EDWARD G. M. D'HAENE
CORNELIS STERK
HERMAN FINTELMAN
Gemeenteziekenhuis
Dordrecht, Netherlands

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Reply

The letter by D'haene and associates raises several important points concerning our recent article "Radionuclide Techniques for Valvular Regurgitant Index" and we would like to respond (*1*).

We are in complete agreement with D'haene et al. that the visual assessment of the intensity of the regurgitant stream and the degree of opacification of the recipient chamber as a measure of the amount of regurgitation is "subjective and semiquantitative." We are well aware of the limitations of this technique as listed in the references cited by these authors and others (*2,3*). However, we would seriously question whether the findings at surgery or at postmortem can be considered physiological either! The authors advocate the use of a "quantitative" assessment of valvular regurgitation, i.e., the difference between total (angiographic) and net forward (Fick or green dye) measurements of cardiac output. Although this approach is theoretically attractive, it is not without its own pitfalls: net forward output can usually be measured accurately but measurement of the angiographically determined output may at times be seriously in error due to (a) ventricular geometry that bears no resemblance to a prolate ellipsoid, (b) use of a single-plane rather than biplane radiographic system, (c) depressed ventricular function and the need to measure small changes in large ventricles, and (d) errors in calculation of the degree of magnification of the image. Thus, designating this approach as "quantitative" may be a little euphemistic. In this regard, it is worth noting that Nichols et al. found considerable variability between both of the above mentioned techniques and the degree of aortic regurgitation as assessed with a catheter tip velocity transducer, which in turn has its own limitations (*3*). In short, there is no "gold" (or even "silver) standard that is consistently accurate. We routinely calculated the regurgitant flow by the angiographic minus Fick/green dye method in our patients. However, we felt that this technique offered no advantage over the "semiquantitative" visual assessment of regurgitation in our patients, in whom one out of three had a markedly depressed left-ventricular ejection fraction.

We agree that, ideally, patients with aortic regurgitation should have been separated from those with mitral regurgitation. Unfortunately, this would have resulted in a large number of small subgroups. However, patients with atrial fibrillation were deliberately excluded from our study in order to eliminate this variable as a source of error.

D'haene and associates correctly point out that Method 2 in our study is not identical to that described by Sorenson et al. (*4*), although it is conceptually similar to their approach. The best method of assessing the regurgitant fraction should theoretically be one using separate regions of interest for end diastole and end systole. This should provide the most accurate assessment of the stroke-volume counts. However, no currently available method, including those with semiautomated edge-detection programs, reliably separates the right ventricle from the right atrium. Therefore, it is a fairly common practice to use either the "stroke-volume image" or a fixed region of interest at end diastole to calculate a regurgitant fraction, despite the known limitation of this technique.

We believe that use of a single end-systolic frame to determine left- and right-ventricular counts is a justifiable approximation in view of the other technical limitations that exist.

We agree with D'haene et al. that different attenuation coefficients for the left and right ventricles (due to breast tissue, localized pericardial effusion, anatomical position, etc.) are a major factor likely to limit the accuracy with which the regurgitant fraction can be obtained using any radionuclide technique. Several different approaches have been developed recently to determine the influence of attenuation in the estimation of left-ventricular volumes. In time, it may well be feasible to include data concerning the regurgitant fraction in reports of radionuclide ventriculography. However, it is our opinion that at the present time, the indiscriminate reporting of such information without adequate caveats concerning the limitations of the technique may result in more confusion than clarity. It remains to be demonstrated convincingly that the present methods of assessing valvular regurgitation by radionuclide ventriculography provide substantially more useful

information concerning the individual patient than a thorough physical examination combined with a noninvasive assessment of left-ventricular ejection fraction.

PASCAL NICOD
JAMES R. CORBETT
BRIAN G. FIRTH
GREGORY J. DEHMER
CARLOS IZQUIERDO
ROY V. MARKHAM
L. DAVID HILLIS
JAMES T. WILLERSON
SAMUEL E. LEWIS
University of Texas Health Science Center
Dallas, Texas

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TABLE 1. RATIOS OF FEMUR-TO-SOFT TISSUE (MEAN ± s.d.), AT 2 hr AFTER INJECTION IN NORMAL SUBJECTS AND IN PATIENTS WITH MALIGNANCIES

	N	Normals	Patients	N
MDP*	57	1.638 ± 0.279	1.756 ± 0.317	128
		n.s.	$p < 0.005$	
HMDP†	66	1.627 ± 0.207	1.655 ± 0.221	142
		$p < 0.005$	$p < 0.005$	
DPD‡	26	1.825 ± 0.385	1.885 ± 0.336	177

* MDP = methylene diphosphonate.
† HMDP = hydroxymethylene diphosphonate.
‡ DPD = dicarboxypropane diphosphonate.

Comparison of Tc-99m MDP, HMDP, and DPD with Respect to Bone-to-Soft Tissue Ratios

To close the gap between comparative studies, either open by design (*1-5*) or by number of patients (*1-3,5,6*), we would like to introduce some results illustrated in Tables 1 and 2. This study was designed to complete the comparison of bone imaging with Tc-99m dicarboxypropane diphosphonate (DPD) and Tc-99m methylene diphosphonate (MDP), published in 1982 (*4*), by including Tc-99m hydroxymethylene diphosponate (HMDP). Accordingly, selection of patients, methods, and aims were identical (*4*). Incubation time of Tc-99m in the diphosphonate vials was 45 min in all cases. HMDP was prepared from commercial kits.*

The results comparing the bone-to-soft tissue ratios showed that HMDP was very close to MDP and that differences between the three agents were very small (Tables 1, 2)—in particular the ratio between os sacrum (cancellous bone) and femoral soft tissue (Table 2). Moreover, as with MDP and DPD, HMDP revealed identical trends: ratios in patients were higher than in normals (this difference was most pronounced with MDP, Table 1) and sacrum-to-femoral soft-tissue ratios decreased with patient's age. Image contrast in patients without skeletal lesions was still the highest with DPD (Tables 1, 2). However, intra-individual comparison in patients with skeletal lesions revealed changes in this ranking (*6*).

Comparative intra-individual studies are bound to include a small number of patients due to ethical reasons. Therefore, small changes in preparation, selection, evaluation, and sequence of choice of agents may play a more important role than in the large number of patients included in inter-individual studies (596 patients in Table 1). On the other hand, it is more effective to compare uptake in lesions than in normal bone. To solve these problems created by an increasing number of bone-seeking diphosphonates similar in action but different in structure, more work is needed to explain the differences in biokinetics at the target, rather than solely to describe them.

TABLE 2. RATIOS OF SACRUM-TO-SOFT TISSUE (MEAN ± s.d.), AT 2 hr AFTER INJECTION, IN NORMALS AND IN PATIENTS WITH MALIGNANCIES

Years of age	N	DPD	Normals	HMDP	N	MDP
20 – 30	7	8.16 ± 3.25	13	7.04 ± 2.35	8	7.53 ± 1.94
40 – 49	6	6.63 ± 2.49	17	6.86 ± 2.03	11	5.93 ± 1.49
50 – 59	8	6.02 ± 1.11	10	5.33 ± 1.76	19	5.68 ± 1.47
60 – 69	5	5.02 ± 0.71	14	5.75 ± 1.62	10	4.78 ± 1.28
>70	—		12	4.61 ± 1.14	8	3.79 ± 1.14
			Patients			
20 – 39	30	7.16 ± 2.10	25	7.71 ± 2.40	11	6.62 ± 2.10
40 – 49	41	7.09 ± 2.27	33	6.56 ± 1.63	26	6.66 ± 1.98
50 – 59	40	6.36 ± 2.00	33	6.23 ± 1.42	33	5.80 ± 1.63
60 – 69	33	5.40 ± 1.56	32	5.18 ± 1.51	41	5.56 ± 1.88
>70	33	5.28 ± 1.36	19	4.82 ± 1.19	17	4.86 ± 1.00