Evaluation and Comparison of Charcot's Triad and Tokyo Guidelines for the Diagnosis of Acute Cholangitis

Tolga Dinc^{1,2} · Selami Ilgaz Kayilioglu² · Faruk Coskun²

Received: 30 March 2016 / Accepted: 26 May 2016 / Published online: 2 June 2016
© Association of Surgeons of India 2016

Abstract Reliability of Charcot's triad has long been questioned. Tokyo Guidelines committee published Tokyo Guidelines in 2007 and 2013. The aim of this study was to retrospectively examine the patients who had been treated with the diagnosis of acute cholangitis and evaluate 2007–2013 Tokyo criteria and Charcot's triad. The files of the patients with acute cholangitis in a referral center were examined retrospectively. All patients were classified and evaluated according to 2007 and 2013 Tokyo criteria and Charcot's triad; and results were compared. It was detected that 51.7 % of patients who did not meet Charcot's triad were in definitive diagnosis group of both Tokyo criteria. Kappa value was calculated as 0.404 in the analysis of consistency between two Tokyo criteria. Two patients who had features sufficient to objectively make the diagnosis of acute cholangitis failed to meet the Tokyo criteria 2007 or 2013. Charcot's triad is not sensitive and specific enough in the diagnosis of acute cholangitis. Revision of Tokyo 2007 criteria caused a change in the diagnostic status of 15 % of the patients. It is remarkable that kappa value can hardly be considered as a sign of moderate agreement between two Tokyo guidelines. Tokyo criteria should be supported and updated.

Keywords Cholangitis · Diagnosis · Guideline · Charcot's triad

✉ Tolga Dinc
tolga_dr@hotmail.com

¹ Department of General Surgery, Ankara Numune Training and Research Hospital, Ankara, Turkey

² Genel Cerrahi Kliniği, Ankara Numune Eğitim ve Araştırma Hastanesi, B-Blok 2. Kat Oda No: 216 Altındağ, Ankara, Türkiye

Introduction

Acute cholangitis was first described by Charcot as hepatic fever in 1877 [1]. In the course of time, this infectious disease of biliary system has been evaluated by different names and criteria [2, 3]. Lastly, Tokyo criteria and revised Tokyo criteria were published in 2007 and 2013, respectively, in an attempt to describe a universal and ideal method for the diagnosis of acute cholangitis [4, 5].

For many years, the diagnosis of acute cholangitis has been made based on Charcot's triad which was described as coexistence of right upper quadrant pain, jaundice and fever, in 1877 [1]. On the other hand, reliability of Charcot's triad has long been questioned. Tokyo Guidelines committee was established from this point of view, and Tokyo Guidelines for the Management of Acute Cholangitis and Cholecystitis was published in 2007 as a result of 4-year work [4, 6]. In 2007, Tokyo guidelines blood tests and diagnostic imaging tools were combined with Charcot's triad for the diagnosis of acute cholangitis [4]. Due to the limitations of these criteria and low sensitivity and specificity, the committee published revised criteria in 2013. In revised 2013 Tokyo guidelines, three main topics are defined for the diagnosis of acute cholangitis: (A) systemic inflammation (A-1, fever and/or shaking chills; A-2 laboratory data for inflammatory response), (B) cholestasis (B-1, Jaundice B-2; abnormal liver function tests), (C) imaging (C-1; Biliary dilatation; C-2; evidence of etiology on imaging, such as stricture, stone, stent etc.) Regarding these three topics, existence of one item in A section and one item in either B or C sections is referred to as "Suspected diagnosis." On the other hand, existence of at least one item from each section is referred to as "Definite diagnosis" [5]. After publication, the criteria have been clinically evaluated in many centers, and accuracy and consistency of these criteria have been investigated [7]. In 2013, this

guideline was revised and republished by the committee [8]. Testing the revised Tokyo criteria in large populations and evaluation of the results are important to achieve this goal. The aim of this single-center study was to retrospectively examine the patients who had been treated with the diagnosis of acute cholangitis and evaluate 2007–2013 Tokyo criteria and Charcot's triad.

Patients and Methods

Ethics committee approval was taken for this study (Ethics Committee 15.02.2016/E-16-786). The patients who were treated for acute cholangitis between the years 2011 and 2014 in our clinic were determined by browsing electronic records. Patient files were retrospectively examined. Patients' symptoms and clinical features (particularly pain and fever), complete blood count and biochemical tests, examinations performed for the investigation of the etiology (endoscopic retrograde cholangiopancreatography, ultrasound, magnetic resonance cholangiopancreatography), etiologic features detected (gallstone, malignancy, trauma, hydatid disease etc.), and disease outcomes were separately recorded. All patients were then classified according to 2007 and 2013 Tokyo criteria. In addition, the patients were also classified according to the status of meeting Charcot's Triad criteria (right upper quadrant pain, fever $>38^{\circ}\text{C}$ and hyperbilirubinemia). "Suspicious Diagnosis" and "Definitive Diagnosis" groups and Charcot's triad groups were evaluated according to 2007 and 2013 Tokyo criteria, and the results were compared.

Statistical Analyses

The SPSS 15.0 (SPSS Inc., Chicago, USA) statistics software was used for statistical analysis. In the groups with non-parametric distribution pattern, comparison between two groups was performed using Mann-Whitney *U* test, while comparison of the mean values was performed by using *t* test in the groups with parametric distribution pattern. Nominal values were compared with Fisher's exact test. *P* value below 0.05 was considered as significant.

Results

The files of a total number of 60 patients (34 male and 26 female patients) who were clinically diagnosed with acute cholangitis and treated between the years 2011 and 2014 were obtained. The mean age of the patients was 64.78 ± 14.79 years. Two of 60 patients were detected to die during treatment period.

The patients were grouped as the patients diagnosed and not diagnosed with acute cholangitis according to Charcot's Triad criteria, while Tokyo guideline was used to group them as the patients with definitive diagnosis, suspicious diagnosis, and no diagnosis.

The number of the patients meeting Charcot's triad criteria was 29 (48.3 %). It was seen that all of these patients were also in definitive diagnosis group according to 2007 Tokyo criteria, while only 23 (79.3 %) of them were in definitive diagnosis group according to 2013 Tokyo criteria and the remaining were in suspicious diagnosis group. On the other hand, it was detected that 12 of 31 patients (51.7 %) who did not meet all Charcot's triad features were in definitive diagnosis group according to both 2007 and 2013 Tokyo criteria (Table 1). When Tokyo 2013 criteria were accepted as gold standard (providing that the evaluation was made based on suspicious diagnosis group), sensitivity, specificity, positive predictive value, and negative predictive value of Charcot's triad were found to be 59.18, 100, 100, and 35.48 %, respectively. Kappa value of Cohen was found to be 0.34 in the evaluation of the consistency between Tokyo 2013 "suspicious diagnosis" criteria and Charcot's triad.

The number of the patients who did not meet the diagnostic criteria was 5 out of 60 patients (8.3 %) in Tokyo 2007 group and 11 (18.3 %) in Tokyo 2013 group. A total number of 46 patients (76.7 %) from both groups were found to meet at least suspicious diagnosis criteria. Nine of 14 patients (64.3 %) who had suspicious diagnosis (and not definitive diagnosis) according to Tokyo 2007 criteria were found to have no diagnosis according to Tokyo 2013 criteria. One patient in Tokyo 2007 group (1.7 %) who did not meet the diagnostic criteria had definitive diagnosis according to Tokyo 2013 criteria (Table 2). Kappa value was calculated as 0.404 in the analysis of consistency between Tokyo 2007 and Tokyo 2013 criteria.

Two patients (3.4 %) were found to die of cholangitis-related complications during follow-up. Both of these patients

Table 1 Number of patients that meet Tokyo criteria comparing to Charcot Triad positivity

	Suspicious diagnosis (Tokyo 2007)	Definitive diagnosis (Tokyo 2007)	Suspicious diagnosis (Tokyo 2013)	Definitive diagnosis (Tokyo 2013)
Charcot triad Positive	29	29	29	23
Charcot triad Negative	26	12	20	12

Table 2 Comparison of Tokyo criteria 2007 and 2013 (Number of patients)

		Suspicious diagnosis (2007)		Definitive diagnosis (2007)	
		Negative	Positive	Negative	Positive
Suspicious diagnosis (2013)	Negative	2	9	11	0
	Positive	3	46	8	41
Definitive diagnosis (2013)	Negative	4	21	18	7
	Positive	1	34	1	34

were detected to have a definitive diagnosis of cholangitis according to Charcot, 2007 and 2013 Tokyo criteria.

Two of the patients who had been followed-up and treated for acute cholangitis in our hospital were found to have no acute cholangitis according to both Tokyo guidelines. Although these two patients who had been clinically diagnosed and treated had features sufficient to objectively make the diagnosis of cholangitis (hydatid cyst rupture into bile ducts in one patient and purulent content detected by endoscopic retrograde cholangiopancreatography [ERCP]), they could not be diagnosed with acute cholangitis according to any Tokyo criteria. One of these patients had previously undergone ERCP for choledocholithiasis, and choledochal stone had been removed. He had again been admitted to outpatient clinic with the complaints of pain and vomiting and hospitalized 2 weeks after discharge. ERCP had been repeated, which had revealed undigested food and phytobezoar in choledoch. The patient had been discharged with no complaints.

Discussion

After publication, accuracy and consistency of Tokyo criteria have been investigated in many centers. In a study, sensitivity of Tokyo 2007 criteria in the diagnosis of acute cholangitis was found to be low (63.9 %) [7]. In the following years, Tokyo Guidelines committee has evaluated the studies on 2007 criteria [5, 9] and the guidelines were again published in 2013 after revision [8]. 2013 criteria aimed to increase the sensitivity especially in the diagnosis of acute cholangitis and decrease false-positive results in the diagnosis of acute cholecystitis [10]. Abdominal pain was excluded from the criteria, and diagnostic examinations were arranged to achieve this goal. It has been observed that the diagnostic sensitivity of Tokyo 2013 guideline which was established after these arrangements has increased to 91.8 % for acute cholangitis [5].

In these studies, one of the following features has been required for definitive diagnosis of cholangitis; the presence of purulent biliary leakage, clinical remission after bile duct drainage, or remission achieved by antimicrobial therapy alone in patients in whom the only site of infection was the biliary tree. Unfortunately, in our study, these features could

not be retrospectively evaluated; Tokyo 2007 criteria and Charcot's triad that is commonly used by physicians were assessed by accepting Tokyo 2013 criteria as gold standard. Furthermore, accuracy of available clinical practices was evaluated by examining the patients who had been diagnosed with "acute cholangitis" in our hospital.

We saw that only 48.3 % of the patients would be diagnosed by an evaluation including only Charcot's triad. In addition, 20 of 31 patients who had not been diagnosed with cholangitis according to Charcot's triad were found to be diagnosed with acute cholangitis according to Tokyo 2013 criteria. As it is obviously understood, Charcot's triad that is commonly used by clinicians is not sensitive and specific enough in the diagnosis of acute cholangitis. Introduction of carefully configured objective evaluation methods like Tokyo criteria is very important.

When Tokyo 2007 and Tokyo 2013 criteria were comparatively examined, it is seen that 9 of 60 patients (15 %) enrolled in our study had "suspicious diagnosis" according to 2007 criteria, while they failed to be diagnosed according to revised Tokyo 2013 criteria. Revision of Tokyo 2007 criteria caused a change in the diagnostic status of 15 % of the patients who had been treated in our hospital for clinical diagnosis of acute cholangitis, which is a considerable rate. On the other hand, 1 of 60 patients (1.7 %) could not be diagnosed according to Tokyo 2007 criteria but had "definitive diagnosis" according to Tokyo 2013 criteria. Despite its low rate, this result created by the difference between two guidelines is interesting. Moreover, it is remarkable that kappa value was found to be 0.404 when consistency between two Tokyo guidelines was analyzed. This result can hardly be considered as a sign of moderate agreement between these criteria. In that case, changes made to increase the diagnostic power enable some patients to have a diagnosis, while it causes overlook in some patients. The most probable cause of this is wide range of clinical finding spectrum of acute cholangitis disease. We suggest that this situation indicates complexity and difficulty of the diagnosis of acute cholangitis and requirement of novel objective diagnostic tools, in addition to clinical diagnostic criteria, in making the diagnosis of acute cholangitis.

A universal gold standard method has not been yet described in making the definitive diagnosis of acute cholangitis.

Some studies have accepted the presence of choledochal purulent fluid or complete remission achieved by acute cholangitis treatment in the patients without another infectious focus as gold standard for acute cholangitis. In our study, all patients who had been discharged after treatment for clinical diagnosis of cholangitis were enrolled. This limited the evaluation of diagnostic power. However, in this way, diagnostic results according to three diagnostic criteria could be compared on the patients with the suspicion of acute cholangitis who are encountered in daily practice. Another limitation of our study is the absence of severity assessment due to retrospective nature of the study and insufficient data. An important part of Tokyo guidelines is composed of severity assessment and related treatment strategies. Our study compared Tokyo guidelines and Charcot's triad only in terms of their diagnostic abilities.

Conclusion

In conclusion, acute cholangitis is a disease which is difficult to diagnose due to its wide spectrum of symptoms and signs. In this sense, Tokyo guidelines are important steps in creating international standards. However, these criteria should be supported and updated by multi-centered, multidisciplinary, prospective, and randomized studies including larger patient groups in order to intensify diagnostic specificity.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. De la Charcot M (1877) *fièvre hépatique symptomatique. Comparaison avec la fièvre uroseptique. Leçons sur les maladies du foie des voies biliaires et des reins*. Bourneville et Sevestre, Paris
2. Reynolds BM, Dargan EL (1959) Acute obstructive cholangitis; a distinct clinical syndrome. *Ann Surg* 150:299–303
3. Longmire WP. Suppurative cholangitis (1971) In: *Critical surgical illness*. Edited by Hardy JD. New York, USA: Saunders; pp. 397–424.
4. Wada K, Takada T, Kawarada Y, Nimura Y, Miura F, Yoshida M et al (2007) Diagnostic criteria and severity assessment of acute cholangitis: Tokyo Guidelines. *J Hepatobiliary Pancreat Surg* 14: 52–8
5. Kiriya S, Takada T, Strasberg SM, Solomkin JS, Mayumi T, Pitt HA et al (2013) TG13 guidelines for diagnosis and severity grading of acute cholangitis (with videos). *J Hepatobiliary Pancreat Sci* 20: 24–34
6. Takada T, Kawarada Y, Nimura Y, Yoshida M, Mayumi T, Sekimoto M et al (2007) Background: Tokyo Guidelines for the management of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Surg* 14:1–10
7. Yokoe M, Takada T, Mayumi T, Yoshida M, Hasegawa H, Norimizu S et al (2011) Accuracy of the Tokyo Guidelines for the diagnosis of acute cholangitis and cholecystitis taking into consideration the clinical practice pattern in Japan. *J Hepatobiliary Pancreat Sci* 18:250–7
8. Takada T, Strasberg SM, Solomkin JS, Pitt HA, Gomi H, Yoshida M et al (2013) TG13: Updated Tokyo Guidelines for the management of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci* 20:1–7
9. Yokoe M, Takada T, Strasberg SM, Solomkin JS, Mayumi T, Gomi H et al (2012) New diagnostic criteria and severity assessment of acute cholecystitis in revised Tokyo Guidelines. *J Hepatobiliary Pancreat Sci* 19:578–85
10. Mayumi T, Someya K, Ootubo H, Takama T, Kido T, Kamezaki F et al (2013) Progression of Tokyo Guidelines and Japanese Guidelines for management of acute cholangitis and cholecystitis. *J UOEH* 35:249–57