Case Report

Successful Transcatheter Edge-to-Edge Mitral Valve Repair via Minithoracotomy in Canine Myxomatous Mitral Valve Disease: Case Report

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Abstract

Transcatheter edge-to-edge mitral valve repair (TEER) for the correction of mitral regurgitation (MR) due to myxomatous mitral valve disease (MMVD) stage B1 in a dog by a hybrid intervention technique via mini-thoracotomy was first reported in Thailand and Southeast Asia. The dog did not show any clinical signs related to congestive heart failure (CHF). Physical examination revealed systolic murmur grade III/VI. Electrocardiographs were recorded and showed normal sinus rhythm. A thoracic radiograph revealed the normal size and shape of the heart (VHS 10.9) and diffuse bronchial pattern in the lungs. A definitive diagnosis of MMVD was made by echocardiography. The dog received MR correction by transcatheter edge-to-edge mitral valve repair (TEER) guided by transesophageal echocardiography (TEE). The procedure was successful, as indicated by the absence of regurgitant jet flow from the left ventricle into the left atrium and the lack of complications. Ten days after the operation, echocardiography, complete blood count, and blood chemistry profiles were obtained, and the dog remained healthy.

Keywords: edge-to-edge mitral valve repair, dog, mini-thoracotomy, MMVD, transcatheter, TEE

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Introduction

Myxomatous mitral valve disease (MMVD) is the most prevalent heart disease in dogs and predominantly affects small- to medium-sized breeds and aged dogs (Borgarelli and Haggstrom, 2010). MMVD is characterized by the thickening and degeneration of the mitral valve leaflets, resulting in their failure to close properly, which leads to mitral regurgitation (MR). Consequently, over time, the left atrium (LA) and left ventricle (LV) become enlarged, and congestive heart failure (CHF) eventually develops, for which furosemide and pimobendan are usually prescribed during the symptomatic phase (Bode *et al.*, 2022).

Currently, the medical treatment of MMVD aims to manage symptoms and improve quality of life or slow the progression of the disease by administering medicine at an appropriate stage. Although medical management is easy to implement, cost-effective, and adjustable based on disease progression, side effects can occur. Current treatments are also less effective in advanced stages, eventually resulting in the dog's death. Recently, a hybrid approach to mitral valve repair known as TEER, combining the conventional surgical procedure and an interventional procedure that does not require cardiopulmonary bypass, has been introduced in the field of veterinary cardiology. This surgery aims to correct the underlying structural defect of the mitral valve and has been suggested as a promising treatment option (Liu *et al.*, 2020).

TEER is an emerging and promising minimally invasive procedure for treating mitral valve disease in dogs, particularly in cases of MMVD, using catheters to deliver repair devices called "V-clamps" to the mitral valve (Sasaki *et al.*, 2021). Studies have shown that TEER can significantly reduce regurgitant volumes and improve clinical symptoms in dogs suffering from MMVD (Liu *et al.*, 2020). The procedure is typically guided by three-dimensional TEE, which allows for real-time imaging and precise placement of the V-clamps. While TEER is being undertaken in a small number of cardiology centers worldwide, this procedure had not previously been performed in Thailand and Southeast Asia. This study is the first to report the performance of TEER with a V-clamp device in canine MMVD stage B1 in Thailand and Southeast Asia.

Case description

Case history: A nine-year-old intact male beagle weighing 11.8 kg was presented to a private animal hospital in Bangkok, Thailand, with a history of systolic murmur grade III/VI with the point of maximal intensity at the left apex. No clinical signs related to cardiovascular disease (e.g., coughing, dyspnea, syncope, exercise intolerance) were observed. Physical examination revealed pink mucous membranes, a strong femoral pulse, no pulse deficit, a heart rate of 107 beats/min, a respiratory rate of 32 breaths per minute, and a systolic blood pressure of 157 mmHg.

Assessment: Complete blood count (CBC), blood chemistry profiles (i.e., creatinine, blood urea nitrogen, alanine transaminase, aspartate aminotransferase, and alkaline phosphatase), and blood parasites were within normal limits. Electrocardiograms (ECG) were obtained and showed a normal sinus rhythm (Figure 1). A thoracic radiograph was taken, and it revealed a normal size and shape of the heart (VHS 10.9) and a diffuse bronchial pattern of the lungs (Figure 2).

Echocardiography was performed using an ultrasound machine (Mindray DC70 X-Insight, Mindray, Shenzhen, China) with 1.0–5.0 MHz phase array transducers (SP5-1E, Mindray, Shenzhen, China) on the right parasternal and left apical views. The two-dimensional echocardiogram revealed structural abnormalities of the mitral valve (e.g., thickening of the mitral valve leaflets) and slight enlargement of both the LA and LV, suggesting chronic volume overload. Color Doppler echocardiography showed regurgitant jet flow into the LA during ventricular systole on the left apical five-chamber view, which indicated the presence of MR (Figure 3A). The two-dimensional echocardiogram revealed a slightly enlarged LA with an LA-to-aortic root ratio (LA/Ao) of 1.63 (Figure 3B), and the normalized left ventricular internal diameter at end-diastole (LVIDDN) obtained from the two-dimensional M-mode view was 1.65 (Figure 3C). Therefore, a diagnosis of MMVD stage B1 was established (Keene *et al.*, 2019).

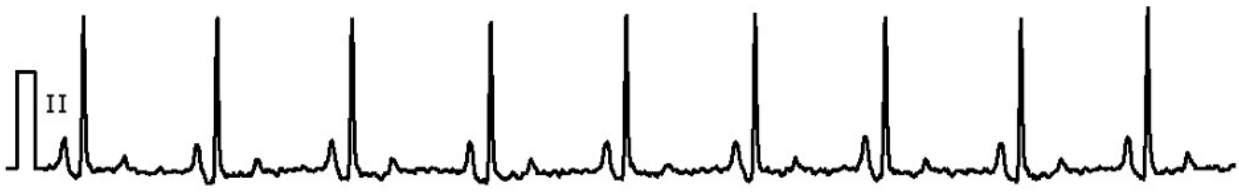

Figure 1 Representative body surface electrocardiograms (Lead II, 25 mm/s, 10 mm/mV) recorded from canine degenerative mitral valve disease, which showed sinus rhythm with a heart rate of 107 beats per minute.

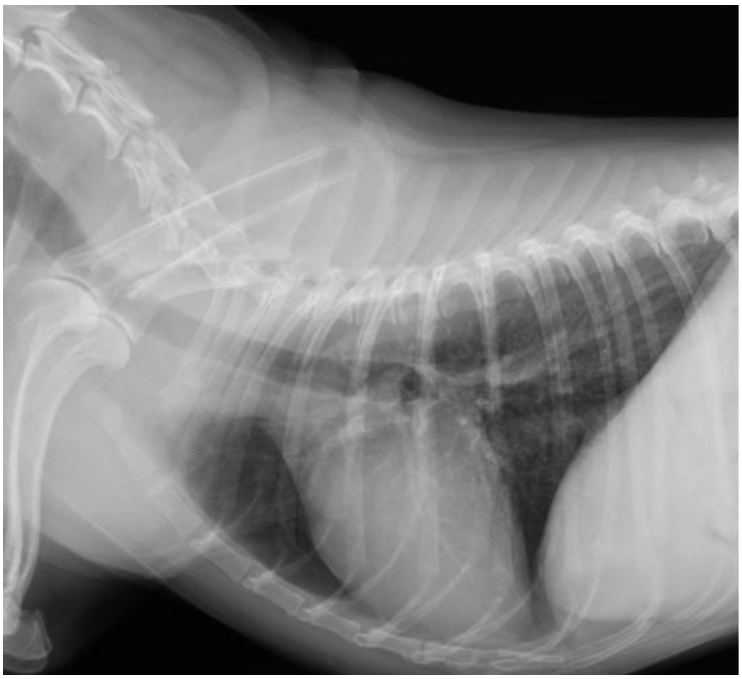

Figure 2 Thoracic radiograph of degenerative mitral valve disease dog on right lateral view showing normal size and shape of the heart (VHS 10.9) and diffuse bronchial pattern of the lung.

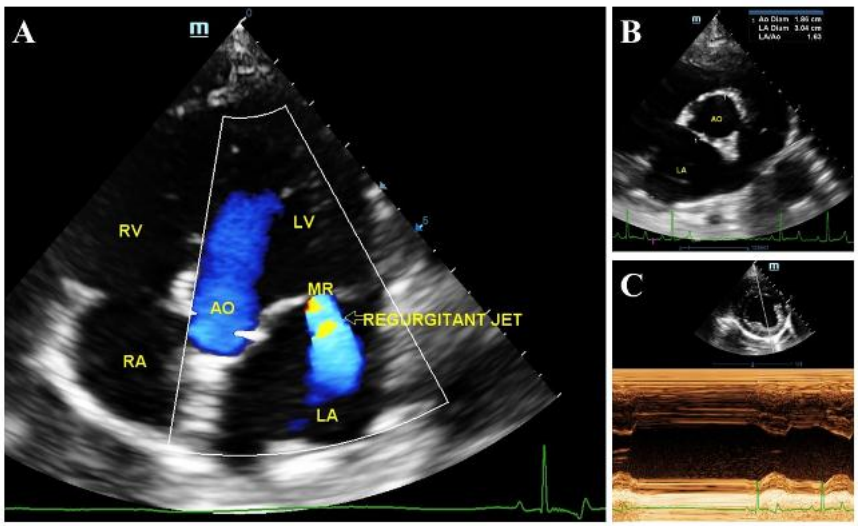

Figure 3 Color Doppler echocardiography shows turbulent flow in the left atrium during systole (A). Two-dimensional view of the left atrium and aorta on the right parasternal short axis view (B). Two-dimensional and M-mode echocardiography shows the left ventricular internal diameter on the right parasternal short axis view at the level of the head of the papillary muscle (C). LV=left ventricle; RV=right ventricle; RA=right atrium; LA=left atrium; Ao=aorta; MR=mitral regurgitation

Transcatheter Edge-to-Edge Mitral Valve Repair (TEER) Technique: TEER was performed on this dog with a V-clamp device (Hongyu Medical Technology, Shanghai, China; Figure 4). The anesthesia method was modified from the methods used in previous studies (Buranakarl *et al.*, 2015; Buranakarl *et al.*, 2016; Pichayapaiboon *et al.*, 2021). In brief, anesthetic induction was achieved with a combination of midazolam (0.3 mg/kg) and morphine (0.5 mg/kg) intravenously, followed by alfaxalone 2 mg/kg intravenously. Then, orotracheal intubation was performed and connected to a ventilator. The animal was mechanically ventilated with 100% oxygen using a volume-cycled ventilator, set at a rate of 8–12 breaths per minute and a tidal volume of approximately 20 mL/kg. This procedure sustained an arterial partial pressure of carbon dioxide from 35–45 mmHg and an arterial partial pressure of oxygen greater than 85 mmHg. Body temperature was regulated to remain within a range of 36.5–37°C utilizing a forced-air warming system. A surgical plane of anesthesia was achieved via inhalation of isoflurane, with the end-tidal concentration of the inhalant maintained between 1.4% and 1.6%. Prophylactic antibiotics (cephazolin 25 mg/kg intravenously) and intravenous fluid (Lactate Ringer Solution 10 mL/kg/hr) were administered via the cephalic vein. The dog was placed in right lateral recumbency. An intravenous catheter was also placed at the right pedal artery and connected with a fluid-filled pressure transducer to monitor invasive arterial blood pressure. Standard limb lead electrocardiograms were set to monitor heart rate and rhythm. After sterile

preparation, a mini-thoracotomy was performed, and the pericardium was incised to expose the apical area. A perioperative intercostal nerve block was also performed with bupivacaine (1 mg/kg). To locate the point for device insertion, a long wooden cotton swab was used with the help of Xplane imaging with a TEE probe (EPIQ7 X7-2t xMATRIX Array Live three-dimensional and two-dimensional TEE, Philips, Bangkok, Thailand) connected to the ultrasound machine (EPIQ CVx, Philips, Bangkok, Thailand). After placing a purse string on the apex, heparinized saline (100 IU/kg) was administered intravenously. The V-clamp delivery system was inserted through the cardiac apex, first into the LV and then into the LA, under echocardiographic guidance with a TEE probe (Figure 5). The mitral valve was captured, and the position of the clip was confirmed utilizing a three-dimensional view (Figure 6). Following confirmation of the clip's position, the V-clamp device was deployed. Subsequently, the delivery system was removed, and the apex was sutured using a purse-string technique. Then, the pericardium and thoracic wall were sutured with synthetic glyconate monofilament 4/0 and polydioxanone monofilament 0/0, respectively. A chest drainage tube was placed before closing the thoracic cavity. The ventilator was discontinued, and the skin was then sutured with a polyamide monofilament suture to complete the procedure. The procedure was successful, as indicated by the absence of a regurgitant jet into the LA and the absence of any complications.

During the postoperative period, continuous rate infusion of morphine 0.12 mg/kg/hr, lidocaine 1.5 mg/kg/hr, and ketamine 0.12 mg/kg/hr were given for 24 hr, followed by morphine (0.3 mg/kg, SC, q12h) and carprofen (4 mg/kg, SC, q12h) for 3 consecutive days to manage postoperative pain. Clinical signs, ECG, and blood pressure were monitored closely. Clopidogrel (2 mg/kg, PO, q24h) was also given for 2 months. Echocardiography, CBC, and blood chemistry profiles were obtained 10 days after surgery. Both the CBC and blood chemistry profiles were within normal limits. The echocardiographic data revealed that the V-clamp device was intact at the mitral valve leaflets. The LA/Ao (1.58) and LVIDDN (1.52) were slightly decreased compared to the values before surgery (Figure 7).

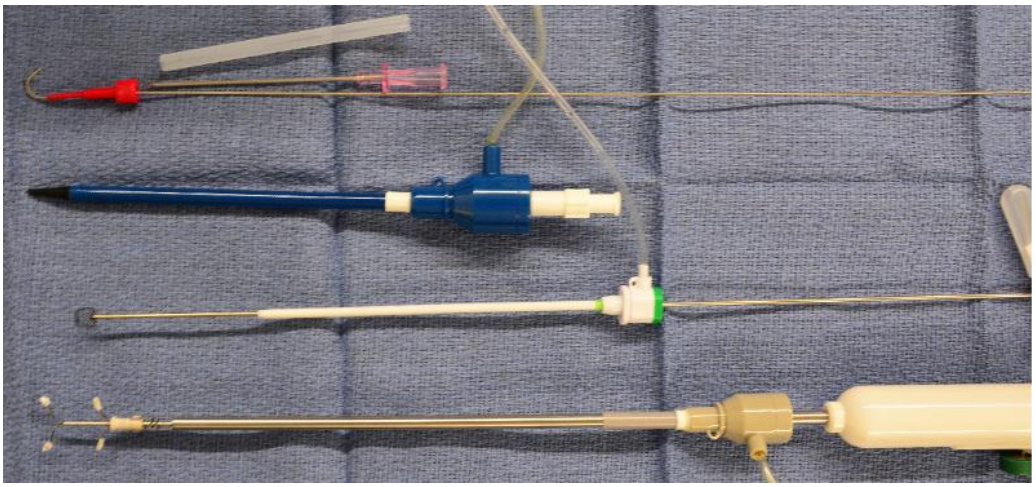

Figure 4 Devices for transcatheter edge-to-edge mitral valve repair (TEER), called "V-clamps."

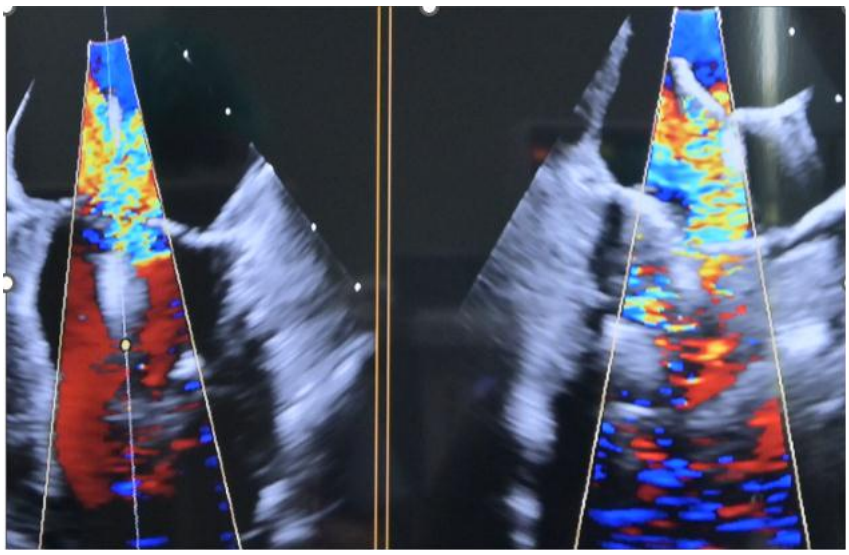

Figure 5 Simultaneous biplane (left: four-chamber view and right: five-chamber view), two-dimensional transesophageal views, and color flow of the TEER delivery system inserted through the cardiac apex position at the mitral valve level. Notice that the mitral valve leaflets were on the upper surface of the lower clip, which was inside the left ventricle, whereas the upper clip was inside the left atrium.

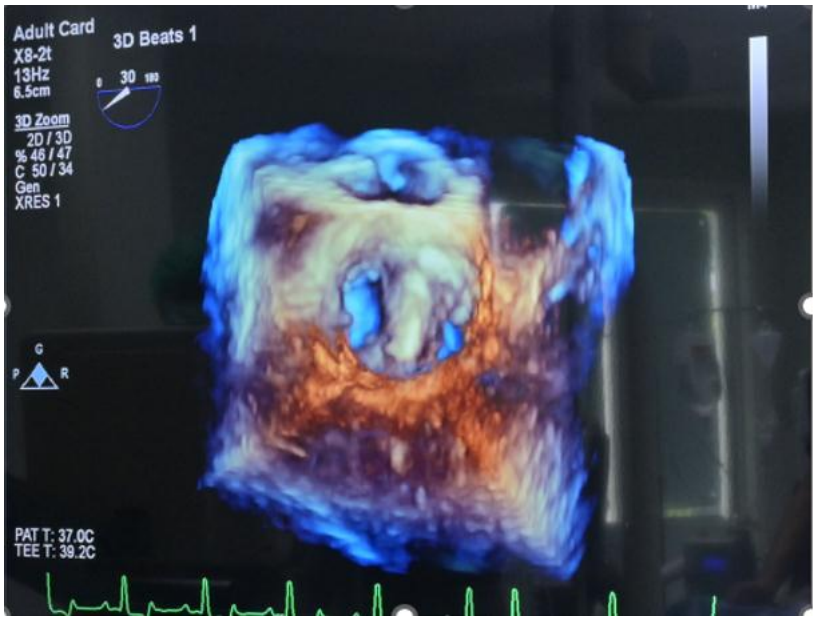

Figure 6 A three-dimensional transesophageal en-face view of the mitral valve with a V-clamp device located at A2-P2 of the mitral valve.

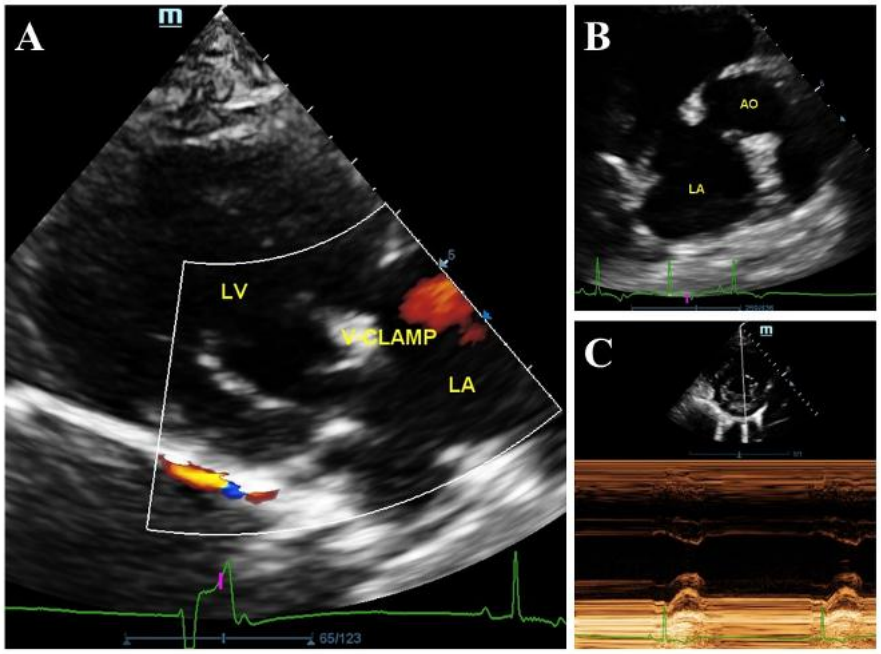

Figure 7 Color Doppler echocardiography shows a V-clamp device with no turbulent flow into the left atrium during systole (A). Two-dimensional view of the left atrium and aorta on the right parasternal short axis view (B). Two-dimensional and M-mode echocardiography shows the left ventricular internal diameter on the right parasternal short axis view at the level of the head of the papillary muscle (C). LV=left ventricle; RV=right ventricle; RA=right atrium; LA=left atrium; Ao=aorta; MR=mitral regurgitation

Discussion

This report presents the first evaluation of the efficacy of TEER utilizing a V-clamp device in a male canine diagnosed with stage B1 MMVD in Thailand and Southeast Asia. Dogs with MMVD stage B1 are known to have a heart murmur of MR and to be asymptomatic for their heart disease. In the current study, the dog exhibited no significant signs of CHF or abnormal ECG results. Common clinical manifestations of CHF include exercise intolerance, coughing, syncope, and pulmonary edema, contingent upon the severity of MR. In the initial stages of the disease, ECG readings may not exhibit alterations; however, advanced stages may show prolonged P wave and QTc intervals (Na *et al.*, 2021). Thoracic radiography serves as a fundamental tool in the diagnostic evaluation of cardiac disease in dogs, as it facilitates the identification of cardiac abnormalities, pulmonary changes, and indicators of heart failure. In the present case, the absence of radiographic evidence of cardiomegaly was inferred from the vertebral heart score (VHS) and vertebral left atrial score (VLAS). This observation aligns with the American College of Veterinary Internal Medicine (ACVIM) guidelines, which establish thresholds of VHS < 11.5 and VLAS <

3, indicating that the canine should be categorized within MMVD stage B1 (Keene *et al*., 2019). Interestingly, a definitive diagnosis of stage B disease requires echocardiography. In the current report, transthoracic echocardiography (i.e., two-dimensional and M-mode) revealed that the LA/Ao was more than 1.60, whereas the LVIDDN was less than 1.70, which indicated that the LA was remodeling, while the LV had mild remodeling after valvular leakage. Therefore, according to the ACVIM consensus guidelines, it was confirmed that the dog had MMVD stage B1.

According to the ACVIM guidelines (Keene *et al*., 2019), no medical treatment is recommended for dogs with MMVD stage B1 because they have not yet been shown to benefit from any treatment. In addition, in most dogs with MMVD stage B1, it takes several years for heart disease to progress to clinical disease, congestive heart failure, and death, and some dogs with MMVD stage B1 have a normal life expectancy (Grosso *et al*., 2023). Although no medical treatment has been shown to slow the progression of disease in dogs with MMVD stage B1, surgical intervention may represent an alternative strategy. The authors do not yet know whether the operation will improve the survival time of dogs with MMVD stage B1 compared with untreated dogs. However, based on the current results and previous reports, we believe that if the mitral clamp can stop valvular leakage or reduce the regurgitant jet to a small amount, the progression of the disease will be very slow. This suspicion must be confirmed by a future clinical trial.

Previously, no surgical options were available for dogs suffering from severe MMVD. With techniques stemming from human medicine, mitral valve repair by surgery now includes valve replacement, valve repair, circumferential annuloplasty, and chordal replacement with expanded polytetrafluoroethylene (Mizuno *et al*., 2013). Until recently, these surgeries required cardiopulmonary bypass, which can be performed only on large breeds; now, the technique has been improved to enable its use in a wide range of dog sizes (Uechi, 2012). The V-clamp has been adopted in a small number of countries. This new approach gains access to the heart through a small incision in the thoracic wall, followed by a needle puncture at the apex of the heart. Guided by TEE, the V-clamp is positioned on the mitral valve leaflets to reduce regurgitation, thus reducing left atrial volume overload. Data about success rates, survival rates, and quality of life after surgery are limited. A previous prospective observation study in eight dogs with MMVD stage B1 reported a success rate of 100% following the procedure (Liu *et al*., 2020). A significant reduction in the severity of MR was also reported (i.e., 87.5% with no detectable MR and 12.5% with trace MR). Furthermore, the transvalvular diastolic pressure gradients, an index of mitral valve stenosis, were unchanged. Similar to the current case report, the dog had MMVD stage B1 without clinical signs of CHF. Possible complications both during and after the procedure are injuries to the mitral valve leaflets due to excessive manipulation of the device during implantation, chordae tendineae rupture while passing the sheath from LV to LA, cardiac tamponade and haemothorax due to puncture to the LA, and acute ischemia and/or stroke due to small thrombi. However, these complications have not been encountered in the current case, nor were they found in the previous publication (Liu *et al*., 2020).

It has been reported that safe anesthetic inductions in dogs with heart disease can be performed using alfaxalone (3–7 mg/kg, IV), etomidate (1.5–3.5 mg/kg, IV), propofol (4–8 mg/kg, IV), or midazolam (0.2–0.3 mg/kg, IM; (Pypendop, 2011)). In the current report, midazolam, morphine, and alfaxalone were used for anesthetic premedication and/or induction. Midazolam, an imidazobenzdiazepine, acts as an agonist on the gamma-aminobutyric acid ($GABA_A$) receptor, which helps to reduce the anesthetic gas required during anesthesia while having a minimal effect on cardiovascular function (Kropf and Hughes, 2018). Alfaxalone, a synthetic neuroactive steroid, induces anesthesia through an interaction with the $GABA_A$ receptor, and it has been shown to have a high margin of safety with minimal cardiorespiratory side effects and few or no cardiovascular changes (Fernandez Castaner *et al*., 2023). Morphine causes analgesia by occupying μ opioid receptors at pre- and post-synaptic sites (Ueyama *et al*., 2008). These drug combinations are routinely used in our patients with heart disease, as they have been shown to have a good safety profile while reducing the amount of isoflurane required, as previously reported (Mayordomo-Febrer *et al*., 2017; Rubio *et al*., 2022). In those reports, a combination of morphine, midazolam, and alfaxalone produced good anesthesia and analgesia and acceptable cardiorespiratory effects in dogs during surgery.

In human patients with HF and severe secondary MR, TEER has been found to reduce death or hospitalization during a 2-year follow-up period (Lerakis *et al*., 2024). In dogs, one study reported that TEER in dogs with MMVD stage B1 can effectively reduce the severity of MR; the study did not report on cardiac function (Liu *et al*., 2020). Another study of TEER implantation in normal, healthy dogs reported that the E/e ratio and radial strain were elevated and that the intraventricular pressure gradients were stable after the operation (Sasaki *et al*., 2021). However, the latter study was performed in normal dogs; therefore, the results cannot be compared with the operation in dogs with MMVD. In our study, echocardiography was performed 10 days post-operation, and it was found that both the LA and LV were smaller than before the operation; however, the cardiac function inferred from the shortening fraction and ejection fraction was not altered. This lack of change in cardiac function may be due to the short period of assessment post-operation and/or the low sensitivity of those parameters. A long-term assessment is needed to investigate the outcome of the TEER procedure in dogs with MMVD.

The procedure may present several limitations. First, transesophageal echocardiography with simultaneous biplane and three-dimensional echocardiography is required. Although traditional TEE with two-dimensional echocardiography combined with fluoroscopy can be employed, it is challenging to accurately locate the precise position of the clamp on the valve leaflets. Second, the delivery

device is composed of a rigid metal rod, which may make it difficult to resolve clamping leakages that are not situated at the A2-P2 position. Third, only three types of the device are currently available for dogs (i.e., type II [front clamp length 14 mm], III [front clamp length 16 mm], and IV [front clamp length 18 mm]). If the mitral valve annulus diameter is excessively large, the device may not be suitable for the procedure. Fourth, due to the size of the dog, only one clip can be used per dog. Therefore, if there are multiple leakages along the mitral edge of the valve, this procedure may not be appropriate.

In conclusion, TEER using a V-clamp is a straightforward and highly effective procedure for reducing MR jets. While TEER necessitates minimal thoracic opening, it does not require cardiopulmonary bypass and can be performed on dogs of various sizes. This advancement in hybrid interventional cardiology holds the potential to significantly improve the quality of life for both pets and their owners and may provide a valuable alternative to the medical management of canine MMVD. Further studies are warranted to evaluate its applicability across different stages of MMVD.

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