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ORIGINAL ARTICLE

The value of Tc-99m (V) dimercaptosuccinic acid in detecting intra-abdominal infection: compared with gallium scan

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Abstract
Objective Gallium-67 (Ga-67) and labeled leukocytes are useful in the detection of an unknown infectious source. However, the delay in the diagnosis of a Ga-67 citrate scan (gallium scan) and the complicated labeling technique of a leukocyte scan are major drawbacks to their clinical use. Recently, Tc-99m (V) dimercaptosuccinic acid (DMSA) has been found to be very useful in the detection of infection. Tc-99m (V) DMSA is inexpensive, easy to prepare, and provides a result within hours. In this study, we evaluated the potential of Tc-99m (V) DMSA scan (DMSA scan) in the detection of intra-abdominal infection.
Methods A total of 33 patients who suffered from an unknown cause of fever after colorectal surgery were enrolled in this study. All patients received both a gallium scan and a DMSA scan. DMSA scintigraphy was performed 3–4 h after an injection of 740 MBq (20 mCi) of Tc-99m DMSA. After completion of the DMSA image, 111 MBq (3 mCi) of Ga-67 citrate was injected intravenously. Gallium scintigraphy was performed after 24 h and later as needed.
Results Of the 33 patients, 17 (51.5%) were diagnosed with intra-abdominal abscesses. For DMSA scans, the sensitivity, specificity, and overall accuracy were 88.2%, 93.7%, and 90.9%, respectively. For gallium scans, the diagnostic sensitivity, specificity, and accuracy were 100%, 87.5%, and 93.9%, respectively. No statistical difference was found in the diagnostic accuracy between these two diagnostic modalities using Fisher's exact test.
Conclusions DMSA scan is a useful alternative to gallium scan in the detection of intra-abdominal infection in patients with colorectal surgery because Tc-99m DMSA is inexpensive, easy to prepare, and most importantly the result can be obtained within hours.

Keywords Tc-99m(V) DMSA · Colorectal surgery · Abdominal infection · Gallium scan

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Introduction

Intra-abdominal infection continues to pose a significant threat to patients, following abdominal surgery. Undiagnosed and untreated sepsis may lead to multiple system organ failure, a common cause of death in postoperative patients. Early detection of intra-abdominal infection followed by surgery/drainage and antimicrobial therapy is crucial for reduction of mortality. Radionuclide techniques are widely used in the detection of infection. Gallium-67 (Ga-67) citrate (gallium) scan was the first radionuclide method to be widely used to image inflammation [1]. The method is relatively inexpensive. Although the reported sensitivity and specificity of

gallium imaging for the detection of abdominal infection have varied [2–4], our previous studies showed very promising results in detecting abdominal infection after colorectal surgery [5–8]. However, a big problem with gallium scan is that the final results usually cannot be obtained within 24 h and may take even longer when physiological bowel activity appears. This becomes a major drawback in its use for the detection of infection. Alternatively, the development of leukocytes labeled with In-111 oxine or Tc-99m hexamethylpropylene amine oxime (HMPAO) supplanted gallium image for the evaluation of suspected intra-abdominal infection [9]. Labeled leukocytes provide more accurate and a quicker diagnosis than gallium imaging. However, In-111 is not available in many countries. Tc-99m HMPAO labeling of leukocytes is expensive and time consuming. In addition, both gallium scan and Tc-99m HMPAO scan may show intense physiologic bowel activity, which may be an obstacle when applied to patients with abdominal surgery. Therefore, the search for a new, quick diagnostic modality still continues.

Tc-99m (V)-dimercaptosuccinic acid (DMSA) was developed as a tumor imaging agent and has been reported to be useful in localizing various tumors such as medullary carcinoma of the thyroid [10], soft tissue tumors [11], lung cancers [12], and bone metastases [13]. Recently, more and more studies have shown the potential of Tc-99m DMSA as an infection-detecting agent [14–16]. Tc-99m DMSA is inexpensive, easy to prepare, and provides results within hours. No obvious bowel activity is noted in a normal Tc-99m DMSA image, which is suitable for the evaluation of abdominal infection.

In this study, we evaluated the diagnostic accuracy of Tc-99m DMSA scan (DMSA scan) in patients who were suspected of having infection after abdominal surgery and the results were compared with those of the gallium scan.

Materials and methods

Between March 2001 and October 2002, 33 patients (13 women, 20 men; mean age 61.8 years) who underwent colorectal surgery were enrolled in this study. All patients suffering from unknown causes of fever after surgery (range 2–14 days; mean 5.3 days) were referred to our department for the detection of occult infectious source. The underlying disease processes were: colorectal cancer, colon rupture, colonic lymphoma, intestinal intussusception, and colon diverticulitis. All patients received both a gallium whole-body scan and Tc-99m DMSA scan.

The diagnosis of a positive infection was based on pus formation, a positive bacteria culture, a positive re-operation result, and/or effective response to antibiotic treatment. Negative reports were verified by adequate out-patient review following hospital discharge that indicated the clinical absence of infection.

DMSA scintigraphy

DMSA scintigraphy was performed 3–4 h after an injection of 740 MBq (20 mCi) Tc-99m (V) DMSA. A dual-headed gamma camera (VARICAM, Elscint, Haifa, Israel) with a low-energy, parallel-hole collimator was used to simultaneously obtain anterior and posterior views of the whole body and local abdominal images. A lateral view was obtained as needed. In addition, SPECT images of the abdomen or any suspicious infectious lesions were also obtained.

Gallium scintigraphy

After completion of DMSA scanning, 111 MBq (3 mCi) Ga-67 citrate was injected intravenously. Gallium scintigraphy was performed 24 h later. A dual-headed gamma camera (VARICAM, Elscint) with a medium-energy, parallel-hole collimator was used to simultaneously obtain anterior and posterior views of the whole body and local abdominal images. A lateral view was obtained as needed. If clinically needed, 48-h or 72-h images were taken. SPECT images of the abdomen or any suspicious infectious lesion were also taken if needed.

Interpretation

The intensity of gallium uptake was recorded using a scale of 0–3: grade 0, no abnormal uptake; grade 1, abnormal activity with intensity less than liver activity; grade 2, abnormal activity equal to liver activity; and grade 3, abnormal activity greater than liver activity. In addition, gallium uptake was classified into two patterns when the intensity of gallium uptake was equal to or greater than 2: changing pattern, in which the pattern of abnormal gallium activity changes or gallium activity decreases during the sequential images, and the unchanging pattern, in which the pattern of abnormal gallium activity does not change during the sequential images. A positive gallium image was defined as a gallium uptake intensity of grade 2 or 3 with an unchanging pattern.

Any abnormal uptake of Tc-99m DMSA in the abdomen was interpreted as a positive study finding. All images were read by two nuclear medicine physicians along with the surgeon who performed the operation.

Interobserver disagreements were resolved by discussion among the observers.

Statistical analysis

We calculated the diagnostic sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of both the DMSA image and the gallium image. Statistical analysis of the results was done with the Statistica for Windows Release 4.5 package (StatSoft, Tulsa, OK, USA) using a two-tailed, Fisher's exact test. $P < 0.05$ was considered statistically significant.

Results

Of the 33 patients, 17 (51.5%) were diagnosed with intra-abdominal infection. Table 1 shows the diagnostic results of the gallium scan and DMSA scan in the detection of infectious foci after colorectal surgery (Fig. 1). The gallium scan detected all the intra-abdominal infections, whereas DMSA scan missed two of the lesions (Fig. 2). Of the 16 patients without infection, the gallium scan showed two cases of false positive results, whereas the DMSA scan showed only one false positive case (Figs. 3, 4). Table 2 shows the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of the gallium scan and the DMSA scan. For gallium scans, the diagnostic sensitivity, specificity, accuracy, negative predictive value, and positive predictive value

Table 1 Diagnostic results of the gallium scan and the DMSA scan in the detection of intra-abdominal infection source after colorectal surgery

Infectious focus	No.	Gallium scan		DMSA scan	
		Positive	Negative	Positive	Negative
Presence	17	17	0	15	2
Absence	16	2	14	1	15

DMSA dimercaptosuccinic acid

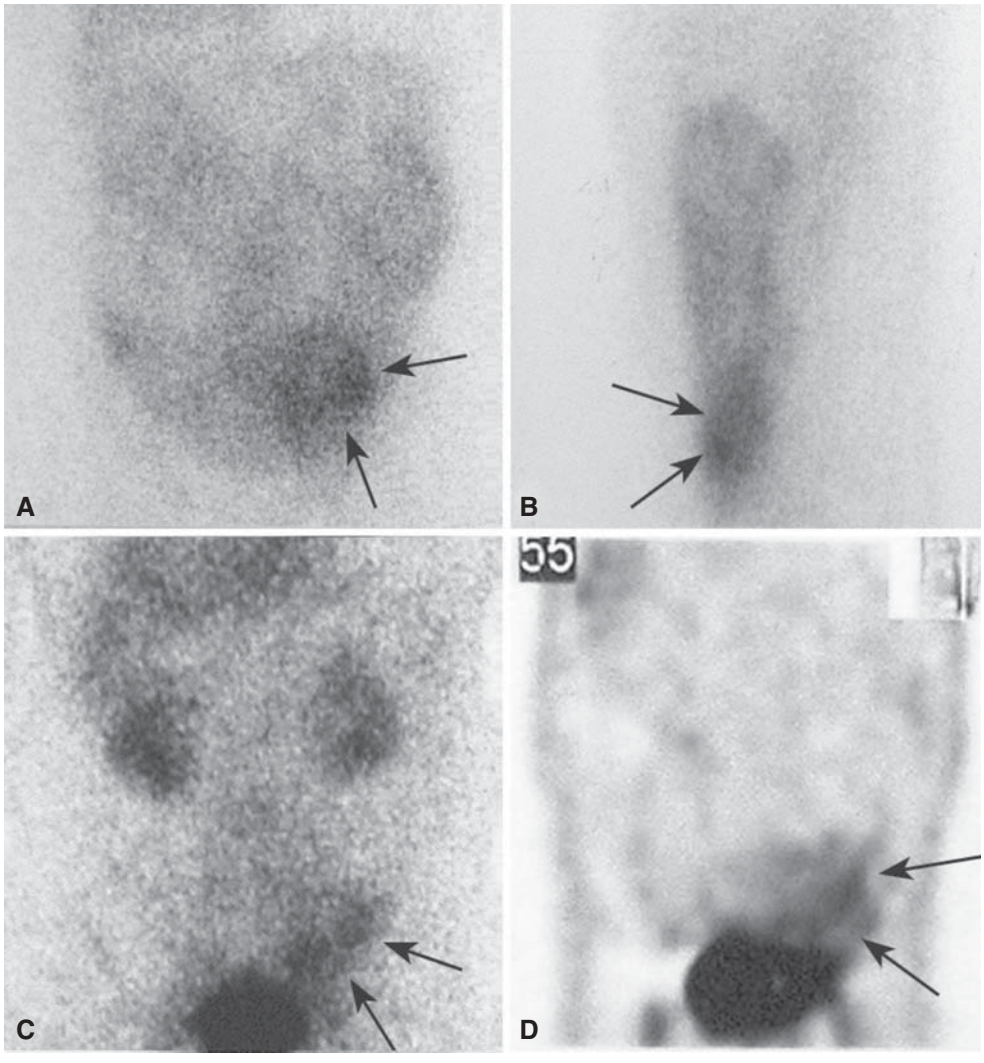

Fig. 1 *Upper row* **A** gallium scan performed 48 h after injection of 111 MBq (3 mCi) gallium-67 citrate shows significant gallium uptake (grade 3) in the left lower abdomen (*arrows*). **A** Anterior planar view of the abdomen. **B** Left lateral planar view of the abdomen. *Lower row* A dimercaptosuccinic acid (DMSA) scan performed 3 h after injection of 740 MBq (20 mCi) of Tc-99m (V) DMSA shows increased DMSA uptake in the left lower abdomen (*arrows*). **C** Anterior planar view of the abdomen. **D** Coronary section of the abdomen SPECT images. The final diagnosis is intra-abdominal abscess in the left lower abdomen

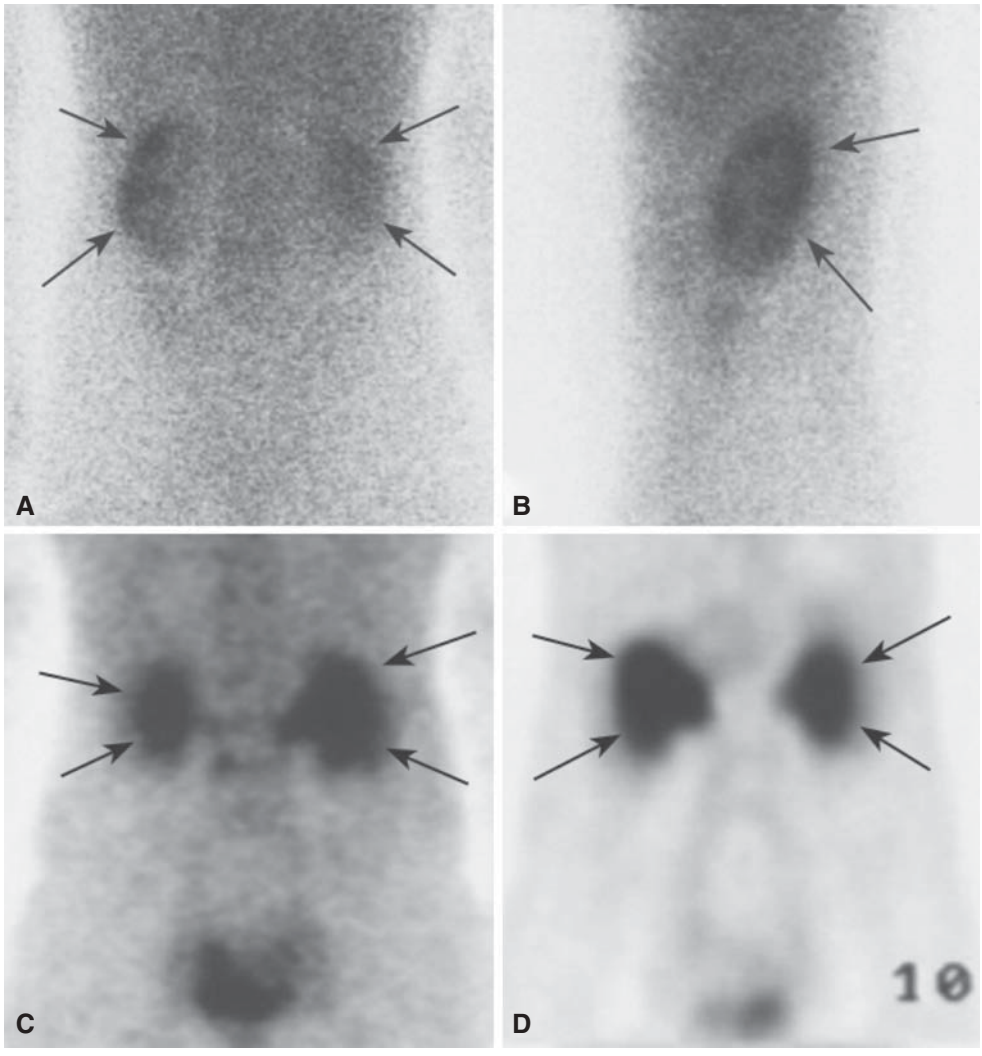

Fig. 2 *Upper row* A gallium scan performed 48 h after injection shows significant gallium uptake (grade 3) in bilateral kidneys (*arrows*). **A** Posterior planar view of the abdomen. **B** Left lateral planar view of the abdomen. *Lower row* A DMSA scan performed 3 h after injection shows intense DMSA uptake in both kidneys. The radioactivity is predominantly physiologic, owing to normal renal excretion of Tc-99m DMSA (*arrows*). It is very difficult to detect renal infection on a DMSA scan because of the physiological renal uptake of Tc-99m DMSA. **C** Posterior planar view of the abdomen. **D** Coronary section of the abdominal SPECT images. The final diagnosis is renal infection. This is a false-negative case of DMSA scan

Table 2 Test characteristics of the gallium scan and the DMSA scan in the detection of intra-abdominal infection source after colorectal surgery

Characteristics	Gallium scan (%)	DMSA (%)
Sensitivity	100	88.2
Specificity	87.5	93.7
Accuracy	93.9	90.9
Negative predictive value	100	88.2
Positive predictive value	89.4	93.7

were 100%, 87.5%, 93.9%, 100%, and 89.4%, respectively. For the DMSA scans, the sensitivity, specificity, overall accuracy, positive predictive value, and negative predictive value were 88.2%, 93.7%, 90.9%, 88.2%, and 93.7%, respectively. Using Fisher's exact test, there were no significant differences in sensitivity ($P = 0.48$), specificity ($P = 0.61$), or accuracy ($P = 1.00$) between these two diagnostic methods in the detection of intra-abdominal infection after colorectal surgery.

Discussion

Intra-abdominal infections are common and are associated with significant morbidity and mortality. Early diagnosis followed by appropriate operative surgical procedures and drainage is the key to managing patients with serious intra-abdominal infections. Most reports agree that computed tomography (CT) is the imaging method of choice for the diagnosis of intra-abdominal abscesses [17, 18]. However, in patients with distortion of normal anatomy due to recent trauma or surgery, an early infection before the development of discrete fluid collections is more difficult to detect with CT. In these clinical situations, radionuclide scanning may be still of some value [18]. Moreover, in patients without localized

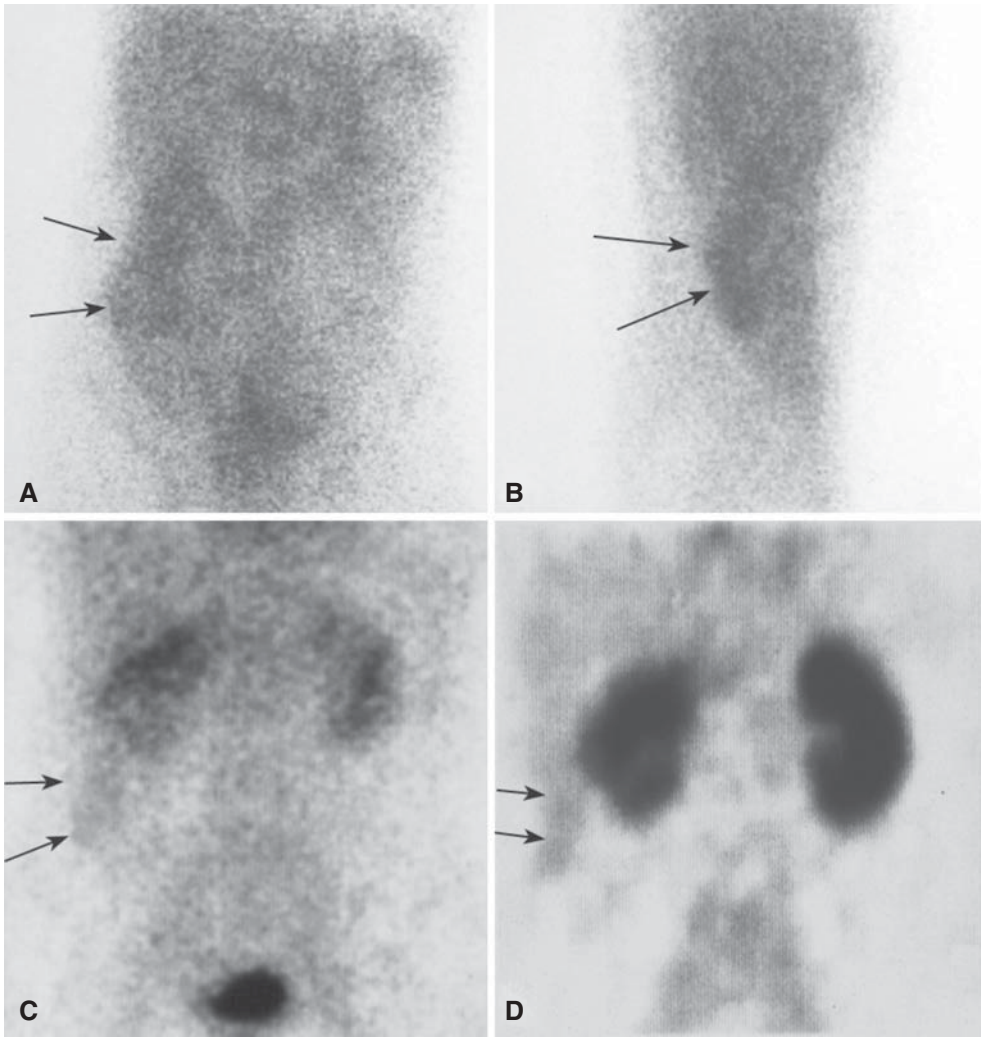

Fig. 3 *Upper row* A gallium scan performed 48 h after injection shows significant gallium uptake in the right abdomen (*arrows*). **A** Anterior planar view of the abdomen. **B** Right lateral planar view of the abdomen. *Lower row* A DMSA scan performed 3 h after injection shows mildly increased DMSA uptake in the right abdomen (*arrows*). **C** Anterior planar view of the abdomen. **D** Coronary section of the abdominal SPECT images. The final diagnosis is bile leakage. The patient was not diagnosed with intra-abdominal infection. We considered this to be a false positive case for both the gallium scan and the DMSA scan

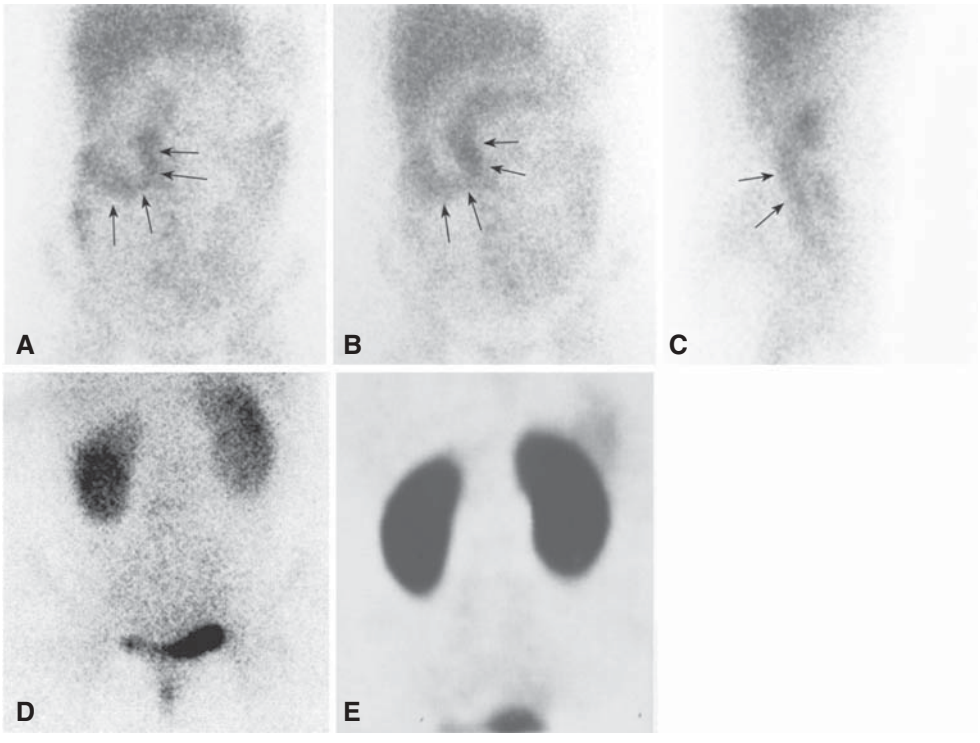

Fig. 4 *Upper row* A gallium scan shows persistent accumulation of gallium uptake in the right transverse colon (*arrows*). **A** A 48-h anterior abdominal planar view. **B** A 72-h anterior abdominal planar view, **C** right lateral planar view. *Lower row* A DMSA scan performed 3 h after injection shows no abnormal DMSA uptake in the abdomen. **D** Anterior planar view of the abdomen. **E** Coronary section of the abdominal SPECT images. This is a false-positive case of gallium scan

signs of abdominal abscess, nuclear medicine imaging still has a role because it allows the entire body to be imaged [18, 19]. Theoretically, a Tc-99m DMSA scan could be an ideal radiopharmaceutical for the evaluation of intra-abdominal infection. In contrast to Ga-67, Tc-99m is cheaper, has better physical characteristics, is more readily available, and is more suitable for everyday clinical use. In addition, no obvious bowel activity is demonstrated in the DMSA scan [20], which is crucial in the evaluation of intra-abdominal infection. Most importantly, the result can be obtained within hours of DMSA scanning. Recently, three infectious cases including one intra-abdominal abscess, one peritonitis, and one psoas muscle abscess have been reported to be detected by a DMSA scan [21–23]. Moreover, a study by Lee et al. [20] revealed very high diagnostic sensitivity, specificity, and an accuracy of 95%, 94%, and 95%, respectively, in the detection and localization of intestinal inflammation using a DMSA scan. They concluded that a DMSA scan is a useful noninvasive diagnostic test for the detection and localization of intestinal inflammation. However, to the best of our knowledge, this is the first systematic study for the evaluation of intra-abdominal infection using DMSA scanning. According to our data, both the DMSA scan and the gallium scan showed good diagnostic accuracy in the detection of intra-abdominal infection in patients with a history of colorectal surgery. Although the diagnostic accuracy of the gallium scan was slightly better than that of the DMSA scan (93.9% vs. 90.9%), there was no statistical difference ($P = 1.00$).

In this study, the gallium scan detected all the infections, whereas the DMSA scan missed two lesions. The gallium scan showed higher diagnostic sensitivity than the DMSA scan (100% vs. 88.2%), whereas there was no statistical difference ($P = 0.48$). The DMSA scan showed two false-negative results, which were all due to renal infections. Tc-99m DMSA is mainly excreted via the urinary system. The high accumulation of Tc-99m DMSA in the kidney and urinary bladder may weaken the ability of the DMSA scan to detect infection in these areas [24]. Therefore, in the evaluation of infection of the urinary system, a gallium scan may be more useful than the DMSA scan. A negative DMSA scan cannot rule out the possibility of urinary infection.

By contrast, the DMSA scan showed higher diagnostic specificity than the gallium scan (93.7% vs. 87.5%), although there was no statistical difference ($P = 0.61$). A high false-positive rate in the evaluation of intra-abdominal abscess is always considered to be a weakness of the gallium scan [25]. A false-positive gallium scan may be caused by non-specific gallium uptake in the normal excretion of gallium into the bowel [25]. Serial imaging is a useful method for distinguishing normal bowel activity from intra-abdominal infection. Normal gallium activity in the bowel will move with time, whereas abscesses will appear unchanged. Most of the normal gallium activity in the bowel can be easily distinguished from the infectious lesion by this method, but a delayed 72 h image or even a 96-h image is usually needed. Delayed diagnosis significantly limits its clinical use. Moreover, some patients with a suspected abdominal abscess may show reduced peristalsis. Then a static area may still represent normal bowel activity and result in a false-positive interpretation. In our study, there were two positive cases in the gallium scan; one resulted from the misinterpretation of normal bowel activity (Fig. 4). The other false-positive case was due to bile leakage over the right upper abdomen, which was proven by bile excretion via the drain tube (Fig. 3). Inflammation, but not infection, was considered clinically, as all bacterial cultures were negative in this case. Accumulation of Tc-99m DMSA was also found in this area in the DMSA scan. We considered the uptake of gallium and Tc-99m DMSA in this inflammatory area caused by bile leakage as false-positive results in our study, because it was not an infection. Both the gallium scan and the DMSA scan failed to differentiate inflammation from infection in our case (Fig. 3).

The mechanism of gallium uptake in infectious sites is not completely understood. Multiple factors are thought to contribute to the accumulation and retention of Ga-67 in inflammatory lesions, including increased capillary permeability at the inflammatory sites, binding of gallium to tissue proteins such as lactoferrin, as well as direct leukocyte and bacterial uptake [26]. The localization mechanism of Tc-99m (V) DMSA in inflammation is not well known either. Some possible mechanisms have been assumed, such as the infiltration of Tc-99m DMSA into the interstitial space due to increased capillary permeability in the inflammatory tissue, Tc-99m DMSA complexes being bound to proteins at the site of inflammation, and the structure of Tc-99m DMSA being similar to that of the phosphate ion [14, 15, 24]. All these factors may play a role in its localization in infection. However, more studies are still needed to elucidate the localization mechanisms.

On the basis of our data, both the gallium scan and the DMSA scan are useful in the detection of intra-abdominal infection in patients after colorectal surgery. The DMSA scan has higher specificity, whereas the gallium scan has a higher sensitivity, although no statistical difference was noted between these two methods. Nuclear medicine imaging may be helpful in the following situations where a patient is suspected of having an

infectious source after colorectal surgery: (1) when an abdominal CT scan is negative, but infection is still suspected clinically; (2) no localized signs of abdominal abscess are demonstrated; (3) the possibility of an unexpected infectious source is considered.

Conclusions

The DMSA scan may play a role in the detection of intra-abdominal infection in patients with colorectal surgery because Tc-99m DMSA is not expensive, is easy to prepare, and, most importantly, provides the result within hours.

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