Echocardiography with Ultrasound Enhancement Agents and the Diagnostic Challenge of Cardiac Masses: Solid Evidence for a Complex Clinical Problem

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Short editorial referring to the article: Diagnostic Performance Of Contrast-Enhanced Echocardiography In Differentiating Cardiac Masses: A Systematic Review And Meta-analysis

The proper characterization of intracardiac masses continues to be one of the most relevant challenges in contemporary cardiovascular imaging. Thrombi, benign tumors, and malignant neoplasms share some similar morphological characteristics in conventional echocardiography, but they entail radically different approaches, prognoses, and therapeutic urgencies. Despite significant advances in cardiovascular imaging diagnostic techniques, critical decisions, such as whether to anticoagulate or operate, investigate or observe, treat urgently or monitor, are still frequently challenging in clinical practice. Echocardiography, although indispensable as an initial method, often fails to differentiate thrombi, benign tumors, and malignant neoplasms in a significant number of patients.[1] Given this scenario, it is legitimate to question: why does echocardiography with ultrasound enhancing agents (UEAs), available for decades, still play a secondary role in many diagnostic algorithms?

The meta-analysis, "Diagnostic performance of contrast-enhanced echocardiography in differentiating cardiac masses", presents important arguments for this context. Using methodological rigor, aligned with PRISMA-DTA and Cochrane Handbook recommendations,[2,3] the authors demonstrate that echocardiography with UEAs has shown exceptional diagnostic performance in two of the most critical dilemmas in clinical practice: differentiating tumors from thrombi and distinguishing benign from malignant tumors.

The results presented are impressive. Echocardiography with UEAs has demonstrated combined sensitivity and specificity of 100% in differentiating between tumors and thrombi, with an AUC close to 1.0. This finding is pathophysiologically consistent, since thrombi are avascular structures, while tumors — whether benign or malignant — have some degree of perfusion detectable by intravascular microbubbles.[4,5] This functional distinction gives echocardiography with UEAs a clear diagnostic advantage over conventional echocardiography, especially in clinical situations in which the decision between anticoagulation and invasive investigation needs to be made quickly and safely.

Even more relevant is the performance of echocardiography with UEAs in differentiating between benign and malignant tumors. The meta-analysis demonstrated a sensitivity of 94.3% and a specificity of 96.1%, with an AUC of 0.976, indicating high discriminatory capacity. These results reinforce previous observations that perfusion patterns, such as intense hyperperfusion, rapid filling, and perfusion heterogeneity, are heavily associated with malignancy.[6,7] Thus, echocardiography with UEAs transcends the merely morphological role and consolidates itself as a functional tool for tissue characterization, a role traditionally reserved for cardiac magnetic resonance imaging.

Given these data, another important question arises: Why do we continue to systematically refer patients to more expensive, less accessible, and often unavailable methods in a timely manner, before fully exploring the potential of echocardiography with UEAs? The answer seems to lie less in scientific evidence and more in cultural, logistical, and training barriers. Echocardiography with UEAs is still underused, often restricted to centers of excellence, despite its excellent safety profile, wide availability, and the possibility of being performed even at bedside in unstable patients or those with contraindications to more complex methods.[5,7]

However, some limitations deserve to be highlighted. The small number of studies included (five prospective cohorts, totaling 381 patients) reflects the scarcity of primary data suitable for diagnostic meta-analyses in this area. In addition, the QUADAS-2 assessment identified methodological concerns in some studies, particularly related to patient selection and the time flow between the index test and the reference standard. These factors limit the unrestricted generalization of the results and reinforce the need for more robust studies, with standardized protocols and greater population diversity.

Despite the significant increase in diagnostic accuracy provided by contrast-enhanced echocardiography in this scenario, the technique presents some pitfalls that require attention when used for this specific purpose. Recent thrombi, although avascular, may show some degree of enhancement with contrast, usually restricted to the periphery of the mass. In the study by Li et al., among the 36 patients diagnosed with thrombi, three showed marked enhancement, all corresponding to recent thrombi.[8] This pattern can make differentiation from cardiac tumors difficult; however, it is important to emphasize that tumors, especially malignant ones, tend to show diffusely

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increased perfusion, involving both the central and peripheral regions of the mass, which helps in diagnostic distinction.

Nevertheless, the findings of this meta-analysis represent an important step in consolidating echocardiography with UEAs as a core method in the evaluation of cardiac masses. The consistency of the findings, the biological plausibility, and the magnitude of the observed effects indicate a solid scientific basis for expanding the use of contrast-enhanced echocardiography in the diagnostic workflow of routine practice. In a scenario where quick and accurate decisions directly impact clinical outcomes, underusing an accessible, safe, and highly accurate method is unreasonable.

In conclusion, the evidence presented in this study reinforces that echocardiography with UEAs not only represents a complementary technique, but also a strategic, accessible tool with high clinical impact. In a scenario where quick and accurate decisions are fundamental, establishing echocardiography with UEAs in the diagnostic algorithms for intracardiac masses, seems not only reasonable, but also necessary.

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