Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Pharmacy and Pharmacology

Journal homepage: https://www.ijpp.org.in/

Review Article

Targeting aortic elasticity: A promising therapeutic avenue in congestive heart failure and cardiac pumping disorders

Abhilash Santhosh Menon*[1], Kailash Kumar[1]

[1] Dept. of Pharmacy Practice, JSS College of Pharmacy, Ooty, Tamil Nadu, India

Abstract

Heart failure (HF), including both preserved ejection fraction (HFpEF) and reduced ejection fraction (HFrEF) phenotypes, remains a growing global health crisis, affecting over 64 million individuals and contributing significantly to morbidity, mortality, and healthcare burden. Although contemporary HF therapies focus largely on myocardial function and neurohormonal modulation, accumulating evidence suggests that the vascular system-particularly the elastic properties of the aorta-plays a crucial and modifiable role in disease progression. Aortic elasticity is central to maintaining optimal ventriculo-arterial coupling, damping pulsatile load, and ensuring coronary perfusion during diastole. However, age-related changes, hypertension, diabetes, and metabolic syndrome promote vascular stiffening, which increases left ventricular (LV) afterload, exacerbates systolic dysfunction, and impairs diastolic relaxation.

Aortic stiffness, quantified by pulse wave velocity (PWV), has emerged as an independent predictor of cardiovascular events and HF hospitalization. Pharmacologic agents that preserve or restore aortic compliance-including RAAS blockers, calcium channel blockers, statins, SGLT2 inhibitors, soluble guanylate cyclase stimulators, AGE cross-link breakers, and GLP-1 receptor agonists-have demonstrated encouraging vascular benefits in both preclinical and clinical studies. Novel therapies targeting extracellular matrix remodeling, endothelial dysfunction, and oxidative stress hold promise in transforming our approach to HF therapy by shifting focus beyond cardiac contractility to vascular health.

This narrative review comprehensively examines the physiology of aortic elasticity, the pathophysiologic mechanisms linking vascular stiffness to heart failure, and therapeutic strategies aimed at reversing or mitigating arterial stiffening. We highlight key trials, mechanistic insights, and potential research directions to promote integration of vascular-targeted therapies in HF management. Emphasizing aortic compliance as a therapeutic goal may help close the current gap in HFpEF treatment, improve long-term outcomes, and redefine cardiovascular care paradigms.

Keywords: Drug therapy, aortic stiffness, congestive heart failure, vascular stiffness, pulse wave analysis.

Received: 23-06-2025; **Accepted:** 24-07-2025; **Available Online:** 25-09-2025

1. Introduction

Congestive heart failure affects over 64 million people worldwide[1], and mortality remains high despite guideline-directed therapy. Recent paradigm shifts have expanded beyond targeting the myocardium to include the vascular system—especially the aorta, whose mechanical properties determine systolic-diastolic dynamics.[2]

Loss of aortic elasticity increases pulse wave velocity (PWV), systolic blood pressure (SBP), and left ventricular (LV) workload, while decreasing coronary perfusion pressure. This is particularly problematic in HFpEF, where increased vascular resistance and impaired ventricular relaxation coexist.[3]

2. Physiology of Aortic Elasticity

The aortic media contains elastin and collagen fibres interspersed with smooth muscle cells. These confer distensibility and recoil, central to the Windkessel effect.[4] With each cardiac cycle, the aorta stores energy during systole and releases it during diastole, maintaining organ perfusion and reducing LV workload.[5]

Key determinants of aortic elasticity include:

1. Elastin/collagen ratio
2. Nitric oxide (NO) bioavailability
3. Extracellular matrix remodeling
4. Inflammation and calcification

*Corresponding author: Abhilash Santhosh Menon
Email: abhilashmenon61@gmail.com

https://doi.org/10.18231/j.ijpp.30920.1758777742

Age, hypertension, diabetes, and oxidative stress accelerate elastin fragmentation, smooth muscle apoptosis, and glycation cross-linking, leading to stiffening.[6,7,8]

3. Pathophysiology: Aortic Stiffness in Congestive Heart Failure

Aortic stiffness contributes differently to different phenotypes of heart failure. In heart failure with preserved ejection fraction (HFpEF), ventriculo-arterial uncoupling is a major determinant of impaired relaxation and diastolic dysfunction. Conversely, in heart failure with reduced ejection fraction (HFrEF), while elevated afterload worsens pump failure, systolic dysfunction remains central. Thus, targeting vascular stiffness may yield more pronounced benefits in HFpEF populations.[9]

Aging is the predominant factor leading to medial elastin degradation, vascular smooth muscle apoptosis, and progressive calcification. Comorbidities such as hypertension, diabetes mellitus, and chronic kidney disease exacerbate stiffening through endothelial dysfunction, oxidative stress, and the accumulation of advanced glycation end-products (AGEs), accelerating loss of compliance and raising pulse wave velocity.[10]

Aortic stiffening elevates afterload and disrupts the pressure-volume relationship of the heart. Early return of reflected pressure waves during systole raises LV wall tension, promoting hypertrophy and fibrosis.[11,12] **(Figure 1)** illustrates the pathophysiologic sequence linking aortic stiffness with increased pulse wave velocity, afterload, and eventual heart failure. Reduced diastolic pressure impairs coronary perfusion, precipitating ischemia and HF exacerbation.[13] **(Table 1)** shows the pathophysiological mechanisms underlying aortic stiffening and their functional consequences.

4. Mechanisms of Arterial Stiffness

Table 1: Cellular and biochemical drivers of vascular stiffening

Pathology	Mechanism	Consequence
Elastin fragmentation	Protease activity (e.g., MMPs)	↓ Compliance
Collagen deposition	TGF-β driven fibrosis	↑ Rigidity
Calcification	Osteogenic differentiation of VSMCs	↑ PWV
AGE cross-linking	Non-enzymatic glycation in diabetes	↓ Elastic recoil
Endothelial dysfunction	↓ NO, ↑ ET-1	↑ Vasoconstriction

Abbreviations: MMPs- Matrix Metalloproteinases; TGF-β- Transforming Growth Factor Beta; PWV- Pulse Wave Velocity; VSMCs- Vascular Smooth Muscle Cells; NO- Nitric Oxide; ET-1- endothelin-1

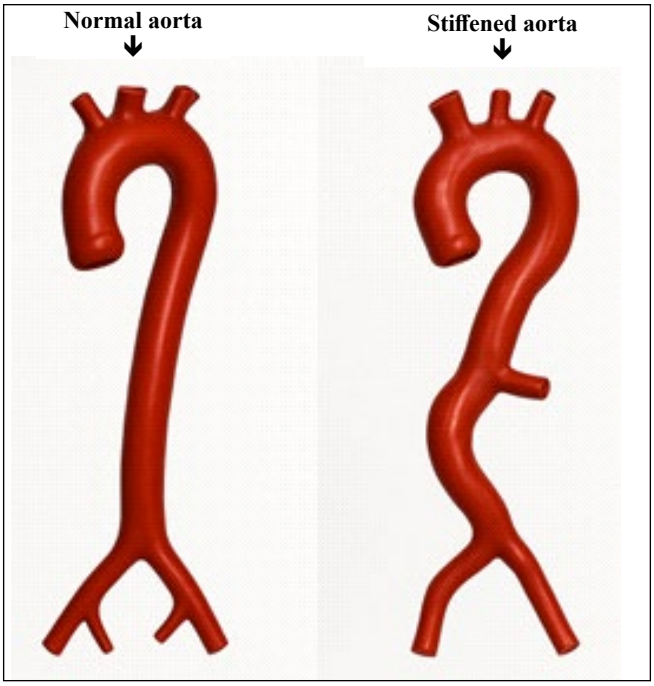


Figure 1 : Comparison of normal and stiffened aortic morphology

5. Pharmacologic Modulation of Aortic Elasticity

Pharmacologic modulation of aortic elasticity has emerged as a promising adjunct to traditional heart failure therapy. While most heart failure treatments have historically focused on improving cardiac contractility or neurohormonal balance, increasing attention is now being directed toward drugs that can directly or indirectly enhance vascular compliance. The aorta, being a dynamic and biologically active vessel, responds to chronic stressors such as hypertension, inflammation, and metabolic dysfunction through maladaptive remodeling—marked by elastin degradation, collagen deposition, and endothelial dysfunction. Reversing or halting these changes pharmacologically may ease ventricular afterload, improve ventriculo-arterial coupling, and ultimately enhance cardiac efficiency.

Recent clinical and translational studies have identified several drug classes capable of modifying arterial stiffness through diverse mechanisms, including anti-fibrotic, anti-inflammatory, glycemic, and nitric oxide-mediated pathways. Rather than focusing solely on symptomatic relief, these agents represent a shift toward disease-modifying vascular therapy. Pharmacological strategies targeting vascular elasticity are summarized in **(Figure 2)**, highlighting key therapeutic classes such as RAAS blockers, SGLT2 inhibitors, soluble guanylate cyclase (sGC) stimulators, and others currently under investigation.

5.1. Renin-Angiotensin-Aldosterone system (RAAS) Inhibitors

1. ACE inhibitors (e.g., enalapril) and ARBs (e.g., losartan) have been shown to attenuate vascular fibrosis, promote nitric oxide (NO) bioavailability, and contribute to a measurable reduction in arterial stiffness.[14,15]

2. RAAS inhibitors reduce Angiotensin II- mediated VSMC hypertrophy and fibrosis, increase endothelial NO bioavailability and stabilize extracellular matrix by reducing metalloproteinase activity.[16,17]
3. **Meta-analysis:** 17 studies show significant PWV reduction with RAAS blockade.[18]

5.2. Calcium Channel Blockers (CCBs)

1. Amlodipine improves aortic compliance, especially in isolated systolic hypertension (ISH).[19] CCBs promote relaxation of VSMC relaxation via L-type calcium channel inhibition and also reduce vascular tone and central blood pressure, thus improving compliance.
2. The **CAMELOT trial** showed reduced cardiovascular events via CCBs partly due to vascular effects.[20]

5.3. Statins

1. Statins have been found to increase eNOS activity and NO production, and reduce oxidative stress and MMP expression, reducing arterial remodeling.[21]
2. The statins atorvastatin and rosuvastatin exert beneficial vascular effects by enhancing endothelial function, diminishing oxidative stress, and lowering arterial stiffness, effects that are observed independently of their actions on lowering low-density lipoprotein (LDL) cholesterol levels.[22,23]
3. **ASCOT-LLA** and **TNT** trials showed secondary benefits on vascular compliance.[24,25]

5.4. Sodium Glucose Co-Transporter 2 (SGLT2) inhibitors

1. SGLT2 inhibitors reduce pulse wave velocity through natriuresis, BP reduction, and weight loss.[26,27]
2. Dapagliflozin and empagliflozin lower blood pressure, improve endothelial function, and reduce arterial stiffness.[28,29,30]
3. **DAPA-HF** and **EMPA-REG OUTCOME** trials confirmed reduced HF hospitalization and CV death.[31,32]

5.5. Soluble Guanylate Cyclase (sGC) stimulators

1. sGC stimulators increase cGMP production and cause VSMC relaxation.[33]
2. Vericiguat activates cGMP signaling independent of NO, improving compliance and reducing fibrosis.[34,35]
3. The **VICTORIA trial** demonstrated reduced HF-related hospitalizations.[36] **SOCRATES-PRESERVED trial** showed reduced vascular fibrosis and stiffening.

5.6. Advanced Glycation Endproducts (AGE) cross-link breakers

1. AGE cross-link breakers cause cleavage of AGE-mediated collagen cross-links.[37]
2. Alagebrium cleaves glycation cross-links in ECM, restoring elasticity in diabetic and aged vessels.[38,39]
3. Preclinical data in rats showed reversal of vascular stiffening and LV hypertrophy.[40]

5.7. Glucagon-Like Peptide-1 (GLP-1) receptor agonists

1. GLP-1 receptor agonists (eg. Liraglutide, Exenatide) increase eNOS phosphorylation via AMPK and NO production in endothelium.[41] They reduce oxidative stress by inhibiting PKC-NADPH oxidase enzyme and lower TNF- α and IL-6 levels to reduce inflammatory signaling.[42]
2. Liraglutide improves endothelial function and reduces inflammation. Some studies show arterial stiffness reduction in T2DM.[43]

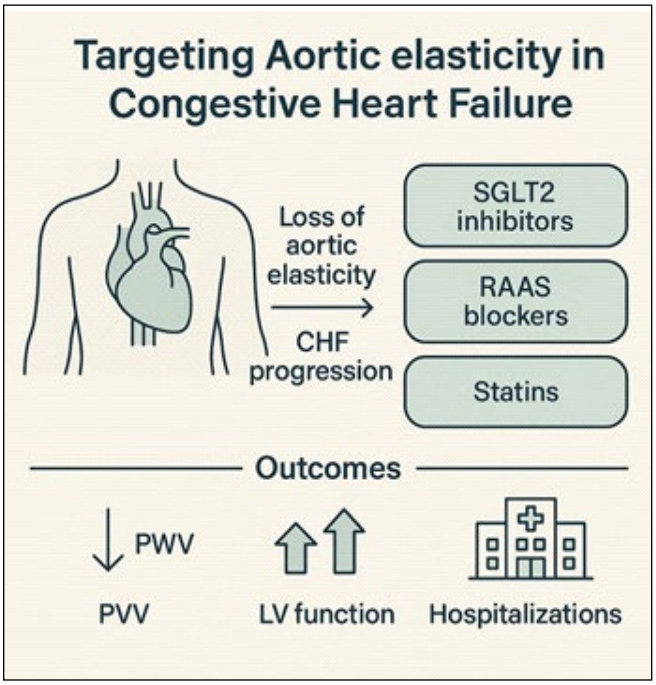


Figure 2 : Improving outcomes in CHF by enhancing aortic compliance

6. Preclinical and Clinical Evidence

6.1. Preclinical highlights

1. **Rodent models:** Enalapril, alagebrium, and SGLT2 inhibitors reduced aortic PWV and improved cardiac output in aged or diabetic mice.[44,45,46,47]
2. **In vitro studies:** GLP-1 and sGC agonists inhibit collagen deposition in human aortic smooth muscle cells.[48]

7. Clinical Trials and Meta-analyses

(Table 2) provides a consolidated overview of major clinical trials that have investigated the association between specific pharmacological interventions and changes in aortic stiffness. The table includes therapeutic agents across various drug classes, outlines the key imaging modalities used—such as MRI, and central blood pressure measurements—and highlights their impact on vascular compliance and heart failure-related outcomes.

Table 2: Key clinical trials evaluating pharmacologic interventions on vascular stiffness, cardiac function, and imaging-based outcomes.

Trial	Drug/Class	Outcome	Imaging/Measure
HOPE	Ramipril	↓ CV events, improved compliance	Brachial-ankle PWV
ASCOT	Amlodipine	↓ stroke risk, improved stiffness	Central BP
DAPA-HF	Dapagliflozin	↓ CV death, ↑ quality of life	MRI, tonometry
VICTORIA	Vericiguat	↓ HF hospitalization	NT-proBNP, PWV
PARAMETER	Sacubitril/Valsartan	↓ aortic stiffness vs. ARB	Central BP, MRI
PARAGON-HF	Sacubitril/Valsartan	Benefit in HFpEF (subgroup)	Diastolic parameters

Abbreviations: CV- Cardiovascular; PWV- Pulse Wave Velocity; BP- Blood Pressure; MRI- Magnetic Resonance Imaging; HF- Heart Failure; NT-proBNP- N-terminal pro-B-type Natriuretic Peptide; ARB- angiotensin Receptor Blocker; HFpEF- Heart Failure with Preserved Ejection Fraction.

(Table 3) summarizes major clinical trials demonstrating efficacy of vascular-targeted therapies in heart failure.

Table 3: Key Clinical Trials Supporting Vascular-Targeted Therapies.

Trial	Drug	Target	HF Subtype/ Special population	Outcomes
Emperor- Preserved	Empagliflozin	Endothelial function, inflammation	HFpEF	↓ CV death & HF hospitalization
Socrates- Preserved	Vericiguat	NO-sGC-cGMP signaling	HFpEF	Improved NT-proBNP, better hemodynamic profile
Parameter	Sacubitril/Valsartan	RAAS inhibition, vascular stiffness	Elderly hypertensive patients	↓ Central aortic stiffness vs ARB

Abbreviations: HFpEF- Heart Failure with Preserved Ejection Fraction; CV- Cardiovascular; HF- Heart Failure; NO-sGC-cGMP- Nitric Oxide- Soluble Guanylate Cyclase- Cyclic Guanosine Mono Phosphate; NT-proBNP- N-terminal pro-B-type Natriuretic Peptide; RAAS- Renin-angiotensin-aldosterone System; ARB- Angiotensin Receptor Blocker.

8. Imaging Modalities for Aortic Elasticity

Aortic stiffness, an early marker of cardiovascular risk, necessitates reliable and reproducible imaging modalities for its assessment. Over the years, non-invasive techniques have evolved to quantify arterial elasticity, enabling clinicians to stratify risk and monitor therapeutic efficacy in real time. Table 4 shows a summary of imaging modalities used to assess aortic elasticity, highlighting their key measures and respective strengths.

Table 4: Common diagnostic modalities for assessing aortic stiffness and arterial compliance with associated strengths.

Modality	Measures	Strength
Carotid-femoral PWV	Gold standard stiffness	Widely validated
MRI	Aortic distensibility, pulse wave imaging	High spatial resolution
Echocardiography	Aortic root expansion, LVAC	Bedside accessible
Applanation tonometry	Central BP, augmentation index	Non-invasive

Abbreviations: PWV- Pulse Wave Velocity; MRI- Magnetic Resonance Imaging; LVAC- Left Ventricular-arterial Coupling; BP- Blood Pressure

Newer imaging modalities, such as four-dimensional (4D) Flow MRI and arterial strain imaging, provide detailed, dynamic visualization of blood flow patterns and aortic wall deformation. These advanced techniques enable precise, region-specific assessment of aortic biomechanics and are increasingly being explored as tools to monitor the efficacy of vascular-targeted therapies in both clinical trials and specialized cardiovascular care settings.[49–52]

9. Future Perspectives

The evolving understanding of aortic stiffness in heart failure pathophysiology presents new avenues for diagnostic and therapeutic innovation. Future management may benefit from a multi-pronged approach that targets not only myocardial dysfunction but also vascular rigidity.

Newer imaging modalities, such as four-dimensional (4D) flow magnetic resonance imaging (MRI) and arterial strain imaging, are poised to revolutionize vascular assessment. These technologies provide high-resolution, dynamic visualization of aortic wall movement and complex hemodynamics, including flow vortices, wall shear stress, and regional strain. They allow for early detection of subtle changes in elasticity before irreversible damage occurs. Unlike static measures, 4D Flow MRI offers a temporal and spatial view of aortic function, making it suitable for monitoring response to vascular-targeted therapies in both

clinical and research settings. As these modalities become more widely adopted, they may offer personalized imaging biomarkers to guide therapy decisions.

Biologic therapies represent an exciting frontier. Gene therapies aimed at restoring elastin production and TGF-β antagonists targeting fibrotic remodeling are under preclinical investigation. If translated successfully, such approaches may directly reverse arterial stiffening at a molecular level.

Multi-target pharmacologic strategies may also gain prominence. Combining myocardial-directed drugs (e.g., beta-blockers, ARNIs) with agents that improve vascular compliance (e.g., sGC stimulators, SGLT2 inhibitors) may achieve synergistic benefits, especially in HFpEF, where single-mechanism drugs have underperformed.

Non-pharmacologic interventions, including aerobic exercise and caloric restriction, have demonstrated significant improvements in arterial compliance and endothelial function. These lifestyle strategies can serve as adjuncts to drug therapy, particularly in aging and metabolic patients.[52]

Finally, AI-guided management systems using digital pulse wave analysis and real-time vascular biomarker integration may facilitate early risk prediction and therapy optimization. By combining wearable technology with cloud-based analytics, AI could help clinicians detect and intervene on vascular dysfunction long before symptoms arise.

Together, these innovations signal a promising future for vascular-focused heart failure care.

10. Conclusion

Focusing on aortic elasticity presents an innovative and hopeful therapeutic strategy in the evolving management of congestive heart failure (CHF), especially in patient populations where conventional treatments have demonstrated limited efficacy or diminishing returns. While left ventricular systolic and diastolic dysfunction have long been central to heart failure paradigms, growing evidence suggests that large-vessel stiffness—particularly of the aorta—is not merely a passive bystander but an active driver of disease progression. Aortic stiffness contributes to increased afterload, impaired coronary perfusion, and early return of reflected pulse waves, which collectively exacerbate ventricular remodeling and compromise cardiac output. Importantly, this process is especially detrimental in HFpEF, where ventriculo-arterial coupling is already tenuous, and minor increases in aortic impedance can disproportionately worsen symptoms and functional capacity.

Contrary to being a consequence solely of aging or long-standing hypertension, aortic stiffness represents a modifiable hemodynamic target. Modern imaging modalities such as carotid-femoral pulse wave velocity (cf-PWV), echocardiographic aortic distensibility, and cardiac MRI-based compliance measures as summarized in **(Figure 3)**. have facilitated more accurate quantification and monitoring of aortic elasticity in clinical settings.

Therapeutic interventions aimed at improving aortic compliance are gaining traction. Agents such as SGLT2 inhibitors, GLP-1 receptor agonists, RAAS blockers, and soluble guanylate cyclase (sGC) stimulators have demonstrated potential in both preclinical and clinical studies to reduce aortic stiffness. By doing so, they not only alleviate symptoms but also appear to reduce hospitalization rates and cardiovascular mortality. This vascular-targeted strategy complements myocardial therapies and opens a new frontier for individualized, mechanism-based heart failure care.

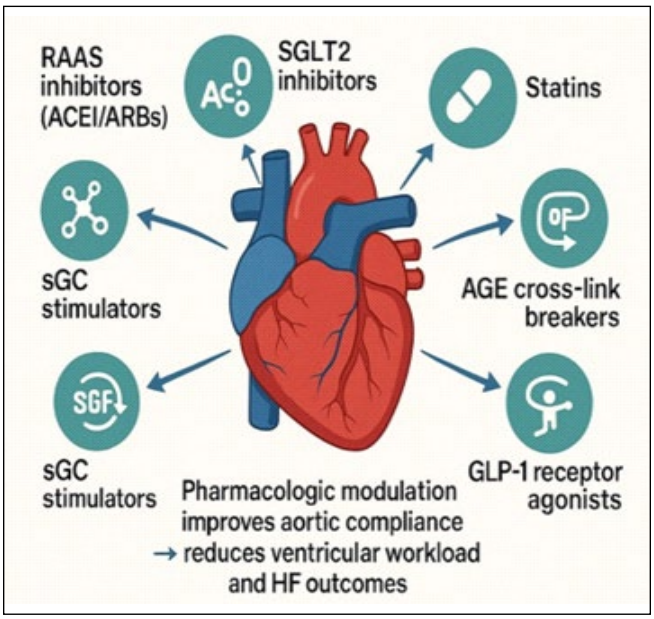


Figure 3: Impact of elasticity-preserving drugs on CHF progression and outcomes.

In addition to pharmacological approaches, upcoming studies should focus on creating specific treatments that directly enhance elastin levels, disrupt AGE cross-links, or adjust vascular smooth muscle activity. Progress in imaging and biomechanical modeling will be crucial for accurately measuring aortic stiffness and directing tailored treatment. There is an urgent need for clinical trials that feature aortic stiffness as a primary endpoint to confirm its importance as both a therapeutic target and a prognostic biomarker.

Ultimately, incorporating vascular-focused approaches into standard CHF treatment could change the paradigm from just alleviating symptoms to altering disease progression at its vascular foundation. As we enhance our knowledge of aortic biomechanics and their impact on cardiac performance, this field presents transformative possibilities for bettering patient results in heart failure across the entire range of ejection fractions.

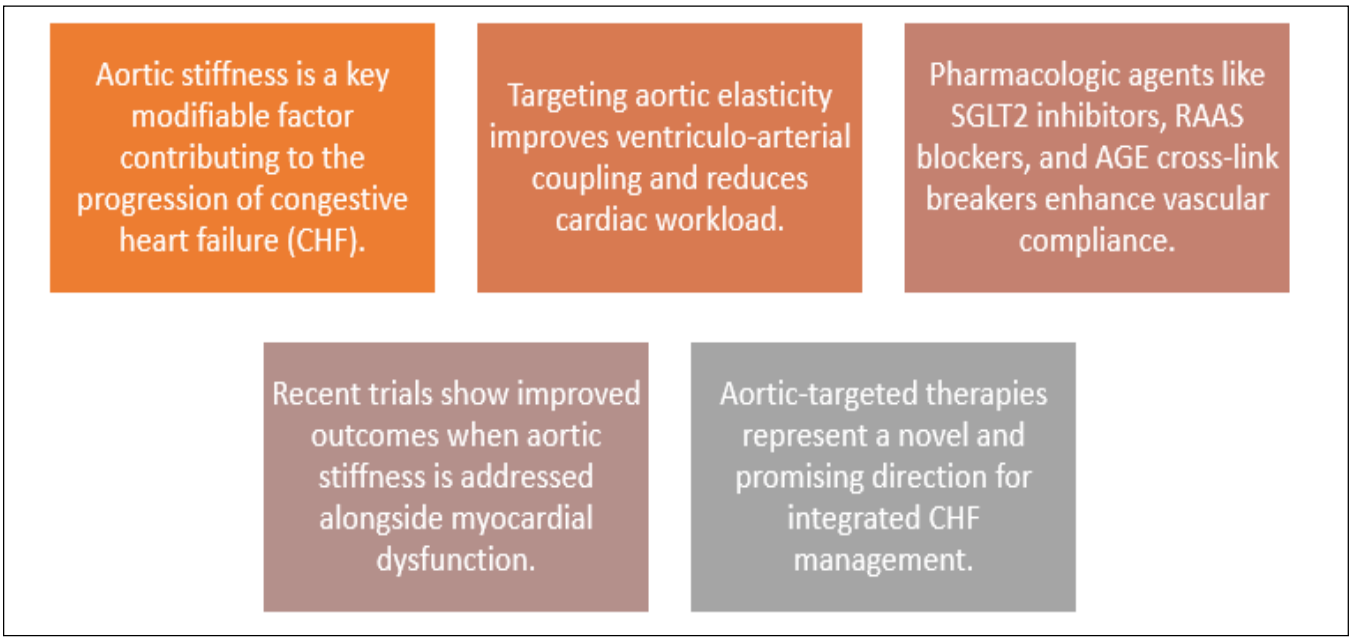
Aortic elasticity is more than a vascular curiosity—it is a clinically actionable determinant of cardiovascular performance and heart failure progression. The aorta's ability

to buffer pulsatile flow and sustain coronary perfusion plays a critical role in maintaining optimal ventriculo-arterial coupling. In both HFpEF and HFrEF, but especially the former, arterial stiffening serves as both a marker and a driver of disease.

Therapeutic strategies aimed at improving aortic compliance—spanning from conventional RAAS blockade to novel interventions like sGC stimulation and AGE cross-link disruption—have shown encouraging results in both preclinical and clinical settings. Their integration into standard HF therapy may offer additive benefits, particularly in patient populations where traditional myocardial-targeted approaches have underperformed.

By expanding our understanding of vascular contributions to HF pathogenesis, clinicians can better stratify patients and personalize therapy. Going forward, incorporating arterial stiffness as a primary endpoint in clinical trials and leveraging advanced imaging modalities may help validate this approach. Targeting aortic stiffness is not merely adjunctive—it may represent the next frontier in heart failure therapeutics.

11. Highlights



12. Authors Contribution

1. **Dr. Abhilash Santhosh Menon:** Conceptualization, Methodology, Writing-Original Draft, Supervision.
2. **Dr. Kailash Kumar:** Writing-Review & Editing, Visualization, Investigation

13. Source of Funding

None

14. Conflict of Interest

None

15. Acknowledgement

None

References

1. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the american college of cardiology/ american heart association joint committee on clinical practice guidelines. *Circulation*. 2022;145(18):e895-e1032.
2. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Heart J.* 2006;27(21):2588–605.
3. Borlaug BA, Paulus WJ. Heart failure with preserved ejection fraction: pathophysiology, diagnosis, and treatment. *Eur Heart J.* 2011;32(6):670–9.
4. Mitchell GF. Effects of central arterial aging on the structure and function of the peripheral vasculature: implications for end-organ damage. *J Appl Physiol (1985).* 2008;105(5):1652–60.
5. Vlachopoulos C, Nichols WW, O'Rourke M, Wilmer W. *McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles*. 6th ed. London: CRC Press; 2011.
6. Lakatta EG and Levy D. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part I: aging arteries: a "set up" for vascular disease. *Circulation.* 2003;107(1):139–46.
7. Zieman SJ, Melenovsky V, Kass DA. Mechanisms, pathophysiology, and therapy of arterial stiffness. *Arterioscler Thromb Vasc Biol.* 2005;25(5):932–43.
8. Safar ME, London GM. Therapeutic studies and arterial stiffness in hypertension: recommendations of the European Society of Hypertension. The Clinical Committee of Arterial Structure and Function. Working group on vascular structure and function of the european society of hypertension. *J Hypertens.* 2000;18(11):1527–35.
9. Kim HL, Jo SH. Arterial stiffness and heart failure with preserved ejection fraction. *J Korean Med Sci*. 2024;39(23):e195.
10. Stirban A, Gawlowski T, Roden M. Vascular effects of advanced glycation endproducts: Clinical effects and molecular mechanisms. *Mol Metab*. 2013;3(2):94-108.
11. Najjar SS, Scuteri A, Lakatta EG. Arterial aging: is it an immutable cardiovascular risk factor? *Hypertension.* 2005;46(3):454–62.
12. Chirinos JA. Arterial stiffness: basic concepts and measurement techniques. *J Cardiovasc Transl Res.* 2012;5(3):243–55.

13. Kass DA. Ventricular arterial stiffening: integrating the pathophysiology. *Hypertension.* 2005;46(1):185–93.
14. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting–enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med.* 2000;342(3):145–53.
15. Mahmud A, Feely J. Arterial stiffness is related to systemic inflammation in essential hypertension. *Hypertension.* 2005;46(5):1118–22.
16. Dengel DR, Pratley RE, Hagberg JM, Goldberg AP. Impaired insulin sensitivity and maximal responsiveness in older hypertensive men. *Hypertension*. 1994;23(3):320-4.
17. Williams B, Lacy PS, Thom SM, Cruickshank K, Stanton A, Collier D, et al. Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit Artery Function Evaluation (CAFE) study. *Circulation.* 2006;113(9):1213–25.
18. Wang KL, Cheng HM, Sung SH, Chuang SY, Li CH, Spurgeon HA, et al. Wave reflection and arterial stiffness in the prediction of 15-year all-cause and cardiovascular mortalities: a community-based study. *Hypertension.* 2010;55(3):799–805.
19. Morgan TO, Anderson A, MacInnis RJ, et al. Effect of different antihypertensive drug classes on central aortic pressure. *Am J Hypertens.* 2004;17(2):118–23.
20. Nissen SE, Tuzcu EM, Libby P, Thompson PD, Ghali M, Garza D, et al. Effect of antihypertensive agents on cardiovascular events in patients with coronary disease and normal blood pressure: the CAMELOT study. *JAMA.* 2004;292(18):2217–25.
21. Raison J, Rudnichi A, Safar ME. Effects of atorvastatin on aortic pulse wave velocity in patients with hypertension and hypercholesterolaemia: a preliminary study. *J Hum Hypertens.* 2002;16(10):705–10
22. Alidadi M, Montecucco F, Jamialahmadi T, Al-Rasadi K, Johnston TP, Sahebkar A. Beneficial Effect of Statin Therapy on Arterial Stiffness. *Biomed Res Int.* 2021;2021:5548310.
23. Upala S, Wirunsawanya K, Jaruvongvanich V, Sanguankeo A. Effects of statin therapy on arterial stiffness: A systematic review and meta-analysis of randomized controlled trial. *Int J Cardiol.* 2017;227:338–41.
24. Sever PS, Dahlöf B, Poulter NR, Wedel H, Beevers G, Caulfield M, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Drugs.* 2004;64(2):43–60.
25. Fitchett DH, Leiter LA, Goodman SG, Langer A. Lower is better: implications of the Treating to New Targets (TNT) study for Canadian patients. *Can J Cardiol.* 2006;22(10):835-9.
26. Chilton R, Tikkanen I, Cannon CP, Crowe S, Woerle HJ, Broedl UC, et al. Effects of empagliflozin on blood pressure and markers of arterial stiffness and vascular resistance in patients with type 2 diabetes. *Diabetes Obes Metab.* 2015;17(12):1180-93.
27. Solini A, Giannini L, Seghieri M, Vitolo E, Taddei S, Ghiadoni L, et al. Dapagliflozin acutely improves endothelial dysfunction, reduces aortic stiffness and renal resistive index in type 2 diabetic patients: a pilot study. *Cardiovasc Diabetol.* 2017;16(1):138.
28. Lopez MDCA, Lax A, Vicente AH, Guillen ES, Hernandez-Martinez A, Palacio MJFD, et al. Empagliflozin improves post-infarction cardiac remodeling through GTP enzyme cyclohydrolase 1 and irrespective of diabetes status. *Sci Rep.* 2020;10(1):13553.
29. Heerspink HJL, Perkins BA, Fitchett DH, Husain M, Cherney DZI. Sodium glucose cotransporter 2 inhibitors in the treatment of diabetes mellitus: cardiovascular and kidney effects, potential mechanisms, and clinical applications. *Circulation.* 2016;134(10):752–72.
30. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med.* 2015;373(22):2117–28.
31. McMurray JJV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med.* 2019;381(21):1995–2008.
32. Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med.* 2020;383(15):1413–24.
33. Armstrong PW, Pieske B, Anstrom KJ, Ezekowitz J , Hernandez AF, Butler J, et al. Vericiguat in patients with heart failure and reduced ejection fraction. *N Engl J Med.* 2020;382(20):1883–93.
34. Gheorghiade M, Greene SJ, Butler J, Filippatos G, Lam CSP, Maggioni AP, et al. Effect of vericiguat, a soluble guanylate cyclase stimulator, on natriuretic peptide levels in patients with worsening chronic heart failure and reduced ejection fraction: the SOCRATES-REDUCED randomized trial. *JAMA.* 2015;314(21):2251–62.
35. Pieske B, Maggioni AP, Lam CSP, Pieske-Kraigher E, Filippatos G, Butler J, et al. Vericiguat in patients with worsening heart failure with preserved ejection fraction: results of the SOluble guanylate Cyclase stimulatoR in heArT failurE patientS with PRESERVED EF (SOCRATES-PRESERVED) study. *Eur Heart J.* 2017;38(15):1119–27.
36. Cheng HS, Ton SH, Kadir KA. Therapeutic agents targeting the AGE-RAGE axis for the treatment of diabetes and cardiovascular disease: a review of clinical evidence. *Clin Diabetes Res.* 2017;1(1):16–34.
37. Asif M, Egan J, Vasan S, Jyothirmayi GN, Masurekar MR, Lopez S, et al. An advanced glycation endproduct crosslink breaker can reverse age-related increases in myocardial stiffness. *Proc Natl Acad Sci U S A.* 2000;97(6):2809–13.
38. Kass DA, Shapiro EP, Kawaguchi M, Capriotti AR, Scuteri A, deGroof RC, et al. Improved arterial compliance by a novel advanced glycation end-product crosslink breaker. *Circulation.* 2001;104(13):1464–70.
39. Wolffenbuttel BH, Boulanger CM, Crijns FR, Huijberts MS, Poitevin P, Swennen GN, et al. Breakers of advanced glycation end products restore large artery properties in experimental diabetes. *Proc Natl Acad Sci U S A.* 1998;95(8):4630–4.
40. Steppan J, Tran H, Benjo AM, Pellakuru L, Barodka V, Ryoo S, et al. Alagebrium in combination with exercise ameliorates age-associated ventricular and vascular stiffness. *Exp Gerontol*. 2012;47(8):565–72.
41. Nystrom T, Gutniak MK, Zhang Q, Zhang F, Holst JJ, Ahrén B, et al. Effects of glucagon-like peptide-1 on endothelial function in type 2 diabetes patients with stable coronary artery disease. *Am J Physiol Endocrinol Metab.* 2004;287(6):E1209–15.
42. Baylan U, Korn A, Emmens RW, Schalkwijk CG, Niessen HWM, Krijnen PAJ, et al. Liraglutide treatment attenuates inflammation markers in the cardiac, cerebral and renal microvasculature in streptozotocin-induced diabetic rats. *Eur J Clin Invest.* 2022;52(9):1–11.
43. Lambadiari V, Pavlidis G, Kousathana F, Varoudi M, Vlastos D, Maratou E, et al. Effects of 6-month treatment with the glucagon like peptide-1 analogue liraglutide on arterial stiffness, left ventricular myocardial deformation and oxidative stress in subjects with newly diagnosed type 2 diabetes. *Cardiovasc Diabetol*. 2018;17(1):1–12. doi: 10.1186/s12933-017-0646-z.
44. Zieman SJ, Kass DA. Advanced glycation endproduct crosslinking in the cardiovascular system: potential therapeutic target for cardiovascular disease. *Drugs.* 2004;64(5):459–70.
45. Shigiyama F, Kumashiro N, Miyagi M, Ikehara K, Kanda E, Uchino H, et al. Effectiveness of dapagliflozin on vascular endothelial function and glycemic control in patients with early-stage type 2 diabetes mellitus: DEFENCE study. *Cardiovasc Diabetol.* 2017;16(1):1–12.
46. Uthman L, Homayr A, Juni RP, Spin EL, Kerindongo R, Boomsma M, et al. Empagliflozin and Dapagliflozin reduce ROS generation and restore NO Bioavailability in tumor necrosis factor α-stimulated human coronary arterial endothelial cells. *Cell Physiol Biochem*. 2019;53(5):865–86.
47. Ikonomidis I, Pavlidis G, Thymis J, Birba D, Kalogeris A, Kousathana F, et al. Effects of glucagon-like peptide-1 receptor

agonists, sodium-glucose cotransporter-2 inhibitors, and their combination on endothelial glycocalyx, arterial function, and myocardial work index in patients with type 2 diabetes mellitus after 12-month treatment. *J Am Heart Assoc.* 2020; 9(9):1–21.

48. Gaspari T, Liu H, Welungoda I, Hu Y, Widdop RE, Knudsen LB, et al. A GLP-1 receptor agonist liraglutide inhibits endothelial cell dysfunction and vascular adhesion molecule expression in an ApoE−/− mouse model. *Diab Vasc Dis Res.* 2011;8(2):117–24.
49. Markl M, Harloff A, Bley TA, Zaitsev M, Jung B, Weigang E, et al. Time-resolved 3D MR velocity mapping at 3T: improved navigator-gated assessment of vascular anatomy and blood flow. *J Magn Reson Imaging.* 2007;25(4):824–31.
50. Hope TA, Markl M, Wigström L, Alley MT, Miller DC, Herfkens RJ. Comparison of flow patterns in ascending aortic aneurysms and volunteers using four-dimensional magnetic resonance velocity mapping. *J Magn Reson Imaging.* 2007;26(6):1471–9.
51. Doltra A, Stawowy P, Dietrich T, Schneeweis C, Fleck E, Kelle S. Magnetic resonance imaging of cardiovascular fibrosis and inflammation: from clinical practice to animal studies and back. *Biomed Res Int*. 2013;2013:676489:1–10. doi: 10.1155/2013/676489.
52. Tanaka H, DeSouza CA, Seals DR. Absence of age-related increase in central arterial stiffness in physically active women. *Arterioscler Thromb Vasc Biol.* 1998;18(1):127–32.

Cite this article: Menon AS, Kumar K. Targeting aortic elasticity: A promising therapeutic avenue in congestive heart failure and cardiac pumping disorders. *Indian J Pharma Pharmacol.* 2025;12(3):129–136