Imaging

Thallium Lung-to-Heart Quantification: Three Methods of Evaluation

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Lung-to-heart quantification, when used in conjunction with visual assessment of 201 TI stress test images, has been found useful in diagnosing cardiac dysfunction. We evaluated three methods of quantification in terms of inter- and intraobserver variability and reproducibility. Fifty anterior 201 Tl stress images were quantified by each of the following methods: Method A (sum region), which involved one region of interest (ROI) in the measurement of pulmonary activity relative to that of the myocardium; Method B (count density), which required two ROIs, the lung-to-heart ratio being dependent on count density; and Method C (maximum pixel), which used the gray scale of the computer to determine the most intense pixels in the lung field and myocardium. Statistical evaluation has shown that the three methods assess clinical data equally well. Method C was found to be most reproducible in terms of inter- and intraobserver variability (p = 0.0016 and 0.0083), followed by Methods A (p = 0.0026 and 0.0129) and B (p = 0.0038 and 0.0135). Although nearly equivalent in terms of statistics, the three methods possess inherent differences and therefore should not be used interchangeably without conversion factors.

Thallium-201 stress test imaging is useful in detecting coronary artery disease (CAD); as an adjunct to this examination, the lung-to-heart ratio provides additional knowledge of cardiac function. Previous studies suggest that increased pulmonary ²⁰¹Tl activity immediately after stress correlates with an increase in CAD (*I*). Furthermore, the lungto-heart ratio is held to be very specific for advanced CAD because increased activity appears to be a function of increased pulmonary capillary wedge pressures, reflecting development of transient, exercise-induced left ventricular failure (2). Given the clinical significance of the lung-to-heart ratio, we have evaluated three methods of quantification in terms of interand intraobserver variability and reproducibility.

MATERIALS AND METHODS

Patient Studies

Fifty patients underwent ²⁰¹Tl stress test imaging. The pro-

tocol included insertion of an i.v. catheter to facilitate ²⁰¹Tl injection and establishment of a baseline 12-lead electrocardiogram. Treadmill exercise (Bruce protocol) (3) was then initiated with continuous monitoring of blood pressure and heart rate. Patients were encouraged to exercise until the development of 2 mm or more of horizontal or downsloping ST segment depression (4). Thallium-201 (2.5–3.0 mCi) was intravenously injected at peak stress, and the patient was exercised an additional 30–60 sec to ensure optimal myocardial uptake of the radionuclide. Imaging commenced within 5 min of termination of exercise with patients supine in the anterior, 45° left anterior oblique, 70° left anterior oblique, and left lateral positions; images were collected for a maximum of 10 min. Redistribution studies were conducted at 3-hr intervals, in the same positions for the same time interval.

Instrumentation and Technique

Image data were collected by a mobile scintillation camera interfaced to a computer.* The camera was peaked on the 60–80 keV mercury x-ray peak of ²⁰¹Tl at a 20% window. A low energy, all-purpose parallel-hole collimator was employed in all studies. Image data were collected in a 64 \times 64 matrix and transferred to a disk.

The anterior stress image was the preferred image for determination of lung-to-heart ratio to yield the best representation of the lung field for the most accurate measurement of ²⁰¹Tl uptake by the lung. Calculations were performed by two independent observers, subjecting each of the 50 anterior thallium images to three different methods of lung-to-heart quantification. One observer repeated the calculations for purposes of defining the intraobserver variability. Lung ²⁰¹Tl activity was expressed as a percentage of the maximal myocardial counts for each image (5). The methods employed were as follows:

Method A: Designated as the "sum region," the observer drew a region of interest (ROI) over the area of myocardium visually qualified as containing the most counts, the anterolateral, inferior, or apical segment. The ROI was then moved to the area of lung also thought to con-

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tain the most activity. The number of counts in each region was then determined; the pulmonary activity divided by the myocardial activity yielded the lung-to-heart ratio.

- Method B: Rather than creating one ROI to serve both the myocardial and the pulmonary regions, Method B, "count density," required the setting of individual ROIs over the myocardium and the lung. The myocardial ROI contained 5-10 pixels, and the pulmonary ROI contained 50-100 pixels. Furthermore, the pulmonary ROI was to be located in the left lung field superior to and separated by a minimum of 5 pixels from the anterolateral wall of the myocardium (I). Primary in this approach is the density of each ROI, an expression of the mean counts per pixel (readily obtained by the computer). The pulmonary density divided by the myocardial density provided the lung-to-heart ratio.
- Method C: The "maximum pixel" method used the 64-shade gray scale featured on the computer. The baseline (lower limit) was set to zero. The upper limit, which controls the displayed images' scale, was decreased until all myocardial pixels reached saturation (maximal intensity). The baseline was then gradually increased until the last lung pixel had just disappeared. At this time, the baseline was equal to either the maximum myocardial pixel or the place at which the last myocardial pixel had just disappeared. The pulmonaryto-myocardial ratio was determined by dividing the counts within the maximum lung pixel by those within the maximum myocardial pixel (5).

RESULTS

Initially, the range of lung-to-heart ratios derived by each method was expressed in terms of a mean \pm standard deviation. Data were subsequently applied to a two-way analysis of variance, specifically, the estimated variance of a proportion test (Fisher test).

Examination of values produced by each method indicated characteristic ranges. With relative consistency, Method B produced the lowest values, ranging from 0.25-0.59 (mean = 0.38). Method A produced mid-range values, from 0.26-0.66 (mean = 0.41), and Method C produced the highest values, ranging from 0.30-0.63 (mean = 0.42) (Table 1).

Interobserver Variability

In comparing the results obtained by each of the two observers using each method, Method C offered the greatest reproducibility (SD = 0.66), Method A showed slightly diminished reproducibility (SD = 1.25), and Method B offered the least

TABLE 1.	Characteristic	Ratios and	Variations
	of Method	Values	

	Mean L/H Ratio %			± S.D. %	
	Observer 1	Observer 2, Trial 1	Observer 2, Trial 2	Inter- observer	Intra- observer
Method A	42.76	40.98	40.49	1.25	1.9
Method B	39.28	37.15	38.41	1.50	1.1
Method C	42.88	41.95	43.19	0.66	0.88

reproducibility (SD = 1.50). Further analysis by the Fisher test essentially confirmed the comparable worth of Methods A, B, and C (p = 0.0026, 0.0038, and 0.0016, respectively).

Intraobserver Variability

Results obtained by one observer on two separate occasions concurred with previous results. Method C was the most reliable (SD = 0.88), Method A was slightly less reliable (SD = 0.9), and Method B was the least reliable (SD = 1.1). The analysis of variance showed Method C (maximum pixel) to vary the least, followed by Methods A and B (p = 0.0083, 0.0129, and 0.0135, respectively).

DISCUSSION

Pulmonary accumulation of 201 Tl is, to a certain degree, an inescapable phenomenon, because the pulmonary extraction fraction of thallium during the initial transit is normally ~ 9% (4). Increased pulmonary capillary wedge pressures resulting from left ventricular dysfunction have been associated with increased pulmonary uptake of thallium, reflected by an elevated lung-to-heart ratio.

Three methods of determining pulmonary-to-myocardial activity were evaluated in terms of inter- and intraobserver variability and reproducibility. Method A followed a single ROI protocol, Method B required the setting of individual ROIs over the myocardium and the lung field, and Method C used the maximum pixel count, identified using the 64-shade gray scale of the computer. Quantification, regardless of the chosen method, resulted in markedly similar outcomes. The differences were statistically negligible.

In reviewing each method, however, subtle distinctions were revealed. Method B yielded relatively lower lung-to-heart ratios than Methods A or C. This can be traced to the averaging of activity within a given ROI, which encompasses pixels of decreased activity surrounding pixels of increased activity.

Method C consistently produced values that fell into a slightly higher range than those produced in Methods A or B, both of which used ROIs. This may be related to the asymmetric configuration of the lung compared with the myocardium. An ROI includes activity over a range of lung thicknesses and represents an average activity, which will necessarily be less than the activity of the maximum pixel (4).

Method A yielded results that fell between the higher and lower lung-to-heart ratios of Methods B and C. Reproducibility was shown to be greatest in Method C. Potential for difference (as a function of observer technique in addition to marginal computer variation) decreased with the elimination of observer contribution (i.e., the setting of ROIs). We currently use Method A in our department.

CONCLUSION

The evidence collected in this study affirms the comparable value of these three methods. Furthermore, each method is equally effective in measuring the same clinical data. Given the assessability of the lung-to-heart ratio and the evidence suggested by Boucher et al. (5), which recognizes the significance of the lung-to-heart ratio in the diagnostic process, it may be advisable for departments engaging in ²⁰¹Tl stress testing to incorporate the lung-to-heart ratio as a routine procedure. It is important to note, however, that these three methods cannot be applied interchangeably without conversion factors; therefore, a single method should be used on a regular basis for purposes of maintaining reproducibility.

FOOTNOTE

*Technicare Inc., Solon, OH.

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