	28
	<0.19	2	101	103
	Total	21	110	131
Sensitivity	90.48% (69.62 to 98.83)	***Positive LR***	11.06 (5.82 to 21)	
Specificity	91.82% (85.04 to 96.19)	***Negative LR***	0.10 (0.03 to 0.39)	
PPV	67.86% (52.65 to 80.03)	***Prevalence***	16.03% (10.21 to 23.45)	
NPV	98.06% (93.1 to 99.47)	***Accuracy***	91.60% (85.47 to 95.73)	

PPV – positive predictive value, NPV – negative predicted value, LR – likelihood ratio

was *Streptococcus pneumoniae*, while one patient was positive for *Haemophilus influenzae* only on CSF Bactigen but negative on CSF culture. These were all community-acquired. Two neurosurgical patients suspected of post-operative ventriculitis were also included. In the Group 2 patients suspected of viral encephalitis, HSV-1 was isolated in three patients and HSV-2 in one patient. In the TBM patients, TB PCR / GeneXpert MTB/RIF was positive in eight patients. Anti-NMDAr antibody was positive in seven patients, and blasts were present in one patient.

Table 1 details the various CSF parameters, including procalcitonin levels, cell counts, chemistries, and microbiological findings. Notably, patients with bacterial meningitis and ventriculitis exhibited significantly higher levels of CSF procalcitonin (median 0.63 ng/mL vs. 0.05 ng/mL, p <0.001) compared to those without. Similarly, the median value of serum procalcitonin was also significantly higher in patients with bacterial meningitis and ventriculitis (median 2.23 ng/mL vs 0.13 ng/mL, p = 0.018) compared to those without.

CSF parameters such as color, transparency, WBC (including neutrophil and lymphocyte counts), and protein showed significant differences between patients with meningitis and ventriculitis, and those without. CSF glucose was significantly decreased in those with bacterial meningitis and ventriculitis (median 2.1 mmol/L vs 3.2 mmol/L, p = 0.002). CSF WBC was significantly higher in Group 1 (median 40 vs 2, p = 0.006) compared to Group 2. Colorless CSF was significantly more common in Group 2 compared to Group 1. Clear transparency was likewise more common in Group 2 than in Group 1. The presence of bacterial growth in CSF culture was significantly and only associated with the bacterial meningitis and ventriculitis group (p = 0.025).

Table 2 shows the comparison of CSF PCT values between Group 1 and TBM patients under Group 2 showing a significantly lower value for TBM (median 0.095 ng/mL vs 0.63 ng/mL, p <0.001).

Table 3 focuses on the diagnostic accuracy of CSF procalcitonin in discriminating bacterial meningitis and ventriculitis. A cutoff value of >0.19 ng/mL for CSF procalcitonin demonstrated a sensitivity of 90.48% and a specificity of 91.82% (Appendix 1). The positive predictive value (PPV) was 67.86%, the negative predictive value (NPV) was 98.06%, the positive likelihood ratio (PLR) of 11.06, and the negative likelihood ratio (NLR) of 0.10.

It was also noted that for every 0.01 increase in a patient's CSF procalcitonin, the odds of having bacterial meningitis and ventriculitis also increased by 3.56%, as shown in Table 4. In addition, patients with ≥0.19 CSF Procalcitonin are 106.61 times more likely to have bacterial meningitis and ventriculitis compared to patients with CSF Procalcitonin of <0.19.

Table 5 summarizes the diagnostic accuracy of serum PCT in differentiating between patients with and without bacterial meningitis and ventriculitis. A threshold of >0.67 ng/mL yielded a sensitivity of 64.29% and a specificity of 73.08% (Appendix 2). The PPV was 39.13%, NPV 88.37%, PLR 2.39, NLR 0.49, and the diagnostic accuracy of the test was 71.21%.

Table 4. Association of CSF Procalcitonin to Predict Bacterial Meningitis and Ventriculitis

CSF Procalcitonin	Crude odds ratio	95% CI	*P*-value
CSF Procalcitonin, 0.01	1.0356	1.0171 to 1.0543	<0.001
CSF Procalcitonin ≥0.19	106.61	21.339 to 532.64	<0.001

Table 5. Diagnostic Accuracy of Serum PCT to Discriminate Bacterial Meningitis and Ventriculitis

		Bacterial Meningitis and Ventriculitis		Total
		Group 1	Group 2	
Serum PCT	≥0.67	9	14	23
	<0.67	5	38	43
	Total	14	52	66
Sensitivity	64.29% (35.14 to 87.24)	***Positive LR***	2.39 (1.32 to 4.33)	
Specificity	73.08% (58.98 to 84.43)	***Negative LR***	0.49 (0.24 to 1.01)	
PPV	39.13% (26.19 to 53.8)	***Prevalence***	21.21% (12.11 to 33.02)	
NPV	88.37% (78.69 to 93.99)	***Accuracy***	71.21% (58.75 to 81.70)	

PPV – positive predictive value, NPV – negative predicted value, LR – likelihood ratio

Table 6 presents a comparative analysis of the diagnostic accuracy of CSF PCT and serum PCT for predicting bacterial meningitis and ventriculitis. The diagnostic accuracy is assessed using the area under the receiver operating characteristic (ROC) curve (AUC). The AUC for CSF procalcitonin is 0.9657 (95% CI: 0.9271 to 1.0000), indicating excellent diagnostic ability. This high AUC value demonstrates that CSF procalcitonin is a highly reliable biomarker for distinguishing patients with bacterial meningitis and ventriculitis from those without the conditions. The AUC for serum procalcitonin is 0.7047 (95% CI: 0.5354 to 0.8740), reflecting fair diagnostic ability. While serum procalcitonin is somewhat useful, it is not as effective as CSF procalcitonin in diagnosing bacterial meningitis and ventriculitis.

Table 6. Diagnostic Accuracy of CSF Procalcitonin Compared to Serum Procalcitonin to Predict Bacterial Meningitis and Ventriculitis

Parameter	ROC area (95% CI)	Diagnostic ability	*P*-value
CSF Procalcitonin	0.9657 (0.9271 to 1.0000)	Excellent	<0.001
Serum Procalcitonin	0.7047 (0.5354 to 0.8740)	Fair	<0.001

Figure 1 graphically illustrates the area under the receiver operating characteristic (ROC) curves for CSF procalcitonin and serum procalcitonin to predict bacterial meningitis and ventriculitis. The ROC curve for CSF PCT shows an area under the curve (AUC) of 0.9657, indicating excellent diagnostic ability. The ROC curve for serum PCT shows a lower AUC value, indicating poorer diagnostic abilities compared to CSF PCT. Figure 1 emphasizes the superior diagnostic performance of CSF PCT over serum PCT.

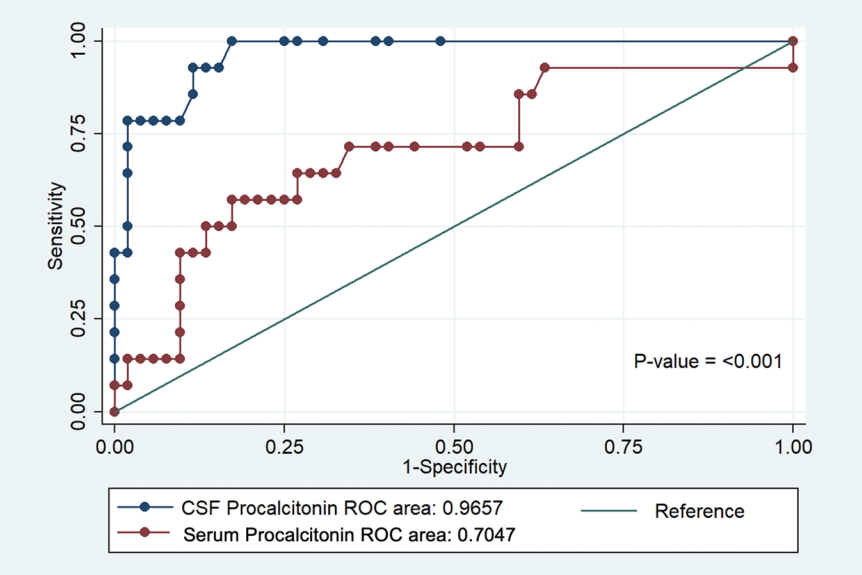

Figure 1. Area under the ROC curves of CSF procalcitonin and serum procalcitonin to discriminate bacterial meningitis and ventriculitis.

DISCUSSION

The findings of this study confirm that CSF procalcitonin is a reliable marker for pediatric bacterial meningitis and ventriculitis with a high sensitivity and specificity. Our results, which extend the comprehensive work of Biasucci et al., showed an AUC for CSF PCT of 96.57% in the ROC analysis[1], making it an excellent test in distinguishing between bacterial meningitis and ventriculitis from the control diseases.

Our study arrived at a CSF PCT cut-off point of 0.19 ng/mL. These results coincide with those published previously; in particular, a study in adults with bacterial meningitis and ventriculitis noted a slightly higher cut-off of 0.2 ng/mL, yielding a sensitivity of 95.2% and specificity of 96%.[23] In pediatrics, early studies on serum PCT achieved a cut-off value of 1–1.5 ng/mL with a sensitivity of 83% and specificity of 93% for distinguishing between bacterial and viral infections.[24] In the last decade, only seven studies have so far looked directly at the utility of CSF PCT in the diagnosis of pediatric bacterial meningitis and tried to establish cut-off values,[7,16,25] with four of them in the neonatal population.[14,26–28] Three studies focused solely on CSF PCT, while the others compared CSF PCT with serum PCT and other markers like ferritin, CRP[7], and lactate.[25] The results yielded cut-offs from 0.085 – 0.33 ng/mL with sensitivities ranging from 55 – 97% and specificities from 58 – 98%. The closest reported cut-off point was 0.22 ng/mL in an Indian study with neonates, showing a sensitivity of 95.2% and specificity of 96%.[26] There is often a trade-off between sensitivity and specificity in that optimizing one may come at the expense of the other. In our study, however, CSF procalcitonin exhibits both high sensitivity and specificity, making it an ideal diagnostic test.

In addition, we found that CSF PCT had a higher specificity (91.82%) than sensitivity (90.48%). Studies on neonatal meningitis, however, showed discordant results with a higher sensitivity than specificity for similar cut-off values.[14,28] In children, however, researchers in China showed that a CSF PCT cut-off of 0.085 ng/mL achieved a sensitivity of 55.17% and a much higher specificity of 95.83%.[16] Finally, a recent meta-analysis reported that the pooled sensitivity of a CSF PCT cut-off of 0.33 ng/mL in children was 96% and specificity of 91%.[1] Again, this variability is understandable and likely reflects differences in study populations, methodologies, and the clinical context wherein sensitivity and specificity are being balanced.

For our purposes, we arrived at the cut-off value of 0.19 ng/mL by maximizing both the sensitivity and specificity. In addition, the PLR for CSF PCT was 11.06, and the NLR at 0.1. Clinically, a PLR greater than 10 or an NLR below 0.1 is generally more useful in indicating diagnostic accuracy. They indicate significant and decisive shifts from pre- to post-test probability.[29] By considering a CSF PCT value of less than 0.19 ng/mL as negative and any value higher than the cut-off as positive, we can conclude that patients testing positive for CSF PCT have an 11-fold higher chance of having bacterial meningitis and ventriculitis. Conversely, a negative CSF PCT result is associated with only a 10% probability of the patient having the disease. In this manner, coupled with its high specificity, CSF PCT will be most valuable in clinical scenarios where the conventional tests are confounded or inconclusive and patients have minimal or subtle signs and symptoms, such as in cases of partially treated bacterial meningitis or ventriculitis and post-neurosurgical patients with or without CSF diversion devices (shunt systems or external ventricular drains (EVDs). It can provide a more accurate diagnosis and contribute to more judicious use of antibiotics, potentially reducing antibiotic resistance.

In a review of ventriculostomy-related infections, the authors emphasized the importance of distinguishing between contamination, colonization, suspected or confirmed ventriculostomy-related infections, and clinically relevant ventriculitis. They noted that conventional parameters like CSF WBC, glucose, protein, Gram stains, and cultures can vary significantly and are highly influenced by surveillance methods like CSF sampling.[30] In our study, only a single procalcitonin determination was done for patients who were suspected and later confirmed to have primary bacterial infection. Because serial measurements of PCT are often more informative than single time-point assessments in monitoring the response to treatment and distinguishing between expected post-operative changes in neurosurgical patients[31], this is another clinical scenario wherein CSF PCT is potentially useful and warrants further study. It is, therefore, recommended that serial procalcitonin determinations be incorporated in future research.

Our research has also demonstrated that the mean CSF PCT in patients with bacterial meningitis and ventriculitis was significantly higher than those without. This was also adequately illustrated by our sub analysis of the patients with TBM in the study, showing that the median value of CSF PCT in TBM patients (median, 0.095 ng/mL; range 0.05 to 0.175) was significantly (p <0.001) lower than that of bacterial meningitis and ventriculitis patients (median, 0.63 ng/mL; range 0.4 to 1.48). This result also justifies our study design to include TBM under Group 2, but we recommend that a study dedicated to discriminating between bacterial meningitis and ventriculitis from TBM be undertaken in the future.

This relationship can be particularly valuable in cases wherein the CSF characteristics may appear indistinguishable from bacterial meningitis, such as in TBM. Tuberculous meningitis can be challenging to confirm due to its paucibacillary nature and atypical clinicoradiologic findings. Among the 14 cases of TBM in our study, only eight were bacteriologically confirmed (57%), while the rest (42%) were diagnosed based on clinical and radiological features. Certain neuroradiologic findings, such as basal enhancement, hydrocephalus, infarcts, and tuberculomas, had sensitivities ranging from 41-89%, with pre-contrast hyperdense exudates in the basal cisterns or the combination of features

mentioned being 100% specific.[32] Therefore, in cases wherein the above characteristics are not present, CSF PCT may help augment the diagnostic toolkit in TBM.

It was also revealed that CSF PCT outperforms serum PCT in distinguishing pediatric bacterial meningitis and ventriculitis from other nonbacterial diseases. Existing literature on this aspect presents conflicting evidence. A systematic review and meta-analysis of 22 studies involving 2,000 patients investigated the diagnostic accuracy of PCT in blood and CSF in bacterial meningitis and found that the overall specificities and sensitivities were 86% and 80% for CSF PCT and 97% and 95% for blood PCT.[12] However, the review included only five studies that focused on CSF PCT, and all were in the adult population with small sample sizes. On the other hand, the work of Biasucci et al., which included 11 studies on CSF PCT, supports the superior sensitivity (96%) and specificity (91%) of CSF procalcitonin compared to serum procalcitonin in children, less so in adults and post-neurosurgical patients.[1] Our study appears congruent with the latter as the population investigated is the same, but further meta-analyses with larger sample sizes can clarify this relationship.

Some studies also suggest that CSF PCT cut-offs may be lower than serum PCT cut-offs for diagnosing bacterial meningitis both in community-acquired and hospital-associated settings. In our study, consistent with most literature, the cut-off for CSF PCT (0.19 ng/mL) was lower than serum PCT (0.67 ng/mL). They hypothesize that CSF PCT may be more specific to CNS infections compared to serum PCT, which can be elevated in systemic infections without CNS involvement.[28]

Additionally, it is recognized that procalcitonin levels are physiologically elevated in the first 2-3 days of life[33], and excluding this population ensured that the CSF values in our study were not falsely increased. A dedicated study designed for neonates must be undertaken.

In our study, we found that the mean CSF white blood cell count in the bacterial meningitis and ventriculitis group was only 40, despite the usual criteria for pleocytosis requiring over 100 WBCs. This might be due to the inclusion of patients with partially treated bacterial meningitis, and prior antibiotic treatment may have influenced these counts. While this approximates a more representative population of bacterial meningitis and ventriculitis in real life, future research will need to consider these factors to clarify their effect on CSF procalcitonin.

The study has several limitations. Bacteriologic and etiologic confirmation of meningitis were not available for some of our patients, and this could have led to bias in how the cases were categorized. We also recognize that some cases lack data pertaining to specific laboratory tests, which were not done either due to the working clinical impression at the time or the non-availability of the test, and this could have led to a measurement bias. We have ameliorated this by including only patients who satisfied the clinical criteria supported by the laboratory parameters and analyzed them in these groups accordingly. By using the conventional CSF parameters to help diagnose the disease entities in the study, we were also unable to compare the diagnostic ability of CSF PCT and these routine CSF tests. Factors such as the timing of PCT sampling, sampling site, and shunt system revisions will need to be included in the design of future studies to test the vigor of procalcitonin in different clinical scenarios seen in children. In addition, PCT testing may not be readily available in all healthcare settings, particularly in resource-limited areas. Studies on cost-effectivity, availability, and turn-around time will impact the uptake of this test into routine practice.

Our findings suggest that incorporating CSF procalcitonin can aid in the diagnosis of pediatric bacterial meningitis and ventriculitis. This study featured a relatively larger sample size than previous research and included post-neurosurgical patients, resulting in increased statistical power and better representation of the target population. When combined with comprehensive patient history, physical examination, and relevant tests, CSF procalcitonin has the potential to serve as a valuable predictor in the stepwise assessment of suspected bacterial meningitis and ventriculitis.

CONCLUSION

CSF procalcitonin has excellent power in discriminating between patients with and without pediatric bacterial meningitis and ventriculitis. Its high sensitivity and specificity make it valuable in clinical scenarios wherein the conventional laboratory tests are inconclusive, supplementing clinical assessment for the early and accurate diagnosis of CNS infections in order to guide management and rational use of antibiotics.

Disclaimer

Any opinions, findings, conclusions, or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the University of the Philippines Manila - Philippine General Hospital.

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Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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REFERENCES

1. Biasucci DG, Sergi PG, Bilotta F, Dauri M. Diagnostic accuracy of procalcitonin in bacterial infections of the CNS: an updated systematic review, meta-analysis, and meta-regression. Crit Care Med. 2024;52(1):112-24. doi:10.1097/CCM.0000000000006017.
2. Tunkel AR, Hasbun R, Bhimraj A, et al. 2017 Infectious Diseases Society of America's Clinical practice guidelines for healthcare-associated ventriculitis and meningitis. Clinical Infectious Diseases. 2017;64(6):e34-e65. doi:10.1093/cid/ciw861.
3. Pan X, Haishaer D, Liu M, Zhou S, Na H, Zhao H. Diagnostic, monitoring, and prognostic value of combined detection of cerebrospinal fluid heparin-binding protein, interleukin-6, interleukin-10, and procalcitonin for post-neurosurgical intracranial infection. Cytokine. 2024;179:156593. doi:10.1016/j.cyto.2024.156593.
4. Lenski M, Huge V, Schmutzer M, et al. Inflammatory markers in serum and cerebrospinal fluid for early detection of external ventricular drain–associated ventriculitis in patients with subarachnoid hemorrhage. J Neurosurg Anesthesiol. 2019;31(2):227-33. doi:10.1097/ANA.0000000000000496.
5. Huy NT, Thao NT, Diep DT, Kikuchi M, Zamora J, Hirayama K. Cerebrospinal fluid lactate concentration to distinguish bacterial from aseptic meningitis: a systemic review and meta-analysis. Crit Care. 2010;14(6):R240. doi:10.1186/cc9395.
6. Mekitarian Filho E, Horita SM, Gilio AE, Nigrovic LE. Cerebrospinal fluid lactate level as a diagnostic biomarker for bacterial meningitis in children. Int J Emerg Med. 2014;7(1):14. doi:10.1186/1865-1380-7-14.
7. Shokrollahi MR, Shabanzadeh K, Noorbakhsh S, Tabatabaei A, Movahedi Z, Shamshiri AR. Diagnostic value of CRP, procalcitonin, and ferritin levels in cerebrospinal fluid of children with meningitis. Cent Nerv Syst Agents Med Chem. 2018;18(1). doi:10.2174/1871524916666160302103223.
8. Panji M, Behmard V, Raoufi MF, et al. Evaluation of biological markers in children's cerebrospinal fluid with bacterial and viral meningitis. Int J Med Lab. 2023;10(3):208-16. doi:10.18502/ijml.v10i3.13745.
9. Dubos F, Korczowski B, Aygun DA, et al. Serum procalcitonin level and other biological markers to distinguish between bacterial and aseptic meningitis in children. Arch Pediatr Adolesc Med. 2008;162(12):1157. doi:10.1001/archpedi.162.12.1157.
10. Scheld WM, Whitley RJ, Marra CM. Infections of the Central Nervous System. In: Scheld WM, Whitley RJ, Marra CM, eds. Fourth edition. Wolters Kluwer; 2014:16-16.
11. Julián-Jiménez A, Morales-Casado MI. Usefulness of blood and cerebrospinal fluid laboratory testing to predict bacterial meningitis in the emergency department. Neurología. 2019;34(2):105-113. doi:10.1016/j.nrl.2016.05.009
12. Wei TT, Hu ZD, Qin BD, et al. Diagnostic accuracy of procalcitonin in bacterial meningitis versus nonbacterial meningitis. Medicine. 2016;95(11):e3079. doi:10.1097/MD.0000000000003079.
13. Vikse J, Henry BM, Roy J, Ramakrishnan PK, Tomaszewski KA, Walocha JA. The role of serum procalcitonin in the diagnosis of bacterial meningitis in adults: a systematic review and meta-analysis. Int J Infect Dis. 2015;38:68-76. doi:10.1016/j.ijid.2015.07.011.
14. Dutta S, Sachdeva N, Pal A, Ray P. Cerebrospinal fluid and plasma procalcitonin for the diagnosis of neonatal bacterial meningitis. J Paediatr Child Health. 2022;58(8):1425-30. doi:10.1111/jpc.16023.
15. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control. 2008;36(5):309-32. doi:10.1016/j.ajic.2008.03.002.
16. Zhang L, Ma L, Zhou X, et al. Diagnostic value of procalcitonin for bacterial meningitis in children: a comparison analysis between serum and cerebrospinal fluid procalcitonin levels. Clin Pediatr (Phila). 2019;58(2):159-65. doi:10.1177/0009922818809477.
17. Viallon A, Bothelo-Nevers E, Zeni F. Clinical decision rules for acute bacterial meningitis: current insights. Open Access Emerg Med. 2016 Apr 19;8:7-16. doi:10.2147/OAEM.S69975.
18. Adhikari S, Gauchan E, BK G, Rao K. Effect of antibiotic pretreatment on cerebrospinal fluid profiles of children with acute bacterial meningitis. Nep J Med Sci. 2013;2(2):135-9. doi:10.3126/njms.v2i2.8963.
19. Malla KK, Malla T, Rao KS, Basnet S, Shah R. Is cerebrospinal fluid C-reactive protein a better tool than blood c-reactive protein in laboratory diagnosis of meningitis in children? Sultan Qaboos Univ Med J. 2013;13(1):93-9. doi:10.12816/0003201.
20. Nigrovic LE, Malley R, Macias CG, et al. Effect of antibiotic pretreatment on cerebrospinal fluid profiles of children with bacterial meningitis. Pediatrics. 2008;122(4):726-30. doi:10.1542/peds.2007-3275.
21. Li W, Sun X, Yuan F, et al. diagnostic accuracy of cerebrospinal fluid procalcitonin in bacterial meningitis patients with empiric antibiotic pretreatment. J Clin Microbiol. 2017;55(4):1193-204. doi:10.1128/JCM.02018-16.
22. World Health Organization. Guidance for National Tuberculosis Programmes on the Management of Tuberculosis in Children: Diagnosis of TB in children. [Internet]. 2014 [cited 2024 July]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK214442.
23. Konstantinidis T, Cassimos D, Gioka T, et al. Can procalcitonin in cerebrospinal fluid be a diagnostic tool for meningitis? J Clin Lab Anal. 2015;29(3):169-74. doi:10.1002/jcla.21746.
24. Gendrel D, Raymond J, Assicot M, et al. Measurement of procalcitonin levels in children with bacterial or viral meningitis. Clin Infect Dis. 1997;24(6):1240-2. doi:10.1086/513633.
25. Nazir M, Wani WA, Kawoosa K, et al. The diagnostic dilemma of traumatic lumbar puncture: current standing of cerebrospinal fluid leukocyte corrections and our experience with cerebrospinal fluid biomarkers. J Child Neurol. 2018;33(7):441-8. doi:10.1177/0883073818761719.
26. Rajial T, Batra P, Harit D, Singh NP. Utility of cerebrospinal fluid and serum procalcitonin for the diagnosis of neonatal meningitis. Am J Perinatol. 2022;39(04):373-8. doi:10.1055/s-0040-1716406.
27. Nagaraj M, Bandiya P, Jagannatha B, Shivanna N, Benakappa N, Bandyopadhyay T. Diagnostic utility of cerebrospinal fluid procalcitonin in neonatal meningitis. J Trop Pediatr. 2022;68(3). doi:10.1093/tropej/fmac043.
28. Reshi Z, Nazir M, Wani W, Malik M, Iqbal J, Wajid S. Cerebrospinal fluid procalcitonin as a biomarker of bacterial meningitis in neonates. J Perinatol. 2017;37(8):927-31. doi:10.1038/jp.2017.73
29. López AF, Cubells CL, García JJG, Pou JF. Procalcitonin in pediatric emergency departments for the early diagnosis of invasive bacterial infections in febrile infants: results of a multicenter study and utility of a rapid qualitative test for this marker. Pediatr Infect Dis J. 2003;22(10):895-904. doi:10.1097/01.inf.0000091360.11784.21.
30. Lozier AP, Sciacca RR, Romagnoli MF, Connolly ES. Ventriculostomy-related infections: a critical review of the literature. Neurosurgery. 2002;51(1):170-82. doi:10.1097/00006123-200207000-00024.
31. Meisner M. Pathobiochemistry and clinical use of procalcitonin. Clinica Chimica Acta. 2002;323(1-2):17-29. doi:10.1016/S0009-8981(02)00101-8.
32. Andronikou S, Smith B, Hatherhill M, Douis H, Wilmshurst J. Definitive neuroradiological diagnostic features of tuberculous meningitis in children. Pediatr Radiol. 2004;34(11):876-85. doi:10.1007/s00247-004-1237-1.
33. Chiesa C, Pellegrini G, Panero A, et al. C-reactive protein, interleukin-6, and procalcitonin in the immediate postnatal period: influence of illness severity, risk status, antenatal and perinatal complications, and infection. Clin Chem. 2003;49(1):60-8. doi:10.1373/49.1.60.

APPENDICES

Appendix 1. Reference Values of CSF Procalcitonin with Respective Sensitivity and Specificity

Correctly Cutpoint	Sensitivity	Specificity	Classified	LR+	LR-
(≥.05)	100.00%	0.00%	16.03%	1.0000	1.0000
(≥.06)	95.24%	58.18%	64.12%	2.2774	0.0818
(≥.07)	95.24%	63.64%	68.70%	2.6190	0.0748
(≥.08)	95.24%	66.36%	70.99%	2.8314	0.0718
(≥.09)	95.24%	70.91%	74.81%	3.2738	0.0672
(≥.1)	95.24%	73.64%	77.10%	3.6125	0.0647
(≥.11)	95.24%	76.36%	79.39%	4.0293	0.0624
(≥.12)	95.24%	79.09%	81.68%	4.5549	0.0602
(≥.14)	95.24%	81.82%	83.97%	5.2381	0.0582
(≥.15)	95.24%	85.45%	87.02%	6.5476	0.0557
(≥.16)	95.24%	86.36%	87.79%	6.9841	0.0551
(≥.17)	90.48%	88.18%	88.55%	7.6557	0.1080
(≥.18)	90.48%	90.91%	90.84%	9.9524	0.1048
(≥.19)	90.48%	91.82%	91.60%	11.0582	0.1037
(≥.21)	85.71%	91.82%	90.84%	10.4762	0.1556
(≥.22)	80.95%	91.82%	90.08%	9.8942	0.2074
(≥.24)	76.19%	92.73%	90.08%	10.4762	0.2568
(≥.26)	76.19%	93.64%	90.84%	11.9728	0.2543
(≥.29)	76.19%	94.55%	91.60%	13.9683	0.2518
(≥.3)	76.19%	95.45%	92.37%	16.7619	0.2494
(≥.38)	76.19%	96.36%	93.13%	20.9524	0.2471
(≥.4)	76.19%	97.27%	93.89%	27.9365	0.2448
(≥.42)	66.67%	97.27%	92.37%	24.4445	0.3427
(≥.44)	61.90%	97.27%	91.60%	22.6984	0.3916
(≥.63)	52.38%	97.27%	90.08%	19.2064	0.4895
(≥.77)	47.62%	97.27%	89.31%	17.4603	0.5385
(≥.82)	47.62%	98.18%	90.08%	26.1906	0.5335
(≥1.1)	42.86%	98.18%	89.31%	23.5715	0.5820
(≥1.13)	42.86%	99.09%	90.08%	47.1430	0.5767
(≥1.16)	33.33%	99.09%	88.55%	36.6668	0.6728
(≥1.48)	28.57%	99.09%	87.79%	31.4287	0.7208
(≥2.2)	23.81%	99.09%	87.02%	26.1906	0.7689
(≥2.31)	23.81%	100.00%	87.79%	0.7619	
(≥2.44)	19.05%	100.00%	87.02%	0.8095	
(≥2.56)	14.29%	100.00%	86.26%	0.8571	
(≥3.69)	9.52%	100.00%	85.50%	0.9048	
(≥4.3)	4.76%	100.00%	84.73%	0.9524	
(>4.3)	0.00%	100.00%	83.97%	1.0000	

Appendix 2. Reference Values of Serum Procalcitonin with Respective Sensitivity and Specificity

Cutpoint	Sensitivity	Specificity	Classified	LR+	LR-
(≥0)	100.00%	0.00%	21.21%	1.0000	
(≥.05)	92.86%	0.00%	19.70%	0.9286	
(≥.06)	92.86%	36.54%	48.48%	1.4632	0.1955
(≥.07)	85.71%	38.46%	48.48%	1.3929	0.3714
(≥.08)	85.71%	40.38%	50.00%	1.4378	0.3537
(≥.09)	71.43%	40.38%	46.97%	1.1982	0.7075
(≥.1)	71.43%	46.15%	51.52%	1.3265	0.6190
(≥.13)	71.43%	48.08%	53.03%	1.3757	0.5943
(≥.15)	71.43%	55.77%	59.09%	1.6149	0.5123
(≥.16)	71.43%	59.62%	62.12%	1.7687	0.4793
(≥.18)	71.43%	61.54%	63.64%	1.8571	0.4643
(≥.2)	71.43%	65.38%	66.67%	2.0635	0.4370
(≥.27)	64.29%	67.31%	66.67%	1.9664	0.5306
(≥.4)	64.29%	69.23%	68.18%	2.0893	0.5159
(≥.46)	64.29%	71.15%	69.70%	2.2286	0.5019
(≥.67)	64.29%	73.08%	71.21%	2.3878	0.4887
(≥.69)	57.14%	73.08%	69.70%	2.1224	0.5865
(≥.81)	57.14%	75.00%	71.21%	2.2857	0.5714
(≥.88)	57.14%	76.92%	72.73%	2.4762	0.5571
(≥1.18)	57.14%	78.85%	74.24%	2.7013	0.5436
(≥1.31)	57.14%	80.77%	75.76%	2.9714	0.5306
(≥1.36)	57.14%	82.69%	77.27%	3.3016	0.5183
(≥1.73)	50.00%	82.69%	75.76%	2.8889	0.6047
(≥1.74)	50.00%	84.62%	77.27%	3.2500	0.5909
(≥3.11)	50.00%	86.54%	78.79%	3.7143	0.5778
(≥3.42)	42.86%	86.54%	77.27%	3.1837	0.6603
(≥5.09)	42.86%	88.46%	78.79%	3.7143	0.6460
(≥5.44)	42.86%	90.38%	80.30%	4.4571	0.6322
(≥5.46)	35.71%	90.38%	78.79%	3.7143	0.7112
(≥7.11)	28.57%	90.38%	77.27%	2.9714	0.7903
(≥8.89)	21.43%	90.38%	75.76%	2.2286	0.8693
(≥9.71)	14.29%	90.38%	74.24%	1.4857	0.9483
(≥11.81)	14.29%	92.31%	75.76%	1.8571	0.9286
(≥19.01)	14.29%	94.23%	77.27%	2.4762	0.9096
(≥24.32)	14.29%	96.15%	78.79%	3.7143	0.8914
(≥59.38)	14.29%	98.08%	80.30%	7.4286	0.8739
(≥78.91)	7.14%	98.08%	78.79%	3.7143	0.9468
(≥200)	7.14%	100.00%	80.30%	0.9286	
(>200)	0.00%	100.00%	78.79%	1.0000	