

Novel therapeutic approach using angiotensin receptor neprilysin inhibitors for managing tricuspid regurgitation with diastolic dysfunction in a mongrel dog

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Abstract

A 10-year-old male mongrel dog weighing 12 kg was presented with history of lethargy, exercise intolerance, persistent coughing, and dyspnea to Referral Veterinary Polyclinic, ICAR-Indian Veterinary Research Institute. Physical examination showed tachycardia, palpable precordial thrills, and a systolic murmur localized to the tricuspid region. Thoracic radiographs revealed enlargement of the right ventricle, and electrocardiography indicated sinus arrhythmia. Hematological and serum biochemical parameters were within normal reference ranges. Echocardiography showed moderate right atrial and ventricular dilatation, significant tricuspid regurgitation (TR - 274 cm/s), and grade I diastolic dysfunction of the left ventricle characterized by reduced transmitral E/A ratio (0.7), prolonged isovolumic relaxation time (72 ms), and increased early mitral inflow deceleration time (217 ms). The dog was treated with Sacubitril/Valsartan (20 mg/kg orally twice daily), Lasilactone (2 mg/kg orally twice daily), and cardiac support (Strong Beat, 1 tablet twice daily). Follow-up at 14 days demonstrated a marked decrease in tricuspid regurgitation with concurrent clinical improvement in symptoms. Subsequent evaluation at 60 days indicated that left sided diastolic function indices were stabilized and modestly optimized under therapy, while systolic performance was preserved. This case highlights the potential of Sacubitril/Valsartan in managing early diastolic dysfunction in dogs and reducing regurgitant burden. Early intervention in mild diastolic dysfunction may prevent disease progression and improve clinical outcomes.

Keywords: Diastolic dysfunction, Echocardiography, Sacubitril/Valsartan, Tricuspid regurgitation

Highlights

- A mongrel dog with tricuspid regurgitation and Grade I diastolic dysfunction managed by Sacubitril/Valsartan.
- Echocardiography showed marked reduction in TR velocity and right heart remodeling in 60 days.
- Sacubitril/Valsartan therapy induced reverse remodeling with preserved systolic and improved diastolic function.
- RAAS inhibition and neprilysin blockade together gave better hemodynamic results than standard therapy.

Tricuspid regurgitation is a relatively common valvular disorder in dogs and often occurs secondary to degenerative valve disease, pulmonary hypertension, or functional annular dilation, leading to chronic volume overload of the right atrium and ventricle (Yamini et al., 2020; Pinkos & Stauthammer, 2021). Progressive right sided volume and pressure overload can induce right atrial and ventricular enlargement, interventricular septal displacement, and altered left ventricular filling dynamics, thereby predisposing to the development of left ventricular diastolic dysfunction (Vezzosi et al., 2018a; Chalermpromma & Surachetpong, 2023). In such patients, increased right sided filling pressures and ventricular interdependence may impair left

ventricular relaxation and compliance, which is reflected by changes in Doppler indices such as a reversed transmitral E/A ratio, prolonged isovolumic relaxation time, and increased early mitral inflow deceleration time (Kibar et al., 2009; Winter et al., 2025). Diastolic dysfunction in dogs is clinically important because it can contribute to congestive signs despite preserved systolic function, and therapeutic strategies that modulate loading conditions and neurohormonal activation may offer meaningful clinical benefit.

In 2015, the introduction of sacubitril/valsartan marked a paradigm shift in HF treatment (Hubers & Brown, 2016). Sacubitril/valsartan (S/V), a combination of a neprilysin inhibitor and an

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angiotensin II receptor blocker respectively, has emerged as a promising therapeutic option in human cardiology for heart failure with preserved ejection fraction and valvular heart disease (Sabbah et al., 2017). These have been shown to effectively reduce all-cause mortality and the frequency of HF-related hospitalizations, surpassing the benefits observed with conventional ACEIs such as enalapril (Jackson et al., 2021). Its dual mechanism of action, enhancing beneficial natriuretic peptides and inhibiting harmful RAAS effects (Saengklub et al., 2021) can have potential benefits in canine patients by reducing volume overload, lowering filling pressures, and interrupting harmful biventricular interactions in diastolic dysfunction and TR.

Preliminary studies in veterinary cardiology have indicated that S/V may mitigate adverse myocardial remodeling, reduce left atrial and ventricular dimensions, and improve systolic function in dogs with myxomatous mitral valve disease. These findings raise the possibility that S/V could offer therapeutic advantages in managing TR and diastolic dysfunction in dogs. This article aims to explore the potential role of sacubitril/valsartan in the management of tricuspid regurgitation and diastolic dysfunction in canine patients, synthesizing available clinical data and discussing its implications for veterinary cardiology.

A 10-year-old male mongrel dog weighing 12 kg was presented to the Referral Veterinary Polyclinic, ICAR-Indian Veterinary Research Institute, Bareilly, Uttar Pradesh with a clinical history characterized by lethargy, persistent coughing, exercise intolerance, and dyspnea. A detailed physical examination revealed normal physiological parameters such as body temperature, mucous membrane color, and capillary refill time. However, palpable precordial thrills, tachycardia, and a systolic murmur over the tricuspid area were detected. The systolic and diastolic blood pressures, measured using a Doppler device (BPL Ultima Prime D), were 141 mmHg and 73 mmHg, respectively. Radiographic imaging of the thorax was performed in both lateral and dorsoventral (DV) projections. The lateral view showed enlargement of the right ventricle (Fig. 1), while on DV view, a bulge was observed between the 7:00 and 10:00 o'clock positions, suggesting mild enlargement of the right atrium and ventricle (Fig. 2). Electrocardiographic evaluation was performed with the dog in right lateral recumbency using a 6-channel electrocardiograph, revealing sinus arrhythmia (Fig. 3). Hematologic and serum biochemical analyses indicated values within normal reference ranges.

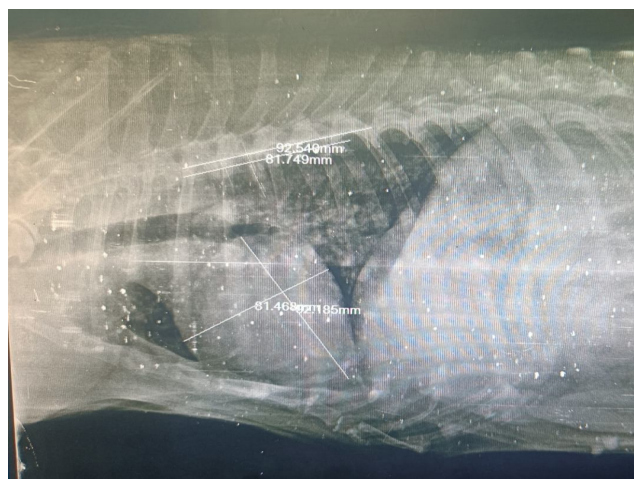


Fig. 1a. Lateral radiograph of dog showing enlargement of right ventricle

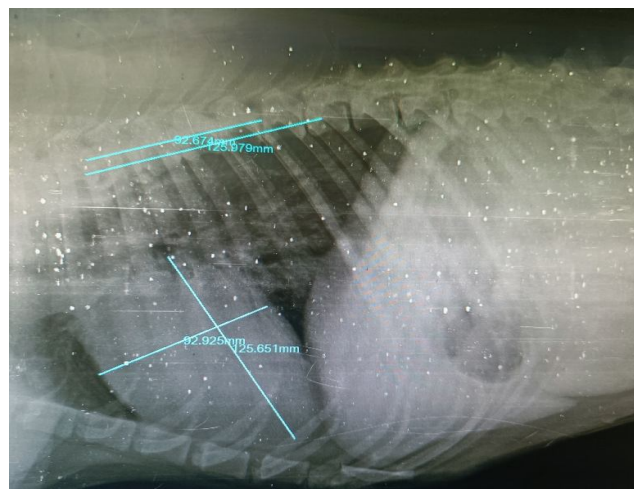


Fig. 1b. Reduction in size of right ventricle post therapy on 14th day



Fig. 2. DV view showing mild enlargement of right atrium and ventricle

Echocardiographic assessment was performed using a Siemens Acuson X300 ultrasound system equipped with a phased-array transducer operating at 2.0–6.0 MHz. Right parasternal long-axis and left apical four-chamber views were used to evaluate 2D, M-mode, and Doppler parameters. The left apical four-chamber view revealed moderate dilation of the right atrium and ventricle, with normal downward displacement of the tricuspid valve, thereby ruling out Ebstein's anomaly. Marked tricuspid regurgitation (274 cm/s) was observed, with the regurgitant jet occupying approximately 30–40% of the right atrial area (Fig. 4). Systolic pulmonary artery pressure, estimated using the simplified Bernoulli equation [$SPAP = 4 \times (TR \text{ velocity})^2 + \text{estimated RA pressure}$], was 40.03 mmHg, suggestive of mild pulmonary hypertension (Vezzosi et al., 2018b). Right ventricular longitudinal systolic function indices such as tricuspid annular plane systolic excursion (TAPSE) were not recorded in this case and therefore could not be incorporated into the assessment of right ventricular performance. Pulsed-wave Doppler assessment of transmitral inflow demonstrated a reversed E/A ratio (0.7) (Fig. 5), indicative of Grade I diastolic dysfunction, along with a prolonged increased deceleration time (217 ms) of early mitral inflow (Fig. 6) and isovolumic relaxation time (72 ms) (Fig. 7) and additional echocardiographic parameters are presented in Table 1. Based on these findings, the case was diagnosed as functional tricuspid regurgitation with secondary mild pulmonary hypertension and Grade I left ventricular diastolic dysfunction.

Therapy was initiated with Sacubitril/Valsartan (Tab. Arney) at a dosage of 20 mg/kg body weight

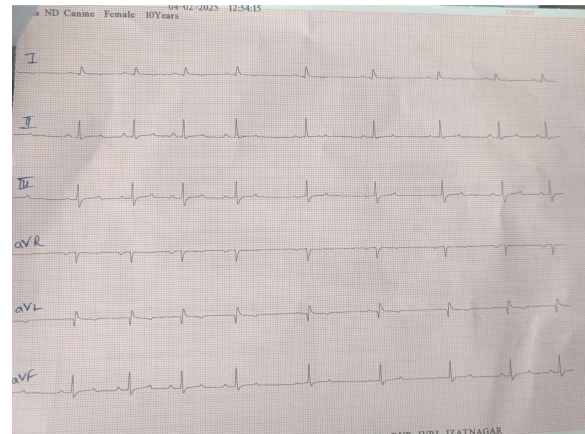


Fig. 3. Electrocardiogram showing sinus arrhythmia in Lead II

orally twice daily (Saengklub et al., 2021), Lasilactone at 2 mg/kg body weight orally twice daily, and cardiac support (Tab. Strong Beat), 1 tablet twice daily. Following the initiation of treatment, tricuspid regurgitation significantly decreased from 274 cm/s to 79 cm/s within 14 days (Fig. 4b), and the dog was clinically stable within 14 days. Sacubitril/Valsartan operates through a dual mechanism: valsartan, an angiotensin II receptor blocker (ARB), inhibits the effects of angiotensin II, while sacubitril, a neprilysin inhibitor, prevents the breakdown of natriuretic peptides. This combination leads to increased levels of beneficial natriuretic peptides, promoting vasodilation, natriuresis, and diuresis, which can reduce preload and afterload, thereby decreasing the volume load on the right ventricle and potentially mitigating tricuspid regurgitation (Imamura et al., 2021; Yang et al., 2022; Zhang et al., 2022).

Table 1. Sequential echocardiographic observations during therapy

Parameter	Day 0	Day 14	Day 30	Day 60
LV Diameter (Peak Systole)	2.00 cm	2.04 cm	2 cm	1.9 cm
LV Diameter (End Diastole)	2.95 cm	3.45 cm	3.31 cm	3.10 cm
IVS Thickness (Peak Systole)	1.30 cm	0.95 cm	0.90 cm	0.89 cm
IVS Thickness (End Diastole)	0.88 cm	0.63 cm	0.61 cm	0.59 cm
LVW Thickness (Peak Systole)	1.20 cm	0.95 cm	0.9 cm	0.87 cm
LVW Thickness (End Diastole)	0.77 cm	0.63 cm	0.63 cm	0.62 cm
EF	62.1%	72.7%	71.37%	70.55%
FS	32.2%	40.9%	39.58%	38.71%
SV	20.86 mL	35.75 mL	31.73 mL	26.75 mL
LA/Ao Ratio	0.91	0.91	0.89	0.88
Mitral Peak E / A Velocities	0.77	0.63	0.62	0.68
E Deceleration Time (DT)	144 ms	144 ms	142 ms	140 ms
Tricuspid Regurgitation (TR)	274 cm/s, Jet occupies ~30-40% RA area	79 cm/s, Jet<10% RA area	65 cm/s, Jet<5% RA area	45 cm/s, trace jet
IVRT	72 ms	72 ms	71 ms	69 ms

Therapeutic role of ARNI in diastolic dysfunction with tricuspid regurgitation in dog

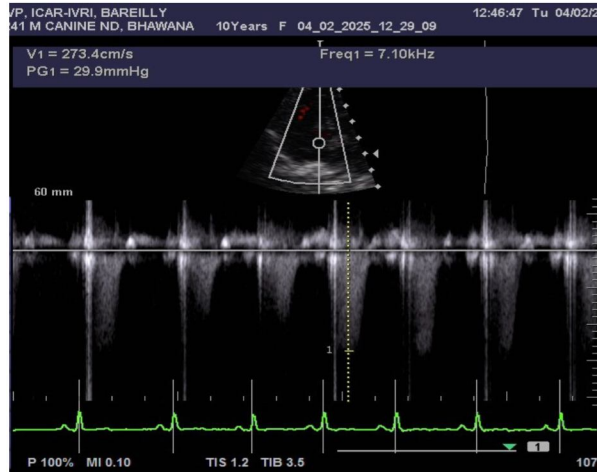


Fig. 4a. Left parasternal apical four chamber view showing Tricuspid Regurgitation (TR=273.4 cm/s)



Fig. 4b. Reduced Tricuspid Regurgitation (TR=78.5 cm/s) after therapy on 14th Day

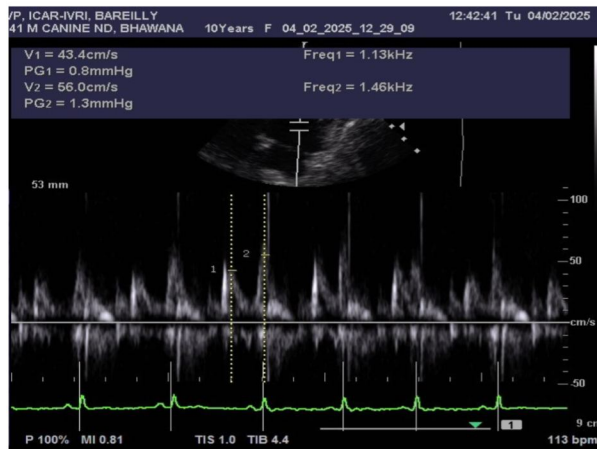


Fig. 5. Pulsed-wave Doppler assessment of transmitral inflow showed a reversed E/A ratio

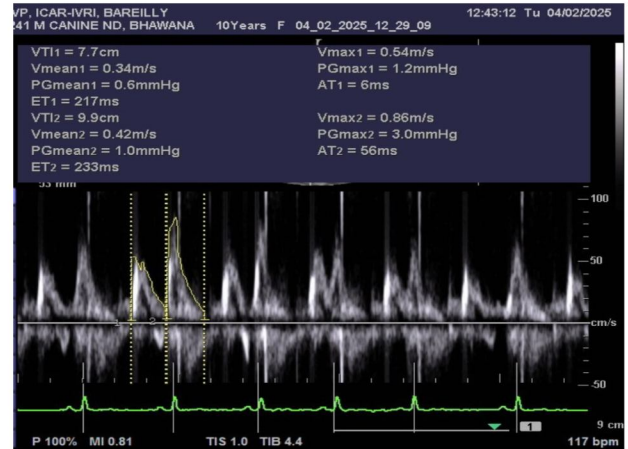


Fig. 6. Increased deceleration time (217 ms) of early mitral inflow

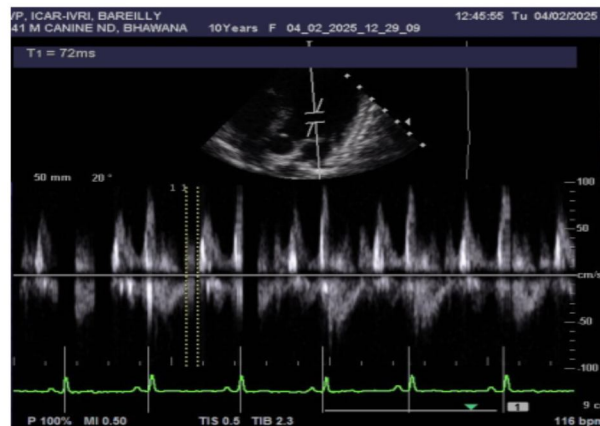


Fig. 7. Prolonged Isovolumic Relaxation Time (72 ms) observed in left parasternal apical four chamber view

Follow-up echocardiography conducted after initiation of therapy showed that the E/A ratio remained below 1, with modest reductions in isovolumic relaxation time (from 72 ms to 69 ms) and deceleration time (from 144 ms to 140 ms). In dogs, Doppler indices such as E/A and IVRT are strongly influenced by preload and heart rate; therefore, part of these changes may reflect shifts in loading conditions rather than direct improvement in myocardial relaxation (Ie et al., 2003). However, the observed trends in diastolic parameters, alongside reductions in left ventricular dimensions and improvement in clinical signs, suggest that sacubitril/valsartan may have contributed indirectly to improved diastolic function by reducing preload, mitigating volume overload, and potentially enhancing myocardial compliance. Complementary measures, including tissue Doppler velocities, E/e' ratios, or estimates of left atrial pressure, would further clarify the direct impact of therapy on myocardial relaxation.

By Day 60, echocardiography revealed that LV end diastolic diameter, after an initial rise from 2.95 cm to 3.45 cm at Day 14, had decreased to 3.10 cm, and interventricular septal and LV free wall thicknesses had fallen from higher to lower values (e.g., IVS systolic 1.30 to 0.89 cm), findings consistent with reduction in cavity and wall dimension and therefore indicative of limited reverse remodeling rather than a marked structural change. Over the same period, the LA/Ao ratio remained within a low-normal range and declined only slightly from 0.91 to 0.88, suggesting no clinically relevant left atrial enlargement at baseline and only subtle early reverse remodeling under therapy. Overall, the sequential M mode measurements in this case are compatible with mild left ventricular reverse remodeling; however, this conclusion should be regarded as provisional because it is based exclusively on one dimensional, load dependent indices that may overestimate true three dimensional alterations in cardiac geometry. These changes are likely secondary to reduced tricuspid regurgitation and improved hemodynamics (Borlaug et al., 2016; Saengklub et al., 2021). While systolic function remain preserved (high ejection fraction and fractional shortening). Systolic function was maintained, as evidenced by elevated ejection fraction and fractional shortening values.

These observations suggest that in canine patients with early LV diastolic dysfunction and concomitant tricuspid regurgitation, Sacubitril/Valsartan reduce the burden of regurgitation over 60 days, preserve systolic function, and may help in beneficial remodeling. The potential of breaking the vicious cycle of elevated filling pressures causing pulmonary hypertension and worsening tricuspid regurgitation is clinically

important. Given that grade-1 LV diastolic dysfunction is relatively mild, early intervention may forestall progression. The dual action of Sacubitril/Valsartan offers a broader mechanistic reach than conventional ACE inhibitors or ARBs alone.

Despite promising findings, the study is subject to several limitations: Doppler indices such as E/A, IVRT, and deceleration time are inherently preload-dependent, meaning observed changes may partially reflect altered hemodynamic states rather than intrinsic improvement in myocardial relaxation. The scope is limited to a single case, which restricts generalizability across breeds, ages, body sizes, and degrees of baseline myocardial fibrosis. Furthermore, structural constraints such as fixed tricuspid annular dilation or leaflet pathology may impose upper limits on the potential reversal of tricuspid regurgitation. Finally, the 60-day observational period may not be sufficient to capture slower, long-term remodeling, especially of diastolic properties, which often evolve more gradually in chronic cardiac disease.

Conflict of interest: The authors declare that they have no conflict of interest.

Author's contributions: BA: Conceptualized and designed the study, conducted the clinical and laboratory investigations, and prepared the initial draft of the manuscript; KM: Assisted in data collection, analysis, and interpretation of results; AS, BS: Helped in echocardiographic examination; PM, RS, NK, KD: Contributed to manuscript editing, critical review, and final approval of the version to be published. All authors contributed significantly to the present study.

Data availability statement: All data generated or analyzed during this study are included in this published article. Additional information related to this case can be provided by the corresponding author upon reasonable request.

Ethical statement: Ethical approval was not required for this study. The owner provided informed consent for treatment and publication of the case details and images

Use of artificial intelligence tools: Author(s) hereby declare that NO generative AI technologies such as Large Language Models (Chat GPT, COPILOT, etc.) and text-to-image generator have been used during writing or editing of this manuscript.

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