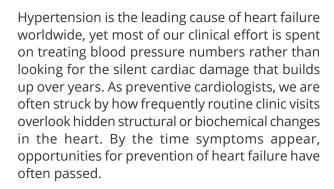
PERSPECTIVES IN **HYPERTENSION**

Early detection of pre-heart failure in hypertension: bringing cardiac biomarkers and echocardiography into everyday practice

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That's why we and our colleagues have been exploring how simple tools we already have, namely serum cardiac biomarkers and echocardiography, can help us identify "pre-heart failure" in people with elevated blood pressure or hypertension before they develop symptoms.

From Numbers to Phenotypes

Contemporary hypertension care relies on office and/or home blood pressure readings plus conventional risk factors such as smoking and dyslipidemia. But these measures tell us little about what's actually happening in the heart. Over the past decades, robust evidence has demonstrated that natriuretic peptides such as NT-proBNP and high-sensitivity cardiac troponins rise in response to subclinical myocardial stress or injury. In large population-based studies, elevated levels of these cardiac biomarkers are common even in stage 1





hypertension and strongly predict future heart failure and cardiovascular events.^{1,2}

At the same time, echocardiography, especially when we look beyond ejection fraction to parameters such as left ventricular mass, left atrial diameter, and diastolic function, can reveal structural and functional changes long before symptoms appear. Put together, cardiac biomarkers and echocardiography provide a much richer picture of heart health than blood pressure alone.

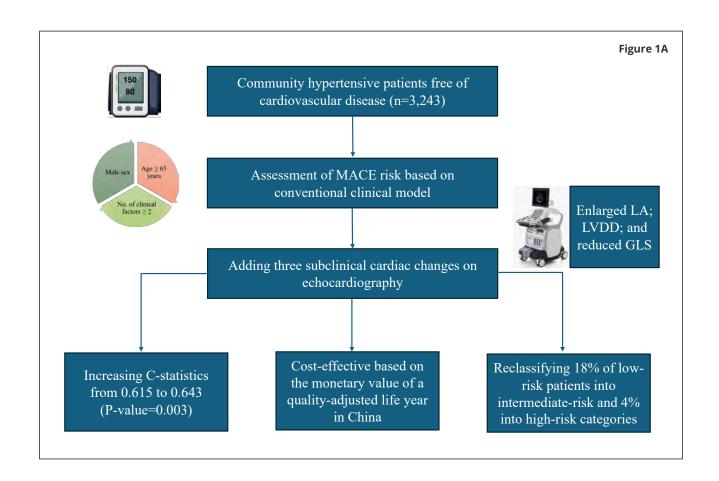
Pre-Heart Failure Is Real and Detectable

The universal definition and classification of heart failure specifically define pre-heart failure, that is individuals with risk factors such as hypertension plus abnormal cardiac structure or function or elevated cardiac biomarkers, but no heart failure symptoms.³ This stage is common in hypertensive populations. For example, in a nationally representative hypertension survey, we found that the weighted prevalence of preheart failure was 42.8%.4 In addition, our recent work showed that pre-heart failure defined by age-specific NT-proBNP cutoffs in the general population approaching 17.1%.5 We further









Risks of ASCVD and HF associated with the three echocardiographic measures

	Hazard ratio (95% CI)		
	Enlarged LA	LVDD	Reduced GLS
ASCVD	1.95 (1.38, 2.75)	1.80 (1.39, 2.33)	1.51 (1.22, 1.87)
HF	3.85 (2.27, 6.55)	5.72 (2.64, 12.39)	4.15 (2.63, 6.53)
P-value*	0.035	0.005	< 0.001

ASCVD, atherosclerotic cardiovascular disease; HF, heart failure; CI, confidence interval; LA, left atrium; LVDD, left ventricular diastolic dysfunction; GLG, global longitudinal strain

ASCVD included coronary heart disease, myocardial infarction, and stroke

*indicated comparison of hazard ratio between ASCVD and HF

Figure 1B

demonstrated the potential of echocardiography for risk reclassification and cost-effectiveness in cardiovascular primary prevention among hypertensive individuals in China (Figure 1A; In Press in the Journal of Hypertension). Notably, conventional echocardiographic parameters, such as left atrial enlargement, were found to confer a higher risk of heart failure than heart attack or stroke (Figure 1B).

Detecting pre-heart failure matters because it identifies hypertensive patients who derive the greatest absolute benefit from intensive blood pressure lowering. For example, in post-hoc analyses of the SPRINT trial, participants with elevated biomarkers saw far larger reductions in heart failure and death than biomarker-negative individuals.6







Why Hypertension Guidelines **Should Catch Up**

Heart Failure guidelines and American Diabetes Association consensus statement already recommend cardiac biomarker screening for highrisk, asymptomatic individuals. But hypertension guidelines have been slow to follow, 7,8 perhaps due to a lack of randomized trials or cost-effectiveness data. Yet the science is clear: elevated NT-proBNP or cardiac troponin in a hypertensive patient signals a malignant cardiac phenotype and should prompt closer monitoring, imaging assessment, and potentially earlier or more intensive therapy.

From our perspective, biomarkers and imaging should be viewed as complementary ones. Posthoc analysis of the SPRINT trial showed that left ventricular hypertrophy carries very different prognostic meaning depending on whether cardiac biomarkers like NT-proBNP or cardiac troponin are elevated; a malignant phenotype that carries four-fold higher risks of heart failure and death.9 This tells us that while cardiac biomarkers can efficiently flag many apparently "low-risk" individuals, echocardiography remains critical for identifying those with structural remodeling who are at especially high risk. A pragmatic 'biomarkerfirst, imaging-second' approach could therefore maximize efficiency while still capturing the hidden malignant cases that matter most for heart failure prevention.

Looking Ahead: Pragmatic and Equitable Solutions

Moving from evidence to implementation will require pragmatic trials of biomarker-guided hypertension management, cost-effectiveness analyses, and simplified algorithms for use in primary care. Point-of-care NT-proBNP testing, portable echocardiography and integration of artificial intelligence may all help us tailor screening to individual risk profiles while keeping it affordable in the future.

A Call to Action

As clinicians, we can begin now. Consider ordering NT-proBNP or high-sensitivity cardiac troponin in your hypertensive patients with other risk factors, unexplained symptoms, or poor blood pressure control. Use echocardiography proactively, not just when ejection fraction falls. Start thinking of hypertension not simply as a number to control, but as a continuum of cardiac risk we can intercept.

If we embed cardiac biomarker and imaging assessment into hypertension care pathways, we can shift from reactive treatment of overt heart failure to proactive prevention of its earliest stages, and ultimately improve outcomes for billions worldwide.

References:

- 1. Pandey A, Patel KV, Vongpatanasin W, Ayers C, Berry JD, Mentz RJ, Blaha MJ, McEvoy JW, Muntner P, Vaduganathan M, et al. Incorporation of Biomarkers Into Risk Assessment for Allocation of Antihypertensive Medication According to the 2017 ACC/AHA High Blood Pressure Guideline: A Pooled Cohort Analysis. Circulation. 2019;140:2076-2088. doi: 10.1161/circulationaha.119.043337
- 2. Hussain A, Sun W, Deswal A, de Lemos JA, McEvoy JW, Hoogeveen RC, Matsushita K, Aguilar D, Bozkurt B, Virani SS, et al. Association of NT-ProBNP, Blood Pressure, and Cardiovascular Events: The ARIC Study. Journal of the American College of Cardiology. 2021;77:559-571. doi: 10.1016/j.jacc.2020.11.063
- 3. Bozkurt B, Coats AJS, Tsutsui H, Abdelhamid CM, Adamopoulos S, Albert N, Anker SD, Atherton J, Böhm M, Butler J, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure: Endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association. European journal of heart failure. 2021;23:352-380. doi: 10.1002/ejhf.2115
- 4. Cai A, Zheng C, Qiu J, Fonarow GC, Lip GYH, Feng Y, Wang Z. Prevalence of heart failure stages in the general population and implications for heart failure prevention: reports from the China Hypertension Survey 2012-15. European journal of preventive cardiology. 2023;30:1391-1400. doi: 10.1093/eurjpc/zwad223











- 5. Cai A, Liu L, Feng Y, Li L, Bozkurt B, Januzzi JL, Jr., Lam CSP, Fonarow GC, Pandey A, Chen LY, et al. Comparison of Fixed vs Age-Adjusted NT-proBNP Cutoffs to Define Pre-Heart Failure. Journal of the American College of Cardiology. 2025;86:625-629. doi: 10.1016/j.jacc.2025.06.041
- 6. Berry JD, Nambi V, Ambrosius WT, Chen H, Killeen AA, Taylor A, Toto RD, Soliman EZ, McEvoy JW, Pandey A, et al. Associations of High-Sensitivity Troponin and Natriuretic Peptide Levels With Outcomes After Intensive Blood Pressure Lowering: Findings From the SPRINT Randomized Clinical Trial. JAMA cardiology. 2021;6:1397-1405. doi: 10.1001/jamacardio.2021.3187
- 7. Mancia G, Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A, Muiesan ML, Tsioufis K, Agabiti-Rosei E, Algharably EAE, et al. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International

Society of Hypertension (ISH) and the European Renal Association (ERA). Journal of hypertension. 2023;41:1874-2071. doi: 10.1097/hjh.000000000003480

- 8. Jones DW, Ferdinand KC, Taler SJ, Johnson HM, Shimbo D, Abdalla M, Altieri MM, Bansal N, Bello NA, Bress AP, et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/ AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2025. doi: 10.1161/ cir.000000000001356
- 9. Ascher SB, de Lemos JA, Lee M, Wu E, Soliman EZ, Neeland IJ, Kitzman DW, Ballantyne CM, Nambi V, Killeen AA, et al. Intensive Blood Pressure Lowering in Patients With Malignant Left Ventricular Hypertrophy. Journal of the American College of Cardiology. 2022;80:1516-1525. doi: 10.1016/j.jacc.2022.08.735

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