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Case Report

Clinical Improvement and Recovery of Systolic Function in Chronic Triple-Vessel Coronary Artery Disease with Controlled Diabetes Mellitus After Long-Term Conservative Management and Adjunctive Hydrogen Nanobubble Infusion Therapy: A Case Report

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Abstract

Background: Chronic coronary artery disease (CAD) with triple-vessel involvement and diabetes mellitus is a high-risk condition that often leads to a recommendation for coronary artery bypass grafting (CABG). This report presents the course of a 67-year-old man with chronic CAD, old myocardial infarction, and controlled diabetes mellitus who declined CABG and underwent conservative management and Hydrogen Nanobubble Infusion Therapy. **Methods:** This retrospective descriptive case report was compiled from history taking, physical examination, and review of medical records from 2012 to 2025. **Case Presentation:** Coronary angiography demonstrated triple-vessel disease, and CABG was recommended, but the patient declined surgery. He was managed with medical therapy, lifestyle modification, Enhanced External Counterpulsation, laser therapy, chelation infusion, and follow-up. Serial echocardiography in 2025 showed mildly reduced to low-normal left ventricular systolic function, regional wall motion abnormalities, and impaired relaxation. After 12 sessions of Hydrogen Nanobubble Infusion Therapy, the patient reported symptomatic improvement, and a follow-up reevaluation reportedly documented an increase in left ventricular ejection fraction from approximately 52% to 62%. **Conclusion:** The post-treatment symptomatic improvement and reported increase in systolic performance are interesting, but causality cannot be established from a single case. The findings should be interpreted as hypothesis-generating and warrant structured investigation.

Keywords: chronic coronary artery disease; triple-vessel disease; diabetes mellitus; hydrogen nanobubble infusion therapy; conservative management; case report

1. Introduction

Chronic coronary artery disease involving multiple epicardial vessels remains a major cause of morbidity and mortality, particularly in older adults with diabetes mellitus [1]. In patients with diffuse multivessel disease, chronic total occlusion, and evidence of previous myocardial injury, revascularization by coronary artery bypass grafting is frequently recommended in order to improve prognosis and reduce ischemic burden [1,2].

In real-world practice, however, not every patient accepts surgical revascularization. Long-term conservative management therefore becomes an individualized strategy that relies on optimal medical therapy, risk-factor control, functional monitoring, and in selected cases, adjunctive non-surgical interventions [1]. This case is notable because the patient remained clinically stable for more

than a decade despite anatomically severe coronary disease, and later experienced meaningful symptomatic improvement after adjunctive Hydrogen Nanobubble Infusion Therapy.

Because the clinical use of molecular hydrogen-based therapy in chronic ischemic heart disease is still emerging [3,4], this report focuses not only on the patient's longitudinal course but also on the biological rationale and interpretive context for Hydrogen Nanobubble Infusion Therapy.

2. Methods

This manuscript was prepared as a retrospective descriptive case report. Data were obtained from direct anamnesis, family-provided history, physical examination at follow-up evaluation, and review of serial medical records dated 2012-2025. The dataset included prior digital subtraction angiography, coronary angiography, serial electrocardiograms, serial echocardiograms, carotid duplex ultrasonography, and laboratory findings from June 2024, January 2025, June 2025, and September 2025. The patient's identity has been anonymized as Mr. K. Interpretation was performed narratively and clinically. Because this is a single-patient observational report without a comparator, no causal inference is claimed for any adjunctive intervention.

3. Case Presentation

Mr. K, a 67-year-old man, was evaluated on 08 September 2025 because of easy fatigability and shortness of breath when walking long distances or performing heavy physical activity. The symptom had been present since 2013. It was most prominent during prolonged walking or strenuous exertion, but it did not occur during lighter-to-moderate activity such as climbing stairs. The symptom improved with rest. He denied chest pain, dizziness, focal weakness, cold sweating, radiating pain, wheezing, cough, nausea, and abdominal bloating.

The illness history began in 2012, when he suddenly experienced unsteady gait and visual dimming after returning home from work late at night. He was still able to sleep, but the next morning the symptoms persisted and worsened to the point that he nearly fell. He was taken to hospital, where a dangerous lesion involving a small cerebral vessel was suspected. He was referred to Gatot Soebroto Army Hospital and underwent digital subtraction angiography (DSA). A general pre-procedure evaluation was reportedly considered normal and safe. After the DSA procedure, the neurologic symptoms resolved.

During hospitalization, however, after transfer from the intensive care unit to the inpatient ward, he developed persistent cough, mild dyspnea, and cold sweating without chest pain. Evaluation showed massive fluid accumulation in the lungs. Supportive treatment with nasal cannula, mask oxygen, and bagging was insufficient, and mechanical ventilation became necessary. He remained on ventilatory support for less than 14 days, after which the pulmonary fluid resolved and the clinical condition improved.

A subsequent cardiac catheterization was performed to assess the coronary circulation. Coronary angiography from 2012 showed a short, normal left main coronary artery; 60% proximal stenosis of the left anterior descending artery (LAD) with total occlusion distal to the first septal branch; 99% proximal stenosis of the left circumflex artery (LCX) with delayed distal filling; and 80% plus 60% proximal stenoses of the right coronary artery (RCA) with total occlusion of the mid RCA. Collateral circulation to the distal LAD and distal RCA was described. The angiographic conclusion was triple-vessel disease and CABG was recommended. The patient declined surgery despite similar recommendations from several hospitals.

He later sought treatment with Dr. Raymond, a cardiologist in Jakarta, and underwent a long-term conservative program consisting of medical therapy, Enhanced External Counterpulsation (EECP), laser therapy, chelation infusion, and routine follow-up. According to the history, an initial course of approximately 10 treatment sessions led to notable symptomatic improvement. Since 2013 he has continued maintenance therapy approximately every two months. No repeat coronary catheterization has been performed to date.

Past medical history included chronic coronary artery disease, old myocardial infarction, and diabetes mellitus for more than 20 years. The diabetes has remained clinically stable with oral medication, and the patient reported no active diabetes-related symptoms. He denied smoking and alcohol consumption. He maintained a disciplined diet with reduced sugar and fat intake, restricted fried foods, limited rice portions, and a preference for olive oil and coconut oil at home. He also performed daily morning walking for approximately 45 minutes without major symptoms.

Regular medications included Carpiaton 100 mg once daily, Nebilet 5 mg once daily, Candotens 16 mg once daily, Lopiten 10 mg once daily, Q-Ten twice daily, Suvesco 40 mg once daily, Ezetrol 10 mg once daily, Fibrinase once daily, Nospirinal 80 mg once daily, Janumet once daily, Gludepatic 500 mg three times daily, Lycoxy once daily, Forxiga once daily, Tride capsule once daily, and Arcalion twice daily. He also underwent routine EECp, laser therapy, and chelation infusion approximately every two months after the 2012 DSA procedure. The principal clinical, electrocardiographic, echocardiographic, vascular, and laboratory findings are summarized in Table 1.

Table 1. Summary of clinical findings.

Domain	Main Findings
Physical examination (September 8, 2025)	General condition good; jugular venous pressure not elevated; single S1-S2, no murmur, no gallop; normal breath sounds without crackles or wheeze; abdomen soft and non-tender; extremities warm with CRT <2 s; no edema.
Neurologic examination	Cranial nerves within normal limits; motor strength 5/5 in upper and lower extremities; sensation preserved; physiologic reflexes +2 symmetrically; pathologic reflexes absent.
Electrocardiography (September 2025)	Old infarct pattern; September 2025 ECG noted normal sinus rhythm, normal axis, old inferior myocardial infarction, and markedly abnormal ECG interpretation.
Echocardiography (January 2025)	LVEF approximately 54.3% by M-mode/Teich and 56.4% by modified biplane; regional hypokinesia involving mid anteroseptal and mid anterolateral wall; impaired LV relaxation; E/A approximately 0.524; medial E/e' approximately 14.1.
Echocardiography (September 2025)	LVEF approximately 54.5% by MM-Teich and approximately 51.5-51.6% by modified methods; left atrial dimension 4.16 cm; persistent segmental wall motion abnormality and impaired relaxation pattern.
Carotid duplex ultrasonography (January 2025)	Irregular calcified plaques in bilateral common carotid/carotid bulb regions without hemodynamically significant stenosis; antegrade flow maintained.
Laboratory examination (June 2024)	HbA1c 7.1%; estimated average glucose 157 mg/dL; LDL direct 73 mg/dL; creatinine 0.91 mg/dL; eGFR >90 mL/min/1.73 m ² ; urine albumin-creatinine ratio (ACR) 46.2 mg/g.
Laboratory examination (June 2025)	HbA1c 7.0%; estimated average glucose 154 mg/dL; creatinine 0.90 mg/dL; eGFR >90 mL/min/1.73 m ² ; urine ACR 37.3 mg/g.
Post-treatment follow-up (September 25, 2025)	After 12 sessions of therapy, the patient reported no current symptoms, improved body strength, and no exertional breathlessness during heavier activity or long-distance walking. A follow-up clinical reevaluation dated 25 Sep 2025 reportedly noted improvement in ejection fraction from about 52% to about 62%.

4. Discussion

This case involves a patient with anatomically severe chronic coronary artery disease, including triple-vessel involvement, chronic total occlusion, previous myocardial infarction, and diabetes mellitus—a combination that would usually support a recommendation for surgical

revascularization [1,2]. Nevertheless, the patient declined CABG and remained on long-term conservative treatment. The key point of interest in this report is not whether conservative management replaced guideline-based revascularization, but whether adjunctive Hydrogen Nanobubble Infusion Therapy may have contributed to the recent symptomatic and functional improvement observed late in the disease course.

The biological rationale for hydrogen-based therapy is grounded in oxidative stress biology [3]. Molecular hydrogen has been reported to act as a selective antioxidant, especially against highly cytotoxic oxygen radicals, while potentially sparing reactive oxygen species that are involved in normal signaling [5]. In chronic ischemic heart disease, persistent oxidative stress, endothelial dysfunction, mitochondrial injury, inflammatory activation, and impaired microvascular regulation all contribute to progressive ventricular dysfunction and reduced exercise tolerance [3,6]. Therefore, a hydrogen-based intervention is biologically plausible as an adjunctive strategy aimed at myocardial protection rather than anatomical revascularization [3].

Preclinical cardiovascular studies support this rationale [7]. In a rat myocardial ischemia-reperfusion model, inhaled hydrogen gas reduced infarct size and attenuated ischemia-reperfusion injury [8]. In a canine model, hydrogen-mediated cardioprotection was associated with mitochondrial ATP-sensitive potassium channels and permeability transition pore modulation, suggesting preservation of mitochondrial integrity during reperfusion injury [7]. These mechanisms are relevant because chronic ischemic myocardium often contains a mixture of scarred tissue, hibernating segments, and viable but metabolically stressed myocardium [9]. Any intervention capable of reducing oxidative damage, stabilizing mitochondria, or improving microvascular function could theoretically improve contractile efficiency in the residual viable myocardium.

Human clinical evidence remains limited but is emerging [3,7]. A first-in-human pilot study reported that hydrogen gas inhalation in patients with post-cardiac arrest syndrome was feasible and did not produce treatment-related serious adverse effects [7]. Another pilot study in ST-elevation myocardial infarction patients undergoing primary PCI suggested that hydrogen gas inhalation was safe and may favor reverse left ventricular remodeling over time, although that study was not powered to demonstrate definitive efficacy [10]. Separate human work has also shown improvement in peripheral endothelial function with high-dissolved-hydrogen water, which supports the broader vascular relevance of hydrogen-based interventions [11]. Collectively, these data do not establish standard-of-care use in chronic coronary artery disease, but they do provide a biologically coherent and clinically relevant background for further exploration.

The specific issue in this case is the use of Hydrogen Nanobubble Infusion Therapy rather than inhaled hydrogen. Nanobubble systems are of particular interest because they may enhance gas stability, facilitate dispersion in liquid media, and potentially improve bioavailability of dissolved gases compared with conventional gas delivery methods [12,13]. Although the exact pharmacokinetic behavior of intravenously delivered hydrogen nanobubbles in chronic cardiac disease is not yet established, the nanobubble platform may offer theoretical advantages as a carrier system [4,13]. At present, however, published clinical evidence specific to intravenous hydrogen nanobubble infusion in chronic triple-vessel coronary artery disease is still insufficient [4,13]. Therefore, the present case should be viewed as a carefully described clinical observation rather than proof of efficacy.

The patient's longitudinal course is also important for interpretation. For more than a decade he had remained relatively stable on medical therapy, lifestyle control, and periodic adjunctive conservative treatments such as EECF, laser therapy, and chelation infusion. Serial echocardiography in early and later 2025 generally showed left ventricular ejection fraction in the low-normal to mildly reduced range, with persistent regional wall motion abnormality and diastolic relaxation impairment. Against this background, the post-treatment change reported after 12 sessions of Hydrogen Nanobubble Infusion Therapy—together with the patient's subjective report of stronger physical condition and disappearance of exertional breathlessness during heavier activity—is clinically noteworthy.

Even so, causality cannot be determined from a single case. Several alternative explanations remain possible: natural physiologic fluctuation, measurement variability between echocardiographic methods and operators [14], changes in loading conditions, cumulative effects of the patient’s longstanding background therapy, or combined rather than isolated treatment effects. The reported increase of ejection fraction to approximately 62% on 25 September 2025 should therefore be presented as a follow-up clinical finding rather than as definitive evidence that Hydrogen Nanobubble Infusion Therapy alone restored systolic function.

Despite these limitations, this case has value for hypothesis generation. It suggests that in carefully selected patients with chronic ischemic heart disease, adjunctive hydrogen-based therapy may deserve prospective study with standardized end points such as repeated echocardiography by the same method, 6-minute walk distance, NYHA functional class, biomarker profiling, endothelial function assessment, and, when clinically justified, follow-up ischemia or perfusion imaging. The case also highlights the need to separate three questions in future research: safety, symptom benefit, and structural/functional cardiac improvement. Demonstrating safety and feasibility is not the same as proving disease-modifying efficacy, but both steps are necessary in the development of a new therapy.

5. Conclusions

This report describes a 67-year-old man with chronic triple-vessel coronary artery disease, old myocardial infarction, and controlled diabetes mellitus who declined CABG and remained on long-term conservative treatment. Over more than ten years, he maintained relative clinical stability, with exertional fatigue and breathlessness mainly during prolonged or heavy activity but no typical angina and no overt signs of active congestive heart failure at the latest evaluation.

After 12 sessions of adjunctive Hydrogen Nanobubble Infusion Therapy, the patient reported meaningful improvement in exercise-related symptoms, and a follow-up clinical reevaluation reportedly documented an increase in left ventricular ejection fraction from approximately 52% to 62%. This finding is clinically intriguing but should be interpreted cautiously. The present case does not establish causation; instead, it supports the need for more rigorous prospective studies on Hydrogen Nanobubble Infusion Therapy as a potential adjunctive strategy in chronic ischemic heart disease.

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Institutional Review Board Statement: The preparation and publication of this retrospective single-patient case report were conducted in accordance with the Declaration of Helsinki. Ethical review and approval were not required because the report was based solely on information documented during routine clinical care. No intervention was prospectively assigned for research purposes, and no additional procedures were performed solely for the preparation of this manuscript.

Informed Consent Statement: Written informed consent was obtained from the patient for publication of this paper and the anonymized clinical information contained herein.

Data Availability Statement: Relevant data supporting this case report are presented within the manuscript. Additional patient-level clinical records are not publicly available because of patient privacy and confidentiality restrictions.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

ACR Albumin-to-creatinine ratio

ATP	Adenosine triphosphate
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
DSA	Digital subtraction angiography
E/A	Ratio of early to late transmitral inflow velocity
E/e′	Ratio of early transmitral flow velocity to early diastolic mitral annular velocity
ECG	Electrocardiography
EECP	Enhanced External Counterpulsation
eGFR	Estimated glomerular filtration rate
HbA1c	Glycated hemoglobin A1c
LAD	Left anterior descending artery
LCx	Left circumflex artery
LDL	Low-density lipoprotein
LV	Left ventricular
LVEF	Left ventricular ejection fraction
NYHA	New York Heart Association
PCI	Percutaneous coronary intervention
RCA	Right coronary artery

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