

# Usefulness and Cost-Effectiveness of Universal Echocardiographic Contrast to Detect Left Ventricular Thrombus in Patients with Heart Failure and Reduced Ejection Fraction

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**Contrast is a recommended but frequently unused tool in transthoracic echocardiography to improve detection of left ventricular thrombus in patients with ejection fraction (EF)  $\leq 35\%$ . The clinical and economic outcomes of a possible solution (i.e., universal contrast use) remain uncertain. To estimate clinical benefit, cost, and cost-effectiveness of a diagnostic strategy of universal use of contrast (vs no contrast) during echocardiography in patients with reduced EF, we created a decision analytic model using echocardiography sensitivity and specificity for left ventricular thrombus detection from a meta-analysis, as well as survival and cost estimates from published literature. Universal contrast use (vs nonuse) did not result in clinical or statistical improvement in estimated life years (8.509 vs 8.504) or quality-adjusted life years (5.620 vs 5.616). The cost of contrast was offset by reductions in subsequent health-care costs, resulting in similar total costs (\$201,569 vs \$201,573). In conclusion, although an intuitively attractive practice improvement strategy, universal contrast use strategy appears to offer no appreciable benefit to quality-adjusted survival or financial outcomes in patients with low EF. © 2018 Published by Elsevier Inc. (Am J Cardiol 2018;■■■:■■■-■■■)**

A substantial proportion of patients referred for a resting echocardiogram have technically difficult studies with sub-optimal visualization of endomyocardial borders,<sup>1</sup> which restrict the accurate assessment of segmental wall motion, ejection fraction (EF), and the presence or absence of left ventricular thrombus (LVT). In a patient population with poorly visualized endomyocardial borders or with low EF, both studies

and guidelines support the routine use of contrast to improve diagnostic accuracy<sup>2-5</sup> to reduce the possibility of missing actionable findings or indicating false-positive results. Accurate detection or exclusion of LVT guides the anticoagulation of affected patients, thereby lowering their risk of stroke and systemic embolization if LVT is present, or avoiding the hazards of unnecessary anticoagulation if LVT is absent.<sup>6,7</sup> We performed a decision analysis to evaluate the benefits, cost, and cost-effectiveness of a possible guideline or laboratory-based policy change to recommend the routine addition of contrast (vs no contrast) in clinically indicated echocardiography for the sentinel assessment of LVT in patients with severely reduced EF ( $\leq 35\%$ ).

## Methods

A decision model was developed to compare the diagnostic strategies of echocardiography with and without contrast in a patient cohort with a mean age of 60 years, as well as the presence of heart failure, reduced EF, and sinus rhythm (Figure 1). For each diagnostic strategy and LVT status, the clinical and economic consequences of positive and negative echocardiography results were modeled using a Markov process (Supplementary Figure 1). Each Markov node contained 9 disease states, with disease and age-dependent transitions among states occurring in monthly cycles over 30 years (Supplementary Table 1). The cohort began in the heart failure state with EF  $\leq 35\%$ , from which transitions could be made to ischemic stroke, bleed, systemic embolism, or death states. Nonfatal major bleeds and systemic embolisms transitioned to the chronic heart failure state. Nonfatal ischemic and hemorrhagic strokes transitioned to poststroke states (either disabled or nondisabled) until transition to death. In

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See page •• for disclosure information.

All authors have been involved in the study design, analysis, and manuscript revision. All authors read and approved the final manuscript. Dr. Douglas is the guarantor who accepts full responsibility for the work and the conduct of the study, had access to the data, and controlled the decision to publish. Dr. Douglas takes responsibility for the integrity of the data and the accuracy of the data analysis. Dr. Douglas contributed to the conception and design of the study, the supervision, data acquisition, analysis, and interpretation, the manuscript drafting, and the critical revision of the manuscript. Dr. Lehman contributed to the conception and design of the study, the data analysis, the data interpretation, the manuscript drafting, and the critical revision of the manuscript. Drs. Cowper, Randolph, Kosinski, and Lopes contributed to the data analysis, the data interpretation, the manuscript drafting, and the critical revision of the manuscript.

**Funding Sources:** This study was funded by an unrestricted educational grant by GE Healthcare, Waukesha, Wisconsin. Model design, inputs, and interpretation were solely at the discretion of the authors, as is this manuscript.

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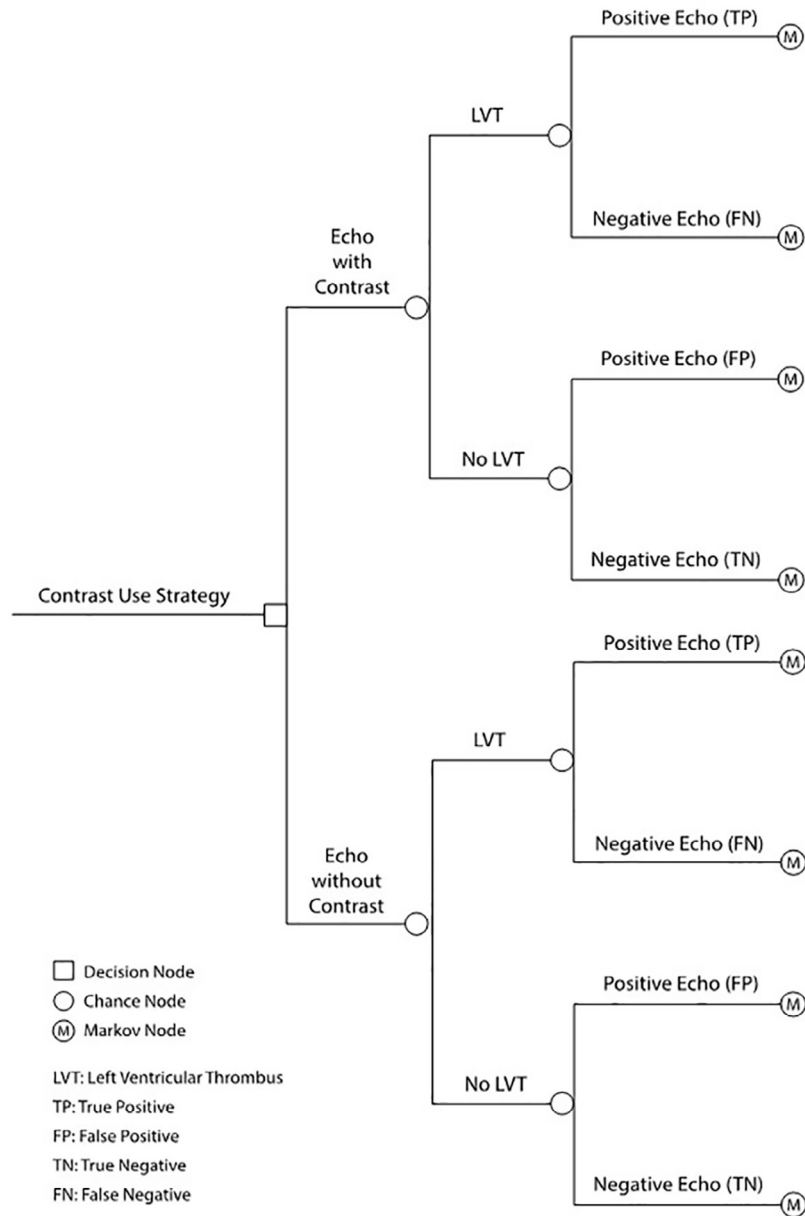


Figure 1. Decision model. The branches of the decision model leading to the Markov nodes are displayed. The Markov node structure is provided in [Supplementary Figure 1](#).

each cycle, costs for acute events and chronic states were applied, along with quality of life adjustments for heart failure, increasing age, acute stroke, systemic embolism, and long-term disabling and nondisabling stroke ([Supplementary Table 1](#)). The validity of survival projections was assessed through comparison to survival estimates from heart failure trials. The decision model was programmed using TreeAge Pro version 2015 (Williamstown, Massachusetts). Supporting analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

Meta-analysis was used to develop estimates for the sensitivity and specificity of echocardiography with and without contrast in the detection of LVT in patients with heart failure and reduced EF. A PubMed and Medline search through March

1, 2016 for MeSH terms “thrombosis and echocardiography AND (Optison OR Definity OR contrast media)” and “thrombosis and echocardiography AND (sensitivity OR specificity)” yielded 136 and 505 articles, respectively. Hand-searching reference lists of included articles resulted in 1 additional study.<sup>8</sup> Twelve articles remained after applying inclusion criteria ( $\geq 30$  participants with reduced EF or recent myocardial infarction, comparison of LVT presence on transthoracic echocardiography with either computed technology, magnetic resonance imaging, surgery, or autopsy examination; data present for calculation of sensitivity and specificity).

A random-effects model (DerSimonian-Laird estimator) was used with Knapp-Hartung standard error adjustment. Proportions (sensitivity and specificity) were summarized on the

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