

EDITORIAL POINT OF VIEW

Cardiac Amyloidosis, Should We See It from the Side or the Front?

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Received: July 16, 2024/Revised manuscript received: August 26, 2024/Accepted: August 26, 2024

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Ann Nucl Cardiol 2024; 10 (1): 4–5

See related articles, pp.23–28 and pp.29–37

If a small decision could critically change the course of the rest of someone's life, what would you do?

Recent studies have revealed that cardiac amyloidosis (CA) is not rare but rather prevalent among the elderly. Two pivotal articles have illuminated this disease as relatively easy to diagnose using well-established imaging techniques, such as bone scintigraphy (1, 2). One notable article by Bokhari demonstrated exceptionally high sensitivity and specificity through semiquantitative measurement using the heart-to-contralateral lung (H/CL) ratio on planar imaging (2). Bokhari's primary findings indicate almost perfect accuracy, potentially leading to widespread acknowledgment of the utility of bone scintigraphy (excluding technetium 99m methylene diphosphonate: $^{99m}\text{Tc-MDP}$) in diagnosing CA. However, as with many quantitative methods in the medical field, subsequent research has shown that the H/CL ratio is not perfect.

H/CL was initially reported by Bokhari, whose first article demonstrated remarkable accuracy. However, subsequent reports showed a decline of accuracy in H/CL, similar to many other proposed quantitative parameters in medical fields. Recent findings suggest that H/CL offers no incremental value over well-executed visual diagnosis. The problem with H/CL are twofold: reliance on planar imaging and using the contralateral lung as the standard (denominator). Why is the contralateral lung used as the denominator for H/CL?

When creating parameters to evaluate abnormal tissue uptake of a tracer, normal tissue that exhibits minimal uptake is typically used as the denominator. For instance, iodine 123 metaiodobenzylguanidine ($^{123}\text{I-MIBG}$) uses the mediastinum as the denominator because it generally shows very low $^{123}\text{I-MIBG}$ uptake. This method has rendered the heart-to-

mediastinum (H/M) ratio a reliable parameter in nuclear cardiology, including in the diagnosis of amyloidosis (3). However, for technetium 99m pyrophosphate ($^{99m}\text{Tc-PYP}$) imaging, using the mediastinum on planar image as the denominator poses a significant problem due to sternal uptake visible on the frontal planar image. This necessitates the use of the contralateral lung as the denominator. However, is the lung scientifically appropriate as a denominator? The answer is likely no, for several reasons. Firstly, contralateral lung activity measured on the frontal planar view may be contaminated by rib uptake. Methodologically, the region of interest (ROI) on the contralateral lung is mirrored from the ROI over the heart. Theoretically, contamination by rib uptake should equally affect both the heart and contralateral lung ROIs, thus minimally impacting the ratio. However, this symmetric contamination is not always achieved. Secondly, using the contralateral lung as the denominator fails to mitigate the influence of high blood pool activity in the heart chambers, a common cause of false-positive results in $^{99m}\text{Tc-PYP}$ imaging (4). If both the denominator and numerator include blood pool activity equally, their effects cancel each other out, minimizing its impact on the parameter. This cancellation effect is not expected when using the lungs as the denominator. Therefore, using the mediastinum, which contains blood pools in large vessels, is considered as a better choice. Thirdly, the lungs may exhibit tracer accumulation. It is well-documented that not only the myocardium but also soft tissues can show amyloid deposition and tracer accumulation (5). Amyloid deposits are also known to occur in lung tissue (6).

To minimize these errors, it is advisable to select the mediastinum as the denominator. One potential solution is to utilize single photon emission computed tomography (SPECT) imaging instead of planar imaging to obtain the mediastinal

DOI: 10.17996/anc.24-00004

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uptake (7). However, incorporating SPECT imaging into busy daily practice can be challenging due to its complexity and time requirements. Another study proposed using the heart-to-mediastinum ratio measured on a very early (15 minutes post-injection) planar image, reporting 100% sensitivity and specificity (8). However, it remains questionable whether a 15-minute incubation period is adequate for achieving optimal tracer accumulation in the myocardium.

In this issue, two articles introduced new and straightforward parameters (9, 10). Coincidentally, both articles recommend the use of lateral planar images. Utilizing this lateral H/M value as a substitute for the H/CL value may be an excellent approach. As noted by the authors, including the aorta in the ROI placed on the mediastinum ensures that both the heart and mediastinum ROIs contain the blood pool, thereby eliminating errors caused by blood pool activity.

The two studies conducted H/M analysis based on the same concept, resulting in some similarities and discrepancies. Hara et al. analyzed 93 patients and using only cases classified as grade 2 or 3 on the frontal planar image, examined the elimination of false positive cases using lateral H/M value (9). Patients classified as grade 0 or 1, typically considered negative in many guidelines, were excluded from their analysis. In other words, Hara et al. focused on avoiding false positives and demonstrated excellent performance in this regard. Saito et al. emphasized accuracy and constructing a precise diagnostic tree. In Saito's study, 116 patients who were classified as grade 0 or 1 in the frontal view, were included in the analysis (10). Thus, Saito and colleagues addressed both false negatives and false positives. The difference between the two studies may be attributed to their differing perspectives.

Despite these differences, both studies successfully demonstrated that incorporating a single lateral planar imaging can yield significant clinical benefits. Considering that planar imaging requires only about one-third to one-fourth the time of SPECT imaging, the addition of an extra lateral planar imaging is particularly noteworthy for its substantial clinical value. Although their results and conclusions differ slightly, the clinical importance of both studies remains equally significant. If a small decision such as acquiring the image from the lateral side or not make change the course of the rest of patients life, what would you do?

See it from the side.

Acknowledgments

None.

Sources of funding

None.

Conflicts of interest

None.

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