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Role of Gallium SPECT-CT in the Diagnosis of Left Ventricular Assist Device Infections

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Abstract

Infection remains a well-established complication after the placement of left ventricular assist devices (LVADs). Defining the extent of infection is a challenging task as there are few effective imaging modalities and no standardized guidelines regarding imaging in the diagnosis of device-related infections (DRIs). The use of gallium with single photon emission tomography-computed tomography (Ga-SPECT-CT) has not been previously reported in localizing DRIs. We reviewed the charts and images of five patients with LVADs who underwent Ga-SPECT-CT for the diagnosis of various types of DRIs. Gallium SPECT-CT further clarified the extent of infections among LVAD patients, allowing for patient-specific tailored treatments including surgical debridement. Gallium SPECT-CT is a useful tool when diagnosing LVAD infections and could potentially be the imaging modality of choice in the near future. With improved imaging studies, such as Ga-SPECT-CT, allowing for earlier and more accurate diagnoses of DRIs, the outcome of such infections is likely to improve.

Keywords

gallium; LVAD; infection

Left ventricular assist devices (LVADs) have become the standard treatment for the management of end-stage heart failure either as a bridge to cardiac transplantation or as long-term mechanical circulatory support when patients are not suitable transplant candidates. Despite the success of this therapy in extending survival and improving patients' quality of life, infection is the primary cause of morbidity limiting the long-term success of this technology.

Infectious complications in recipients of LVAD technologies can be ventricular assist device (VAD) specific or VAD related. The former includes pump, cannula, pocket, and percutaneous driveline infections, which can be limited to the exit site or burrow deeper into the driveline tunnel. Ventricular assist device–related infections include infective endocarditis, blood stream infections, mediastinitis, and sternal wound infections.^{1–6}

There are few effective imaging modalities and no standardized guidelines for the use of imaging studies in the diagnosis of LVAD-associated infections. Computed axial tomography (CT) is limited by artifact from the device itself, and magnetic resonance imaging is contraindicated due to the metallic components that comprise the LVAD. Ultrasonography, while useful in detecting fluid collections around the LVAD pump (which resides in a preperitoneal pocket that separates the device from the abdomen), cannot definitively ascertain the presence of infection. Alternatively, nuclear medicine studies appear to be a viable option for localizing and determining the extent of a device-related infection (DRI). To the best of our knowledge, the role of gallium single photon emission tomography (Ga-SPECT)-CT has not been studied in localizing infections among LVAD recipients. The purpose of this review was to highlight nuclear medical imaging using gallium as a useful tool in determining the extent of LVAD infections.

Materials and Methods

Gallium-67 SPECT-CT imaging was performed on five patients with LVADs with suspected DRIs between July 2008 and May 2012. These specific patients were chosen as they all had LVAD infections that were not responding to conventional antibiotic therapy, and further diagnostics were necessary to localize the extent of their infections. All patients had a HeartMate II LVAD, which has an inflow cannula inserted into the left ventricular apex and an outflow graft inserted into the ascending aorta. A percutaneous driveline, attached to an external power source, tunnels under the skin of the right lower abdomen and connects to the pump internally. Electronic medical records were retrospectively reviewed for microbiological data and Ga-67 SPECT-CT imaging. This study qualified for exemption by the institutional review board at Montefiore Medical Center.

The average assist device support time was 774 days. All patients were referred for Ga-67 SPECT-CT imaging if a DRI was suspected or to monitor response to antimicrobial therapy. Two patients underwent additional Ga-67 SPECT-CT imaging for suspicion of new infection and to assess the response to therapy. Three hundred to 370 MBq of Ga-67 citrate was injected to the patient. Whole body and SPECT-CT imaging was performed 48 hours later. Medium-energy collimation, energy window, acquisition time settings (30 s per projection for SPECT), and matrix size (64 × 64) were adjusted to Ga-67 imaging characteristics. Single photon emission tomography-CT data were processed with the Volumetric for Hawkeye version 1.0 software on a Xeleris workstation (GE Healthcare, Marlborough, MA). For slice reconstruction, an ordered-subset expectation maximization algorithm was used, with two iterations and 10 subsets, followed by three-dimensional filtering (Butterworth, order 10, 0.35 frequency cutoff). Attenuation correction was performed by means of CT-acquired transmission maps. During the time interval represented in this case series, SPECT software was updated from Pegasys (ADAC Laboratories, Milpitas, CA) to HERMES

(Hermes Medical Solutions, Stockholm, Sweden). The latter allows greater postacquisition image manipulation and facilitates compilation with diagnostic CT scans for enhanced spatial resolution.

Results

Case 1

A 75-year-old man underwent LVAD placement in December 2009. His postoperative course was complicated by gastrointestinal bleeding requiring exploratory laparotomy with subsequent ligation of vessels and placement of a gastrostomy tube. Approximately 18 months after LVAD placement, the patient began to have purulent drainage from the driveline exit site. Wound cultures from the exit site grew *Serratia*, *Klebsiella*, and *Enterobacter*. The patient underwent a CT abdomen/ pelvis, which demonstrated thickening along the tract of the driveline in the subcutaneous tissues where it exits the right anterior abdominal wall. He was treated with a brief course of intravenous antimicrobials followed by oral therapy. One month after the drainage began, the patient was readmitted with renal failure and persistent drainage from the driveline exit site. Cultures from the wound continued to grow *Serratia*. Due to persistent drainage from the exit site, Ga-67 SPECT-CT was performed to determine the extent of infection he was not responding to conventional therapy. Anterior whole body image and SPECT-CT fusion images were obtained. Figure 1A showed a focal area of intense radiotracer activity overlying the right abdomen corresponding to skin contamination on the SPECT-CT images consistent with a superficial driveline infection (Figure 1B and C). The patient continued on antibiotic therapy and had some improvement in amount of drainage. Two months later, he was noted to have increasing drainage at the driveline exit site and was treated with another course of antibiotics. Wound cultures from the exit site continued to grow *Serratia*. He then underwent another CT, which revealed no collection around the LVAD. The patient continued to have drainage with *Serratia* growing from the wound the following month and continued on antimicrobial therapy. He underwent another gallium, without SPECT-CT, to further establish the extent of infection as the drainage was persistent and not responding to various antibiotic regimens. The images were consistent with extension of the prior infection of the LVAD as demonstrated by linear uptake in the right abdominal wall (Figure 2). The patient never developed bacteremia and remained clinically stable, and it was decided no surgical intervention be done at this time. Three months after the second gallium study that showed infection extension, the patient was readmitted to the hospital with fever and increasing drainage from the driveline exit site. Cultures from the wound now demonstrated emergence of drug-resistant organisms. The patient's antibiotic regimen was again broadened. Once clinically stable, the patient was discharged home to continue a lifelong antibiotic course as he refused surgical intervention. Finally, after nearly a year of LVAD infection, the patient was admitted with altered mental status and fungemia. He underwent an additional gallium study that was consistent with more extensive infection compared with prior studies 6 months earlier (Figure 3). The images demonstrated uptake along the entire length of the driveline to the point of entry of the LVAD. An LVAD exchange was offered to the patient, yet he refused and expired within 3 weeks. There was no postmortem performed.

Case 2

A 43-year-old man underwent LVAD placement in July 2008. He developed purulent, methicillin-resistant *Staphylococcus aureus* (MRSA)-positive, drainage from the driveline exit site approximately 5 months after device placement. His blood cultures were also positive for MRSA at that time. Gallium-67 SPECT-CT imaging was obtained shortly thereafter, with a clinical suspicion for deep driveline infection and subsequent LVAD endocarditis. Gallium-67 SPECT-CT imaging demonstrated activity adjacent to the heart, tracking across the abdomen and into the thoracic cavity. This was interpreted to represent an infection of the LVAD, driveline and outflow tract, respectively. A planar whole body anterior image demonstrates tracer activity along the driveline (Figure 4A). Fused SPECT-CT transaxial and coronal images confirm tracer concentration in the site of the driveline and the LVAD (Figure 4B and C, respectively). The patient underwent LVAD exchange 13 days after Ga-67 SPECT-CT imaging, at which time LVAD endocarditis was definitively diagnosed and intraoperative cultures from the pump were positive for MRSA. Left ventricular assist device endocarditis is defined as the isolation of the same microorganism from more than one blood culture and histopathologic evidence of infection involving the inflow/ outflow conduits or the porcine valves at the time of transplantation or autopsy.⁶ The patient continued antimicrobial therapy after exchange; however, he had adherence issues. He subsequently developed abdominal pain and leukocytosis, which prompted a repeat Ga-SPECT-CT 7 months later. Imaging showed no active signs of infection, and patient remained clinically stable, on antibiotics, without any further intervention as of July 2012.

Case 3

A 45-year-old man underwent LVAD placement in March 2010. Five months after device placement, the patient developed drainage from the driveline exit site. Wound cultures from the site were polymicrobial, growing *Klebsiella*, *Stenotrophomonas*, and MRSA. Despite a prolonged course of antimicrobials, the patient had persistent purulent drainage from driveline exit site and ultimately developed septicemia with MRSA. He underwent Ga-67 SPECT-CT imaging later that month to determine the extent of infection. A planar whole body anterior image demonstrated uptake in the right anterior upper quadrant representing an infected driveline. In addition, there was uptake noted in the midsternal region that was thought to be secondary to prior sternotomy (Figure 5A). Fused Ga-67 SPECTCT imaging demonstrates increased radiotracer uptake along the driveline and sternal uptake as well. In addition, there is uptake noted in the left chest that may represent infection in the LVAD (Figure 5B and C). The patient was diagnosed with a polymicrobial deep driveline infection and MRSA septicemia. Due to the findings on gallium and the patients deteriorating clinical status, he underwent debridement of the driveline and was maintained on broad antimicrobial coverage with clinical improvement. Four months after the initial Ga-67 SPECT-CT imaging, the patient returned to the hospital with recurrent septicemia and was found to have *Klebsiella pneumoniae* and MRSA growing from blood cultures. Left ventricular assist device endocarditis secondary to a deep driveline infection was suspected due to persistent fevers and bacteremia, despite antibiotic therapy. Repeat Ga-67 SPECT-CT imaging demonstrated improvement in the previously seen infectious foci; however, residual infection remained in both the driveline and the LVAD (Figure 6). The patient eventually underwent LVAD exchange for persistent DRI and was diagnosed with LVAD endocarditis

and pocket infection, with intraoperative device cultures positive for MRSA. The patient improved clinically after device exchange and was discharged on suppressive antibiotic therapy, ultimately receiving cardiac transplantation.

Cases 4 and 5

Two additional patients underwent Ga-67 SPECT-CT imaging for localization of LVAD infection and were found to have negative results, as demonstrated by a lack of increased radiotracer activity. Case 4 was a 44-year-old man with MRSA bacteremia who underwent Ga-67 SPECT-CT imaging to determine the extent of infection. This patient had a negative scan, allowing physicians to treat the patient with a limited course of antibiotics for a presumed endovascular infection and eliminated the concern for a DRI. Case 5 was a 60-year-old man who underwent a Ga-67 SPECT-CT for increased drainage from driveline exit site and a concern for a deep driveline infection. Images were negative for infection. Clinical follow-up of both patients supported the negative findings of Ga-67 SPECT-CT imaging.

Discussion

Nuclear medicine imaging is a promising modality to confirm the presence and extent of DRIs. The use of nuclear imaging in the diagnosis of LVAD infections was first described in a case of a 57-year-old man with a Novacor (Rueil-Malmaison Cedex, France) N100 portable LVAD with recurrent fevers and MRSA septicemia. Several investigations, not described in detail, failed to determine the exact focus of infection. The patient eventually underwent immunoscintigraphy, with Tc-99m-labeled anti-NCA 95 antigranulocyte antibodies, and a suspected focus was found on the outflow tract of the LVAD. The patient subsequently underwent an exchange of the valves of both the in- and outflow tracts. Postoperative microscopic findings revealed gram-positive bacteria on the outflow graft valve, which confirmed the diagnosis of LVAD endocarditis.⁷ Roman *et al.*⁸ later described the use of indium-111 WBC whole body and SPECT scintigraphy to identify an infected retained driveline in a patient following heart transplant with persistent fever. More recently, Litzler *et al.*⁹ described several cases in which leukocyte SPECT-CT led to an accurate diagnosis of DRI, establishing both the anatomic location and the extent of infection.

Gallium-67, an analog of ferric iron (Fe^{3+}), was first noted in 1971 to accumulate in sites of inflammation. Gallium-67 is primarily bound to the circulating iron-binding proteins transferrin and lactoferrin. Ga-67 transferrin is delivered to sites of increased capillary permeability and blood flow, whereas B-cells take up Ga-67 lactoferrin into intracytoplasmic granules, which are released at the site of infection. In addition, bacterial and fungal organisms may bind Ga-67 directly *via* iron-scavenging proteins, which allows for the diagnosis of infection in neutropenic patients.^{10,11}

Today, Ga-67 imaging is used in the evaluation of several potentially infectious conditions, including fever of unknown origin, fever in an immunosuppressed host, suspected vertebral osteomyelitis, chronic osteomyelitis, and various pulmonary infections, specifically *Pneumocystis jiroveci* pneumonia. Gallium-67 imaging is also very useful for imaging chronic infections in patients receiving prolonged antibiotics courses. With the addition of fused SPECT-CT imaging, a significantly higher specificity can be attained compared with

that achieved with the individual modalities in the diagnosis of acute infections.^{11–14} Our institution uses Ga-67 with SPECT-CT, specifically, as this method of nuclear imaging is commonly used in cases of chronic infection and chronic causes of fever of unknown origin (FUO). Infections among LVAD recipients often become chronic as the device itself is a large surface area susceptible to biofilm formation.

There appear to be no overt contraindications to using gallium citrate. It has been occasionally associated with allergic reactions and adverse events including skin rash and nausea. The safety and efficacy has not been established in the pediatric population.¹⁴

The potential advantages of using nuclear imaging studies to diagnose DRIs are significant. In particular, patients with bacteremia or FUO, those with recurrent bacteremia after successful antibiotic therapy, and those with percutaneous site infections that fail to heal with antibiotic and local wound therapies are practical clinical scenarios where Ga-67 SPECT-CT imaging can be a useful diagnostic tool. Localizing an infection to a specific part of the LVAD has allowed for tailored treatment. In addition, localizing subcutaneous infections would likely require shorter courses of antibiotics compared with deeper infections that may require surgical drainage or ultimately lead to device exchange for infection.

Wickline and Fischer¹⁵ described possible difficulties when using Ga-67 imaging to aid in the diagnosis of LVAD infections. They noted that few data exist regarding sensitivity and specificity for imaging infection in implanted cardiac devices and report concern regarding the inflammatory process that commonly accompanies wound healing causing false results. It was also noted that the physiologic appearance in blood, bones, bowel, and other organs can obfuscate the diagnosis. Other disadvantages to the utilization of Ga-67 are that it may interfere with bowel and renal activity, as well as delayed imaging times of 24–48 hours.¹⁴

The use of Ga-67 SPECT-CT imaging has not been previously reported in localizing infection in LVAD recipients. Our institution has not used nuclear medicine imaging modalities aside from Ga-67 SPECT-CT in the diagnosis of LVAD infection. We demonstrated several instances in which Ga-67 SPECT-CT imaging was used to determine the extent of infection and suggest that Ga-67 SPECT-CT imaging is a useful tool in the diagnosis of LVAD infections. Among the cases described, Ga-67 SPECT-CT imaging was instrumental in determining the extent of infection, allowing tailored drug and surgical management when appropriate. Two patients underwent LVAD exchange as a result of Ga-67 SPECT-CT imaging, which demonstrated involvement of the pump itself, signifying a deep-seated infection unlikely to respond to antimicrobial therapy alone. One patient was found to have only a superficial driveline infection when a deep driveline infection was suspected; this prevented the patient from undergoing an unnecessary device exchange. With improved imaging studies, such as Ga-67 SPECT-CT imaging, allowing for earlier and more accurate diagnoses, the outcome of LVAD-related infections is likely to improve.

Although our experience, as reflected in this small case series, is limited, we recommend the implementation of nuclear medicine techniques, notably Ga-SPECT-CT, when patients with LVAD infection are not responding to appropriate antimicrobials as expected, as well as

when accessing response to therapy. We suggest using nuclear medicine imaging modalities when managing complicated infections among LVAD recipients as current conventional methods are fraught with tremendous limitations in this patient population.

Conclusions

Ga-SPECT-CT is a useful noninvasive tool for diagnosing LVAD infections and delineating their extent. This imaging modality can allow for earlier detection of such infections and lead to more prompt initiation of the appropriate management measures, leading to improved clinical outcomes.

Moreover, it can be used to assess for response to therapy. It remains unclear if Ga-SPECT-CT is superior to other nuclear imaging modalities in the diagnosis of LVAD infections. Future research should be dedicated to this clinical query.

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Figure 1. Planar whole body anterior image shows a focal area of intense radiotracer activity overlying the right abdomen (A). This activity corresponds to skin contamination on the single photon emission tomography images, which is consistent with a superficial driveline infection (B and C).

Figure 2.

The planar whole body anterior image shows tracer activity along the driveline (A). Fused single photon emission tomography-computed tomography transaxial and coronal images confirm tracer concentration in the site of the driveline and the left ventricular assist device (B and C).

Figure 3.

Planar whole body anterior image shows more extensive driveline infection than seen on prior study (A). Fused single photon emission tomography-computed tomography transaxial (B) and coronal (C) images confirm tracer concentration uptake along the driveline and along the entire course of the driveline to the point of entry of the left ventricular assist device.

Figure 4.

A planar whole body anterior image demonstrates a curvilinear uptake anteriorly in the right upper quadrant. This uptake represents an infected driveline, whereas the uptake in anterior midline was likely related to prior median sternotomy (**A**). Fused single photon emission tomography-computed tomography transaxial and coronal images confirm tracer concentration along the driveline (**B and C**).

Figure 5.

Planar whole body anterior image demonstrates uptake in the right upper quadrant representing an infected driveline (A). Fused single photon emission tomography-computed tomography transaxial (B) and coronal (C) images confirm tracer concentration in the site of the driveline in the right upper quadrant. Uptake in the midsternal region may be secondary to prior median sternotomy. There is also uptake demonstrated in the lower left chest, which may be consistent with extension of driveline infection to include the left ventricular assist device.

Figure 6.

Partial improvement in the previously seen infectious foci along the driveline; however, residual focus of infection has progressed toward the left ventricular assist device in the left lower chest on whole body planar image (A). Corresponding fused single photon emission tomography-computed tomography transaxial (B) and coronal (C) images demonstrate increased activity specifically along the deep driveline.