Biomedicine Advances

Biomed adv 2026;3(3):x-x
doi:10.34172/bma.85
https://biomedad.ae

Editorial

Cardiac Patch as a Superior Clinically Translatable Approach for Cardiac Regenerative Medicine

Sara Pahlavan[1*]

[1]Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran

***Corresponding Author:** Sara Pahlavan, Email: s.pahlavan@royan-rc.ac.ir

Received: May 2, 2026, **Revised:** May 29, 2026 **Accepted:** June 10, 2026, **ePublished:** June 25, 2026

A failing heart is far more challenging than a single organ insufficiency, as it can progress to a deteriorating condition with multi-organ impact and life-threatening outcomes.[1] Current therapeutic approaches focus on decelerating disease progression rather than restoring or preserving cardiac function.[2] Therefore, a shift toward more restorative biomedical approaches, including regenerative medicine, is necessary.[3]

Considerable research has been dedicated to cell-, gene-, and tissue-based therapies for heart failure. Over the past two decades, multiple cell types have been used for cardiac stem cell therapy, including bone marrow-derived multipotent stem cells, human pluripotent stem cells (hPSCs), and hPSC-derived cardiac progenitor cells and cardiomyocytes.[4] However, according to available reports, the observed therapeutic effects have not been clinically significant, and this approach has not become standard therapy. Limited retention and no signs of remuscularization have been suggested as underlying reasons, because a failing heart requires a substantial number of new contracting cardiomyocytes to restore sufficient pumping function. In contrast, tissue-based models have appeared promising in this regard. Engineered heart tissue, or cardiac patch, is a three-dimensional (3D) laboratory-grown model comprising different types of heart muscle cells as well as extracellular matrix. In principle, these tissues are formed from pre-differentiated cells derived from cardiogenic differentiation of hPSCs. Signs of remuscularization have been observed following implantation of 3D tissue-engineered allografts and xenografts in small and large animal models.[5-12] Importantly, large animal studies—particularly the 2025 report by Jebran and colleagues on allograft engineered heart muscle (EHM)—provided early proof-of-concept for the safety and efficacy of this new approach in heart failure, findings that could not be conclusively derived from small animal studies alone.[12-17] In xenograft models, the observed effects were determined to be partially induced by immune responses [18] or paracrine mechanisms [19, 20], rather than by remuscularization.

These findings led to the authorization of the first-in-patient Phase 1/2 clinical trial (ClinicalTrials.gov NCT04396899), named BioVAT-HF-DZHK20 in Germany, which aims to explore the safety and efficacy of allograft EHM. Primary results from an early BioVAT-HF patient receiving 10 EHM implants recapitulated large animal findings with respect to safety and remuscularization of the failing heart.[12] Furthermore, these results provided the basis for protocol revisions,

Author's Biosketch

Sara Pahlavan is a member of Cardiovascular Group at Royan Institute for Stem Cell Biology and Technology. She studied Biology in her B.Sc and graduated in M.Sc of Physiology from Shiraz University. During her undergraduate studies, she got interested in physiology of cardiac cells, specifically excitation-contraction coupling. To pursue her interest, she moved to Germany and started her graduate studies in Professor Peter Lipp's lab at Universitäts Klinikum des Saarlandes. There, she learned state of the art technologies such as simultaneous "patch-clamp" and "Ca^{2+}imaging" to study excitation-contraction coupling in cardiomyocytes. Furthermore, she used transgenic mice to study pathophysiology of inherited cardiac diseases with respect to electrophysiology and/or Ca^{2+}machinery. Toward the end of her PhD studies, she got interested in using patient-specific iPSC-derived cardiomyocytes to study cardiac disease in human cardiac cells and to test new drugs. To pursue this goal, she moved to United States and started her postdoctoral fellowship in Professor Martin Morad's lab at Medical University of South Carolina. There she could develop a new genetically-encoded Ca^{2+}probe to study Ca^{2+}induced Ca^{2+}release and Ca^{2+}sparks in cardiomyocytes of healthy and patient-specific iPSC-derived cardiomyocytes. She joined Royan Institute at 2015 and currently she works as an Associate Professor in cardiovascular Group.

such as increasing the dose of EHM implants to up to 20.[12] Unlike intramyocardial injections, epicardial EHM implants have shown no signs of arrhythmia, reducing concerns regarding this major adverse effect.[12-16]

In a nutshell, EHM studies have revived hopes for a novel cell-based therapy for heart failure and have demonstrated that these tissue-engineered models are superior to other non-myocyte grafts, as they result in functional remuscularization.[5,21] The findings of the currently ongoing clinical trial will be critical for future decision-making regarding next-generation therapies for advanced heart failure.[22]

Competing Interests
None declared.

Ethical Approval
Not applicable.

Funding
None.

Intelligence Use Disclosure
None.

References
1. Harjola VP, Mullens W, Banaszewski M, Bauersachs J, Brunner-La Rocca HP, Chioncel O, et al. Organ dysfunction, injury and failure in acute heart failure: from pathophysiology to diagnosis and management. A review on behalf of the Acute Heart Failure Committee of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur J Heart Fail 2017;19(7):821-36. doi:10.1002/ejhf.872
2. Netala VR, Teertam SK, Li H, Zhang Z. A comprehensive review of cardiovascular disease management: cardiac biomarkers, imaging modalities, pharmacotherapy, surgical interventions, and herbal remedies. Cells 2024;13(17):1471. doi:10.3390/cells13171471
3. Jacques E, Suuronen EJ. The progression of regenerative medicine and its impact on therapy translation. Clin Transl Sci 2020;13(3):440-50. doi:10.1111/cts.12736
4. Le TY, Thavapalachandran S, Kizana E, Chong JJ. New developments in cardiac regeneration. Heart Lung Circ 2017;26(4):316-22. doi:10.1016/j.hlc.2016.11.002
5. Zimmermann WH, Melnychenko I, Wasmeier G, Didié M, Naito H, Nixdorff U, et al. Engineered heart tissue grafts improve systolic and diastolic function in infarcted rat hearts. Nat Med 2006;12(4):452-8. doi:10.1038/nm1394
6. Weinberger F, Breckwoldt K, Pecha S, Kelly A, Geertz B, Starbatty J, et al. Cardiac repair in guinea pigs with human engineered heart tissue from induced pluripotent stem cells. Sci Transl Med 2016;8(363):363ra148. doi:10.1126/scitranslmed.aaf8781
7. Gao L, Gregorich ZR, Zhu W, Mattapally S, Oduk Y, Lou X, et al. Large cardiac muscle patches engineered from human induced-pluripotent stem cell-derived cardiac cells improve recovery from myocardial infarction in swine. Circulation 2018;137(16):1712-30. doi:10.1161/circulationaha.117.030785
8. Querdel E, Reinsch M, Castro L, Köse D, Bähr A, Reich S, et al. Human engineered heart tissue patches remuscularize the injured heart in a dose-dependent manner. Circulation 2021;143(20):1991-2006. doi:10.1161/circulationaha.120.047904
9. Jabbour RJ, Owen TJ, Pandey P, Reinsch M, Wang B, King O, et al. In vivo grafting of large engineered heart tissue patches for cardiac repair. JCI Insight 2021;6(15):e144068. doi:10.1172/jci.insight.144068
10. Stüdemann T, Rössinger J, Manthey C, Geertz B, Srikantharajah R, von Bibra C, et al. Contractile force of transplanted cardiomyocytes actively supports heart function after injury. Circulation 2022;146(15):1159-69. doi:10.1161/circulationaha.122.060124
11. Riegler J, Tiburcy M, Ebert A, Tzatzalos E, Raaz U, Abilez OJ, et al. Human engineered heart muscles engraft and survive long term in a rodent myocardial infarction model. Circ Res 2015;117(8):720-30. doi:10.1161/circresaha.115.306985
12. Jebran AF, Seidler T, Tiburcy M, Daskalaki M, Kutschka I, Fujita B, et al. Engineered heart muscle allografts for heart repair in primates and humans. Nature 2025;639(8054):503-11. doi:10.1038/s41586-024-08463-0
13. Chong JJ, Yang X, Don CW, Minami E, Liu YW, Weyers JJ, et al. Human embryonic-stem-cell-derived cardiomyocytes regenerate non-human primate hearts. Nature 2014;510(7504):273-7. doi:10.1038/nature13233
14. Liu YW, Chen B, Yang X, Fugate JA, Kalucki FA, Futakuchi-Tsuchida A, et al. Human embryonic stem cell-derived cardiomyocytes restore function in infarcted hearts of non-human primates. Nat Biotechnol 2018;36(7):597-605. doi:10.1038/nbt.4162
15. Shiba Y, Gomibuchi T, Seto T, Wada Y, Ichimura H, Tanaka Y, et al. Allogeneic transplantation of iPS cell-derived cardiomyocytes regenerates primate hearts. Nature 2016;538(7625):388-91. doi:10.1038/nature19815
16. Romagnuolo R, Masoudpour H, Porta-Sánchez A, Qiang B, Barry J, Laskary A, et al. Human embryonic stem cell-derived cardiomyocytes regenerate the infarcted pig heart but induce ventricular tachyarrhythmias. Stem Cell Reports 2019;12(5):967-81. doi:10.1016/j.stemcr.2019.04.005
17. Shiba Y, Fernandes S, Zhu WZ, Filice D, Muskheli V, Kim J, et al. Human ES-cell-derived cardiomyocytes electrically couple and suppress arrhythmias in injured hearts. Nature 2012;489(7415):322-5. doi:10.1038/nature11317
18. Vagnozzi RJ, Maillet M, Sargent MA, Khalil H, Johansen AKZ, Schwanekamp JA, et al. An acute immune response underlies the benefit of cardiac stem cell therapy. Nature 2020;577(7790):405-9. doi:10.1038/s41586-019-1802-2
19. Gnecchi M, He H, Liang OD, Melo LG, Morello F, Mu H, et al. Paracrine action accounts for marked protection of ischemic heart by Akt-modified mesenchymal stem cells. Nat Med 2005;11(4):367-8. doi:10.1038/nm0405-367
20. Gao L, Wang L, Wei Y, Krishnamurthy P, Walcott GP, Menasché P, et al. Exosomes secreted by hiPSC-derived cardiac cells improve recovery from myocardial infarction in swine. Sci Transl Med 2020;12(561):eaay1318. doi:10.1126/scitranslmed.aay1318
21. Didié M, Christalla P, Rubart M, Muppala V, Döker S, Unsöld B, et al. Parthenogenetic stem cells for tissue-engineered heart repair. J Clin Invest 2013;123(3):1285-98. doi:10.1172/jci66854
22. Evidence that engineered muscle could patch up failing hearts. Nature 2025. doi:10.1038/d41586-025-00193-1