The time for radionuclide ventriculography resurrection is coming

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Left ventricular ejection fraction (LVEF) is the most widely used and easily available index of LV function. Almost all patients with suspected or documented heart disease undergo LVEF assessment at some point. There are nowadays, many different, invasive and non-invasive techniques for measuring LVEF including contrast ventriculography, echocardiography, magnetic resonance imaging (MR), computed tomography angiography (CT), and nuclear techniques. The nuclear techniques include the equilibrium radionuclide angiography (ERNA) referred to also as multigated angiography (MUGA), first-pass radionuclide ventriculography, gated single-photon computed tomography (SPECT) with myocardial perfusion imaging, and SPECT ERNA.

Until the 1970s, the most commonly employed method of determining LV volumes and EF was LV contrast angiography performed at the time of cardiac catheterization. In 1971, Strauss et al¹ described a new revolutionary “scintiphotographic method for measuring LVEF in man without cardiac catheterization.” As reported by Ashburn et al in the Seminars in Nuclear Medicine in 1973,² this procedure made it possible to have multiple determinations of LVEF and volumes without additional administrations of radioactivity, allowing acquisition in different projections to evaluate wall motion of the various surfaces of the heart. Our

knowledge of the physiological changes of LV function during exercise was enhanced from the application of ERNA. The introduction of computers further improved the potential widespread use of this technique,³ preparing the grounds for semi-automated measurement of LV function. It is of historical interest to know that these results were obtained by acquiring data on 12 K, 16 bits minicomputer system, recorded on magnetic tape and transferred them to a “large-scale digital computer as powerful as 200 k, 32 bits”!

In 1977, Borer et al⁴ demonstrated the feasibility of continuous monitoring and analysis of LV function during exercise allowing an accurate assessment of the presence and functional severity of ischemic heart disease. Global and regional dysfunction during exercise could easily be documented by ERNA. Specific features of ERNA were count- based measurement of LVEF independent from geometrical assumption and high reproducibility.

Van Royen et al⁵ compared side by side echocardiographic and quantitative radionuclide LVEF: their conclusion was that LVEF determined by ERNA and echocardiography showed good agreement. Both methods provided clinically valuable measurements of LV function. However, when a precision was required for reproducible measurements, ERNA was the method of choice.

Checking on PubMed with the following search terms, “radionuclide ventriculography,” “Radionuclide angiography,” “ERNA,” “MUGA,” “scintigraphic angiocardiology,” “radionuclide cineangiography,” “scintiphotographic,” “gated scintiphotography,” “radio isotopic angiocardiology,” “radionuclide angiocardiology,” or “ejection fraction,” we found 2591 published papers on this topic. The use of ERNA reached its highest peak in the decade 1985-1995 (Figure 1), with a slow but progressive decline since.

The main reason for this decline is most likely the emergence of reliable competing modalities including

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Figure 1. MedLine check of peer reviewed paper on equilibrium radionuclide angiography published in the last five decades.

MR, echocardiography, and gated SPECT with myocardial perfusion tracers. The present day application of ERNA is limited mainly to monitoring LV performance during chemotherapy or when the quality of images by other methods is suboptimal or could not be performed or when there is discordance between clinical judgement and imaging results. Many drugs, including anthracycline, alkylating agents, tyrosine kinase inhibitors, monoclonal antibodies, anti-metabolites, anti-microtubule agent, monoclonal antibodies, and drugs like interferon or bleomycin may affect LV function and require accurate LV function assessment during treatment.

The spectrum of cardiotoxicity may be associated with dysrhythmias, hypertension, pulmonary hypertension, right ventricular dysfunction, vasospasm, acute cardiac event, and heart failure (HF). Patients with a baseline LVEF $\geq 50\%$ and a drop of EF $\geq 10\%$ during chemotherapy and a final EF below 50% are at risk of HF, while patients with a baseline EF of 30-50% and a drop below 30% are at the highest risk of HF.

These patients should discontinue chemotherapy with doxorubicin and its analogs. For these reasons, a systematic follow-up is required with EF determination every 4-8 weeks.⁶

Thus, considering the number of patients undergoing chemotherapy, how can we explain the decline in the use of ERNA in clinical practice when it has been clearly demonstrated to be useful for serial monitoring?⁷

There are several possible reasons to explain this circumstance: (1) planar imaging is limited by the overlap of different cardiac structures (right and left ventricle in the anterior projection, left ventricle and left atrium in the “best septal” view) affecting the calculation of LVEF, especially in the presence of mitral regurgitation, (2) The valvular function cannot be explored, (3) The volumes of heart chambers are only roughly determined, and (4) The radiation exposure and using the currently administered dose (740 MBq).

We should keep in mind that oncology patients are evaluated systematically by CT and PET/CT and/or other Nuclear Medicine procedures, and as recently pointed out by Rehani⁸, the individual patient dose received through diagnostic imaging may exceed an effective dose of 100 mSv. It is well known from the Hiroshima bomb observations that there is a linear relationship between exposure and incidence of cancer for an effective dose exceeding 50 mSv. The effective dose from 740 MBq of ^{99m}Tc—albumin or ^{99m}Tc—labeled red blood cells is 5.18 mSv according to ICRP publication 80.⁹ The question is: is it justified to administer 740 MBq of radiolabeled red blood cells, with an additional 5.18 mSv for each evaluation of LV function to such patients when other methods with no risk for exposure to ionizing radiations are currently available?

In this issue of the Journal of Nuclear Cardiology®, Duvall et al¹⁰ showed that due to improved count sensitivity with the high-efficiency SPECT, a 50% reduction in injected activity is achievable while maintaining a short imaging times of 5 minutes, with further reduction possible at longer imaging times. It is therefore conceivable to hypothesize that an effective dose below 1 mSv per study is achievable and hence less than 5-6 mSv for LV function monitoring during entire treatment course of cancer patients.

Gated blood pool SPECT angiography is a mature methodology and is well validated by a large body of literature as reported in the bibliography cited in the Duvall paper. The measurements of left and right ventricular EF are not affected by the overlap of different cardiac chambers and it can be corrected for attenuation and for scatter. All manufactures provide acquisition and processing protocols with resolution recovery for gated SPECT allowing the acquisition with half the administered activity for traditional dual headed SPECT.

The high quality of CZT SPECT can further improve the quality of gated blood pool SPECT. The accuracy of gated MPI-SPECT has been documented in comparison to MR^{11,12} but not yet for gated blood pool SPECT by CZT cameras. A comparison between MR and CZT gated blood pool ventriculography for measuring right and left ventricular EF and volumes will be an important next step.

Disclosure

The authors have no conflict of interest nothing to disclose.

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