The Influence of Early Adoption of Non-enhanced Computed Tomography on Management of Patients with Pyogenic Liver Abscess

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Research Article

Keywords: Pyogenic liver abscess, computed tomography, early diagnosis, hospital stay

Posted Date: April 13th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1529770/v1

Abstract

Pyogenic liver abscess (PLA) is an infectious disease and causes high in-hospital mortality. It has no specific symptoms and is difficult to be diagnosed early in the emergency department. Therefore, early diagnosis is an urgent need for clinicians. Ultrasound has been widely used to detect lesions of PLA. However, the sensitivity of ultrasound is affected by the size and location of lesions and clinician's experience. We conducted a retrospective study to assess the effects of early adoption of non-enhanced computed tomography (CT) scanning (i.e., receiving CT scanning within 48 hours after admission) on treatment and disease status of patients with PLA. This study enrolled 76 hospitalized patients with PLA in department of digestive disease, who received CT examination during 2014 to 2021. Of the enrolled patients, 56 received an early CT scan and 20 received a late CT scan. Results showed that the length of hospitalization in the early CT group was significantly shorter than the late CT group (15.0 days vs. 20.5 days; $p = 0.035$). Besides, the median time to initiating drainage after admission was also significantly shorter in the early CT group than the late CT group (1.0 days vs. 4.5 days; $p < 0.001$). The early CT group was also associated with significantly lower prescription rates of antibiotics. Our findings revealed that to conduct early CT scanning within 48 hours of admission may assist in early diagnosis of PLA and be beneficial to disease recovery.

Introduction

Pyogenic liver abscess (PLA), a life-threatening disease, is defined as the liver filled with pus caused by bacterial invasion which is associated with in-hospital mortality rate of up to 2.2–5.6%[1–3]. The incidence of liver abscess is diverse, ranging from 1.0–17.6 cases per 100,000 between countries[3]. Similar to infective diseases, patients with PLA usually have nonspecific symptoms (abdominal pain, fever, nausea, vomiting, etc.) and laboratory findings (elevated white blood cells, C-reactive protein, hepatic enzymes, etc.). Hence, patients with suspected PLA are usually treated with empirical antibiotics at first. Drainages are mostly applied for the abscess ≥ 3 cm[4], and percutaneous drainages are more common than surgical drainages due to lower morbidity and mortality rates[5]. Although adequate antibiotics combined with percutaneous drainages can effectively reduce mortality, delayed diagnosis still results in poor prognosis of patients due to rapid progression to sepsis[6–8]. Therefore, early diagnosis of patients with PLA remains a challenge for emergency clinicians.

Ultrasound and computed tomography (CT) imaging are traditional tools to identify hepatic lesions. Due to the convenience and availability in the real-world settings, ultrasound has become the preferred tool for the initial detection of liver abscess. However, some liver lesions cannot be diagnosed based on ultrasound due to the small size or location with poor visualization (e.g., segment 7/8 of the liver). The sensitivity of ultrasound (85%) was also reported to be lower than CT scan (97%)[9,10]. CT scans are recommended for confirming PLA if negative or nonspecific findings using ultrasound are observed but are not commonly applied in the initial examination[11]. A better tool used for early diagnosis with PLA is an unmet clinical need.

In China, CT imaging is a gold standard for assessing intra-abdominal infection[12]. We conducted a study to evaluate the feasibility of early CT imaging on examining patients with PLA and measure its effects on disease status. This study retrospectively collected data of patients with PLA who received non-enhanced CT examinations; and compared disease characteristics, treatment strategy, and disease status between patients receiving early CT scans (within 48 hours after admission) and those receiving late CT scans (> 48 hours after admission).

Methods

Study design

It was a retrospective study to obtain clinical data of 76 patients hospitalized at Department of Digestive Disease of Xiamen Chang Gung Hospital, China and analyze the disease status and management after the early examination using non-enhanced CT to diagnose as PLA. Patients with PLA who were hospitalized and received CT examination from January 2014 to June 2021 were included; patients who had amebic liver abscess, aged ≤ 14 years, or underwent surgery for PLA were excluded. Enrolled patients were divided into (1) the early CT group, with patients receiving a CT scan within 48 hours after admission; and (2) the late CT group, with patients receiving a CT scan > 48 hours after admission. The primary endpoint was the difference in length of hospital stay between groups. Secondary endpoints included time to initiating percutaneous drainage after admission and antibiotic prescription rates during hospitalization.

This study was approved by the institutional review board (IRB) of Xiamen Chang Gung Hospital (IRB number: XMCGIRB2021037), and conducted per the applicable local regulations and the ethical principles outlined in the Declaration of Helsinki. The informed consent was waivered due to due to secondary use of deidentification data.

Variables

Data collected from medical charts included demographics, disease characteristics, laboratory results, use of antibiotics and percutaneous drainage, hospitalization records, and body temperature during hospitalization. PLA severity was determined by using quick sequential organ failure assessment (qSOFA) and systemic inflammatory response syndrome (SIRS) at baseline. qSOFA is an assessment for identifying the severity of intra-abdominal infections; qSOFA ≥ 2 means patients with severe infection (score range: 0–3 points)[12,13]. SIRS is used to determine the level of inflammatory status; patients may have severe inflammatory response if SIRS meets ≥ 2 criteria.

Statistical methods

Continuous variables were compared using two sample t-tests or Wilcoxon rank-sum tests. Categorical variables were analyzed using Chi-square tests or Fisher's exact tests. A significant difference was defined as a P-value < 0.05. Data analyses were performed using Statistical Analysis Software (SAS®) version 9.4 (SAS Institute, Cary, NC, USA).

Results

Data of 76 eligible patients diagnosed with PLA were included and analyzed; of these, 56 patients receiving an CT scan within 48 hours after admission (i.e., the early CT group) and 20 patients receiving an CT scan > 48 hours after admission (i.e., the late CT group) (Fig. 1). Table 1 presents the comparison of demographic data and comorbidities between early CT and late groups. Overall, there was no significant difference between the groups. The median age was 55.6 years (range 24–78) and 51.8 years (range 15–93) in the early CT and late CT groups, respectively. Males accounted for a higher proportion of both groups (62.5% vs. 75.0%). For the early CT group, 42.9% of patients had diabetes mellitus, 17.9% had hypertension, and 10.7% had gallstones or bile duct stones; for the late CT group, 30.0% had hypertension, 25.0% had diabetes mellitus or gallstones, and 15.0% had cholangitis. Disease characteristics and severity of PLA were also comparable between groups (Table 2). Biliary origin was the main cause of PLA in both groups (30.4% in early CT; 40.0% in late CT). On average, the number of lesions was 1.6 in the early CT and 1.2 in the late CT group, with a diameter of 5.9 ± 3.02 cm and 6.5 ± 2.70 cm, respectively. Lesions were mostly located in the right lobe of liver in both groups (75.0% vs. 70.0%). Both groups had low risks of developing sepsis and low systemic inflammatory response (qSOFA ≤ 1 and SIRS < 2).

Table 1
Comparison of baseline demographics and comorbidities between early and late CT groups

	Early CT, n = 56	**Late CT, n = 20**	**P-value**
Age (years)			
N	56	20	0.322
Median (range)	55.6 (24.0, 78.0)	51.8 (15.0, 93.0)	
Gender, n (%)			
Male	35 (62.5)	15 (75.0)	0.312
Comorbidity, n (%)			
Diabetes mellitus	24 (42.9)	5 (25.0)	0.158
Hypertension	10 (17.9)	6 (30.0)	0.253
Biliary disease			0.164
None	39 (69.6)	11 (55.0)	
Gallstones	6 (10.7)	5 (25.0)	
Bile duct stone	6 (10.7)	0 (0.0)	
Cholangitis	3 (5.4)	3 (15.0)	
Cholecystitis	2 (3.6)	1 (5.0)	

To compare differences between groups, two sample t-tests or Wilcoxon rank-sum tests were used for continual variables; Chi-square tests or Fisher's exact test were applied for categorical variables.

Abbreviation: CT, computed tomography; PLA, pyogenic liver abscess

Table 2
Comparison of baseline disease characteristics and severity between early and late CT groups

Characteristics of PLA	Early CT, n = 56	Late CT, n = 20	P-value
Pathophysiology, n (%)			
Unknown	36 (64.3)	12 (60.0)	0.675
Biliary origin	17 (30.4)	8 (40.0)	
Hematogenous spread	2 (3.6)	0 (0.0)	
Hepatocellular carcinoma	1 (1.8)	0 (0.0)	
Number of lesions			
N	56	19	0.396
Mean ± SD	1.6 ± 1.45	1.2 ± 0.50	
Location of lesions, n (%)			
Right lobe	42 (75.0)	14 (70.0)	0.317
Left lobe	7 (12.5)	5 (25.0)	
Bilateral	7 (12.5)	1 (5.0)	
Dimeter of lesion (cm)			
N	56	20	0.416
Mean ± SD	5.9 ± 3.02	6.5 ± 2.70	
SIRS			
N	56	20	0.300
Mean ± SD	1.6 ± 1.17	1.9 ± 1.29	
qSOFA			
N	56	20	0.535
Mean ± SD	0.3 ± 0.57	0.2 ± 0.41	

To compare differences between groups, two sample t-tests or Wilcoxon rank-sum tests were used for continual variables; Chi-square tests or Fisher's exact test were applied for categorical variables.

Abbreviation: CT, computed tomography; PLA, pyogenic liver abscess; SD, standard deviation; SIRS, systemic inflammatory response syndrome; qSOFA, quick sequential organ failure assessment

Laboratory data are summarized in Table 3. Generally, the laboratory results were comparable between the two groups, except for white blood cells (WBC). The WBC level of patients in the early CT group was significantly lower than the late CT group ($11.4 \pm 5.52 \times 10^9$/L vs. $15.4 \pm 5.26 \times 10^9$/L; $p = 0.006$).

Table 3
Comparison of baseline laboratory data between early and late CT groups

	Early CT, n = 56	**Late CT, n = 20**	**P-value**
White blood cells (× 10^9/L)			0.006*
N	56	20	
Mean ± SD	11.4 ± 5.52	15.4 ± 5.26	
Hemoglobin (g/L)			0.379
N	56	20	
Mean ± SD	126.7 ± 18.61	122.5 ± 17.16	
Platelet (× 10^9/L)			0.299
N	56	20	
Mean ± SD	232.5 ± 146.18	239.2 ± 94.58	
Hs-CRP (mg/L)			0.883
N	56	20	
Mean ± SD	187.6 ± 109.60	196.4 ± 128.35	
AST (U/L)			0.706
N	56	20	
Mean ± SD	100.3 ± 130.80	82.1 ± 68.45	
ALT (U/L)			0.782
N	56	20	
Mean ± SD	90.5 ± 103.47	94.2 ± 84.54	
Total bilirubin			0.608
N	56	20	
Mean ± SD	34.7 ± 52.74	28.1 ± 21.25	
Albumin (g/L)			0.928
N	56	20	
Mean ± SD	32.7 ± 7.06	32.6 ± 5.82	
Creatinine (μmol/L)			0.616
N	56	20	

	Early CT, n = 56	Late CT, n = 20	P-value
Mean ± SD	87.2 ± 49.69	81.1 ± 16.78	
BUN (mmol/L)			0.860
N	56	20	
Mean ± SD	6.5 ± 7.09	5.4 ± 2.51	
ALK (U/L)			0.262
N	49	19	
Mean ± SD	184.8 ± 152.24	206.9 ± 167.89	
GGT (U/L)			0.821
N	47	19	
Mean ± SD	164.4 ± 155.33	170.5 ± 173.02	

To compare differences between groups, two sample t-tests or Wilcoxon rank-sum tests were used for continual variables; Chi-square tests or Fisher's exact test were applied for categorical variables.

*P-value < 0.05 considered as a significant difference

Abbreviation: CT, computed tomography; SD, standard deviation; AST, aspartate aminotransferase; ALT, alanine aminotransferase; Hs-CRP, high-sensitivity C-reactive protein; BUN, blood urea nitrogen; ALK, alkaline phosphatase; GGT, gamma-glutamyltransferase

Table 4 displays the comparison of outcomes and therapies between the early and late CT groups. We observed that patients who received CT imaging early had shorter hospitalization stay and initiated drainages sooner. Compared with the late CT group, the early CT group showed significantly shorter hospital stay (early CT vs. late CT = 15.0 days vs. 20.5 days; $p = 0.035$) and significantly shorter median time to initiating drainages (1.0 day vs. 4.5 days; $p < 0.001$). Furthermore, the proportion of patients treated with 2nd generation cephalosporin or fluoroquinolone in the early CT was significantly lower than the late CT group (2nd generation cephalosporin: 32.1% vs. 85.0%; $p < 0.001$; fluoroquinolone: 14.3% vs. 35.0%; $p = 0.046$). However, the duration of fever and body temperature during hospitalization were not significantly different between the groups (data not shown).

Table 4
Comparison of clinical outcomes and treatments between early and late CT groups

	Early CT, n = 56	Late CT, n = 20	P-value
Length of hospitalization (days)			
N	56	20	0.035*
Median (range)	15.0 (3.0, 68.0)	20.5 (6.0, 37.0)	
Receiving drainage after admission (days)			
N	36	16	
Median (range)	1.0 (1.0, 9.0)	4.5 (2.0, 30.0)	< 0.001*
Numbers of antibiotics prescription Use of 2nd generation cephalosporin	18 (32.1)	17 (85.0)	< 0.001*
Use of 3rd generation cephalosporin	33 (58.9)	8 (40.0)	0.145
Use of 4th generation cephalosporin	5 (8.9)	1 (5.0)	0.576
Use of fluoroquinolone	8 (14.3)	7 (35.0)	0.046*

To compare differences between groups, two sample t-tests or Wilcoxon rank-sum tests were used for continual variables; Chi-square tests or Fisher's exact test were applied for categorical variables.

Note: Patients might receive more than one antibiotic during the hospitalization.

*P-value < 0.05 considered as a significant difference

Abbreviation: CT, computed tomography; PLA, pyogenic liver abscess; SD, standard deviation

Discussion

The intra-abdominal infection such as PLA can lead to high mortality rate caused by sepsis if not recognized early and managed promptly. How to promptly provide a precise diagnosis and optimal therapy is crucial. With the routine clinical practice of using CT imaging for identifying intra-abdominal infection in China, this two-arm, retrospective study collected clinical data to evaluate the effects of early adoption of non-enhanced CT imaging (i.e., within 48 hours after admission) on the disease status and recovery in patients with PLA. For patients receiving an early or late CT scan, the disease severity of PLA (i.e., SIRS, qSOFA, and CRP) was comparable though the WBC level in the early CT group was significantly lower than the late CT group. This study revealed that the hospital stay of patients with PLA receiving an early CT scan was shorter than those receiving a late CT scan. Additionally, patients with an early CT scan received drainages earlier and had lower burden of antibiotic use during hospitalization. These findings imply that early CT scan within 48 hours after admission may enable early diagnosis of PLA for effective and prompt treatment.

Compared with other Western studies, outcomes of patients receiving CT scan within 48 hours after admission in the current study were also more favorable, as reflected by a shorter length of stay (15.0 days) than other Western real-world studies (Italy: 24 days; UK: 22 days)[6,14] and a morality rate of 0% versus other studies (Italy: 11 patients [10.1%]; UK: 8 patients [12.3%])[6,14]. In the comparison with Asian studies, the length of hospital stay and in-hospital mortality in our study were also better than a Taiwanese study (19.6 days; 6.3%)[15]; and similar to another Chinese study (14.5 days; 1.5%)[8]. Although the differences in patients and disease characteristics (lesion size, pathogenesis, and comorbidity) between studies and races are inevitable, CT scanning conducted in early 48 hours may be a potential first-line diagnostic tool for identifying liver abscess. Early diagnosis allows physicians plan treatment strategy ahead, which may contribute to improve disease status and a faster recovery.

On the other hand, early adoption of CT scanning for patients with PLA also significantly shorten the time to initiating drainages after admission, and was associated with lower prescription rate of 2nd generation cephalosporin and fluoroquinolone and higher prescription rate of 3rd generation cephalosporin. Considering that *Klebsiella pneumoniae*, a gram-negative bacterium that is sensitive to 3rd generation cephalosporin, is the most common pathogen causing PLA in Asia, such treatment pattern was in line with the general practice that patients with PLA were usually treated with 3rd generation cephalosporin[16–18]. On the other hand, broad-spectrum antibiotics were preferred to treat patients in the late CT group, implying that the clinician might give broad-spectrum antibiotics to treat infections without a precise diagnosis for patients receiving a late CT scan. Taken together, these results suggested that early adoption of CT scanning may achieve early diagnosis and assist clinicians in treating patients with adequate antibiotics combined with drainages, resulting in the reduction of length of hospital stay and in-hospital mortality.

Furthermore, 51.7% of eligible patients (n = 29; data not shown) in the current study had the lesion located in segment 7/8 of liver. This study also presented that first-line CT scanning in the emergency department enabled to detect the lesion in the liver segment early where ultrasound examination may fail to detect the lesion thoroughly.

There are some limitations in this study. First, our findings were not generalizable because it was a single-center study conducted in China. Second, the number of enrolled patients per group was imbalanced, despite their baseline data were generally homogeneous. Third, we observed that the WBC level was significantly lower in the early CT group (lesion size: 5.9 cm) than the late CT group (lesion size: 6.5 cm), and such difference may bias the comparison of disease status and management between groups. Results should be interpreted with caution due to the imbalance in the patient pool, and a randomized-controlled study is required to validate our findings. Forth, 56.5% of patients (n = 43) were infected by *Klebsiella pneumoniae*, diverse pathogens causing PLA may influence the therapeutic decision and strategy; therefore, results need to be interpreted with care[2,19]. Final, to our knowledge, this study might be the first research to evaluate the impact of adopting early CT imaging on PLA patients in comparison with late CT imaging. The cutoff time duration of applying CT was defined by emergency clinicians' experience. However, these data also reflected the routine management of PLA in China.

Conclusion

The retrospective study showed that early adoption of non-enhanced CT scanning for patients with suspected pyogenic liver abscess enabled to reduce the length of hospital stay and led to patients receiving drainages earlier after admission.

Declarations

Funding: Xiamen Chang Gung Hospital Science Project (CMRPG1E0875, CMRPG1G0161).

Acknowledgement: The authors acknowledge the assistance from Formosa Biomedical Technology Corp. CRO Division in the statistical analysis and editorial support.

Author Contributions: Conceptualization: Y.B.L., Y.N.H. ,Data acquisition: T.Y.C,X.B.L.,G.M.Y,J.C.L, P.X.L,C.K.Y., Formal analysis: T.Y.C, P.T.C.,H.S.H. Y.C.W.,Funding acquisition: Y.B.L., Methodology: C.G.Z,Y.B.L., Y.N.H. ,Project administration: Y.B.L., Y.N.H. Writing - original draft: Y.B.L, H.S.H. Writing - review & editing: Y.B.L,W.T.C. Approval of final manuscript: all authors.

Data availability: The data of this study are available from the corresponding author, upon reasonable request. T.Y.C. and Y.B.L. have full access to all the data in the study and take responsibility for the integrity of the data, the accuracy of the data analysis, and the conduct of the research.

Ethics approval and consent to participate ：The study protocol was reviewed and approved by the Institutional Review Board of Xiamen Chang Gung Hospital (approval number: AF-IRB-003-01.0). Because of the retrospective nature of the study, written patient consent was waived by the Institutional Review Board of Xiamen Chang Gung Hospital. All methods were conducted in accordance with the guidelines of the Declaration of Helsinki.

Consent for publication:Not applicable.

Competing interests：The authors declare that they have no competing interests.

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Figures

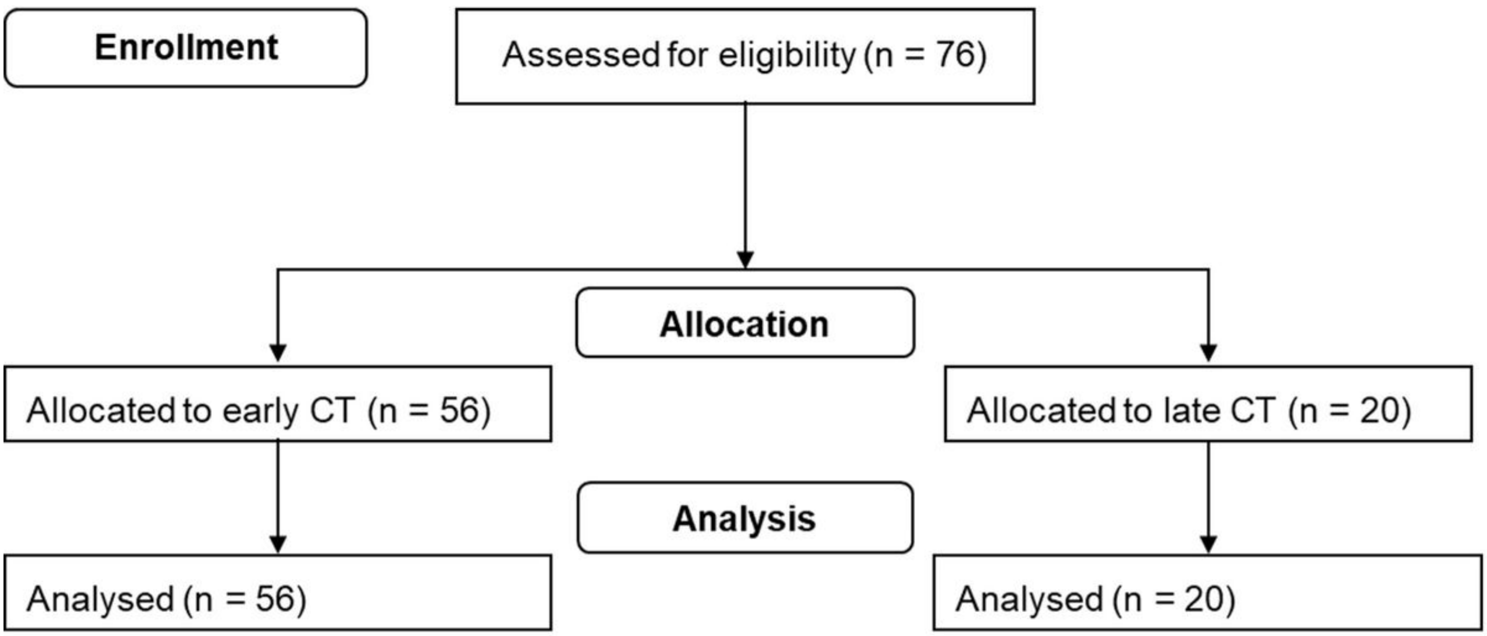

Figure 1 Patient disposition

Figure 1

Eligible patients who were examined using CT imaging within 48 hours after admission were categorized into the early CT group; those who were examined using CT imaging over 48 hours after admission were categorized into the late CT group.