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Radionuclide Techniques for Valvular Regurgitant Index

We have read with much interest the article by Nicod et al. (*1*) and the accompanying Teaching Editorial (*2*). We started our study of valvular disease 4 years ago and are glad that the general interest in this topic is growing. Nevertheless, we would like to make some comments regarding the methods and results of Nicod et al. (*1*).

1. These authors compared their results with cineaortography (CAG), a technique considered as subjective and semiquantitative. Although it is a widely accepted and applied method, in our view it cannot serve as a "gold standard" or true reference technique. The method is invasive and nonphysiological, and relies on the assumptions that there is uniform mixing of the indicator or contrast material and that the forward flow remains undisturbed (*3*). It is hard to see that these assumptions are fulfilled after injection of, e.g., 50 ml of contrast material within 1 to 2 sec at a place 3 to 4 cm above the aortic valve. It is very doubtful whether there is, in reality, an arithmetical linear relationship between the amount of regurgitated blood and the subjective classification criteria 0 to 4+.

Several authors have discussed the discrepancies that could be found between CAG estimates of regurgitation and surgical or postmortem findings (*3–6*). Baron (*7*) stressed the possibility of false-positive findings caused by faulty catheter placement or ventricular extrasystoles.

Although all of these methods have their own specific problems in clinical practice, we advocate, as a "gold standard", the combination of quantitative angiography and dye-dilution or Fick-based methods to measure, respectively, total and forward stroke volume. A useful, perhaps "silver standard" could be the combination of quantitative angiography and thermodilution. In the recent literature the method using stroke-count ratio (SCR) was compared with a combination of angiography and Fick/dye dilution (*8*), angiography and Fick (*9*), angiography and thermodilution (*10,11*). Acceptable correlation-coefficients of 0.85, 0.81, 0.75 and 0.95, respectively, could be found. We therefore regret that Nicod et al. (*1*) used for evaluation a debatable, suboptimal reference technique such as CAG.

2. We regret also that the authors did not treat patients with aortic insufficiency (AI) and with mitral insufficiency (MI) as separate groups. In our opinion, the technical difficulties are clearly different in these two categories. The quantification of isolated chronic AI seems to be the easiest and most straightforward. In a large percentage of MI patients, atrial fibrillation is present and ECG gating in these cases is unreliable, degrading estimates of the SCR. These enlarged left atria (LA) can be difficult to separate from the left ventricle (LV) and may lie partially behind the right ventricle (RV). In our hands, Fourier phase-amplitude analysis in these cases can give estimates of LA size that are unreliable compared with those derived from echocardiography. It may be impossible to correct the LV counts for these atrial contributions. In MI patients it can also be difficult to exclude involvement of the right heart with minor or moderate tricuspid insufficiency.

We agree with Sorenson et al. (*8*) that an experienced observer can differentiate visually between dominating AI or MI by inspection of the direction of the LV long axis. Nicod and colleagues (*1*) did not comment on this, or on the ECG gating problems encountered in patients with atrial fibrillation.

3. The authors correctly stated that the biggest problem in the SCR method remains the accurate and precise definition of the end systolic (ES) or end diastolic (ED) regions of interest (ROI) of the RV. As long as there are no well-evaluated automatic techniques available for the RV, comparable with the numerous and widespread edge-finding programs for the LV ROI, the SC of the RV has to be estimated by a subjective, operative-dependent method. The authors compared three methods of assessing the SCR: a first one with fixed ED ROI for each ventricle; a second with variable ROI for RV and LV, and a third using a stroke-volume image. They incorrectly regarded the second method as the same as Sorenson's (*8*), who made use, however, as we do, of a semiautomated edge-finding program, for LV ED, LV ES, and background estimation, instead of the fully manual method of Nicod for both ventricles and background. Another difference is that Sorenson determined separately for each ventricle the nadir in the volume curve to get the ES frames. The third method based on stroke-count images assumes that systole in RV and LV is always synchronous. Aside from this, there is another argument against the use of stroke-volume images as well as fixed ED ROI, not mentioned by Nicod: during contraction the heart can actually move out of the ROI to a certain extent, due to superposition of rotational, translational, and respiratory movements. These movements are highly patient-dependent and seem to influence mostly the right heart in an unpredictable, variable way. This point is also mentioned by Manyari (*9*) against the single-ROI method.

4. It is rather easy to imagine that the SCR may be inaccurate with a low EF, since in that case both ED and ES counts are high, and the subtraction of two large numbers will result in a small and inaccurate difference. This effect is most prominent in patients with poor contractile function of both ventricles.

5. A final problem requiring discussion is that the SCR method assumes equal counting efficiency for the two ventricles and for systole and diastole. This may cause trouble if there is an unevenly distributed absorber between ventricles and collimator, for example, the female breasts. In patients with exudative pericarditis there can be an asymmetric fluid distribution in the pericardial space, especially in the supine position. Also unclear is the question of the influence of various degrees of LV and/or RV hypertrophy on estimates of SCR. We performed a study in a young male professional football player and calculated a RF value of −0.50 or a L/R SCR of 0.67. The RV ROIs were very easy to trace in this case. In our series, this was the only patient with a result pointing to moderate-to-severe valvular dysfunction in the right heart. Further examinations excluded any valve disease or an intracardiac shunt as a cause. We feel that the LV SC must have been underestimated because of high photon absorption in the very hypertrophic LV wall.

Finally, we should like to cite Pierson et al. (*13*): "All currently applied cardiovascular nuclear medicine measurements discard more information than they capture." In our opinion this is still true for the present situation. We feel it is the moral duty of nuclear medicine (and radiology) to extract maximum information from a study for a given exposure to radiation. In the case of gated blood-pool scintigraphy this means that it is imperative to try to get more parameters, not only the EF, from a given study. In this context we also strongly advocate the routine use of first-pass angiography in combination with GBP. With visual inspection this may serve as a rough and independent control of the SCR estimate, besides giving information about global anatomy.

In this context, the approach recently described by Glass et al. (*14*) seems to be rewarding. They also used a combination of first-pass angiography and GBP, calculating the forward EF of the LV by first-pass angiography and deconvolution analysis, and total EF by GBP, to get the regurgitant fraction from these two EF values. In this way all mentioned problems with the definition of the RV can be circumvented, making this a very attractive alternative.

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