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EDITORIAL
Thallium-201-Chloride for the Detection of Viable Myocardium

Although thallium-201-chloride has been widely used for the detection of myocardial ischemia/infarction, the utilization of this agent for the definition of viable myocardium is a more recent, and somewhat controversial, application. That thallium uptake might serve as a clinical marker of viability is perhaps not surprising—this monovalent cation is dependent upon the Na^+-K^+ ATPase system to achieve myocardial accumulation (*1–3*). Previous studies using the fetal mouse heart organ culture model have demonstrated that thallium uptake is reduced only when irreversible cell injury has occurred (*2,4*). At a more practical level, the "coupling" of myocardial perfusion and contraction in most clinical circumstances would in fact predict that regional thallium uptake is indicative of regional myocardial viability.

Initially applied in patients using a "dual-injection" technique, the work of Pohost and colleagues at the Massachusetts General Hospital (*5*) defined the practice of "stress-redistribution" thallium imaging, an approach that became the convention for coronary artery disease (CAD) detection. While it has become accepted that the presence of thallium redistribution is indicative of myocardial viability, it has become equally clear that a "fixed" thallium perfusion abnormality is not invariably predictive of the presence of myocardial "scar." Of particular relevance are those studies that have demonstrated resolution of such apparently "fixed" defects after coronary angioplasty or bypass surgery (*6,7*) and those that have documented preserved "metabolic function" in myocardial segments

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with "fixed" perfusion defects (*8–10*).

Whereas thallium uptake immediately after injection primarily reflects regional blood flow, the determinants of thallium redistribution are more complex. It has been proposed that both differential thallium clearance from ischemic versus nonischemic zones and continued thallium uptake in initially hypoperfused zones contribute to this phenomenon (*11–15*). Budinger et al. have proposed mathematical models to describe redistribution that emphasize the contribution of blood flow, available tracer concentration, and washout/clearance rates (*16,17*). In essence, these models suggest that thallium redistribution reflects available tracer concentration during the postexercise period, and that "relative available activity" changes over time ("endogenous reinjection").

A number of investigators have proposed modifications of conventional stress redistribution imaging protocols that take advantage of the above determinants of thallium redistribution. Specifically, 8–24-hr delayed redistribution imaging (*18–21*) and rest reinjection techniques (*22–24*) have been applied to clarify the true "persistence" of thallium perfusion abnormalities. With respect to reinjection, it should be emphasized that such images reflect both redistribution kinetics and the status of regional blood flow at the time of the second injection. Editorial comments regarding these approaches have appeared in recent months (*25–27*).

In this issue of the *Journal*, Perlmutter and colleagues describe the use of ribose infusion in the course of conventional myocardial perfusion imaging to "facilitate" thallium redistribution (*28*). This clinical study derives from previous work by this group in an experimental occlusion-reflow model which suggested that intravenous ribose infusion enhanced thallium clearance from normally perfused as compared to ischemic myocardial regions (*29*). It was also observed that this differential clearance resulted from "a non-flow dependent metabolic effect of ribose on monovalent cation kinetics."

The present study reports the results of a placebo-controlled crossover trial of ribose infusion in a group of 17 patients with known (n = 14) or clinically suspected (n = 3) CAD. Ribose was administered over 30 min immediately following acquisition of initial, postexercise planar thallium images. Repeat imaging was performed at 1 and 4 hr after initial thallium injection. Images were analyzed using quantitative circumferential profile analysis. Coronary angiography and biplane left ventriculography were performed in a subset of 14 patients. Regional wall motion and regional perfusion were subsequently correlated. It should be emphasized that each patient underwent the serial exercise thallium studies while receiving medical therapy for clinically stable ischemic heart disease.

The major findings of the study are summarized as follows:

1. Ribose infusion was associated with an approximate 2-fold enhancement of detection of reversible perfusion abnormalities when compared to post-saline control thallium images.
2. This apparent "facilitation" of thallium redistribution was observed in 13 of 17 patients. In addition, 7 of 13 patients who had quantitative coronary angiographic analysis had at least one additional myocardial region identified as ischemic/viable after ribose imaging.
3. In the 54 regions with reversible thallium defects and available wall motion data, 50 had evidence of "viability" as manifested by intact wall motion.
4. No significant differences in whole blood thallium activity were observed between the ribose and saline studies.
5. Thallium clearance was accelerated at both 1 and 4 hr following ribose infusion in normally perfused as compared to ischemic myocardial regions.

Thus, findings 1–3 re-emphasize the limitations of conventional delayed thallium imaging for the delineation of ischemic, viable myocardium; findings 4 and 5 suggest that ribose infusion, by means of a differential effect upon thallium clearance from ischemic versus normally perfused myocardium, provides an alternative mechanism to circumvent the above limitations.

While the study is intriguing from an observational vantage point, several issues regarding these data merit comment. First, the data presented in Figure 3 do not corroborate the authors' claim that 75 "reversible" defects were detected in these 17 patients. For example, Figure 3B assigns a total of 62 reversible defects at 4 hr. Does this imply that 13 of the reversible defects at 1 hr become "fixed" at 4 hr? If so, what is the potential explanation and significance of this finding? Furthermore, this figure does not provide information describing the number of normally perfused regions in these patients. Presumably, these normal regions are included in the "saline-negative, ribose-negative" assignment category.

Second, it is of interest that of the "reversible" defects identified in this patient group only 25 (Fig. 5B) were observed in the 13-patient catheterization subset in coronary vascular territories subtended by vessels with ≥50% epicardial stenosis. This suggests that the majority of reversible defects were observed in patients with non-critical CAD. It is also surprising that detection of reversible defects appeared to be facilitated most typically in the left circumflex vascular distribution. This territorial preference would not be pre-

dicted on the basis of the mechanism proposed by the investigators.

Third, it bears emphasizing that the data reported in the present study derives from a group of patients with symptomatically stable CAD and a low incidence (4 of 17) of prior infarction. In fact, it is perhaps surprising that perfusion abnormalities were detected with such frequency in a population of patients with relatively mild coronary disease. It might have been helpful to provide the raw quantitative data, in some form, upon which segmental assignment (RD+ versus RD−) was based. In addition, because a number of reversible defects appear to have been detected in vascular territories supplied by vessels with non-critical disease, it would be of interest to study the effects of ribose infusion on thallium kinetics in patients free of CAD.

Fourth, I would concur with the authors' contention that this preliminary study should perhaps be repeated and compared to alternative imaging protocols such as delayed redistribution, rest reinjection, and perhaps "infusion scintigraphy" as recently described by Burns et al. (*30*). Furthermore, with respect to "viability" detection, the presence of preserved regional systolic function, as detected in the vast majority of segments with redistribution in this population, would presumably preclude the need to perform additional imaging. It would be of interest to assess the utility of ribose infusion in patients with regional akinesis/dyskinesis and fixed thallium defects on conventional delayed images.

Thus, the data presented by Perlmutter and colleagues reemphasize the limitations of conventional thallium imaging vis-a-vis detection of myocardial "viability"—specifically, conventional 4-hr images failed to detect redistribution in approximately 40% of myocardial regions in this group of patients. Because the ribose infusion technique would preserve the single-injection/dual-image protocol, this approach might well enhance the role of thallium-201-chloride in the evaluation of complex CAD patients. Although comparative studies utilizing previously described modifications of thallium imaging are lacking, this technique may provide an alternate means by which the kinetics of myocardial thallium redistribution could be "manipulated" to optimize detection of viable myocardium.

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SELF-STUDY TEST

Pulmonary Nuclear Medicine

Questions are taken from the *Nuclear Medicine Self-Study Program I*, published by The Society of Nuclear Medicine

DIRECTIONS

The following items consist of a heading followed by lettered options related to that heading. Select the one lettered option that is best for each item. Answers may be found on page 318.

1. A 45-year-old white housewife with a 40 pack-year smoking history presents with progressive shortness of breath and an 8-pound weight loss. She denies febrile episodes, frequent respiratory infections, or excessive sputum production, but she has a dry cough. Her husband is bisexual. Clinical and laboratory examinations reveal cervical and inguinal lymphadenopathy and liver function abnormalities. Her ^{67}Ga scintigram is shown in Figure 1. Which *one* of the following is the most likely diagnosis?

A. bronchogenic carcinoma with lymph node metastases
B. Hodgkin's lymphoma
C. acquired immunodeficiency syndrome with *Pneumocystis carinii* pneumonia
D. sarcoidosis
E. hypersensitivity pneumonitis

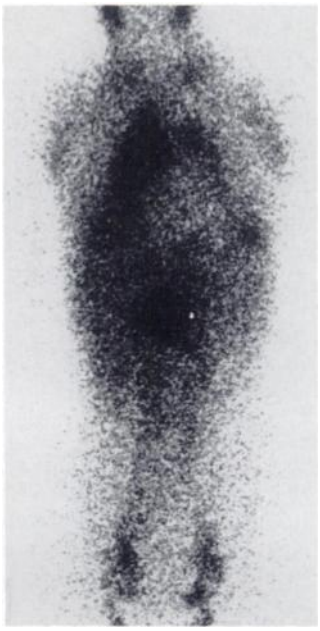

Figure 1

2. Which *one* of the following properties of a radioaerosol is *least* important in determining its rate of clearance from the lung?

A. solubility
B. lipophilicity
C. droplet size
D. pulmonary blood flow rate
E. alveolar-capillary membrane permeability