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# Combination of Coronary Artery Bypass Grafting and Autologous CD133+ Bone Marrow Stem Cell Therapy in a Patient With Severe Ischemic Heart Failure: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ADE 1 Tri Wisesa Soetisna
E 1 Stephanie Wirakarsa
E 2 Hillary
B 1 Ferdinand Wong
B 1 Mark Kevin Devian
and collaborators*

1 Division of Adult Cardiac Surgery, Department of Thoracic and Cardiovascular Surgery, National Cardiovascular Center Harapan Kita, Jakarta, Indonesia
2 Department of Cardiology and Vascular Medicine, National Cardiovascular Center Harapan Kita, Jakarta, Indonesia

* A full list of authors is available on the website

**Corresponding Author:** Tri Wisesa Soetisna, National Cardiovascular Center Harapan Kita, Jl. Letjen S. Parman Kav. 87, 11420, Jakarta, Indonesia
Phone: +62 812-9090-7000, e-mail: tricts2000@yahoo.com

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**Conflict of interest:** None declared

**Patient:** Male, 69-year-old

**Final Diagnosis:** Chronic heart failure due to coronary artery disease involving three vessels (CAD 3VD) with low LVEF, chronic hypertension, mild renal insufficiency, no history of diabetes, and regular smoking

**Symptoms:** Chest discomfort • dyspnea

**Clinical Procedure:** —

**Specialty:** Cardiac surgery

**Objective:** Unusual or unexpected effect of treatment

**Background:** Severe ischemic heart failure with left ventricular ejection fraction (LVEF ≤35%) remains a major therapeutic challenge despite optimal medical therapy and surgical revascularization. Coronary artery bypass grafting (CABG) alone may not fully restore infarcted myocardium. Autologous CD133+ bone marrow stem cell (BMSC) therapy has been proposed as a regenerative adjunct to enhance myocardial recovery. We report the long-term clinical and functional outcome of a patient with advanced ischemic cardiomyopathy treated with combined CABG and CD133+ BMSC implantation.

**Case Report:** A 69-year-old man with multivessel coronary artery disease and severely reduced LVEF (20.4%) presented with New York Heart Association (NYHA) class III symptoms. He underwent CABG combined with intraoperative transepicardial and transseptal injection of autologous CD133+ BMSC without perioperative complications. At 6 months, functional capacity improved (6-minute walk distance from 240 m to 446 m), and NYHA class improved to I. At 2-year follow-up, further structural and functional improvement was observed, including increased LVEF of up to (63%), reduced ventricular volumes, decreased scar size, and improved wall motion score index. Peripheral blood microRNA profiling showed dynamic changes during follow-up.

**Conclusions:** This single-patient case describes a favorable long-term clinical and structural trajectory after combined CABG and autologous CD133+ stem cell therapy in severe ischemic heart failure. However, as an uncontrolled case observation, causality cannot be inferred, and the relative contributions of CABG, CD133+ cell implantation, and patient-specific recovery remain uncertain. These findings should be interpreted as observational and hypothesis-generating.

**Keywords:** Coronary Artery Bypass • Bone Marrow Cells • Regenerative Medicine • Ventricular Dysfunction

**Full-text PDF:** https://www.amjcaserep.com/abstract/index/idArt/953693





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## Introduction

Patients with severely reduced left ventricular ejection fraction (LVEF ≤ 35%) often present with extensive myocardial infarction and limited viable myocardium, resulting in limited functional recovery following coronary artery bypass grafting (CABG) alone. CABG combined with stem cell therapy has been explored as a potential approach to myocardial repair, supported by the regenerative capacity of stem cells, including their ability to proliferate and differentiate [1,2].

Autologous CD133+ bone marrow–derived stem cells have been investigated as a potential therapeutic option due to their capacity for myocardial retention and regenerative properties. Intramyocardial delivery during CABG provides an opportunity for targeted cell administration to ischemic regions [3]. However, previous clinical studies, including randomized trials, registry analyses, meta-analyses, and prior first-treated-patient cases of CD133+ implantation during CABG, have already explored this approach. The incremental contribution of the present case lies in its detailed long-term within-patient follow-up, which integrates structural, functional, and molecular parameters and highlights delayed recovery patterns in a patient with severe ischemic cardiomyopathy.

This case report is therefore observational and hypothesis-generating, illustrating the trajectory of recovery over 2 years after combined CABG and CD133+ cell implantation, without claiming causality. By providing a comprehensive temporal profile of clinical, imaging, and molecular data, this report offers contextual insight into the potential role of adjunctive CD133+ therapy in a selected cohort of patients with severe ischemic heart failure.

## Case Report

A 69-year-old man presented with recurrent dyspnea, chest discomfort, and progressive limitation of daily activities for more than 1 year and was classified as New York Heart Association (NYHA) class III. Vital signs were stable, and physical examination revealed no remarkable findings. The patient was a regular smoker, with no history of alcohol or substance abuse. His medical history included chronic hypertension and mild renal insufficiency, with no diabetes mellitus and no previous coronary interventions.

Coronary computed tomography angiography demonstrated multivessel coronary artery disease involving the left anterior descending, left circumflex, and right coronary arteries. Transthoracic echocardiography revealed severely reduced left ventricular systolic function with a LVEF of 20.4%. Baseline cardiac magnetic resonance imaging showed left ventricular end-systolic volume (LVESV) of 122.2 mL, left ventricular end-diastolic volume (LVEDV) of 153.6 mL, wall motion score index (WMSI) of 2.6, and myocardial scar size of 20%. Functional assessment revealed a 6-minute walk distance of 240 m, and the vascular endothelial growth factor (VEGF) level was 101.8 pg/mL (Table 1). The patient was then diagnosed

**Table 1.** Cardiac MRI findings, 6-minute walk test (6MWT) results, and vascular endothelial growth factor (VEGF) levels at baseline, 6-month follow-up, and 2-year follow-up. MicroRNA (miRNA) analysis was additionally performed at the 2-year follow-up.

| | Baseline | 6 months | 2 years |
|---|---|---|---|
| LVEF (%) | 20.40 | 18.96 | 63.00 |
| LVESV (mL) | 122.20 | 355.15 | 23.00 |
| LVEDV (mL) | 153.60 | 438.25 | 62.00 |
| WMSI | 2.60 | 2.00 | 1.00 |
| Scar size (%) | 20.00 | 38.15 | 9.00 |
| 6MWT (m) | 240.00 | 446.00 | 378.0 |
| VEGF | 101.80 | 51.35 | 19.66 |
| **MicroRNA analysis (2-year follow-up only)** | **Expression level** | | **Regulation** |
| miRNA 221-3p | 5.12 | | Upregulated |
| miRNA 221-5p | 3.40 | | Upregulated |
| miRNA 126-3p | 1.05 | | Downregulated |
| miRNA 126-5p | 8.08 | | Upregulated |

Abbreviations: LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVEDV, left ventricular end-diastolic volume; WMSI, wall motion score index; 6MWT, 6-minute walk test; VEGF, vascular endothelial growth factor. miRNA expression levels were assessed only at the 2-year follow-up.





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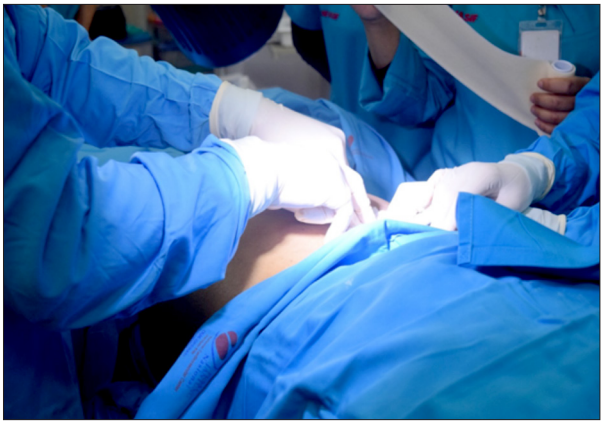

**Figure 1.** Bone marrow aspiration procedure from the posterior iliac crest.

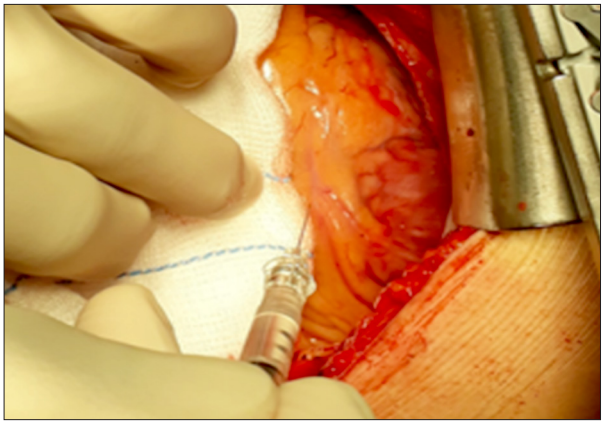

**Figure 2.** Intraoperative injection of the CD133+ stem cells along the transseptal segment.

with chronic heart failure due to coronary artery disease involving 3 vessels with low LVEF. Written informed consent for publication was obtained from the patient.

Autologous bone marrow (190-210 mL) was aspirated from the posterior iliac crest 1 day before surgery (**Figure 1**). CD133+ cells were isolated with a purity of 84.4% to 90.1% and viability of 94.4% to 95.2%, distributed into twenty 1-mL syringes, and stored at 4 to 8 °C. CABG was performed using the left internal mammary artery to graft the left anterior descending artery and saphenous vein grafts to the posterior descending artery and first diagonal coronary artery, with a Y-graft to the second obtuse marginal artery. After release of the aortic cross-clamp, 30 trans-epicardial intramyocardial injections (0.5 mL each) were administered to hypokinetic regions, followed by 10 transseptal injections into the interventricular septum under transesophageal echocardiographic guidance (**Figure 2**). Aortic cross-clamp and cardiopulmonary bypass times were 60 and 100 minutes, respectively. No intraoperative complications occurred. Postoperatively, the patient was extubated on day 2, discharged from intensive care on day 4, and released from the hospital on day 9 without complications.

At 6-month follow-up, the NYHA functional class improved from III to I, and the 6-minute walk distance increased from 240 m to 446 m. VEGF levels decreased from 101.80 pg/mL to 51.35 pg/mL, and WMSI improved from 2.6 to 2.0. Despite this clinical improvement, cardiac magnetic resonance imaging (MRI) showed a marked transient increase in left ventricular volumes, with a slight decrease in LVEF from 20.40% to 18.96%, an increase in LVESV from 122.2 mL to 355.15 mL, an increase in LVEDV from 153.6 mL to 438.25 mL, and an increase in scar size from 20% to 38.15%. These values were confirmed from the cardiac MRI assessment and are reported as measured. The discordance between the imaging findings and clinical status was interpreted as a transient, nonlinear remodeling pattern rather than clinical deterioration, as the patient showed no clinical worsening or adverse events at this time point.

At 2-year follow-up, the remodeling pattern had improved, with LVEF increasing to 63% (**Figure 3**), LVESV decreasing to 23 mL, LVEDV decreasing to 62 mL, scar size decreasing to 9%, and WMSI improving to 1.0. The 6-minute walk distance was 378 m, which was lower than the 6-month value of 446 m but remained higher than the baseline value of 240 m. Therefore, the functional outcome was interpreted as sustained improvement compared with baseline, but not as continuous progressive improvement from 6 months to 2 years. VEGF levels declined further to 19.66 pg/mL. Peripheral blood microRNA profiling revealed sustained modulation of miR-221-3p, miR-221-5p, and miR-126-5p. The overall study timeline is illustrated in **Figure 4**. The patient remained clinically stable without adverse events.

## Discussion

This case documents sustained structural improvement observed after combined CABG and autologous CD133+ bone marrow stem cell implantation in a patient with advanced ischemic cardiomyopathy. The patient in this case also showed improvement in functional capacity from baseline. There was a slight decrease in the 6-minute walk distance between the 6-month and 2-year follow-up, but it was still an increase from baseline. However, because this is a single-patient case report, the relative contribution of CABG, CD133+ cell implantation, natural recovery, and patient-specific factors cannot be determined. Bone marrow–derived stem cells have been investigated as potential therapeutic agents because of their ability to home to sites of myocardial injury and their low immunogenicity. CD133+ cells, in particular, exhibit higher myocardial retention than non-selected bone marrow cells, and combined transepicardial and transseptal delivery may enable targeted delivery to ischemic myocardial regions [4-6].







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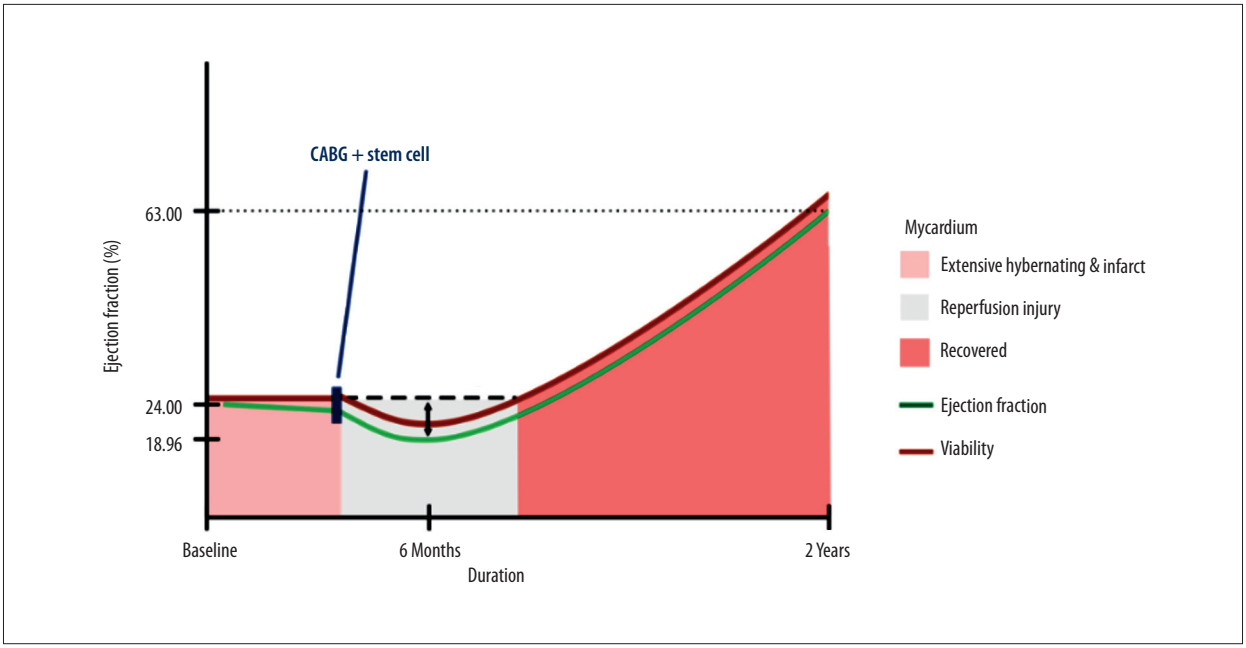


**Figure 3.** Effect of reperfusion on myocardial viability and contractile function over the course of 2 years.

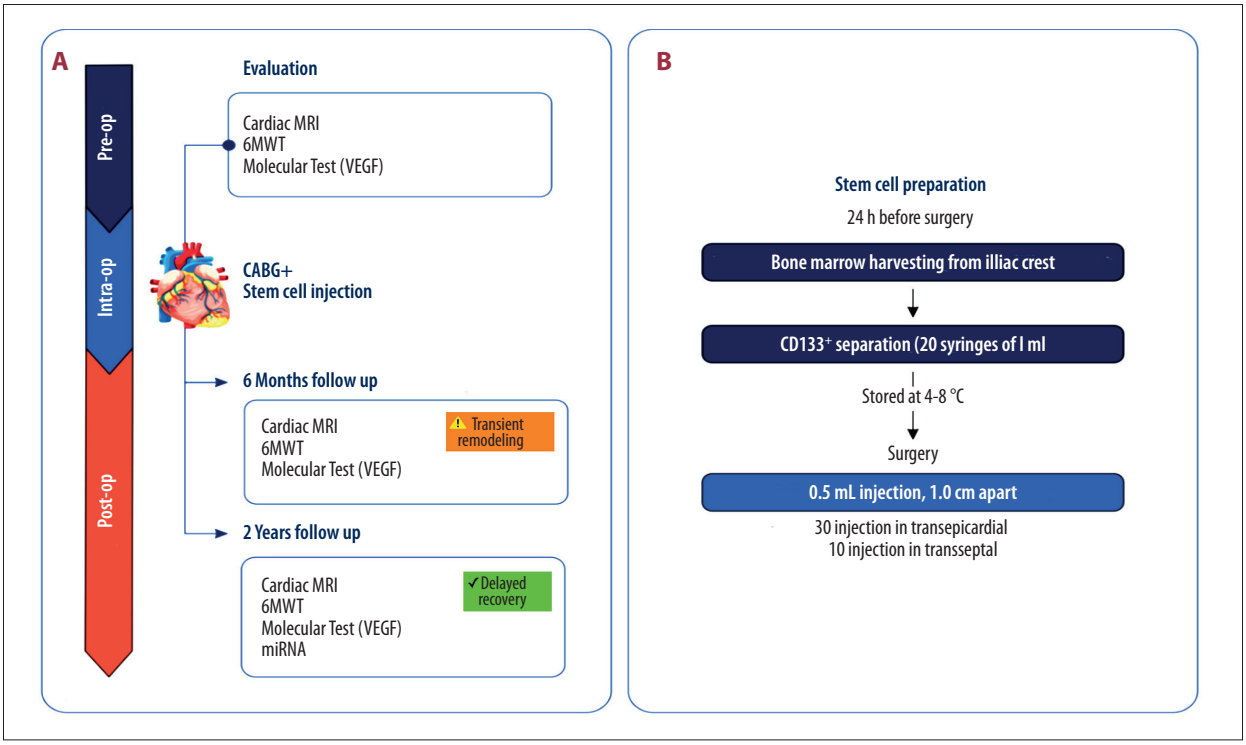


**Figure 4. Study outline and stem cell implantation protocol.** (**A**) The patient underwent preoperative evaluation with cardiac magnetic resonance imaging (MRI), the 6-minute walk test (6MWT), and measurement of vascular endothelial growth factor (VEGF) before surgery. These assessments were repeated at 6 months and 2 years after surgery. MicroRNA (miRNA) analysis was additionally performed at the 2-year follow-up. (**B**) Bone marrow was harvested from the iliac crest 24 hours before surgery. CD133+ cells were isolated and aliquoted into 20 syringes, each containing 1 mL, and stored at 4 to 8 °C until implantation. During surgery, 0.5-mL injections were performed 1 cm apart (30 injections in the transepicardial area and 10 injections in the transseptal area).





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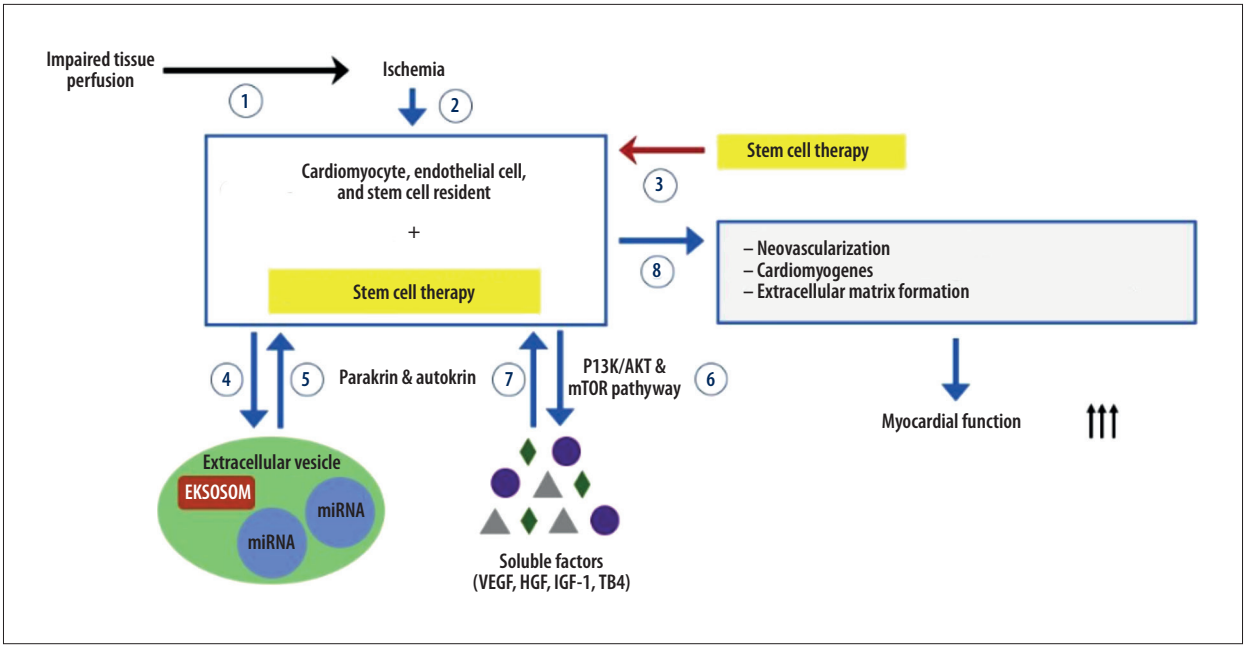


**Figure 5.** A summary of stem cell intracellular communication through paracrine and autocrine pathways leading to improvement of myocardial function.

Transient deterioration in ventricular parameters observed at early follow-up may reflect reperfusion injury and inflammatory responses following surgical revascularization. Similar delayed recovery patterns have been reported in patients with hibernating myocardium, in whom myocardial functional restoration may require prolonged periods after CABG [7-10]. Long-term functional improvement has also been described by Nesteruk et al, who reported gradual recovery of left ventricular performance for up to 5 years following combined CABG and stem cell therapy [4]. In the present case, the 6-month cardiac MRI findings showed transient worsening of structural parameters, including a decrease in LVEF from 20.40% to 18.96%, an increase in LVESV from 122.2 mL to 355.15 mL, an increase in LVEDV from 153.6 mL to 438.25 mL, and an increase in scar size from 20% to 38.15%. This early deterioration was not accompanied by clinical worsening or adverse events, and by the 2-year follow-up, LVEF had increased to 63%, LVESV had decreased to 23 mL, LVEDV had decreased to 62 mL, and scar size had decreased to 9%.

The increase in LVEF from 20.40% at baseline to 63% at 2 years is exceptional and should be interpreted cautiously. CABG alone can improve ventricular function when viable or hibernating myocardium is successfully revascularized, particularly over longer follow-up periods. At the same time, adjunctive CD133+ cell implantation may have contributed through paracrine and angiogenic mechanisms, although this cannot be confirmed in a single case [11]. Therefore, the marked improvement observed in this patient is most plausibly explained by a combination of complete surgical revascularization, delayed recovery of viable but dysfunctional myocardium, possible adjunctive biological effects of CD133+ cell implantation, and patient-specific factors, rather than by stem cell therapy alone.

Experimental studies suggest that bone marrow-derived stem cells may attenuate adverse left ventricular remodeling in ischemic myocardium, in part through paracrine-mediated effects [12]. The gradual improvement in left ventricular function observed in this patient is consistent with previous reports describing delayed recovery after combined revascularization and regenerative therapy [9,12-15].

Functional recovery, reflected by improvement in WMSI and exercise capacity, may suggest improvement in regional myocardial function after combined treatment, but it does not establish that adjunctive stem cell therapy directly enhanced myocardial viability [16]. The accompanying molecular changes should also be interpreted as exploratory observations. Dynamic microRNA expression and declining VEGF levels may be temporally associated with vascular remodeling, inflammatory resolution, or myocardial recovery processes (**Figure 5**) [17-19]. However, these biomarker changes do not establish a mechanistic relationship or prove that the observed clinical improvement was mediated by stem cell-related regeneration. Rather, they provide hypothesis-generating observations that may inform future studies evaluating molecular responses after combined CABG and cell-based therapy.

Patient-related factors may also influence therapeutic response. Absence of diabetes mellitus may have favored stem







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cell function, as hyperglycemia is known to impair stem cell viability and regenerative capacity [20]. Although reduced renal function has been associated with diminished responsiveness in some studies, this patient exhibited favorable recovery despite mild renal insufficiency. These findings suggest that comorbidities may modify recovery patterns, but their influence cannot be determined from this single case.

This report is limited by its single-patient design, precluding causal inference or generalization. The marked long-term improvement observed after combined CABG and CD133+ cell implantation should therefore be regarded as hypothesis-generating rather than evidence of therapeutic efficacy. Nevertheless, it highlights the potential role of adjunctive CD133+ stem cell therapy during CABG in carefully selected patients with severe ischemic heart failure. Larger prospective studies are warranted to define optimal patient selection, refine delivery strategies, clarify biological mechanisms, and determine long-term clinical benefit.

## Conclusions

This case describes the long-term clinical, structural, functional, and molecular follow-up of a single carefully selected patient with severe ischemic heart failure who underwent combined CABG and autologous CD133+ bone marrow stem cell implantation. Over 2 years, the patient showed a favorable trajectory in several clinical and imaging parameters. Because this is a single uncontrolled case observation, causal benefit from CD133+ cell therapy cannot be inferred. The relative contributions of CABG, CD133+ cell implantation, natural recovery, and patient-specific factors remain uncertain. Therefore, these findings should be interpreted as descriptive and hypothesis-generating. Further prospective studies are needed to clarify patient selection, delivery strategies, biological mechanisms, and the long-term clinical value of adjunctive cell-based therapy during CABG in severe ischemic heart failure.

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### Department and Institution Where Work Was Done

National Cardiovascular Center Harapan Kita, Jakarta, Indonesia.

### Patient Consent

Obtained.

### Statement

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### Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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