

Role of thoracic and abdominal tomography in identifying a potential source of infection in patients with acute fever of unknown focus

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Abstract

Objectives: To evaluate the relationship between clinical features evaluated at admission to the emergency department (ED) and the presence of infection on thoracic and abdominal tomography (CT) scans in patients with acute febrile illness without clinical clues. **Methods:** Patients aged 18 years and over who presented to ED with acute fever between January 1, 2020 and December 31, 2020 and underwent CT imaging (thoracic and abdomen) as a diagnostic test (CT) were included in the study retrospectively. The patients were divided into two groups according to the presence and absence of a source of infection on CT. The clinical and demographic data of the patients were evaluated. The effect of clinical factors on the presence of infection in CT scans was determined using the logistic regression analysis. **Results:** Among the 173 patients included in the study, the CT scans were positive for the source of infection in 31.2% (n=54) and negative in 68.8% (n=119). In the multiple logistic regression analysis, age [?] 65 years [odds ratio (OR):2.72, 95% confidence interval (CI):1.15-4.35, p<0.001], presence of comorbidity (OR:2.37, 95% CI:1.08-4.14, p=0.033), and procalcitonin positivity (PCT) (OR:2.54, 95% CI:1.29-4.95, p=0.006) were identified as risk factors for the presence of infection in CT. **Conclusion:** Age, presence of comorbidity, and PCT level should be considered when deciding on the use of CT in determining the source of infection in acute febrile patients without clinical clues.

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Results: Among the 173 patients included in the study, the CT scans were positive for the source of infection in 31.2% (n=54) and negative in 68.8% (n=119). In the multiple logistic regression analysis, age [?] 65 years [odds ratio (OR):2.72, 95% confidence interval (CI):1.15-4.35, $p<0.001$], presence of comorbidity (OR:2.37, 95% CI:1.08-4.14, $p=0.033$), and procalcitonin positivity (PCT) (OR:2.54, 95% CI:1.29-4.95, $p=0.006$) were identified as risk factors for the presence of infection in CT.

Conclusion: Age, presence of comorbidity, and PCT level should be considered when deciding on the use of CT in determining the source of infection in acute febrile patients without clinical clues.

Keywords: Acute fever, Emergency department, Infection, Tomography

What's already known about this topic?

Fever is one of the most common symptoms of patients presenting to the emergency department. Acute fever may be due to the source of infection, as well as various other causes, including pulmonary embolism, intracranial hemorrhage, drugs, and malignancy.

What does this article add?

Infectious diseases can also progress to serious conditions, such as sepsis, which can sometimes be fatal. Therefore, it is crucial to determine the cause of fever to initiate appropriate treatment. However, there is still no consensus among clinicians regarding the use of CT in patients with acute fever without clinical clues. Therefore, in this study, we examined the use of CT in the identification of sources of infection in patients with acute fever of unknown origin. We investigated whether there was any predictor of the source of infection in thoracic and abdominal CT scans undertaken to explore the etiology of fever.

Review criteria: how did you gather, select and analyze the information you considered in your review?

The data of the study were obtained from the hospital electronic database. Clinical, biochemical and radiological imaging reports were collected and analyzed.

Message for the clinic: what is the 'take-home' message for the clinician?

While CT can be the gold standard method to obtain important findings in the presence of appropriate indications, it can also have negative results in terms of patient and cost-effectiveness when used incorrectly and inappropriately. We found that the most important risk factors affecting the presence of infection in CT were age, presence of comorbidity, and PCT positivity. The presence of one or more of the identified risk factors can assist clinicians in deciding on the use of CT in patients with acute fever without clinical clues.

1. INTRODUCTION

Fever is one of the most common symptoms of patients presenting to the emergency department (ED).¹ It is an important diagnostic problem that concerns all branches of medicine since it can be due to infectious or non-infectious causes.² Infectious diseases can also progress to serious conditions, such as sepsis, which can sometimes be fatal. Therefore, it is crucial to determine the cause of fever to initiate appropriate treatment. In the initial evaluation of patients presenting to ED with fever, a comprehensive history is taken and a

physical examination is performed followed by necessary diagnostic tests. In this process, patients with acute fever of unknown focus are particularly difficult to manage for clinicians.

In recent years, radiological imaging methods, which have been increasingly developed, have become diagnostically important for most patients and diseases. In particular, computed tomography (CT) is an easily accessible imaging method found in almost all EDs in today's conditions. The use of CT in EDs has significantly increased due to the increase in accessibility to the device, shortening of examination times with technological developments, and medicolegal reasons.³ Studies have reported that CT plays a beneficial role in determining the source of infection in patients with sepsis of unknown origin.⁴ However, there is still no consensus among clinicians regarding the use of CT in patients with acute fever without clinical clues. Therefore, in this study, we examined the use of CT in the identification of sources of infection in patients with acute fever of unknown origin. We investigated whether there was any predictor of the source of infection in thoracic and abdominal CT scans undertaken to explore the etiology of fever.

2. MATERIALS AND METHODS

2.1. Patient selection

This study retrospectively reviewed the records of patients who presented to the ED of our hospital with the complaint of high fever between January 1, 2020 and December 31, 2020. The case presentations were classified using the International Classification of Disease-10 coding system. Accordingly, the patients diagnosed with the R50-50.9 codes in this system (fever with chills, fever of other and unknown origin, persistent fever, and unspecified fever) were screened, and of these patients, those aged 18 and over who underwent thorax and abdomen CT imaging as a diagnostic test were included in the sample. Patients with incomplete records, cases in which CT findings were not reported by a radiologist, those with a history of trauma, those who used empirical antibiotics, and those under the age of 18 years were excluded from the study. Local ethics committee approval was obtained for the study (ethics committee number: 2021/01-79).

2.2. Data collection and processing

Clinical data were obtained from the hospital electronic database. The patients' demographic characteristics, vital signs at the time of admission to ED, examination findings, chronic diseases, and radiological and laboratory findings were recorded. The CT images evaluated in the study had been acquired using a 128-slice CT device (GE Revolution EVO, USA). The CT findings reported by radiologists were used to evaluate the results. According to the radiologists' CT reports, the patients were divided into two groups according to whether the source of infection was positive or negative in these reports.

Acute fever of unknown origin was defined as the absence of a history or physical examination finding that could explain the possible cause of fever, absence of non-specific symptoms (such as runny nose, cough, abdominal pain, diarrhea, pain, and burning sensation when urinating), normal values of parameters that would suggest an infection in the urine analysis (bacteriuria, pyuria, and nitrite), and absence of infiltration on chest X-ray. High fever was accepted as a body temperature that was measured as 38.3 degC or higher in ED at least once during treatment (5).

2.3. Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc. Chicago IL, USA) v. 15.0. Number, percentage (%), median, and mean \pm standard deviation values were used to define data. The normal distribution of data was tested with the Kolmogorov-Smirnov test. Student's t-test was used to compare normally distributed data, the Mann-Whitney U test to compare non-normally distributed data, and Pearson's chi-square or Fisher's test to compare categorical variables. The univariate and multivariate logistic regression analyses were undertaken to determine the relationship between the presence of the source of infection and clinical risk factors in thoracic and abdominal CT. Variables with a p value of <0.1 in the univariate logistic regression analysis were included in the multivariate logistic regression analysis. A p value of <0.05 was considered significant in all comparisons.

3. RESULTS

A total of 173 patients with a mean age of 47.6 \pm 16.4 years were included in the study. Of the patients, 57.8% (n=100) were male and 49.2% (n=73) were female. The demographic and clinical characteristics of the patients are given in Table 1. The source of infection was detected in the thoracic and abdominal CT scans of 31.2% (n=54) of the patients. Gender, diastolic blood pressure, respiratory rate, and body temperature did not statistically significantly differ between the patients with and without an infection source detected on CT. There was also no significant difference between these two groups in relation to the white blood cell (WBC) and C-reactive protein (CRP) levels (Table 2). Of the patients, 41% (n=71) had one or more comorbidities. In the single logistic regression analysis, age, systolic blood pressure, heart rate, procalcitonin (PCT), and presence of comorbidity were evaluated as risk factors for the presence of infection in the thoracic and abdominal CT scans. According to the multiple logistic regression analysis, age \geq 65 years [odds ratio (OR):2.72, 95% confidence interval (CI):1.15-4.35, $p < 0.001$], presence of comorbidity (OR:2.37, 95% CI:1.08-4.14, $p = 0.033$), and PCT positivity (OR:2.54, 95% CI:1.29-4.95, $p = 0.006$) were determined as risk factors for the presence of infection in CT (Table 3).

4. DISCUSSION

As a result of this study, we found that 31.2% (n=54) of the patients who underwent thoracic and abdominal CT scans due to acute fever of unknown focus were positive for the source of infection. There were significant differences in age, presence or absence of chronic disease, and PCT level between the patients with and without an infection source on CT. We determined that the most important risk factors affecting the presence of infection on CT were age \geq 65 years, presence of comorbidity, and PCT positivity.

Acute fever may be due to the source of infection, as well as various other causes, including pulmonary embolism, intracranial hemorrhage, drugs, and malignancy.² Every person experiences fever many times in their lives. Most causes of acute fever are related to viral infections but patients may sometimes unexpectedly face serious conditions, such as sepsis and septic shock.⁶ The detection of the fever focus quickly and accurately with CT scans is very important for the initiation of appropriate treatment and survival;⁴ therefore, the use of CT in ED has increased in recent years.⁷ However, CT has certain disadvantages, such as deterioration in kidney function due to contrast agent use, exposure to radiation, and additional costs.⁸ Therefore, CT imaging should be performed after careful benefit/risk assessment of the advantages and disadvantages of this method. In our study, a source of infection was detected in CT scans in patients with comorbidities, those aged \geq 65 years, and those with PCT positivity. If clinical benefit is presumed to be high in these patients, thoracic and abdominal CT scans can be performed to detect the focus of fever.

Advances in CT technology have allowed this imaging modality to be used both as a diagnostic and triage method.⁹ However, this can raise concerns in terms of the appropriate use of resources. The reasons for using CT to detect the source of infection in acute febrile patients without clinical clues in ED are blood parameters, such as WBC, CRP, and PCT being significantly higher than normal.^{10,11} and the need to determine whether there is an occult focus of infection and decide on hospitalization or outpatient treatment.¹² In a previous study, PCT was found to be useful in the diagnosis of infection and had a higher diagnostic value than CRP in patients admitted to ED due to fever.¹³ PCT appears to be an earlier and better marker than inflammatory response parameters, such as CRP and leukocyte count in sepsis and serious infections.¹⁴ From these data, it can be concluded that clinicians often consider CT scans for possible infectious disease due to increased inflammatory markers. In the current study, we found that positive PCT was an effective parameter in detecting possible sources of infection in CT.

Diseases seen in the geriatric population may show a different course compared to other age groups and have more dramatic results. In the elderly, one of the most common causes of hospitalization is infections. The main reasons for this are the weakening of cellular and humoral immunity with aging, deterioration of physiological functions, such as the cough reflex, and comorbidities creating predisposition to infectious diseases. It may not always be possible to identify infections without delay in the elderly since they mostly progress with atypical findings in this population.¹⁵ The presence of fever in the elderly is a more serious

indicator of disease compared to the younger age group. Delayed diagnosis and treatment and more severe infections increase morbidity and mortality rates.¹⁶ The results of our study indicate that thoracic and abdominal CT scans should be used more aggressively in elderly patients with high fever without clinical clues.

Study Limitations

The limitation of our study is that it had a retrospective and single-center design. Therefore, there is a need for further studies involving many centers.

5. CONCLUSIONS

While CT can be the gold standard method to obtain important findings in the presence of appropriate indications, it can also have negative results in terms of patient and cost-effectiveness when used incorrectly and inappropriately. We found that the most important risk factors affecting the presence of infection in CT were age, presence of comorbidity, and PCT positivity. The presence of one or more of the identified risk factors can assist clinicians in deciding on the use of CT in patients with acute fever without clinical clues.

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Declaration of conflicting interests

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Table legends

Table 1 . Patient characteristics

Table 2. Baseline characteristics of the patients according to CT findings and infection source

Table 3. Univariate and multivariate analyses of predictive factors for the source of infection in CT

Table 1 . Patient characteristics

Variable (n = 173)	
Age (years)	47.6 ± 16.4
Gender, male	100 (57.8%)
Vital sign	
Systolic BP at ED triage (mmHg)	121 (110-138)
Diastolic BP at ED triage (mmHg)	75 (70-80)
Pulse at ED triage (bpm)	116 (92-128)
Respiratory rate at ED triage (bpm)	18 (18–21)
Temperature at ED triage (°C)	38.6 (38.3-39.9)
Oxygen saturation at ED triage (%)	94 (90-96)
Inflammatory biomarkers	
PCT (ng/mL)	0.7 (0.5-2.5)
CRP (mg/L)	144 (91-245)
WBC (× 10 ⁹ /L)	15.0 (10.0-24.6)
Presence of comorbidity	71 (41.0%)
Source of infection (n= 54)	
Respiratory system infection	25(46.3%)
Intra-abdominal infection	29(53.7%)

BP=blood pressure; ED=emergency department; CRP=C-reactive protein;

PCT=procalcitonin; WBC=white blood cells; CRP reference: <5 mg/L. PCT reference: <0.25 ng/mL

Table2. Baseline characteristics of the patients according to CT findings and infection source

Variable	Thoracic and abdominal CT findings	Thoracic and abdominal CT findings	P-value
	Infection-negative (n = 119)	Infection-positive (n = 54)	
Age	44.2 ± 15.2	55.1 ± 16.5	<0.001
<65 years	102 (85.7%)	33 (61.1%)	<0.001
[?]65 years	17 (14.3%)	21 (38.9%)	

Variable	Thoracic and abdominal CT findings	Thoracic and abdominal CT findings	
Gender			0.355
Female	53 (44.5%)	20 (37.0%)	
Male	66 (55.5%)	34 (63.0%)	
Vital sign			
Systolic BP at ED triage (mmHg)	122 (100-145)	109 (100-132)	0.008
Diastolic BP at ED triage (mmHg)	78 (70-82)	74 (70-80)	0.258
Pulse at ED triage(bpm)	108 (92-126)	117 (96-128)	0.035
RR at ED triage (bpm)	18 (18-21)	18 (18-22)	0.835
Temperature at ED triage (°C)	38.4 (38.2-39.0)	38.6 (38.3-39.9)	0.791
Oxygen saturation at ED triage (%)	95 (90-96)	94 (90-96)	0.821
Inflammatory biomarkers			
PCT (ng/mL)	0.5 (0.2-1.3)	1.6 (0.7-3.9)	0.001
CRP (mg/L)	148 (93-224)	166 (95-254)	0.241
WBC ($\times 10^9/L$)	16.7 (10.1-28.4)	15.1 (10.5-20.7)	0.183
Comorbidities			0.003
Absent	79 (66.4%)	23 (42.6%)	
Present	40 (33.6%)	31 (57.4%)	

Data are presented as mean \pm standard deviation, median (25%-75% quartiles) or n (%) BP=blood pressure; RR=respiratory rate; ED=emergency department; CRP=C-reactive protein; PCT=procalcitonin; WBC=white blood cell

Table 3. Univariate and multivariate analyses of predictive factors for the source of infection in CT

Variables	Univariate logistic regression	Univariate logistic regression	Univariate logistic regression
	OR	95% CI	P-value
Age [?] 65 years	3.28	1.48-8.74	<0.001
Gender	1.14	0.84-1.57	0.355
Pulse at ED triage	1.23	1.09-1.47	0.035
Positive PCT (ng/mL)	2.92	1.47-5.35	0.001
Systolic BP at ED triage (mmHg)	1.60	1.42-1.78	0.008
Presence of comorbidity	2.68	1.20-4.87	0.003

ED=emergency department; PCT=procalcitonin; BP=blood pressure