



Case Report

Exercise echocardiography for a differential diagnosis in a patient with radiation-induced heart disease: A case report



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ABSTRACT

Advances in radiation therapy (RT) have dramatically improved the survival rates of patients with cancer, but radiation-induced heart disease (RIHD) has become an emerging problem, which is complex and multifaceted. A 65-year-old man with a medical history of chemoradiotherapy for esophageal cancer, who had multiple admissions for acute heart failure (AHF), was readmitted to our hospital. Transthoracic echocardiography at rest revealed left ventricular diastolic dysfunction, moderate aortic stenosis with mild aortic regurgitation, and mild mitral regurgitation (MR). A diagnosis of RIHD was obtained, however, the main cause of the AHF was not clearly understood. Exercise echocardiography (ExE) revealed an exacerbation of the MR and exercise-induced pulmonary hypertension (EIPH), and the severe dynamic MR was considered to be the main cause of the AHF. A transcatheter edge-to-edge repair (TEER) with a MitraClip (Abbott Vascular, Menlo Park, CA, USA) was performed, and the post-procedural ExE showed the mitigation of the dynamic MR and EIPH. He had no further heart failure admissions for more than one year.

Our case showed that ExE may be useful in the management of patients with RIHD, and a TEER with a MitraClip may be an effective treatment for RT-related dynamic MR.

Learning objective: Radiation therapy (RT) has improved the survival rates of patients with cancer, but which involves radiation-induced heart disease (RIHD). RIHD is complex and multifaceted, and RT-related valvular disease may be underestimated with transthoracic echocardiography at rest alone. Then exercise echocardiography may be useful in the management. It is important to perform an individualized approach including medical therapy, surgery, and percutaneous intervention by a heart team.

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Introduction

Advances in radiation therapy (RT) have dramatically improved the survival rates of patients with cancer, but late side effects such as radiation-induced heart disease (RIHD) have become an emerging problem [1]. RIHD is a late onset, irreversible, and progressive disease after radiation to the mediastinum, and endothelial injury, oxidative stress and inflammation, and endoplasmic reticulum and mitochondrial damage are considered to be the main causes. The patients sometimes have multiple heart diseases, and its management may be difficult. We herein report a patient with RIHD and dynamic mitral regurgitation (MR), who had repeated admissions for acute heart failure (AHF) within

a short period, in which exercise echocardiography (ExE) was useful in the management.

Case report

The patient was a 65-year-old man with a medical history of chemoradiotherapy, with a total of 60 Gy of radiation, for esophageal cancer about 20 years previously. Although his symptoms were generally stable during daily life, he had multiple admissions for AHF (5 times over a 2-year period), all of which occurred with a sudden onset of flash pulmonary edema. He was prescribed azosemide 30 mg/day, azilsartan 40 mg/day, nifedipine 20 mg/day, and bisoprolol 2.5 mg/day to strengthen the management of blood pressure (BP), and his BP and volume status were well controlled. However, he was readmitted to our hospital with sudden dyspnea. On the initial assessment, the pulse rate was 102 beats/min, BP 178/82 mmHg, respiratory rate 28 breaths/min, and oxygen saturation 96 % on 10 L of oxygen. A physical examination

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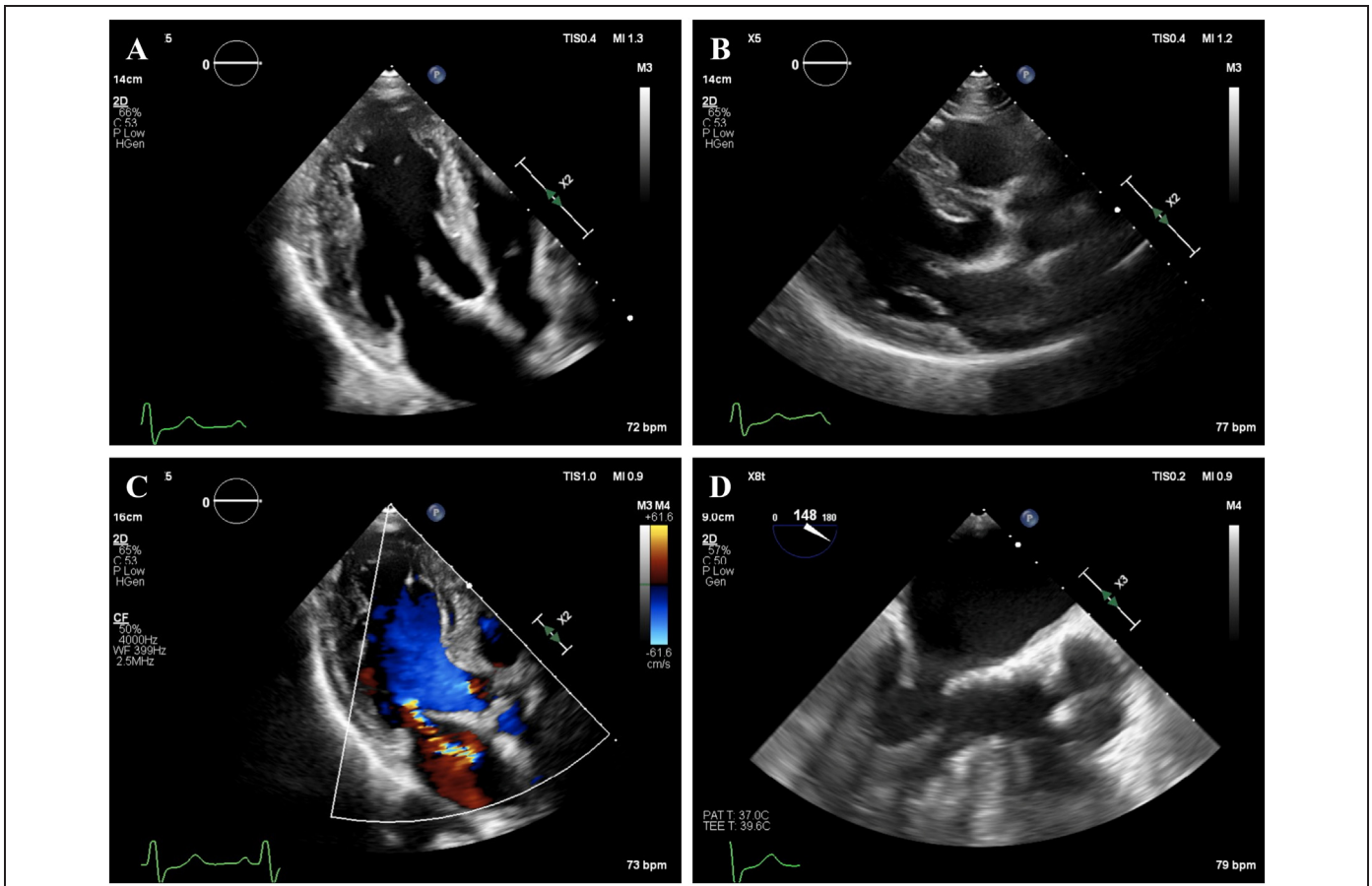


Fig. 1. Pre-procedural transthoracic and transesophageal echocardiography. Transthoracic echocardiography (TTE) showed (A, B) diffuse thickened mitral leaflets without calcifications, thickening and calcifications of the aortic-mitral curtain, and (C) mild mitral regurgitation. (D) Transesophageal echocardiography also showed the same findings as the TTE.

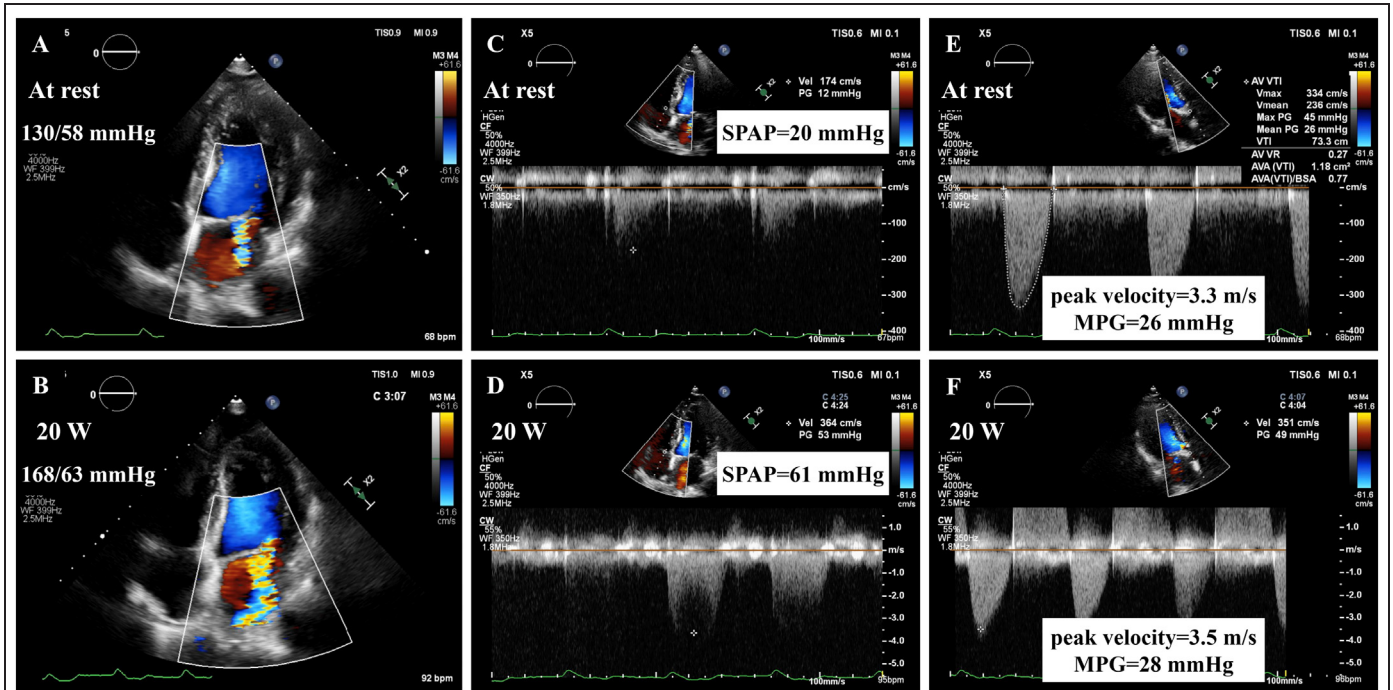


Fig. 2. Pre-procedural exercise echocardiography. The mitral regurgitation (MR) increased from mild at rest (A) to severe at 20 W (B), and the systolic pulmonary arterial pressure (SPAP) increased from 20 mmHg (C) to 61 mmHg (D) (right atrial pressure was estimated at 8 mmHg). The MR was evaluated with a qualitative assessment of regurgitant jet area by color Doppler because a proximal isovelocity surface area could not be clearly revealed. (E, F) The severity of the aortic stenosis did not change [peak velocity from 3.3 m/s to 3.5 m/s and mean pressure gradient (MPG) from 26 mmHg to 28 mmHg].

revealed jugular venous distension and wheezing and crackles over the entire lungs, but no pretibial edema was found. The electrocardiogram exhibited sinus rhythm and complete left bundle branch block. Chest radiography revealed bilateral pulmonary edema. The blood tests exhibited an elevated brain natriuretic peptide level (553.1 pg/mL, normal value; <18.4 pg/mL). He was again diagnosed with AHF, and noninvasive positive pressure ventilation and intravenous nitroglycerin resolved the hypoxia and dyspnea.

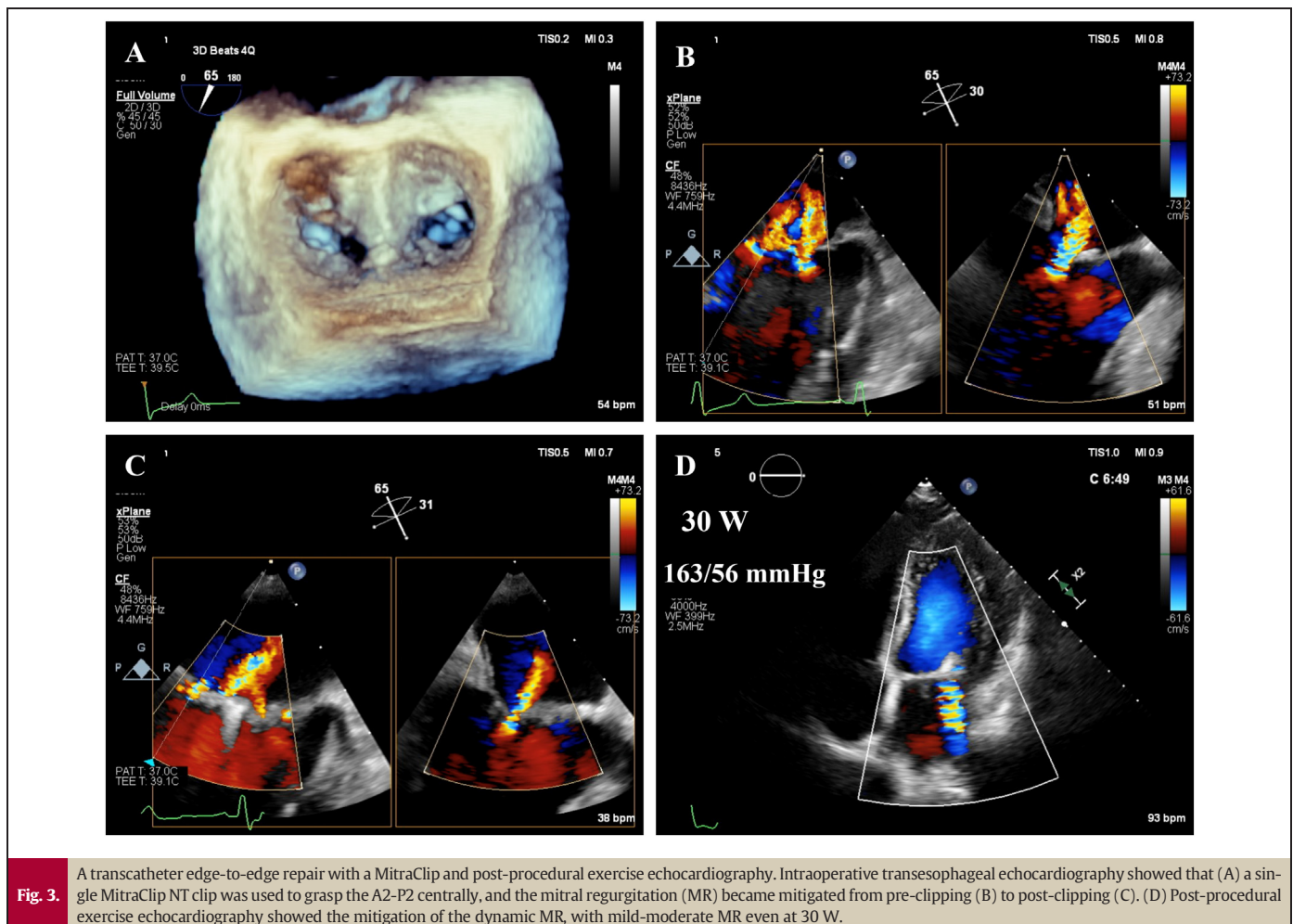
Transthoracic echocardiography (TTE) revealed a nondilated left ventricle (LV) with an ejection fraction of 55 % and stroke volume index of 56.5 mL/m², diastolic dysfunction (an E/A ratio of 0.9 and E/E' of 22.3), mild MR, mild aortic regurgitation, and moderate aortic stenosis (AS) in the aortic valve area by a continuity equation of 1.18 cm², peak velocity of 3.3 m/s, mean pressure gradient of 26 mmHg, but no obvious intraventricular dyssynchrony was observed. The TTE showed diffuse thickened mitral leaflets without calcifications in addition to thickening and calcifications of the aortic-mitral curtain (AMC) (Fig. 1A-C). Transesophageal echocardiography also showed the same findings as the TTE (Fig. 1D). The mean transmitral valve gradient was 1.5 mmHg, and the mitral valve area by planimetry on 3D imaging was 3.35 cm². The cardiac catheterization revealed mild coronary artery stenosis with calcifications and a mean transaortic gradient of 30 mmHg.

A diagnosis of RIHD was obtained because he had RT including of the heart and multiple heart diseases, however, the main cause of the AHF was not clearly understood. ExE was performed. The MR increased from mild at rest to severe at 20 W, and the systolic pulmonary arterial pressure (SPAP) increased from 20 mmHg to 61 mmHg, but the severity of the AS did not change (Fig. 2; Online Videos 1, 2). An elevation in the

BP (from 130/58 mmHg to 168/63 mmHg) was also observed, and the exercise stress test was stopped at 20 W because of worsening dyspnea. That result suggested that the dynamic MR was the main cause of the AHF.

The dynamic MR was considered to be related to not only the post-radiation valvular damage including the restricted motion of the diffuse thickened mitral leaflets but also the AS and diastolic dysfunction, and an intervention for the aortic and mitral valves was thought to be imperative to prevent readmissions. The heart team selected a percutaneous valve technique instead of a double valve replacement, because such a surgery was expected to have a high surgical risk due to the concomitant post-radiation damage including an adhesion of the pericardium, porcelain aorta, and calcifications of the AMC, which were seen in computed tomography. After a discussion whether a transcatheter edge-to-edge repair (TEER) with a MitraClip (Abbott Vascular, Menlo Park, CA, USA) or a transcatheter aortic valve implantation (TAVI) should be performed first, the heart team gave priority to a TEER with a MitraClip for dynamic MR over a TAVI for moderate AS because of the ExE results. A TAVI was planned to be added if he had repeated admissions or the AS worsened to a severe state after the procedure.

Because his condition was stabilized by medical therapy, he was discharged once. However, he was readmitted for the seventh time within a week, and a TEER with a MitraClip was performed during that admission. A single MitraClip NT clip was used to grasp the A2-P2 centrally, and the MR was mitigated (Fig. 3A-C). There was no concomitant mitral stenosis, the mean transmitral valve gradient was 3.5 mmHg, and the combined planimeted mitral valve orifice area was 1.96 cm². The post-procedural ExE revealed the mitigation of the



dynamic MR, with mild-moderate MR even at 30 W, and the SPAP could not be measured due to a notable decrease in the tricuspid regurgitation (Fig. 3D; Online Video 3). The AS remained moderate in the TTE. Six months later, the ExE revealed no progression of the dynamic MR. He had no further admissions for more than one year, in contrast to multiple admissions before the procedure.

Discussion

The course in this patient provided the two following important clinical suggestions: 1) ExE may be useful in the management of patients with RIHD, and 2) a TEER with a MitraClip may be an effective treatment for RT-related dynamic MR.

ExE may be useful in the management of patients with RIHD. ExE is an established method for evaluating the hemodynamic response to exercise stress testing and the risk stratification of cardiovascular events [2]. In this case, TTE at rest revealed mild MR, but ExE revealed severe MR with exercise-induced pulmonary hypertension. An intervention for the mitral valve was prioritized because of the ExE results. Patients with RIHD sometimes have multiple heart diseases including pericardial disease, cardiomyopathy, coronary artery disease, valvular disease, and conduction abnormalities [1,3]. The management of RIHD may be difficult, and RT-related MR may be underestimated with TTE at rest alone. To the best of our knowledge, this is the first case in which ExE was useful for diagnosing the cause of AHF in a patient with RIHD.

A TEER with a MitraClip may be an effective treatment for RT-related dynamic MR. RT-related MR is associated with progressive mitral leaflets thickening with or without calcifications, resulting in the restricted motion, and this can occur alone or in the context of concomitant post-radiation cardiac findings [4,5]. In this case, an elevation in the BP, the AS, and diastolic dysfunction were considered to exacerbate the MR. RT-related valvular disease may progress to severe dysfunction requiring surgery, but surgery is associated with a high surgical risk due to concomitant post-radiation mediastinal and cardiac damage [1,3–5]. A porcelain aorta is associated with a high risk of cerebral embolisms, and thickening of the AMC is associated with an increased mortality [6,7]. Percutaneous valve techniques offer an attractive alternative strategy for such patients with a high surgical risk. It is unclear whether a TEER with a MitraClip for dynamic MR has favorable clinical outcomes, and the data on the efficacy in patients with RIHD are lacking. However, Izumo et al. reported that a TEER with a MitraClip was associated with a better prognosis in patients with exercise-induced secondary MR, and Scarfò et al. reported the effectiveness for RT-related MR, as shown in our case [5,8].

In this patient, the AS never met the criteria of severe since the first admission, and a TEER with a MitraClip was performed first. However, an improvement in the MR after the TAVI for severe AS was reported,

and surgery would be selected for patients with a low surgical risk or patients who are unsuitable for percutaneous valve techniques [9]. The management of RIHD needs an individualized approach.

Herein, we reported a patient with RIHD and dynamic MR, who had repeated admissions for AHF within a short period. Our case showed that ExE may be useful in the management of patients with RIHD, and a TEER with a MitraClip may be an effective treatment for RT-related dynamic MR.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jccase.2022.07.002>.

Declaration of competing interest

The authors declare that there is no conflict of interest.

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