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Adherence to the IDSA guidelines for brain imaging before lumbar puncture in community-acquired meningitis

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Abstract

Background: The Infectious Diseases Society of America (IDSA) has published guidelines indicating the criteria for brain imaging before lumbar puncture (LP) among patients with community-acquired meningitis (CAM). However, data on adherence to the guidelines and associated outcomes are currently limited. *Methods:* We conducted a prospective observational study among patients with CAM from January 2018 to March 2019 in the emergency department (ED) of a tertiary-care hospital in Thailand. Physicians' IDSA guidelines adherence rate for brain imaging before LP was determined. Clinical outcomes were compared between patients undergoing the procedures according and not according to the guidelines. *Results:* Of the 101 patients screened, 69 were included. The physicians' guidelines non-adherence rate for brain imaging before LP was 38%. The most common non-adherent practice was performing brain imaging despite no indication (96%). By multivariable logistic regression analysis, the only independent factor associated with non-adherence to the guidelines was caring patients with no indications for brain imaging before LP ($P<0.001$). The patients in the guidelines-adherent group were more-likely than those in the guidelines-non-adherent group to have underlying AIDS and present with seizure, while the 30-day survival rates were not different between the two groups (88% vs. 85%). *Conclusions:* Our study suggests a significant non-adherence to the guidelines due to the over-investigation of the physicians in patients with no indications for brain imaging before LP. Interventions to improve physicians' knowledge about these indications and practice are needed for better care of patients with CAM.

Keywords: community-acquired meningitis, adherence, IDSA guidelines, lumbar puncture, brain imaging

INTRODUCTION

Community-acquired meningitis (CAM) is a serious infection with high morbidity and mortality.[1] Accurate and timely diagnosis of CAM is critical for early empiric antimicrobial therapy to improve survival. Although lumbar puncture (LP) to obtain cerebrospinal fluid (CSF) for examination is an important diagnostic procedure, it should be performed with caution or not be performed in some patients at-risk for complications associated with LP, especially life-threatening brain herniation. In 2004, the Infectious Diseases Society of America (IDSA) published guidelines which describe indications for performing brain imaging prior to LP. The indications include immunocompromised state, history of central nervous system (CNS) disease, new onset of seizure, papilledema, abnormal level of consciousness, and focal neurologic deficit.[2] While performing brain imaging could guide which patients LP should be done with caution or be avoided, the procedure could also delay antimicrobial initiation and other supportive treatment. In some cases, antimicrobial therapy is empirically initiated long before LP, thus reducing the yield for recovering causative pathogens and the chance to accurately diagnose and treat the patients with CAM.

With the increase in the incidences of physicians being sued and malpractice lawsuits, "defensive medicine" has been practiced in many settings. These include performing unnecessary diagnostic tests and invasive procedures and prescribing unnecessary treatment and needless hospitalization.[3] Defensive medicine could raise the cost of healthcare in each patient and may put patients at-risk for complications related to unnecessary tests, procedures, and treatments.

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Over investigating patients with CAM using brain imaging may increase cancer risks associated with radiation, in cases of performing multiple high-dose examinations in a short period of time[4], while other risks include contrast-induced nephropathy and allergic reactions.[5]

A previous study conducted in the US demonstrated that 60% of clinicians did not adhere to the IDSA guidelines in regard to performing brain imaging prior to LP and a computed tomography (CT) of the brain was ordered when not indicated in 64% of patients with CAM.[6] However, factors associated with non-adherence and the associated outcomes were not prospectively assessed. In addition, none of the previous studies have described physician's adherence to the IDSA guidelines in Asian countries.

The primary objective of this study was to determine physicians' adherence to the IDSA guidelines regarding brain imaging before LP in patients with CAM in a tertiary referral hospital in Thailand. The secondary objectives were to assess factors associated with the guidelines non-adherence, the knowledge of the first contact physicians in the emergency department (ED) about indications for brain imaging before LP and the outcomes associated with non-adherence to the guidelines.

METHODS

This study was conducted among patients who were diagnosed with CAM and identified prospectively in the ED of Thammasat University Hospital (TUH), a tertiary-care center in central Thailand during the period from 1 January 2018 to 31 March 2019. Patients were initially diagnosed of CAM by the physicians in the ED. The investigators reviewed the list of these patients to assess the eligibility. Inclusion criteria were adults aged ≥ 18 years, signs and symptoms compatible with meningitis (fever and headaches and/or stiff of neck and/or alteration of consciousness and/or focal neurological deficits) and CSF white blood cell of ≥ 5 cell/mm^3). Exclusion criteria were patients who had intracranial devices, recent neurosurgery within 3 months, referral to other healthcare facilities for further management, referral to the ED and already treated for CAM from other healthcare facilities and declined participation. Informed consent was obtained from all eligible patients or legal representative if the patients could not give the consent. This study was approved by the Research Ethics Committee of Faculty of Medicine, Thammasat University.

Demographic data, comorbid conditions, clinical presentations, duration to brain imaging, LP and antimicrobial administration, CSF profiles, final diagnoses, treatment and outcomes including survival at 7, 14 and 30 days were collected. All brain imaging in this study were performed using CT with contrast. The radiation exposure was 2 millisieverts (mSv) and the slice thickness was 10 mm. The patients were followed-up for the primary and secondary outcomes until discharged from TUH. A telephone call and chart review were conducted if the patients were discharged before the outcomes could be assessed. Adherence to the IDSA guidelines was defined as patients undergoing brain imaging before LP according to the described indications[2], while patients undergoing the brain imaging without the indications or not undergoing the brain imaging despite having the indications were considered non-adherence to the guidelines. Appropriate antimicrobial therapy was defined as use of (an) antimicrobial agent(s) that 1) was/were active against the causative pathogen(s) and 2) was/were according to the TUH and IDSA guidelines. In case that the causative pathogens could not be identified, use of antimicrobial therapy for the most-likely pathogens based on epidemiology, clinical and laboratory data was considered appropriate. Duration to brain imaging, LP, and antimicrobial therapy was defined as the time from the patients' presentation to the time brain imaging and LP were performed and antimicrobial therapy was initiated.

We used a questionnaire to assess the knowledge about the indications for brain imaging before LP among the first contact physicians taking care of the study patients. The questionnaire comprised a question "which of the followings are the indications for brain imaging before LP in patients with CAM according to the IDSA guidelines" and the 6 indications with provided checkboxes. The physicians can put a mark on any of the checkboxes if they think it/they is/are indication(s) described in the guidelines.

Based on the rate of non-adherence to the IDSA guidelines in a previous study[6], the sample size needed to have statistical power of 80%, significant level of 0.05 and error of 0.12 was 65. All statistical analyses were performed using SPSS 2018 software, version 25 (IBM Corp.). Data were presented in numbers (percentage) and median with interquartile range (IQR). Categorical variables were compared using the $\chi 2$ or Fisher exact test as appropriate while the continuous variables were compared using Mann-Whitney U

test or Kruskal-Wallis test. Multivariable logistic regression analysis was performed to determine factors associated with non-adherence to the guidelines. All *P*-value <0.05 was considered statistically significant.

RESULTS

One-hundred and one patients were diagnosed of CAM during the study period. Thirty-two patients were excluded (Figure). Of the 69 included patients, 40 (58%) were male, and the median age was 42 years (IQR, 42-75 years). The three most common underlying diseases were acquired immune deficiency syndrome (AIDS) (19%), diabetes mellitus (7%), and chronic liver disease (6%). The most common indication for brain imaging before LP was immunocompromised status (28%). Other clinical presentations, CSF profiles and final diagnoses are shown in Table 1.

All 68 brain imaging were performed using CT of the brain while one patient did not undergo CT of the brain despite having an indication (Figure). There were 26 patients who underwent CT of the brain not according to the IDSA guidelines (25 patients underwent CT of the brain despite no indication and one patient not undergoing CT of the brain despite an indication) (Figure 1). The rate of guidelines non-adherence was 26/69 (38%). All CT of the brain of the 25 patients in non-adherence group revealed normal findings. Compared to the patients in the adherence group, those in the non-adherence group were more-likely to have bacterial meningitis as final diagnosis and normal CT finding, had longer duration of symptoms and less-likely to have AIDS and indications for brain imaging before LP (Table 1). By multivariable logistic regression analysis, adjusted for age, AIDS, duration and presenting symptoms, physicians were less likely to adhere to the guidelines when caringfor patients with no indications for brain imaging (over-investigation by ordering CT of the brain without indication); adjusted odds ratio 1062.65, 95% confidence interval 59.23-19067.05; *P*<0.001). For treatment, there were no significant differences between the two groups in regards to type of first contact physician, the rates of appropriate empirical and definite antimicrobial therapy and duration to CT, LP and antimicrobial administration (Table 2). The rates of 30-day survival were comparable between the two groups (88% vs. 85%) as were the rates of 7- and 14-day survival (Table 2). No

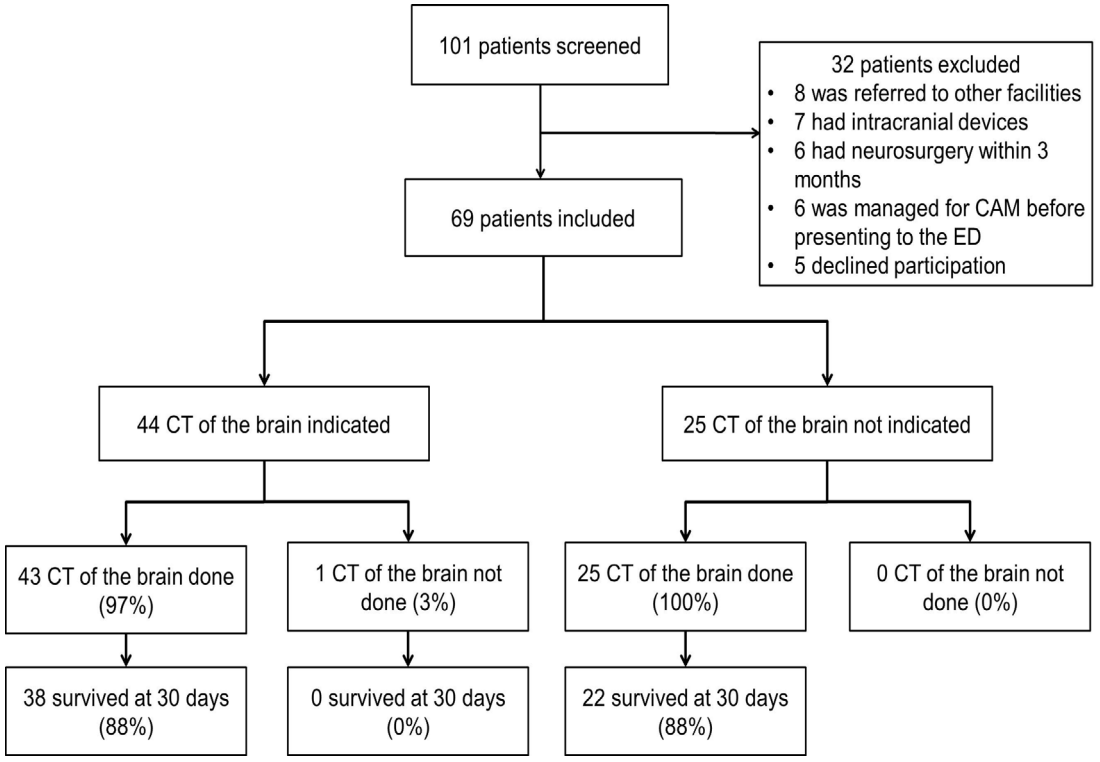

Figure 1. Study flow.
CAM = community-acquired meningitis; CT = computed tomography; ED = emergency department.

Table 1: Baseline demographic and clinical characteristics of patients undergoing brain imaging before lumbar puncture adherent and non-adherent to the IDSA guidelines

Characteristic	All (N=69)	Adherence group (N=43)	Non-adherence group (N=26)	*P*[a]
Male sex	40 (58)	24 (56)	16 (62)	0.64
Age (years, median, IQR)	42 (42-75)	41 (33-56)	46 (35-68)	0.14
Underlying disease				
AIDS	13 (19)	13 (30)	0 (0)	**0.002**
DM	5 (7)	2 (5)	3 (12)	0.28
Chronic liver disease	4 (6)	2 (8)	2 (5)	0.60
Non-AIDS immunodeficiency	1 (1)	1 (2)	0 (0)	0.43
Hypertension	1 (1)	1 (2)	0 (0)	0.43
Duration of symptom[b] (hours, median, IQR)	48 (24-96)	48 (24-96)	72 (48-78)	**0.03**
Presenting symptom				
Fever	48 (70)	28 (65)	20 (77)	0.30
Headache	26 (40)	16 (37)	10 (39)	0.91
Alteration of consciousness	19 (28)	12 (28)	7 (27)	0.92
Focal neurological deficit	3 (4)	3 (7)	0 (0)	0.16
Seizure	8 (12)	8 (19)	0 (0)	**0.01**
Nausea and vomiting	1 (1)	0 (0)	1 (4)	0.19
Having indication(s) for brain imaging[c]				
Immunocompromised status	19 (28)	18 (42)	1 (4)	**0.001**
Alteration of consciousness (GCS < 10)	14 (20)	13 (30)	1 (4)	**0.008**
New onset seizure	9 (13)	9 (21)	0 (0)	**0.01**
Focal neurological deficit	3 (4)	3 (7)	0 (0)	0.16
Papilledema	1 (1)	0 (0)	1 (4)	0.19
History of CNS disease	0 (0)	0 (0)	0 (0)	--
Brain imaging performed before lumbar puncture[d]	68 (99)	43 (100)	25 (96)	0.19
Brain imaging findings[d]				**0.03**
Normal	58/68 (85)	33/43 (77)	25/25 (100)	
Leptomeningeal enhancement	8/68 (12)	8/43 (19)	0/25 (0)	
Parenchymal abscess	2/68 (3)	2/43 (4)	0/25 (0)	
CSF profile				
Opening pressure (cmH_2O, median, IQR)	24 (24-36)	24 (17-25)	24 (20-27)	0.52
WBC count (cells/µL, median, IQR)	253 (253-3965)	247 (57-666)	1072 (130-3010)	0.06
PMN predominance	43 (62)	21 (49)	22 (85)	**0.003**
RBC count (cells/µL, median, IQR)	85 (85-3000)	58 (0-1300)	143 (15-745)	0.68
CSF protein (mg/µL, median, IQR)	199 (199-746)	178 (97-430)	287 (152-418)	0.30
CSF sugar (mg/dL, median, IQR)	40 (40-80)	41 (20-69)	37 (9-60)	0.31
Positive CSF Gram's or AFB staining	4 (6)	1 (2)	3 (12)	0.11
Positive CSF culture	24 (35)	15 (35)	9 (35)	0.26
Final diagnosis				**0.01**
Bacterial meningitis[e]	42 (61)	21 (49)	21 (81)	
Viral meningitis	10 (15)	6 (14)	4 (15)	
Tuberculous meningitis	8 (12)	7 (16)	1 (4)	
Cryptococcal meningitis	9 (13)	9 (21)	0 (0)	

NOTE:

Data are in numbers (%) unless indicated otherwise.

[a] Comparison between adherence and non-adherence groups

[b] Time from the onset of symptom to the time of presentation

[c] Indications according to the Infectious Diseases Society of America guidelines.[2] Each patient could have one or more indications for brain imaging before lumbar puncture.

[d] All patients underwent computed tomography of the brain.

[e] Causative pathogens were *Streptococcus agalactiae* (N = 12), *Streptococcus pneumoniae* (N = 4), *Streptococcus gallolyticus* (N = 3), *Streptococcus suis* (N = 2), *Klebsiella pneumoniae* (N = 2), *Listeria monocytogenes* (N = 1), methicillin-sensitive *Staphylococcus aureus* (N = 1), viridans group streptococci (N = 1), and not identifiable (N = 16).

AFB = acid-fast bacilli; AIDS = acquired immune deficiency syndrome; CNS = central nervous system; CSF = cerebrospinal fluid; DM = diabetes mellitus; GCS = Glasgow coma scale; IDSA = Infectious Diseases Society of America; IQR = interquartile range; PMN = polymorphonuclear; RBC = red blood cell; WBC = white blood cell.

Table 2: Characteristics of treatment and outcomes among patients undergoing brain imaging before lumbar puncture adherent and non-adherent to the IDSA guidelines

Characteristic	Adherence group (N=43)	Non-adherence group (N=26)	*P*
First contract physicians who provided care in the ED			0.99
Internal Medicine resident	20 (46)	12 (46)	
General practitioner	17 (40)	10 (39)	
Emergency Medicine resident	6 (14)	4 (15)	
Appropriate initial antimicrobial therapy[a]	35 (81)	21 (81)	0.95
Appropriate definite antimicrobial therapy[a]	43 (100)	26 (100)	1.00
Receipt of adjunctive corticosteroid	1 (2)	2 (8)	0.28
Duration to CT of the brain[b] (minute, median, IQR)	162 (120-256)	178 (110-417)	0.55
Duration to lumbar puncture[c] (minute, median, IQR)	327 (214-483)	304 (221-531)	0.61
Duration to initial antimicrobial administration[d] (minute, median, IQR)	375 (230-634)	386 (237-556)	0.87
Duration to definite antimicrobial administration[d] (minute, median, IQR)	5,400 (4,680-7,200)	4,800 (3,120-6,600)	0.67
Outcomes			
Survival at 7 days	41 (95)	25 (96)	0.87
Survival at 14 days	40 (93)	23 (89)	0.51
Survival at 30 days	38 (88)	22 (85)	0.65

NOTE:
Data are in numbers (%) unless indicated otherwise.
[a] Defined as use of (an) antimicrobial agent(s) that 1) was/were active against the causative pathogen(s) and 2) was/were according to the TUH and IDSA guidelines. In case that the causative pathogens could not be identified, use of antimicrobial therapy for the most-likely pathogens based on epidemiology, clinical and laboratory data was considered appropriate.
[b] Defined as the time from patients' presentation to the time CT of the brain was performed.
[c] Defined as the time from patients' presentation to the time lumbar puncture was performed.
[d] Defined as the time from patients' presentation to the time such antimicrobial therapy was initiated.

CT = computed tomography; ED = emergency department; IDSA = Infectious Diseases Society of America; IQR = interquartile range; TUH = Thammasat University Hospital.

patient developed contrast-induced nephropathy or allergic reactions.

There were 53 first contact physicians taking care of the 69 study patients (24 internal medicine residents, 21 general practitioners and 8 emergency medicine residents). The knowledge about the indications for brain imaging before LP was fair among these physicians (Table 3). The median number of the indications correctly selected in the questionnaire was significantly higher among Internal Medicine residents compared to other physicians while the most common indication unknown to the physicians was history of central nervous system (CNS) disease (Table 3).

DISCUSSION

Our study is the first to investigate the adherence of physicians in performing brain imaging before LP according to the IDSA guidelines in Thailand. We found that the rate of non-adherence to the

Table 3: Knowledge about the indications for lumbar puncture before brain imaging of the IDSA guidelines among the physicians in the Emergency Department

Indications correctly selected	All (N = 53)	Internal Medicine residents (N = 24)	General practitioner (N = 21)	Emergency Medicine residents (N = 8)	*P*[a]
Indications (% correctly selected)					
Focal neurological deficit	49 (93)	24 (100)	18 (85)	7 (88)	0.17
Papilledema	47 (88)	24 (100)	16 (76)	7 (88)	**0.04**
Abnormal level of consciousness (GCS<10)	42 (79)	19 (79)	16 (76)	7 (88)	0.80
Immunocompromised status	39 (74)	21 (88)	12 (57)	6 (75)	0.07
New onset of seizure within 1 week	35 (66)	17 (71)	13 (62)	5 (63)	0.80
History of central nervous system disease	16 (37)	12 (50)	4 (19)	0 (0)	**0.01**
Median number of the indications correctly selected (IQR)[b]	4 (3-5)	5 (4-6)	4 (3-4)	4 (3-5)	**0.004**

NOTE:

[a] Comparison between physicians who were general practitioners, Internal Medicine residents and Emergency Medicine residents

[b] The total number of correct indications are 6.

GCS = Glasgow Coma Scale; IQR = interquartile range.

guidelines was 38% and physicians were less likely to adhere to the guidelines when caring for patients with no indications for brain imaging since they ordered CT of the brain in all of these patients. These findings suggest over-investigating practice among physicians in the given setting. Although, the over-investigation did not have impact on short-term survivals, duration to LP and duration to antimicrobial administration in this study, it incurred unnecessary patients' radiation exposure of 2 mSv and additional cost ($US 250 per test) without any benefits on revealing abnormal findings of the brain.

We further assessed the knowledge about the indications for brain imaging before LP among the physicians in the ED. The knowledge of the physicians was at moderate level and varied among the type of physicians. In addition, there was a gap of knowledge on some indications including history of CNS disease, new onset of seizure within 1 week and immunocompromised status. The finding suggests interventions to improve knowledge about the indications among the first contact physicians in the ED and to be tailored according to each type of the physicians.

The lower non-adherence rate in this study compared to that reported in the previous study of 60%[6] might be due to the differences in clinical practices between Thailand and the US. Given that the most common non-adherence practice was performing brain imaging without an indication in both settings, this suggests a higher rate of over investigation in the US where malpractice lawsuit is prevalent.[7] In addition, higher proportion of our patients had history and presented with signs and symptoms consistent with the indications for brain imaging before LP compared to the patients in the US study. This may lead to better recognition of the patients who need brain imaging and adherence to the guidelines in this study.

It should be noted that survival rates within 30 days after presentation were not significantly different between patients in adherence and non-adherence groups. This may be explained by the overall low mortality rate in the study cohort, high rates of CT of the brain performed and treatment provided by similar type of the first contact physicians. In addition, several treatment characteristics that impact mortality including appropriate empirical and definite antimicrobial administration, duration to LP and duration to antimicrobial administration[8,9] were also comparable between the two groups.

The study limitations include the single site study that may preclude result generalizability, the screening process relying on initial diagnosis of CAM by the first contact physicians and the small sample size that may have inadequate power to detect the differences in the secondary outcomes between groups. Despite the limitations, this study

is the first to evaluate physicians' adherence to the IDSA guidelines regarding brain imaging before LP in patients with CAM, factors associated with the guidelines non-adherence, the knowledge of the first contact physicians about indications for brain imaging before LP and the outcomes associated with non-adherence to the guidelines in an Asian country.

In conclusion, our study indicates a significant rate of non-adherence to the IDSA guidelines for performing brain imaging before LP in patients with CAM presented to a Thai tertiary-care center. The most common non-adherence practice was performing brain imaging before LP without an indication, which represented over-investigation. The over-investigation may be due to lack of knowledge about the indications and/or being afraid of subsequent malpractice lawsuits. Although the over-investigation did not have significant impact on short-term survival, it did not offer any clinical benefits, yet increased healthcare cost and put the patients at unnecessary risk for radiation exposure. Further studies are required to evaluate interventions to improve knowledge about indications for brain imaging before LP and the impact of adherence to the IDSA guidelines on outcomes among patients with CAM.

DISCLOSURE

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