EM - ORIGINAL

Role of Gallium-67 scintigraphy in the evaluation of occult sepsis in the medical ICU

Wei-Chun Chen · Kuen-Daw Tsai · Chia-Hung Chen · Ming-Shian Lin · Chuan-Mu Chen · Chuen-Ming Shih · Wei Chen

Abstract Patients in intensive care units (ICUs) frequently have multiple infections or persistent fever despite management. The aim of this study was to evaluate the diagnostic contribution of gallium-67 scintigraphy in ICU patients with suspected occult sepsis. One hundred and seventeen patients (>18 years) who had undergone gallium-67 scintigraphy in the ICU of our medical center over a 3-year period were retrospectively reviewed and analyzed. Patients were categorized into Group 1 ($n = 84$), those with a known infectious source, but who still had persistent fever or sepsis despite antibiotic treatment or abscess drainage; or Group 2 ($n = 33$), those without an evident infectious source after clinical, physical, and imaging studies. Among the 117 patients, 19 (16.2%) had a new diagnosis. In Group 1, 12 patients (14%) had a new infection, including pneumonia (4 patients), bed sore infection (2 patients), pulmonary tuberculosis (2 patients), leg cellulitis (1 patient), psoas muscle abscess (1 patient), osteomyelitis (1 patient), and infective endocarditis (1 patient). In Group 2, seven patients (21.2%) had a new infectious source, including septic arthritis (3 patients), osteomyelitis (2 patients), neck abscess (1 patient), and cholecystitis (1 patient). Significant differences were not observed between patients with positive and negative findings on gallium-67 scintigraphy in characteristics, underlying diseases, laboratory data, and outcomes. Gallium-67 scintigraphy helped to detect new or additional infectious sites, particularly bone, joint, and soft tissues. However, differences in hospital stay and mortality were not observed between patients with positive and negative findings.

Keywords Gallium scan · Sepsis · Fever · Intensive care

Abbreviations

ICU	Intensive care unit
^{67}Ga	Gallium-67
AST	Aspartate aminotransferase
LOS	Length of stay
BUN	Blood urea nitrogen
APACHE	Acute physiology and chronic health evaluation
GCS	Glasgow coma scale

W.-C. Chen · K.-D. Tsai
Division of Pulmonary and Critical Care Medicine, China
Medical University Beigang Hospital, Yunlin, Taiwan

C.-H. Chen · C.-M. Shih
Division of Pulmonary and Critical Care Medicine, China
Medical University Hospital, Taichung, Taiwan

M.-S. Lin · W. Chen (✉)
Division of Pulmonary and Critical Care Medicine, Chia-Yi
Christian Hospital, #539 Jhongsiao Rd, Chia-Yi, Taiwan
e-mail: peteralfa2004@yahoo.com.tw

C.-M. Chen · W. Chen
Department of Life Sciences,
National Chung Hsing University, Taichung, Taiwan

C.-M. Shih (✉) · W. Chen
Department of Respiratory Therapy,
China Medical University, Taichung, Taiwan
e-mail: d10326@mail.cmuh.org.tw

Introduction

Despite the advances in diagnostic modalities and antibiotics, sepsis remains a critical problem with high morbidity and mortality in the intensive care unit (ICU) [1]. Identification of an infectious source in septic patients is usually

based on clinical, biochemical, and microbiologic data and radiologic imaging. The most common infectious sources in the ICU are pneumonia, urinary tract infections, bloodstream infections, surgical site infections, and catheter-related infections [2–5]. However, in a few cases, the site of infection is difficult to determine, and is thus defined as occult sepsis [6, 7]. In addition, ICU patients frequently have multiple infections and non-infectious causes of fever [3, 8], and these may increase the complexity of the diagnosis of infection. Thus, a systematic and comprehensive diagnostic tool to solve this problem is needed.

Nuclear medicine has played an important role in the evaluation of patients suspected of harboring infection for decades, including the use of ^{99m}Tc-methylene diphosphonate (MDP), ^{67}Gallium-citrate (^{67}Ga), and ^{111}In-oxine- and ^{99m}Tc-hexamethylpropyleneamine oxime (HMPAO)-labeled autologous leukocytes [2, 9, 10]. However, studies investigating the application of nuclear medicine to fever of unknown origin or occult sepsis in critically ill patients are limited [6, 7, 11]. ^{67}Gascintigraphy has been used for localizing infections for more than three decades. The radionuclide, ^{67}Ga, emits four principal gamma-rays suitable for imaging: 93, 184, 296, and 388 keV. About 90% of circulating ^{67}Ga is in the plasma, and nearly all of it is bound to transferrin. Increased blood flow and increased vascular membrane permeability result in increased delivery and accumulation of transferrin-bound ^{67}Ga at inflammatory foci. In addition, ^{67}Ga also binds to lactoferrin and leukocytes, which are present in high concentrations in inflammatory foci [2]. Several studies prove that ^{67}Ga scanning is clinically effective in the localization of infectious sources [12–17]. Among these studies, only one used ^{67}Ga scans to detect sources of fever in ventilated, critically ill patients [14]. However, the sample size of that study was relatively small, and characteristically focused on ventilated patients, and those with acute respiratory distress syndrome (ARDS).

Infections in the ICU are usually complicated and critical, necessitating prompt diagnosis and management. In our clinical practice, ^{67}Ga scans are usually suggested by infectious disease specialists or intensivists if a critically ill patient has suspected occult sepsis or persistent fever of unknown origin. The aim of this study was to evaluate the diagnostic contribution of ^{67}Gascintigraphy in patients with occult sepsis in our medical ICU.

Materials and methods

Enrolled patients

We retrospectively reviewed the charts and associated medical information of all patients (>18 years) who had undergone ^{67}Ga inflammation scanning in our medical ICU

from January 2003 to December 2006. Our hospital, China Medical University Hospital (CMUH), is a university-affiliated, 2,000-bed (40-bed medical ICU) tertiary medical center in Taiwan. All intensivists in our medical ICU are certified by the Taiwan Society of Pulmonary and Critical Care Medicine.

In our clinical practice, patients who have a fever of unknown origin or occult sepsis (suspected infection with systemic inflammatory response syndrome), despite extensive diagnostic workup, can be further examined by ^{67}Ga scanning. An extensive diagnostic workup, including careful history taking, physical examination, microbiological, and serological data, plain radiography, ultrasonography, and computed tomography (CT), was done for most of the patients as routine practice by our ICU doctors and infection specialists. During the 3-year period, 123 critically ill patients had ^{67}Ga scans, and 6 of these patients were excluded because of missing data or incomplete diagnostic workup prior to ^{67}Ga scanning. The study was approved by the Institutional Review Board of the China Medical University Hospital (CMUH).

Gallium-67 scintigraphy

Total body imaging was conducted 24–72 h after intravenous injection of 3–6 mCi of ^{67}Ga citrate. Planar scintigraphy was performed with a dual-head, variable-angle digital γ-camera with a medium-energy collimator at the three main energy peaks of ^{67}Ga: 93, 184, and 300 keV. For routine survey studies, imaging was usually carried out at 1 and 3 days post-injection. The day 1 study was rarely definitive and served as a baseline to help distinguish physiologic bowel activity in abdominal scans from pathologic activity [11]. All patients underwent bowel preparation the evening before the scan in order to reduce the normal accumulation of ^{67}Ga in the colon. The normal biodistribution of ^{67}Ga, which can be variable, includes the bone, bone marrow, liver, genitourinary and gastrointestinal systems, and soft tissues. The results of the ^{67}Ga scans were interpreted by the staff of the Department of Nuclear Medicine of CMUH, and were judged to be normal if no accumulation of gallium was detected except at the sites of physiological uptake. If a patient had a positive finding in the ^{67}Ga scan, we consulted a specialist to confirm the diagnosis and to prescribe further management strategies.

Data collection and definitions

We analyzed the following clinical and laboratory parameters: age, gender, body mass index, clinical features, Glasgow Coma Scale (GCS), underlying diseases, causes of admission, Acute Physiology and Chronic Health Evaluation (APACHE) II score, complete blood counts,

biochemistry data, bacteriology, occurrence of complications, and duration of ICU stay and outcomes. Sepsis and septic shock were defined in accordance with the criteria of the International Sepsis Definitions Conference [18]. Respiratory failure was defined as the requirement of mechanical ventilation support according to the judgment of the clinical physicians and disease progress.

Because of the probability of multiple infections in critically ill patients, the patient population was divided into two groups: Group 1, patients with a pre-existing infectious site (those with a known infectious source, but who still had persistent fever or sepsis despite antibiotic treatment or abscess drainage); or Group 2, patients without a pre-existing infectious site (those without an evident infectious source after thorough clinical, physical, and imaging studies). After performing the ^{67}Ga scans, patients in Group 2 were further divided into new diagnosis and negative findings groups according to clinical judgment and the results of the scans. Patients with new diagnosis were those who had a newly discovered infectious source. Similarly, patients in Group 1 were further divided into three groups: new diagnosis, confirmed infection, and negative findings. Confirmed infection was diagnosed if the infectious source detected by the ^{67}Ga scan was the same as the source already known in patients with a pre-existing infectious site.

Statistical analysis

The data were compiled and analyzed using commercial statistical software (SPSS for Windows, version 13.0, Chicago, IL, USA). All continuous data were expressed as mean $\pm$ standard deviation (SD) and compared using a two-tailed Student's t test. Categorical variables were reported as a percentage and compared using chi-square or Fisher's exact tests, when appropriate. A p value <0.05 was considered statistically significant.

Results

Patient characteristics

The 117 enrolled patients included 64 men (54.7%) and 53 women (45.3%), with a mean age of 68.2 years (range 22–90 years). The most common concomitant underlying disease was diabetes mellitus ($n = 50$, 42.7%), followed by hypertension ($n = 47$, 40.2%), stroke ($n = 25$, 21.4%), and end-stage renal disease ($n = 21$, 17.9%) (Table 1). The mean APACHE II score was 18.7 $\pm$ 7, and 77 (65.8%) patients had respiratory failure requiring mechanical ventilation on the first day of ICU admission. The most common diagnosis at admission was fever of unknown origin

Table 1 Characteristics of the 117 enrolled patients on the first day of ICU admission

Characteristics	Value
Age	68.2 $\pm$ 13.8 (22–90)
Gender, male/female	64/53 (54.7%/45.3%)
Body mass index, kg/m^2	22.9 $\pm$ 3.8 (15.5–35.3)
Underlying diseases	
Diabetes mellitus	50 (42.7%)
Hypertension	47 (40.2%)
Stroke	25 (21.4%)
End-stage renal disease	21 (17.9%)
Malignancy	8 (6.8%)
Liver cirrhosis	4 (3.4%)
APACHE II	18.7 $\pm$ 7 (12–36)
GCS	9.8 $\pm$ 3 (3–15)
Vasopressor use	64 (54.7%)
Respiratory failure	77 (65.8%)

APACHE acute physiology and chronic health evaluation, *GCS* glasgow coma scale

($n = 27$, 23.1%), followed by neurogenic/cerebrovascular disorder ($n = 17$, 14.5%), pneumonia or pleural infection ($n = 15$, 12.8%), urinary tract infection ($n = 13$, 11.1%), and cardiovascular disorder ($n = 10$, 8.5%) (Table 2).

Diagnostic evaluation

Among the 117 patients who underwent ^{67}Gascintigraphy, 19 (16.2%) were found to have a new diagnosis. Because of the complexity of infections in critically ill patients, we further divided them into two groups (Fig. 1). Eighty-four patients had a pre-existing infectious site (Group 1), and 33

Table 2 Categories of diagnosis at admission among the 117 patients

Diagnosis	n (%)
Sepsis of unknown origin	27 (23.1)
Neurogenic disorder	17 (14.5)
Pneumonia or pleural infection	15 (12.8)
Urinary tract infection	13 (11.1)
Cardiovascular disorder	10 (8.5)
Bone or soft tissue infection	8 (6.8)
Metabolic disorder	5 (4.3)
Intra-abdominal infection	4 (3.4)
Drug overdose	4 (3.4)
Malignancy-related complication	3 (2.6)
Hepatic failure	2 (1.7)
Gastrointestinal bleeding	2 (1.7)
Catheter-related infection	2 (1.7)
Acute renal failure	2 (1.7)

Fig. 1 Flow chart of the 117 patients with occult sepsis who underwent gallium-67 scans in the medical ICU
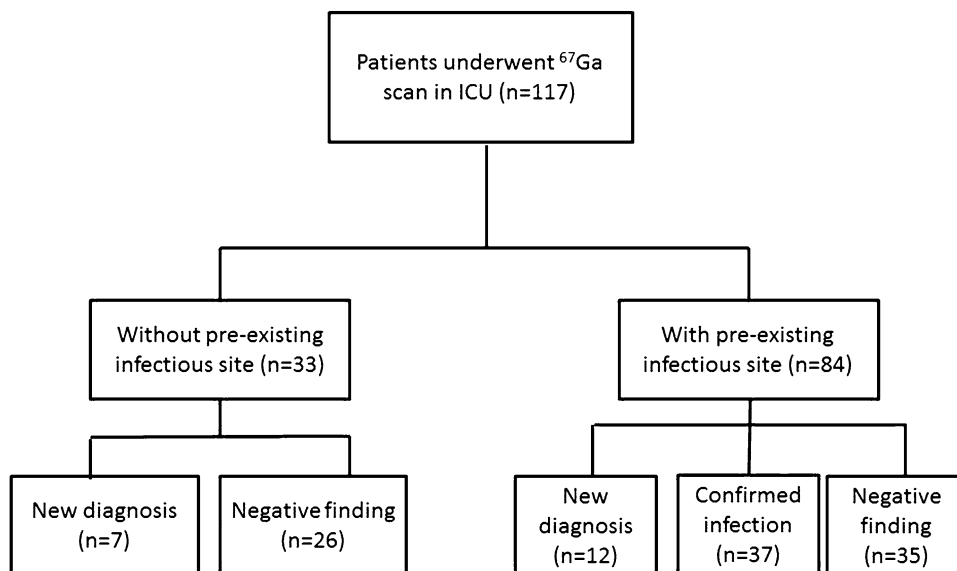
did not have a pre-existing infectious site (Group 2). After performing ^{67}Ga scans, seven patients (21.2%) in Group 2 were found to have a new infectious source, including septic arthritis ($n = 3$), osteomyelitis ($n = 2$), neck abscess ($n = 1$), and cholecystitis ($n = 1$). In Group 1, 12 patients (14.3%) were found to have a new infectious source including pneumonia ($n = 4$), bed sore infection ($n = 2$), pulmonary tuberculosis ($n = 2$), leg cellulitis ($n = 1$), psoas muscle abscess ($n = 1$), osteomyelitis ($n = 1$), and infective endocarditis ($n = 1$). Thirty-seven patients (44%) were confirmed to have the same infectious source as that known before the test, and 35 patients (41.7%) had negative findings. All 19 patients with a newly diagnosed infectious source under went further sepsis management, including treatment with new antibiotics, abscess drainage, debridement of bed sores, and surgery.

Effect of ^{67}Ga scanning

Comparing the clinical features and outcomes of Group 2 patients, there were no significant differences between patients with positive and negative findings on the ^{67}Ga scans in general characteristics, underlying diseases, laboratory data, and outcomes. However, there were trends of higher serum C-reactive protein levels (20.34 ± 14.48 vs. 10.01 ± 9.79 mg/dl, $p = 0.077$) and in-hospital mortality rates (71.4 vs. 26.9%, $p = 0.071$) in patients with positive findings on ^{67}Ga scans (Table 3).

Comparing the clinical features and outcomes of Group 1 patients, there were no significant differences between the patients with positive and negative findings on the ^{67}Ga scans in general characteristics, underlying diseases, laboratory data, and outcomes (Table 4).

Discussion

We found that ^{67}Ga scintigraphy was helpful in detecting new or additional infectious sites in 21.2% of patients without a pre-existing infectious site and 58.3% of patients with a pre-existing infectious site. Among the newly diagnosed infections ($n = 19$), the most common sources detected by the scans were bone/joint infections ($n = 6$, 31.5%) and soft tissue infections ($n = 5$, 26.3%). Comparing the clinical features and outcome of these patients further, we found no significant differences between patients with positive and negative findings on the ^{67}Ga scans in general characteristics, underlying diseases, laboratory data, and outcomes.

^{67}Ga scintigraphy has been used as a screening procedure to detect areas of inflammation or infection for decades. Although it lacks specificity, its sensitivity is high in detecting infections, abscesses, and some neoplasms. Because of these characteristics, it has been used as a convenient imaging tool to help in the evaluation of cases of fever of unknown origin [11], even though there are certain drawbacks. The major drawbacks are that localization of abdominal infections is hampered by normal bowel excretion and unfavorable physical characteristics on γ-camera imaging [19]. However, this is easily overcome by the complementary role of abdominal CT. Almost all abdominal infectious and inflammatory processes can be diagnosed in their early stages by abdominal CT.

Surprisingly, the most common newly diagnosed infections detected by the scans were bone/joint infections (31.5%) and soft tissue infections (26.3%). This is probably because most intensivists rely on CT or ultrasonography as their screening tool for patients with suspected occult sepsis. CT and ultrasonography have a limited ability in diagnosing bone or joint infection.

Table 3 Comparison of the clinical features and outcomes between positive and negative findings on gallium scans in the 33 occult sepsis patients without pre-existing infectious sites

Clinical feature	Gallium scan positive ($n = 7$)	Gallium scan negative ($n = 26$)	p value
Age	68.57 ± 13.30	65.19 ± 18.45	0.665
GCS	11.71 ± 2.63	9.38 ± 3.84	0.142
APACHE II score	21.14 ± 8.36	18.27 ± 7.54	0.388
Shock	1 (14.3%)	16 (61.5%)	0.039
Acute respiratory failure	3 (42.9%)	19 (73.1%)	0.186
Underlying diseases			
Diabetes mellitus	3 (42.9%)	8 (30.8%)	0.661
Liver cirrhosis	0 (0%)	1 (3.8%)	1.000
End-stage renal disease	7 (14.3%)	7 (20%)	0.559
Stroke	0 (0%)	8 (30.8%)	0.154
Laboratory data			
WBC count (10^3/per mm^3)	13.222 ± 4.422	17.313 ± 8.375	0.227
Hemoglobin (g/dl)	9.157 ± 2.000	10.513 ± 3.468	0.333
Platelet (10^3/per mm^3)	185.286 ± 87.410	211.088 ± 129.392	0.624
AST (IU/l)	84.00 ± 92.73	69.25 ± 80.10	0.732
BUN (mg/dl)	73.33 ± 40.63	42.15 ± 31.89	0.060
Albumin (g/dl)	1.70 ± 0.69	2.76 ± 0.98	0.107
C-reactive protein (mg/dl)	20.34 ± 14.48	10.01 ± 9.79	0.077
Outcome			
LOS in ICU, days	26.14 ± 13.87	44.38 ± 81.12	0.563
Total LOS, days	47.57 ± 38.39	94.23 ± 125.50	0.344
In-hospital mortality	5 (71.4%)	7 (26.9%)	0.071

ICU intensive care unit, *AST* aspartate aminotransferase, *LOS* length of stay, *BUN* blood urea nitrogen, *APACHE* acute physiology and chronic health evaluation

Table 4 Comparison of clinical features and outcomes between positive and negative findings on gallium scans in the 84 occult sepsis patients with pre-existing infectious sites

Clinical feature	Gallium scan positive ($n = 49$)	Gallium scan negative ($n = 35$)	p value
Age	68.41 ± 12.65	70.06 ± 11.84	0.547
GCS	10.10 ± 3.47	9.49 ± 3.98	0.453
APACHE II score	17.43 ± 6.66	20.46 ± 7.00	0.067
Shock	26 (53.1%)	21 (60.0%)	0.652
Acute respiratory failure	36 (73.5%)	24 (68.6%)	0.634
Underlying diseases			
Diabetes mellitus	24 (49%)	15 (42.9%)	0.660
Liver cirrhosis	1 (2.0%)	2 (5.7%)	0.568
End-stage renal disease	7 (14.3%)	7 (20%)	0.559
Stroke	10 (20.4%)	7 (20%)	1.000
Malignancy	3 (6.1%)	4 (11.4)	0.443
Laboratory data			
WBC count (10^3/per mm^3)	13.851 ± 8.066	14.163 ± 6.675	0.855
Hemoglobin (g/dl)	10.62 ± 2.26	10.61 ± 2.27	0.968
Platelet (10^3/per mm^3)	167.577 ± 102.05	194.333 ± 129.066	0.310
AST (IU/l)	86.65 ± 294.06	121.54 ± 347.64	0.669
BUN (mg/dl)	46.33 ± 33.92	47.16 ± 30.18	0.914
Albumin (g/dl)	2.23 ± 0.66	2.35 ± 0.60	0.547
C-reactive protein (mg/dl)	16.72 ± 12.54	13.48 ± 9.35	0.320
Outcome			
LOS in ICU, days	25.39 ± 13.87	22.03 ± 12.02	0.251
Total LOS, days	63.82 ± 70.20	84.46 ± 112.36	0.304
In-hospital mortality	15 (30.6%)	15 (42.9%)	0.260

ICU intensive care unit, *APACHE* acute physiology and chronic health evaluation, *LOS* length of stay

Identification of fever sources is difficult in the ICU because critically ill patients frequently have multiple infections. In addition, some microorganisms, such as *Klebsiella pneumoniae* and *Staphylococcus aureus* have the potential to cause metastatic infection, and some may require surgical intervention [20]. Another type of nuclear medicine, F-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT), also plays an important role in localizing these disseminating infectious processes [21, 22]. However, performing ^{18}F-FDG PET/CT is quite expensive, and is not supported by the health insurance system in Taiwan. As a result, we routinely use ^{67}Ga scintigraphy to detect suspected occult sepsis in patients with pre-existing infections when they have persistent fever or systemic inflammatory response syndrome despite antibiotic and medical management. In our study, we found that the infectious source was confirmed in 44% of patients with pre-existing infections. This is helpful for intensivists because it can guide their clinical judgment and treatment strategies.

There are some limitations to our study. First, it took 2–3 days to complete the ^{67}Ga study. This delay may in turn result in delayed treatment of the sepsis in some cases. Second, the final diagnosis in negative ^{67}Ga scintigraphy findings may be underestimated because of the sensitivity of the test. Third, it is a retrospective study, and the time point for performing the scans was not the same for all enrolled patients. However, all the patients had fever or suspected occult sepsis despite thorough studies and standard management. As a result, our study can offer clinical intensivists a method of dealing with this problem when it occurs.

Fever or infection control in the ICU is a critical issue despite the improvement of biochemical and imaging techniques. Our study showed that ^{67}Ga scintigraphy helped in detecting new or other infectious sites, particularly bone, joint, and soft tissue. However, no differences were observed in hospital stay and mortality between patients with positive and negative findings on ^{67}Ga scintigraphy.

References

1. Calandra T, Cohen J (2005) The international sepsis forum consensus conference on definitions of infection in the intensive care unit. Crit Care Med 33(7):1538–1548
2. Love C, Palestro CJ (2004) Radionuclide imaging of infection. J Nucl Med Technol 32(2):47–57 (quiz 58–59)
3. Marik PE (2000) Fever in the ICU. Chest 117(3):855–869
4. Richards MJ, Edwards JR, Culver DH, Gaynes RP (1999) Nosocomial infections in medical intensive care units in the United States. National Nosocomial Infections Surveillance System. Crit Care Med 27(5):887–892
5. Richards MJ, Edwards JR, Culver DH, Gaynes RP (2000) Nosocomial infections in combined medical-surgical intensive care units in the United States. Infect Control Hosp Epidemiol 21(8):510–515
6. Minoja G, Chiaranda M, Fachinetti A, Raso M, Dominioni L, Torre D, De Palma D (1996) The clinical use of 99m-Tc-labeled WBC scintigraphy in critically ill surgical and trauma patients with occult sepsis. Intensive Care Med 22(9):867–871
7. Kao CH, Wang YL, Liao SQ, Wang SJ (1992) Tc-99m HMPAO labelled WBCs in the detection of occult sepsis in the intensive care unit. Intensive Care Med 18(1):15–19
8. Green RJ, Clarke DE, Fishman RS, Raffin TA (1995) Techniques for evaluating fever in the ICU. A stepwise approach for detecting infectious and noninfectious causes. J Crit Illn 10(1):67–71
9. Palestro CJ (2009) Radionuclide imaging of infection: in search of the grail. J Nucl Med 50(5):671–673
10. Palestro CJ, Love C, Tronco GG, Tomas MB (2000) Role of radionuclide imaging in the diagnosis of postoperative infection. Radiographics 20(6):1649–1660 (discussion 1660–1663)
11. Maderazo EG, Hickingbotham NB, Woronick CL, Sziklas JJ (1988) The influence of various factors on the accuracy of gallium-67 imaging for occult infection. J Nucl Med 29(5):608–615
12. Grubstein A, Bernstine H, Steinmetz AP (2007) Chest CT and gallium-67 SPECT scintigraphy scan co-registration in a post-heart transplantation patient with unresolved fever. Isr Med Assoc J 9(11):827–828
13. Lee JK (2003) Gallium-67 citrate imaging before and after treatment of acute Q fever. Clin Nucl Med 28(12):998–999
14. Meduri GU, Belenchia JM, Massie JD, Eltorky M, Tolley EA (1996) The role of gallium-67 scintigraphy in diagnosing sources of fever in ventilated patients. Intensive Care Med 22(5):395–403
15. Knockaert DC, Mortelmans LA, De Roo MC, Bobbaers HJ (1994) Clinical value of gallium-67 scintigraphy in evaluation of fever of unknown origin. Clin Infect Dis 18(4):601–605
16. Suga K, Nakagi K, Kuramitsu T, Itou K, Tanaka N, Uchisato H, Nakanishi T, Utsumi H, Yamada N (1991) The role of gallium-67 imaging in the detection of foci in recent cases of fever of unknown origin. Ann Nucl Med 5(1):35–40
17. Knockaert DC, Mortelmans LA, Deroo MC, Bobbaers HJ (1989) Clinical value of gallium-67 scintigraphy in the investigation of fever or inflammation of unknown origin in the ultrasound and computed tomography era. Acta Clin Belg 44(2):91–98
18. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, Opal SM, Vincent JL, Ramsay G (2003) 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Intensive Care Med 29(4):530–538
19. Becker W, Meller J (2001) The role of nuclear medicine in infection and inflammation. Lancet Infect Dis 1(5):326–333
20. Chen W, Chen CH, Chiu KL, Lai HC, Liao KF, Ho YJ, Hsu WH (2008) Clinical outcome and prognostic factors of patients with pyogenic liver abscess requiring intensive care. Crit Care Med 36(4):1184–1188
21. Vos FJ, Bleeker-Rovers CP, Sturm PD, Krabbe PF, van Dijk AP, Cuijpers ML, Adang EM, Wanten GJ, Kullberg BJ, Oyen WJ (2010) 18F-FDG PET/CT for detection of metastatic infection in gram-positive bacteremia. J Nucl Med 51(8):1234–1240
22. Van Riet J, Hill EE, Gheysens O, Dymarkowski S, Herregods MC, Herijgers P, Peetermans WE, Mortelmans L (2010) (18)F-FDG PET/CT for early detection of embolism and metastatic infection in patients with infective endocarditis. Eur J Nucl Med Mol Imaging 37(6):1189–1197