# Diagnostic value of <sup>99m</sup>Tc-HM-PAO leukocyte scintigraphy and computer tomography in patients with sternal wound infections

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# Abstract

METHODS: 99mTc-HM-PAO leukocyte scintigraphy (LS) and computer tomography (CT) were carried out on 19 patients after cardiac surgery; 10 patients with a high clinical probability of an infected sternal wound (group II) and additionally 9 postoperative patients without clinical symptoms of infection, as a control group (group I). LS was carried out with mixed, autologous leukocytes, labelled with 99mTc-HM-PAO in vitro. CT scans were obtained with the use of intravenous contrast material. Findings from the LS of control patients (group I) were as follows: a cold area in the view of the sternum, a «biffed sternum» and a diffuse, increased lung uptake of leukocytes. The CT scans of the control group showed focal oedema, focal haematoma and moderate sternal abnormalities. The CT findings of a welldefined fluid collection in the retrosternal space led to one control patient being classified as having a retrosternal abscess. In the group II, the LS finding of an increased leukocyte uptake and the CT finding of a structural irregularity of the sternum, or of air or fluid collection in the retrosternal space, were taken as signs of infection. In 11 of the 13 cases, the infection was verified clinically: 9 of these proved positive on LS and 8 on CT. LS

Correspondence to: Miklós Papós, Department of Nuclear Medicine, Albert Szent-Györgyi Medical University H-7620 Szeged, Korányi fasor 8, Hungary Tel: (+36 62) 455375, fax: (+36 62) 311170 e-mail: pavicsl@comser.szote.u-szeged.hu was positive in cases with either superficial or deep processes. In all cases, CT revealed whether the infection was limited to the presternal space or whether the sternum and mediastinum were also involved.

CONCLUSIONS: LS and CT are sensitive methods for the early detection of postoperative sternal wound infections. CT is superior for the exact localisation of the process, while specific signs of infection can be differentiated from those of uninfected sternotomy by the use of LS. A combination of LS and CT is suggested in the diagnosis of poststernotomy infection.

Key words: sternotomy, wound infection, 99mTc-HM-PAO leukocyte scintigraphy, CT

# Introduction

Wound infection following sternotomy remains a complication with an incidence of 1–3% (1–3). It may be localised to the superficial soft tissues, to the sternum and/or to the retrosternal spaces. The diagnosis of sternal wound infection can be based on the local symptoms (erythema, purulent drainage, sternal instability), laboratory findings (leukocyte count, erythrocyte sedimentation rate, C-reactive protein, etc.) and chest X-ray examination (4). Imaging methods such as leukocyte scintigraphy (LS) and computer tomography (CT) can also play an important role in the diagnostic strategy. With CT, despite its good morphological resolution, a differentiation between the signs caused by sternotomy alone, and those caused by infection, could be difficult (5). 99mTc-hexamethylpropylene amine oxime (HM-PAO) LS has been described as a useful method for the detection of mediastinitis and osteomyelitis after sternotomy (6). Abnormalities seen on CT and LS may be caused by infection, but may also be a consequence of a normal sternotomy (5, 7, 8, 9). Separate analysis of the signs caused by sternotomy or infected complications therefore appears reasonable.

The aim of this study was to establish the diagnostic value of LS and CT in the detection and localisation of sternal wound infections.

## **Patients and methods**

## Patients

Nine patients (5 males, 4 females, aged 42–67 years, mean: 53.4 years) without clinical symptoms of infection were investigated a mean of 13 days (range: 10–17 days) following the sternotomy (Group I). Six of the patients underwent valve replacement and 3 coronary artery bypass grafting (Table 1).

Thirteen investigations were carried out on 10 patients (8 males, 2 females, aged 42–72 years, mean: 54.6 years) with typical clinical symptoms of sternal wound infection (Group II). Four patients underwent valve replacement and 6 coronary artery bypass grafting. Six studies were made within the first 30 postoperative days, 2 between the 30th and 60th postoperative days, and 2 one year after surgery (Table 2).

The study was performed with the permission of the Local Ethical Committee of the University.

## LS examinations

In vitro leukocyte labelling was achieved by a routine method (10) with some modifications. 60 ml of venous blood was collected in a syringe containing 6 ml of 3.8% sodium citrate and 12 ml of 6%

dextran. After spontaneous sedimentation of the erythrocytes, the supernatant was centrifuged at 100xg for 5 min, and the mixed leukocyte pellet was collected. 99mTc-HM-PAO was performed by adding 1700-2300 MBq 99mTc in 5 ml to HM-PAO (BRAIN-SPECT, OSSSKI, Budapest, Hungary). The mixed leukocytes were resuspended in 1 ml of 99mTc-HM-PAO (340-460 MBq). After incubation of the leukocytes for 10 min at room temperature, the unbound 99mTc-HM-PAO was removed by centrifugation. The label-ling efficacy was measured and the viability of the labelled cells was checked with the trypan blue exclusion test. Images were taken from the chest in the anterior and anterior oblique views 30 min and 2, 4 and 20–24 hours following re-injection of the labelled cells. LS and CT studies were carried out within 48 hours in each case.

## **CT** examinations

All patients were scanned in the supine position with a Siemens Somatom DRG scanner using contiguous 8 mm scans from the level of the manubrium to the diaphragm. Intravenous contrast medium was used routinely (Omnipaque 300, Nycomed).

Three anatomical areas were evaluated:

1. presternal soft tissue (skin integrity, subcutaneous fat planes, the presence or absence of subcutaneous air or fluid collection),

#### Table 1. Scintigraphic and CT findings in patients in Group I (controls)

| Case | Type of surgery | Postoperative<br>time | Scintigraphic<br>findings | CT<br>findings | Diagnosis |  |
|------|-----------------|-----------------------|---------------------------|----------------|-----------|--|
| no.  |                 |                       |                           |                |           |  |
| 1.   | CABG            | 11 days               | Ν                         | Ν              | healed    |  |
| 2.   | VR              | 16 days               | С                         | Ai, E          | healed    |  |
| 3.   | VR              | 12 days               | I, C                      | Ai, E          | healed    |  |
| 4.   | VR              | 13 days               | Ν                         | Ν              | healed    |  |
| 5.   | VR              | 10 days               | I, B                      | A, E           | healed    |  |
| 6.   | VR              | 13 days               | В                         | Ν              | healed    |  |
| 7.   | VR              | 15 days               | Ν                         | Ab, G, E       | healed    |  |
| 8.   | CABG            | 17 days               | Ν                         | G, E           | healed    |  |
| 9.   | CABG            | 14 days               | I, B                      | G, E           | healed    |  |

VR: valve replacement, CABG: coronary artery bypass grafting, N: normal, I: increased lung uptake, C: cold lesion, B: «biffed» sternum, Ai: air, G: sternal midline «gap», E: oedema, Ab: abscess

#### Table 2. Scintigraphic and CT findings in patients in Group II

| Case | Type of surgery | Postoperative<br>time | Scintigraphic<br>findings | CT<br>findings | Bacteriology | Diagnosis |
|------|-----------------|-----------------------|---------------------------|----------------|--------------|-----------|
| no.  |                 |                       |                           |                |              |           |
| 1.   | VR              | 17 days               | I, D                      | М              | +            | М         |
| 1*.  | VR              | 4 months              | С                         | Ν              | not done     | HE        |
| 2.   | VR              | 17 months             | Н                         | М              | +            | OM        |
| 2*.  | VR              | 20 months             | I, H                      | OM             | +            | OM        |
| 3.   | VR              | 20 days               | I, H                      | Μ              | +            | OM        |
| 3*.  | VR              | 2 months              | В                         | E              | not done     | HE        |
| 4.   | CABG            | 28 days               | В, Н                      | E              | +            | SI        |
| 5.   | CABG            | 15 days               | В                         | Ai, E          | +            | SI        |
| 6.   | VR              | 10 days               | Н                         | Μ              | +            | М         |
| 7.   | CABG            | 30 days               | I                         | Μ              | +            | М         |
| 8.   | CABG            | 15 days               | Н                         | Ai, E          | +            | SI        |
| 9.   | CABG            | 5 days                | B, D                      | Μ              | +            | М         |
| 10.  | CABG            | 12 months             | I, H                      | OM             | +            | OM        |

\*: repeated study, VR: valve replacement, CABG: coronary artery bypass grafting, I: increased lung uptake, C: cold lesion, B: «biffed» sternum, D: diffuse leucocyte accumulation, H: hot spot, N: normal, Ai: air, E: edema, M: mediastinitis, OM: osteomyelitis, HE: healed SI: superficial inflammation 2. bony sternum (adequacy of the approximation, the presence or absence of midline «gaps», sternal «step-offs»),

3. retrosternal space (the preservation of soft tissue planes and the presence or absence of air and fluid in the anterior mediastinum).

## Results

## LS, cell labelling

The mean labelling efficacy was 62.2% (range 50–77%) in Group I and 67.2% (range 47–83%) in Group II. The separation and labelling procedure caused no change in the viability of the leukocytes, which was found to be 100% in all cases.

## Group I (controls)

Physiological leukocyte distribution was detected in 4 of the 9 control patients, a decreased leukocyte uptake (cold lesions) in the view of the sternum in 2 cases (Figure 1), and the pattern of a «biffed sternum» in 3 patients. There was a persistent high leukocyte accumulation in the lung in 3 cases. The LS findings of a cold spot in the sternum, a «biffed sternum» and an increased lung uptake of leukocytes were regarded as normal consequences of sternotomy (Table 1). No increased leukocyte uptake in the view of the sternum was found in the control group.

In 3 patients, CT examination revealed no changes. The scans showed air collection in the presternal soft tissue in 3 other patients. The approximation of the sternum was uneven in every patient, but in only 2 cases was the midline «gap» over 2 mm. Anterior mediastinal abnormalities (mild oedema) were present in 6 patients. In one patient on the basis of the CT findings of a welldefined fluid collection in the retrosternal space, abscess was classified; however, this was not supported by either the clinical data or the LS. This result was considered to be false-positive (Table 1).

#### Group II

Infection of the sternal wound was verified by surgical exposure in 10 basic studies and in 1 of the 3 repeated examinations. The diagnosis was superficial wound inflammation in 3, osteomyelitis involving the sternum in 4 and mediastinitis in 4 cases. The culture results were as follows: *Staphylococcus epidermidis* and/or *S. hominis* in 6 cases, *Staphylococcus aureus, Enterobacter cloacae* or *Pseudomonas aeruginosa* in 1 case each, and a mixed infection of *Micrococcus* and *Streptococcus alpha-haemolyticus* in another patient.

An increased leukocyte uptake was found by LS in 9 of the 11 cases with infected complications. The leukocyte accumulation was found circumscribed in 7 cases (Figure 2) and diffuse in 2 patients (Figure 3). The LS patterns of superficial inflammation, osteomyelitis and mediastinitis were similar (although all patients with osteomyelitis had an LS finding of a circumscribed leukocyte accumulation). LS did not permit exact establishment of the extent of the depth of the inflammatory process. Two studies on patients with wound infections proved false-negative. In these cases only LS findings of uninfected sternotomy were detected. LS proved negative in 2 cases without clinical signs of infection (repeated studies) (Table 2).

Normal postoperative CT signs (air collection and oedema) were revealed in 3 out of 11 examinations on 10 patients with

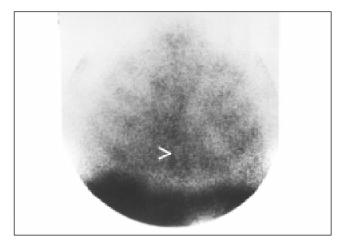


Figure 1. LS of a patient with uncomplicated wound healing. A decreased leukocyte uptake in the view of the sternum (arrow) (patient 2, group I).

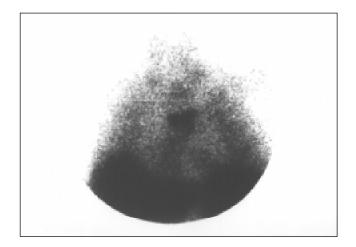


Figure 2. LS of a patient with osteomyelitis following sternotomy. A circumscribed, increased leukocyte accumulation in the view of the sternum, with a diffuse increased lung uptake of the leukocytes (patient 10, group II).

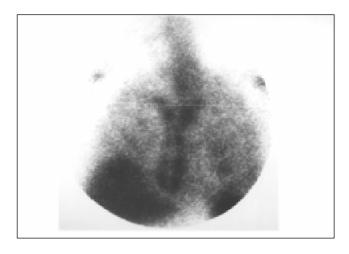


Figure 3. LS of a patient with mediastinitis, as a complication following sternotomy. «Biffed sternum» and diffuse, increased leukocyte accumulation (patient 9, group II).



Figure 4. CT of a patient with wound healing without complication. Widening of the anterior mediastinum and mild oedema, midsternal gap (patient 8, group I).



**Figure 5.** CT of a patient with an infected complication following sternotomy. Irregularity of bone margins and midline «gap» due to osteomyelitis (patient 10, group II).

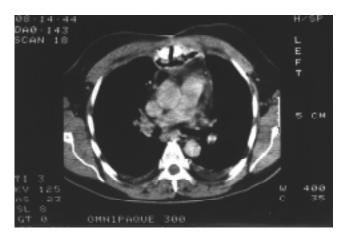


Figure 6. CT of a patient with infected complication following sternotomy. Midsternal gap, well-defined retrosternal fluid and air collection due to mediastinitis (patient 1, group II).

symptoms of poststernotomy wound infection (Figure 4). All of them proved to have a superficial wound infection. Two of the 11 cases were classified as having sternal osteomyelitis (Figure 5), which was confirmed by surgical exposure. In 6 of the 11 cases, CT examination demonstrated infection involving the anterior mediastinum. Surgery revealed either mediastinitis (4 patients) (Figure 6) or osteomyelitis associated with only mild infectious signs in the anterior mediastinum (2 patients) in these 6 cases. CT examination showed normal postoperative changes (normal situation or oedema) in 2 of the 3 repeated examinations following complete recovery (Table 2).

## Discussion

Sternal wound infections can be localised to the superficial soft tissues, or to the sternum, and/or the mediastinum may be also involved (3). Staphylococcus, Enterobacter or Pseudomonas species are the pathogenic agents frequently responsible for the infection (3,11). Typical clinical symptoms, such as erythema, a purulent discharge and sternal instability, are usually apparent in the first or second postoperative week (12,13). A purulent discharge from the wound is the most frequent sign of the infection; this can be detected in 70–90% of the cases (14). The diagnostic value of imaging methods such as CT, bone scintigraphy, 67Ga scintigraphy, or LS has not yet been elucidated. CT has been found to be a useful tool for distinction between wound infection and sternotomy (9). In contrast, Carrol suggested that signs due to sternotomy cannot be distinguished from the signs of infection by means of CT (5). Because of the accumulation of the radiopharmaceutical in scars, neither bone scintigraphy nor 67Ga scintigraphy is a useful method to differentiate between infected complications and normal wound recovery (15,16). HM-PAO LS was found to be a useful method for the detection of mediastinitis and osteomyelitis following sternotomy (6,7).

A decreased leukocyte uptake in cases of fracture, bone necrosis, osteomyelitis or malignant bone lesions has already been observed (17–19). Coronary artery bypass grafting performed with internal mammary artery can cause a decrease in the blood supply of the sternum. This may also be responsible for the decreased uptake of radiopharmaceuticals in the region of the sternum (20). In patients after sternotomy without infection, a persistent diffuse lung uptake of the labelled leukocytes in the late images was found more frequently than usual. Pulmonary leukocyte retention may be due to the activation of leukocytes (21), to damage to the cells during the separation and labelling procedure (22) or to vascular or interstitial injury of the lung tissue (23). Since the viability of the labelled cells checked by trypan blue exclusion test was found to be 100% in all cases in our studies, it is concluded that non-specific activation of the leukocytes may be responsible for the pulmonary leukocyte retention in the control group. This non-specific activation might be due to the interstitial parenchymal injury or some clinically less significant bronchopulmonary inflammation, possibly as a consequence of the routine mechanical ventilation in the early postoperative period.

CT evaluation of the control group indicates that postoperative changes may still be present 2–3 weeks after the operation. The presternal soft tissues return to normal rapidly and air is seldom seen beyond the first week. Smaller defects in sternal closure (midline «gap» or «step-off») are so common that they are of only limited diagnostic value. In most cases, mild oedema or focal fluid collections persist in the anterior mediastinum (8).

In our study in the majority of cases with sternal wound infections, an increased leukocyte accumulation was detected by LS. In agreement with Cooper, only the increased leukocyte uptake can be regarded as a scintigraphic sign of wound infection. In contrast with our findings, Cooper found the LS to be more sensitive (7). Our results, however, agreed with the findings of Oates, based on investigations with 111In LS (24). An increased leukocyte uptake in the view of the lungs was detected in 5 of the patients with clinical signs of infection. This pattern, however, was frequently found in the control group as well. We conclude, therefore, that it cannot be interpreted as a specific sign of infection.

The other very important question is the correct localisation of the inflammatory process. Planar LS imaging, which was applied in the recent study, seems not to be useful for the estimation of the depth of the inflammation. LS combined with SPECT acquisition might be a promising method for increasing the adequate localisation of the inflammation (25). In patients with suspected poststernomy infection, CT examination can accurately reveal the localisation and depth of the infection, and allows an adequate distinction between superficial and deep processes. However, it must be emphasised that postoperative changes in the mediastinum may mimic diffuse mediastinitis or a mediastinal abscess (9).

As normal postoperative changes may overlap significantly with the signs of poststernotomy infection (8), CT scans must be interpreted only in the full knowledge of the clinical symptoms, laboratory findings and abnormalities revealed by other imaging methods.

In conclusion, LS and CT are sensitive methods for the early detection of postoperative sternal wound infection. CT is superior for the exact localisation of the process; while specific signs of infection can be differentiated from those of uninfected sternotomy by the use of LS. A combination of LS and CT is suggested in the diagnosis of poststernotomy infection.

## References

- Grossi EA, Culliford AT, Krieger KH, et al. A survey of 77 major infectious complications of median sternotomy: a review of 7949 consecutive operative procedures. Ann Thorac Surg 1985; 40: 214–223.
- Kohman LJ, Coleman MJ, Parker FB Jr. Bacteremia and sternal infection after coronary artery bypass grafting. Ann Thorac Surg 1985; 40: 214–223.
- Loop FD, Lytle BW, Cosgrove DM. Maxwell Chamberlain memorial paper. Sternal wound complications after isolated coronary artery bypass grafting: early and late mortality, morbidity, cost of care. Ann Thorac Surg 1990; 49: 179–186.
- Carter AR, Sostman HD, Curtis AM, Swett HA. Thoracic alterations after cardiac surgery. AJR 1983; 140: 475–481.
- Carrol CL, Brooke Jeffrey R Jr, Pederle MP, Vernacchia FS. CT evaluation of mediastinal infections. J Comput Assist Tomogr 1987; 11: 449–454.

- Browdie DA, Bernstein RW, Agnew R, Damle A, Fischer M, Balz J. Diagnosis of poststernotomy infection: comparison of three means of assessment. Ann Thorac Surg 1991; 51: 290–292.
- Cooper JA, Elmendorf SL, Teixeira JP, McCandless BK, Foster ED. Diagnosis of sternal wound infection by technetium-99m-leukocyte imaging. J Nucl Med 1992; 33: 59–65.
- Goodman LR, Kay HR, Teplick SK, Mundth ED. Complications of median sternotomy: computed tomographic evaluation. AJR 1983; 141: 225–230.
- Kay HR, Goodman LR, Teplick SK, Mundth ED. Use of computered tomography to assess mediastinal complications after median sternotomy. Ann Thorac Surg 1983; 36: 706–714.
- Danpure HJ, Osman S, Caroll MK. In vitro studies to develop a clinical protocol for radiolabeling mixed leukocytes with 99mTc-HMPAO. Nucl Med Comm 1987; 8: 280 (summary).
- Sarr MG, Gott VL, Townsend TR. Mediastinal infection after cardiac surgery. Ann Thorac Surg 1984; 38: 415–423.
- Jimenez-Martinez M, Arguero-Sanchez R, Perez-Alvarez JJ, Mina-Castaneda. Anterior mediastinitis as a complication of median sternotomy incisions: diagnostic and surgical considerations. Surgery 1970; 67: 929–934.
- Thurer RJ, Bognolo D, Vargas A, Isch JH, Kaiser GA. The management of mediastinal infection following cardiac surgery. J Thorac Cardiovasc Surg 1974; 68: 962–968.
- Hutchinson JE III, Green GE, Mekhjian HA, Kemp HG. Coronary bypass grafting in 376 consecutive patients with three operative deaths. J Thorac Cardiovasc Surg 1974; 67: 7–16.
- Harjula A, Jarvinen A, Matilla S, Porkka L. Experience with single photon emission computerized tomography (SPECT) in follow up of sternotomy healing. Scand J Thor Cardiovasc Surg 1985; 19: 59–62.
- 16. Hoffer P. Gallium and infection. J Nucl Med 1980; 21: 484–488.
- Brown ML, Hauser MF, Aznarez A, Fitzgerald RH. Indium-111 leukocyte imaging the skeletal photopenic lesions. Clin Nucl Med 1986; 11: 611–613.
- Datz FL, Thorne DA. Cause and significance of cold bone defects on indium-111-labeled leukocyte imaging. J Nucl Med 1987; 28: 820–823.
- Mok YP, Carney WH, Fernandez-Ulloa M. Skeletal photopenic lesions in In-111 WBC imaging. J Nucl Med 1984; 25: 1322–1326.
- Petrick SI, Glowniak JV, Hovaguimian H, Gad M. Assessment of sternal viability after sternotomy in patients with and without internal mammary artery bypass. J Nucl Med 1991; 32: 1025 (summary).
- Ussov WYu, Petres AM, Hodgson HJF, Hughes JMB. Quantification of pulmonary uptake of indium-111 labelled granulocytes in inflammatory bowel disease. Eur J Nucl Med 1994; 21: 6–11.
- 22. Peters AM. Granulocyte kinetics and methods of evaluating cell performance. Nucl Med Comm 1988; 9: 687–692.
- Ussov WYu, Peters AM, Savill J, Pusey CD, Gaskin G, Hodgson HJ, Goldman JM, HUGHES JMB. Relationship between granulocyte activation, pulmonary granulocyte kinetics and alveolar permeability in extrapulmonary inflammatory disease. Clin Sci (Chol H) 1996; 91: 329– 335.
- Oates E and Payne DD. Postoperative cardiothoracic infection: diagnostic value of indium-111 white blood cell imaging. Ann Thorac Surg 1994; 58: 1442–1446.
- Bitkover CZ, Gardlund B, Larsson SA, Aberg B, Jacobsson H. Diagnosing sternal wound infection with 99mTc-labeled monoclonal antigranulocyte antibody scintigraphy. Ann Thorac Surg 1996; 62: 1412– 1416.