

# M-Mode Echocardiographic Assessment of Tiletamine-Zolazepam Anaesthetic Effects on Domestic Cat Hearts

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## ABSTRACT

**Background:** Tiletamine–zolazepam is a widely utilized anaesthetic combination in feline medicine, offering rapid dissociative anaesthesia, muscle relaxation, and sedation with comparatively mild cardiovascular effects. M-mode echocardiography is a principal noninvasive modality for assessing feline cardiac structure and function and detecting clinically significant heart disease.

**Aims:** This study aimed to evaluate the effects of tiletamine–zolazepam anaesthesia on M-mode echocardiographic parameters in cats. The results are intended to provide scientific evidence regarding the safety and reliability of this anaesthetic combination in facilitating accurate cardiac assessment.

**Methods:** A total of 19 clinically healthy cats aged 1–4 years underwent echocardiographic examination before and after intramuscular administration of tiletamine–zolazepam anaesthesia at a dose of 10 mg/kg body weight. M-mode echocardiography was used to examine structural parameters including IVSd, IVSs, LVIDd, LVIDs, LVPWd, LVPWs, EDV, ESV and systolic function indicators such as SV, EF, FS, HR, and CO. All measurements were obtained in triplicated and averaged to minimize variability. Statistical comparisons between pre- and post-anaesthetic values were analysed using a paired t-test with a 95% confidence level.

**Results:** Most structural parameters did not change significantly following anaesthesia ( $p > 0.05$ ), suggesting that cardiac morphology was preserved. Significant alterations were observed in left ventricular pump function including increased LVPWd ( $p = 0.002$ ) and decreased SV ( $p = 0.033$ ), EF ( $p = 0.026$ ), FS ( $p = 0.036$ ), and CO ( $p = 0.047$ ). All values remained within normal physiological limits.

**Conclusion:** Tiletamine–zolazepam is widely regarded as a relatively safe anaesthetic agent for short-term use in cats. Depressive effects on myocardial contractility and ventricular ejection capacity necessitate thorough cardiovascular surveillance throughout the anaesthetic period.

## INTRODUCTION

Tiletamine–zolazepam is a commonly used anaesthetic combination in feline clinical practice due to its rapid onset and balanced pharmacological effects. Tiletamine acts as an anesthetic dissociative anaesthetic inducing rapid analgesia and immobilisation. Zolazepam is a benzodiazepine derivative that provides sedation,

anxiolysis and muscle relaxation (Nejamkin et al., 2020). The complementary actions of these agents produce a stable anaesthetic plane suitable for short diagnostic and minor surgical procedures. Compared with several other anaesthetic protocols, tiletamine–zolazepam is often considered relatively safe because it exerts minimal depressive effects on the cardiovascular

system, an important consideration in feline patients that may have subclinical heart disease (Lee et al., 2018).

Evaluation of cardiac structure and function is an essential part of feline clinical assessment, particularly because cats are predisposed to primary cardiomyopathies. Among the available diagnostic tools, echocardiography is the most widely used noninvasive technique for assessing the feline heart. This imaging modality provides real-time visualisation of cardiac chambers, myocardial walls, valves, and blood flow patterns, making it essential for diagnosing both congenital and acquired heart diseases in dogs and cats (Noviana & Kurniawan, 2013). M-mode (motion mode) echocardiography is a fundamental method for quantitative cardiac evaluation. Its high temporal resolution allows precise measurement of dynamic cardiac motion throughout the cardiac cycle.

Using M-mode imaging, clinicians can determine the left ventricular internal diameters in diastole and systole, the interventricular septal thickness, and the left ventricular posterior wall thickness. These structural measurements enable further calculation of indices that reflect myocardial contractility and systolic performance, including fractional shortening (FS) and ejection fraction (EF) (Noviana et al., 2018; Patel et al., 2021). Such parameters are highly valuable for detecting early or subtle changes in cardiac function.

These echocardiographic variables are particularly important in identifying cardiovascular disorders such as hypertrophic cardiomyopathy (HCM), the most common primary heart disease in cats. HCM is characterised by ventricular myocardial thickening and impaired diastolic function and in some cases may progress to systolic dysfunction (Gaia de Sousa et al., 2025; Schober&Chetboul, 2015). Accurate measurement of ventricular wall thickness and chamber dimensions is therefore important for differentiating normal anatomical variation from pathological remodelling (Payne et al., 2015; Brahmwar et al., 2024).

Anaesthetic agents can affect heart rate, myocardial contractility, preload, and afterload, potentially altering echocardiographic measurements obtained during sedation or anaesthesia. Understanding these effects is critical to avoid misinterpretation of cardiac function. This study was designed to evaluate the influence of tiletamine–zolazepam anaesthesia on M-mode echocardiographic parameters in domestic cats. The findings are anticipated to provide scientific evidence regarding the safety and dependability of this anaesthetic combination in supporting accurate and clinically meaningful cardiac assessment.

## MATERIALS AND METHODS

Nineteen clinically healthy domestic cats aged between 1 and 4 years were included in this study. All animals underwent echocardiographic examination under two conditions: before anaesthesia and after administration of a tiletamine–zolazepam anaesthetic combination. Prior to the procedures, all cats were acclimatised for seven days at the Veterinary Teaching Hospital, School of Veterinary Medicine and Biomedical Sciences, IPB University. During the acclimatisation period, each cat received routine anthelmintic and antiparasitic treatments according to body weight and recommended dosages to assure optimal baseline health status.

A comprehensive physical examination and cardiovascular evaluation was performed at the end of the acclimatisation period to assess general health and confirm suitability for inclusion in the study. The physical examination included inspection, palpation, and cardiac auscultation to rule out detectable structural or functional cardiovascular abnormalities prior to echocardiographic assessment.

### Anaesthetic Protocol

Food was withheld for 8–12 hours before anaesthesia to reduce the risk of peri-anaesthetic complications such as regurgitation or aspiration (Cistola et al., 2004; Shin et al., 2024). Baseline physical and echocardiographic examinations were conducted during the fasting period before anaesthetic administration.

Anaesthesia was induced using an intramuscular injection of tiletamine–zolazepam at a dose of 10 mg/kg body weight (Kucharski & Kiełbowicz, 2021). Depth of anaesthesia was assessed every 5 minutes by monitoring the loss of the tail-pinch and toe-pinch reflexes until a surgical plane of anaesthesia was achieved (Young et al., 2024; Imani et al., 2021). Post-anaesthetic echocardiographic examination was performed once a stable anaesthetic plane had been established, typically within 5–10 minutes after injection.

### Echocardiographic Examination

Echocardiographic evaluation was performed using a two-dimensional ultrasound system (Mindray® M6 Vet). A phased-array transducer with a frequency range of 7.5–10 MHz was used for all examinations. Cats were positioned appropriately and the transducer was placed at the right parasternal window, between the fourth to fifth intercostal spaces to obtain standard long-axis and short-axis views of the left ventricle. These images were then used to generate M-mode

recordings for quantitative analysis (Boon, 2011; Penninck & d’Anjou, 2015).

M-mode measurements included interventricular septal thickness in diastole and systole (IVSd, IVSs), left ventricular internal diameter in diastole and systole (LVIDd, LVIDs), and left ventricular posterior wall thickness in diastole and systole (LVPWd, LVPWs). Systolic function parameters were also calculated including end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), ejection fraction (EF), fractional shortening (FS), heart rate (HR), and cardiac output (CO). EDV, ESV, SV, EF, FS, and CO were calculated using the Teichholz formula based on M-mode left ventricular internal diameter measurements. Each parameter was measured in three consecutive cardiac cycles, and the mean value was used for analysis to minimise operator-dependent variability.

#### Data Analysis

A repeated-measures design was employed, with each cat undergoing cardiac function assessment three times at each observation point, both before and after administration of the tiletamine–zolazepam anaesthetic combination. For statistical analysis, the mean of the three measurements was

calculated. Data normality was assessed using the Shapiro–Wilk test. Normally distributed data were analysed with a paired t-test, while non-normally distributed data were analysed using the Wilcoxon signed-rank test with a 95% confidence interval.

## RESULTS AND DISCUSSION

Figure 1 presents representative cardiac images acquired using the M-mode echocardiographic technique. These images were analyzed to assess cardiac morphometry in domestic cats before and after tiletamine–zolazepam anaesthesia. Comparative analysis of pre- and post-anaesthetic measurements identified several statistically significant functional changes, whereas most structural parameters remained stable, as summarised in Table 1.

Statistical analysis showed that the majority of M-mode echocardiographic variables did not differ significantly following anaesthesia ( $p > 0.05$ ), indicating that fundamental cardiac morphology was largely maintained under the influence of tiletamine–zolazepam. Structural parameters that showed no significant changes included interventricular septal thickness in systole (IVSs;  $p = 0.82$ ), left ventricular

**Table 1.** Mean ( $\pm$  SD) M-mode echocardiographic parameters in cats were measured before (pre-anaesthesia) and after (post-anaesthesia) administration of a tiletamine–zolazepam anaesthetic combination. P-values indicate the results of statistical comparisons between pre- and post-anaesthetic measurements. Statistical significance was defined as  $p < 0.05$ .

Variable	Pre Anestesi	Post Anestesi	P-value	Significant
IVSs	0.66 $\pm$ 0.10	0.66 $\pm$ 0.13	0.8195322	No
LVIDs	0.60 $\pm$ 0.13	0.65 $\pm$ 0.22	0.25563184	No
LVPWs	0.73 $\pm$ 0.13	0.74 $\pm$ 0.13	0.70008596	No
ESV	0.56 $\pm$ 0.30	0.81 $\pm$ 0.74	0.10509126	No
IVSd	0.42 $\pm$ 0.08	0.44 $\pm$ 0.11	0.3943817	No
LVIDd	1.37 $\pm$ 0.13	1.29 $\pm$ 0.22	0.10315007	No
LVPWd	0.41 $\pm$ 0.08	0.48 $\pm$ 0.10	0.0019864	Yes
EDV	4.95 $\pm$ 1.32	4.33 $\pm$ 2.08	0.13935173	No
SV	4.36 $\pm$ 1.15	3.61 $\pm$ 1.42	0.03302244	Yes
EF	88.36 $\pm$ 5.25	83.29 $\pm$ 9.52	0.02641515	Yes
FS	56.11 $\pm$ 8.04	49.63 $\pm$ 11.37	0.03608126	Yes
HR	186.98 $\pm$ 26.82	185.86 $\pm$ 28.61	0.87657363	No
CO	0.79 $\pm$ 0.25	0.65 $\pm$ 0.38	0.04720357	Yes

Description: IVSs/d = interventricular septal thickness in systole/diastole; LVIDs/d = left ventricular internal diameter in systole/diastole; LVPWs/d = left ventricular posterior wall thickness in systole/diastole; EDV = end-diastolic volume; ESV = end-systolic volume; SV = stroke volume; EF = ejection fraction; FS = fractional shortening; HR = heart rate; CO = cardiac output.

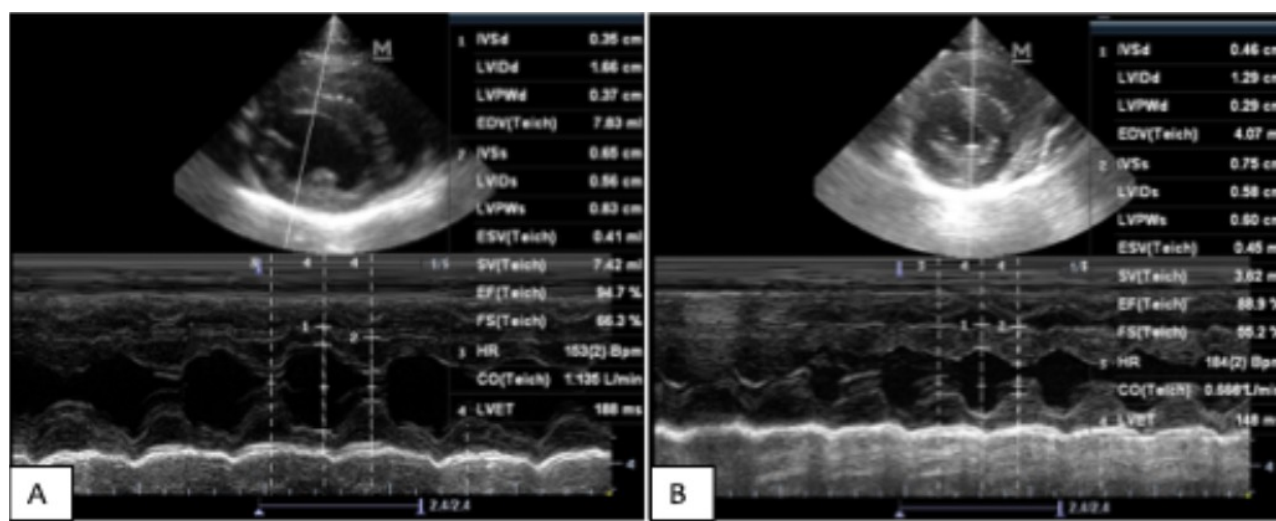
internal diameter in systole (LVIDs;  $p = 0.26$ ), left ventricular posterior wall thickness in systole (LVPWs;  $p = 0.70$ ), interventricular septal thickness in diastole (IVSd;  $p > 0.05$ ), left ventricular internal diameter in diastole (LVIDd;  $p = 0.39$  and  $0.10$ ), end-diastolic volume (EDV;  $p = 0.14$ ), and heart rate (HR;  $p = 0.88$ ).

Several parameters of left ventricular systolic performance changed significantly after anaesthesia ( $p < 0.05$ ). Diastolic left ventricular posterior wall thickness (LVPWd) rose from  $0.41 \pm 0.08$  to  $0.48 \pm 0.10$  ( $p = 0.002$ ). Stroke volume (SV) dropped from  $4.36 \pm 1.15$  to  $3.61 \pm 1.42$  ( $p = 0.033$ ), while ejection fraction (EF) fell from  $88.36 \pm 5.25$  to  $83.29 \pm 9.52$  ( $p = 0.026$ ). Fractional shortening (FS) decreased from  $56.11 \pm 8.04$  to  $49.63 \pm 11.37$  ( $p = 0.036$ ). Cardiac output (CO) also decreased significantly from  $0.79 \pm 0.25$  to  $0.65 \pm 0.38$  ( $p = 0.047$ ). Heart rate remained stable, with no significant difference between pre- and post-anaesthetic values ( $p = 0.88$ ). Overall, these findings indicate reduced left ventricular systolic pumping efficiency after tiletamine–zolazepam administration. Heart rate did not change significantly, indicating that the observed decline in cardiac output was mainly driven by reduced stroke volume rather than alterations in chronotropic activity.

Anaesthesia is widely used in veterinary medicine to facilitate diagnostic and surgical procedures by inducing unconsciousness, analgesia, and muscle

relaxation. These effects are achieved through pharmacologic depression of the central and peripheral nervous systems (Bailey et al., 2025).

Tiletamine–zolazepam is a widely used injectable anaesthetic combination in small animal practice. Tiletamine is a dissociative anaesthetic that induces a cataleptoid state with profound analgesia and amnesia by antagonising N-methyl-D-aspartate (NMDA) receptors. Zolazepam is a benzodiazepine that enhances inhibitory neurotransmission by potentiating  $\gamma$ -aminobutyric acid (GABA) receptors, resulting in sedation, anxiolysis, and muscle relaxation (Yanmaz et al., 2017). An anaesthetic combination of tiletamine–zolazepam offers practical advantages including rapid onset, ease of administration, and a duration of action suitable for short procedures. Compared with some inhalational agents and other injectable induction protocols, tiletamine–zolazepam is generally associated with only moderate cardiovascular effects in many species, although cardiorespiratory responses vary by dose and species (Hampton et al., 2019). Subtle functional and physiologic changes detectable by measures such as echocardiography, haemodynamic monitoring, or heart rate variability have been reported even in clinically healthy animals (Saha et al., 2007; Cistola et al., 2004).



**Figure 1.** M-mode echocardiography results in cats using the right parasternal view (RPS) before (A) and after (B) administration of tiletamine–zolazepam combination anaesthesia. The left ventricle was examined to assess structural parameters and systolic function, including left ventricular wall diameter and thickness, as well as EF, FS, SV, CO, and HR values calculated using the Teichholz method.

Significant reductions in stroke volume (SV), ejection fraction (EF), fractional shortening (FS) and cardiac output (CO) were observed following administration of tiletamine–zolazepam, indicate a decrease in left ventricular systolic performance during anaesthesia. Fractional shortening and ejection fraction are widely accepted echocardiographic indices of systolic function, reflecting the degree of myocardial fibre shortening and the efficiency of ventricular emptying, respectively. Decreases in these parameters therefore indicate reduced contractile performance. The concurrent reduction in SV demonstrates that each systolic contraction delivered a smaller volume of blood into the systemic circulation, which in turn contributed to the observed decline in CO despite relative stability in heart rate (Panprom et al., 2024; Sabatini et al., 2013).

Echocardiographic and heart-rate variability changes in cats under certain injectable anaesthetic protocols, supporting the interpretation that such regimens can transiently suppress systolic performance. Dissociative agents may alter sympathetic tone, while benzodiazepines can attenuate central sympathetic outflow and peripheral vascular resistance. Direct negative inotropic actions on cardiac myocytes have been described for some anaesthetic agents (Liu et al., 2019; Panprom et al., 2024).

A significant increase in left ventricular posterior wall thickness during diastole (LVPWd) was identified. Increased wall thickness may raise concern regarding structural change in the context of anaesthesia, such alterations are more likely to reflect transient functional or loading-related effects. Mild increases in ventricular wall thickness have been described in sedated or anaesthetised cats and are generally attributed to altered myocardial relaxation dynamics or temporary changes in diastolic wall tension rather than true hypertrophy (Ward et al., 2012).

The lack of significant changes in interventricular septal thickness (IVSd, IVSs), left ventricular internal diameters during diastole and systole (LVlDd, LVlDs), and ventricular volumes (end-diastolic volume [EDV] and end-systolic volume [ESV]) supports the interpretation that anaesthesia primarily influences myocardial performance rather than cardiac structure or major loading conditions. Maintenance of these dimensional parameters suggests that overall chamber geometry and preload were preserved during anaesthesia, thereby reducing confounding effects on systolic indices. This consideration is clinically relevant

because substantial changes in preload or afterload can independently affect indices such as ejection fraction (EF) and fractional shortening (FS), potentially leading to misattribution of impaired systolic function to intrinsic myocardial disease (Cuijpers et al., 2020). Reductions in systolic function indices while chamber dimensions remained unchanged, supporting that modest declines in EF and FS under anaesthesia most likely reflect transient pharmacological myocardial depression rather than acute structural remodelling (Bagardi et al., 2023).

Cardiovascular responses to tiletamine–zolazepam have been evaluated in several studies using different administration routes and dosages. Nejamkin et al. (2020) described reductions in systolic arterial pressure and respiratory rate following high-dose buccal administration, while oxygen saturation remained within normal limits. The observed decline in blood pressure was attributed to peripheral vasodilation, and overall cardiovascular tolerance was deemed acceptable in healthy cats. These findings align with the present results, which demonstrate reductions in systolic functional indices without evidence of severe haemodynamic compromise. Tiletamine–zolazepam may induce mild cardiovascular depression that is generally well tolerated in animals without underlying cardiac disease (Caulkett et al., 2000).

Dissociative anaesthetic combinations are known to exert dose-dependent depressive effects on the cardiovascular system and therefore require caution in patients with pre-existing cardiac pathology. Cats with hypertrophic cardiomyopathy (HCM) may be especially vulnerable, as reductions in preload or changes in contractility can exacerbate dynamic left ventricular outflow tract obstruction and impair diastolic filling (Simon & Steagall, 2020). Pharmacokinetic properties also influence clinical response as tiletamine has a longer elimination half-life than zolazepam. Allowing dissociative effects to persist after sedative and muscle-relaxant effects have diminished. Recovery may therefore be accompanied by excitatory phenomena such as vocalisation or dysphoria (Duke-Novakovski et al., 2016).

The importance of continued monitoring throughout induction, maintenance and recovery when both cardiovascular and neurological responses may fluctuate. The physiological effects of tiletamine–zolazepam are strongly dose-dependent. Higher doses have been associated with tachycardia, decreased arterial blood pressure and

more pronounced reductions in myocardial contractility. While respiratory depression is typically milder than with many other anaesthetic agents, it may still include hypoventilation, transient apnoea, or hypoxaemia at elevated doses or in compromised patients (Pattanapon et al., 2018; Hampton et al., 2019; Lumb et al., 2007). Due to the close interrelationship between the cardiovascular and respiratory systems, poor ventilation can worsen myocardial stress caused by hypoxaemia or acid–base imbalances. Ensuring proper oxygenation and ventilation is crucial for safe anesthesia management.

Adverse effects reported in cats include hypersalivation, vocalisation and transient muscle rigidity, particularly when higher doses are administered without appropriate premedication (Kim et al., 2007). Regarding the central nervous system, tiletamine may increase cerebral blood flow and oxygen consumption, making it less suitable for patients with head trauma, increased intracranial pressure or certain neurological disorders. The effect on intraocular pressure appears minimal, which may be advantageous in selected ophthalmic cases (Jang et al., 2015). These specific effects illustrate the importance of tailoring anaesthetic protocols to individual patient needs and comorbidities.

Tiletamine–zolazepam is sometimes combined with other agents, such as xylazine or ketamine to enhance muscle relaxation and analgesia. The combinations can improve handling and procedural conditions, also potentiate cardiovascular depression. Protocols involving  $\alpha_2$ -adrenergic agonists cause marked reductions in heart rate and blood pressure through increased vagal tone and peripheral vasoconstriction followed by reflex changes in cardiac output (Shin et al., 2024).

The echocardiographic alterations observed in this study are most consistent with transient pharmacological modulation of myocardial contractility rather than structural cardiac change. All post-anaesthetic values remained within recognised physiological reference ranges for healthy cats. This outcome is clinically reassuring and supports the use of tiletamine–zolazepam as a practical option for short-term anaesthesia in cats without cardiovascular disease, provided that appropriate monitoring is implemented. These results also have important implications for the interpretation of diagnostic imaging.

Echocardiographic measurements performed under anaesthesia can depress actual systolic function because of myocardial depression caused by anaesthetic agents. The observed increase in LVPWd during diastole is most likely attributable to transient functional or loading-related changes induced by anaesthesia rather than true myocardial hypertrophy, as supported by the absence of concurrent increases in interventricular septal thickness or ventricular chamber dimensions.

## CONCLUSION

Tiletamine–zolazepam administration results in a measurable reduction in left ventricular systolic performance and modest changes in myocardial wall thickness in healthy cats. Despite these effects, all echocardiographic parameters remained within established feline cardiac reference ranges. These findings indicate that tiletamine–zolazepam is suitable for short-term anaesthesia in healthy cats, provided that cardiovascular monitoring is maintained and echocardiographic results obtained under anaesthesia are interpreted with caution.

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## AUTHORS CONTRIBUTION

H.F.K. contributed to the conceptualisation of the study, data collection, echocardiographic examinations, data analysis, and manuscript drafting. D.N. served as principal investigator and first supervisor, contributing to study design, research supervision, data collection, and data interpretation. L.M., as the second supervisor, contributed to the study design, research implementation, data collection, and echocardiographic examinations. N.D.U., D.P.P., and D.Z.R. participated in the research and contributed to data collection and

echocardiographic examinations. All authors read, reviewed, and approved the final manuscript.

“The authors declare that there is no conflict of interest with any parties in this research”.

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