

Subclinical Subaortic Stenosis in a Golden Retriever

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THE CASE

A 12-month-old intact female golden retriever is presented for a wellness examination and to discuss the pros and cons of breeding the patient versus pursuing ovariohysterectomy. The owner would like her to produce one litter of puppies prior to being spayed.

On physical examination, the patient is bright, alert, and responsive. She is extremely energetic with a good BCS (4/9) and appropriate musculature. Cardiovascular examination reveals pink mucous membranes, no obvious jugular venous distension, and a normal heart rate and rhythm with normal synchronous femoral pulses. Auscultation is difficult and brief because the patient is rambunctious and panting. Despite the panting, she is eupneic with clear bronchovesicular sounds. A grade II/VI left basilar systolic heart murmur is auscultated. A murmur had not previously been documented at her puppy wellness visits. The owner has not observed any coughing, trouble breathing, exercise intolerance, or syncope at home, and the patient appears subclinically affected.

Diagnostic investigation of the heart murmur via echocardiography is discussed with the owner but declined due to the patient's lack of clinical signs and the costs associated with additional testing.

What are the next steps?

THE CHOICE IS YOURS ...

CASE ROUTE 1

To provide information on breeding and caring for a pregnant bitch and neonatal puppies and plan to spay the patient after the puppies have been weaned, go to page 28.

CASE ROUTE 2

To avoid providing additional recommendations regarding breeding and ovariohysterectomy to the owner until a diagnostic investigation with a cardiologist has been pursued, go to page 32.

CASE ROUTE 1

Because the patient appears healthy and subclinically affected by the soft murmur, you suspect an innocent, benign flow murmur. There is no urgency to push for expensive echocardiography that may reveal no abnormalities. Thus, you provide information on breeding and caring for a pregnant bitch and neonatal puppies and plan to spay the patient after the puppies have been weaned.

Case Progression

The pros and cons of echocardiography at this stage are discussed with the owner. Based on the location and intensity of the heart murmur and the patient's breed, the most likely differentials include a benign aortic flow murmur and subclinical subaortic stenosis (SAS). Even with mild SAS, dogs typically have a normal lifespan. The owner is relieved that the dog is likely to have a normal lifespan and elects not to spend additional money on echocardiography.

The patient is bred and uneventfully gives birth to 5 healthy puppies. The puppies are successfully

weaned. On patient auscultation as part of the preanesthetic examination for ovariohysterectomy, the same grade II/VI left basilar systolic murmur is observed. The patient is in excellent health and encountered no complications during pregnancy or birth, so an ovariohysterectomy is pursued using typical anesthetic and surgical protocols.

Clinical Considerations

Incidental murmurs are common in small animals, particularly in young dogs or dogs that may be subjected to high-stress environments,^{1,2} and determining whether a grade I/VI to grade III/VI systolic murmur is pathologic (ie, structural cardiovascular lesion is present) or nonpathologic (ie, functional or innocent murmur) based on auscultation alone can be difficult. Guidelines are available to help determine the best approach for treating these murmurs.^{3,4} Criteria such as a murmur that can be heard at all times (at rest or with activity), that is loud through the majority of systole, that is diastolic or continuous in nature, that is grade III/VI or higher intensity, or that is accompanied by abnormal heart sounds (eg, gallop rhythms, split heart sounds, clicks, arrhythmias) is more likely to be pathologic in nature as compared with a murmur that is characterized as soft, focal, or short or with a systolic murmur that is softer or absent at rest, which is more likely to represent a nonpathologic murmur. Localization of the point of maximal intensity, timing, and grade of the murmur in conjunction with patient signalment can help either heighten or decrease the concern for any potential underlying cardiovascular disease. A grade II/VI murmur in a young healthy golden retriever, as in this patient, could represent a functional murmur or indicate a lesion such as mild SAS. Even if mild SAS is present, it is unlikely to substantially impact the lifespan and health of this patient.^{5,6} More important clinical implications arise in patients being considered for breeding.

SAS is a common obstructive congenital heart defect in large-breed dogs, with a strong prevalence in golden retrievers.⁷ Hereditary transmission is suspected via an autosomal recessive trait.⁸

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CHF = congestive heart failure
SAS = subaortic stenosis

Dogs with moderate-to-severe SAS are at an increased risk for arrhythmias, sudden death, infective endocarditis,^{9,10} and other complications (eg, congestive heart failure [CHF]).⁵

Anesthetic considerations for cardiac disease are best determined via echocardiography to evaluate the severity of the cardiovascular lesion and secondary chamber enlargement, cardiac function, and fluid tolerance. General recommendations and anesthetic goals for patients with underlying structural cardiac disease include maintaining heart rate and limiting vasodilation. Extreme fluctuations in heart rate and blood pressure should be avoided. Tachycardia and hypertension should be avoided in patients with aortic stenosis, as there are fewer cardiovascular reserves and these extremes may worsen myocardial work against a fixed obstruction.

It is important to maintain adequate preload and optimize ventricular filling in patients with SAS or other underlying disease processes that can impair ventricular compliance (eg, hypertrophic cardiomyopathy). Inappropriate preload or volume contraction can contribute to myocardial oxygen deficit, which may precipitate arrhythmias. Cardiac output for these patients can be highly dependent on heart rate; thus, bradycardia can result in a significant decrease in cardiac output. Cardiac output is a product of heart rate and stroke volume. Alternatively, tachycardia can result in decreased coronary artery perfusion.

The use of certain drugs that can alter hemodynamics and/or precipitate arrhythmias should be avoided, including α_2 agonists (eg, dexmedetomidine), ketamine (due to increased myocardial oxygen demand), acepromazine, and anticholinergics (unless indicated for bradycardia).¹¹ Because patients with SAS have an increased risk for endocarditis due to blood flow turbulence and endothelial damage, prophylactic antibiotics (eg, cefazolin) are recommended intraoperatively. Although there is no evidence-based medicine to support that postoperative antibiotics are neces-

sary, their use is common among some cardiologists, in part due to the difficulty of treating endocarditis if it develops and the serious sequelae that may result (eg, acute CHF, immune-mediated disease [eg, glomerulonephritis, polyarthritis], thromboembolic disease, arrhythmias). Endocarditis can result in permanent damage to the cardiac valves, causing significant regurgitation, and is difficult to treat due to the relatively avascular composition of the heart valves. Therefore, antibiotics are sometimes administered intra- and postoperatively if there is a concern about an increased risk for endocarditis; it may be easier (and less costly) to prevent endocarditis and/or prophylactically treat it with antibiotics as compared with treating the endocarditis itself. Antibiotics should not be administered to every patient; the cardiologist should discuss with the pet owner the degree of risk for the development of endocarditis and determine appropriate antibiotic use based on the severity of the lesion.

Outcome

The patient recovers from anesthesia and surgery uneventfully and is discharged the next day. Five days later, the patient is presented for evaluation of lethargy and inappetence. On auscultation, the grade II/VI systolic murmur is still present and a new diastolic murmur is audible. Other examination findings include hyperkinetic pulses with a wide pulse pressure and fever (104.1°F [40.1°C]). Neutrophilia with a left shift and monocytosis are present on CBC results. An echocardiogram reveals mild SAS with moderate aortic insufficiency and aortic valve endocarditis.

Inappropriate preload or volume contraction can contribute to myocardial oxygen deficit, which may precipitate arrhythmias.

The patient is hospitalized for 6 days for supportive care and treatment. Paired blood cultures (obtained prior to starting antibiotics to reduce the chance of a false negative result) are submitted, and amoxicillin–clavulanic acid (13.75 mg/kg PO q12h) is started empirically to provide broad-spectrum coverage against common bacteria that lead to endocarditis (eg, *Staphylococcus* spp, *Streptococcus* spp, *Escherichia coli*).¹² The patient begins to improve, and treatment with antibiotics—guided by paired blood culture results (ie, culture yielded *Streptococcus canis* susceptible to amoxicillin–clavulanic acid)—is continued for 8 weeks after documentation that the vegetative lesions have resolved. Of note, a negative blood culture does not rule out the presence of endocarditis, and response to antibiotic therapy should be monitored closely. Diagnosing and treating endocarditis can be complex, requiring frequent follow-up and monitoring via echocardiography, and is beyond the scope of this article.¹²

When the 5 puppies are presented for examination prior to being homed, 3 puppies have left basilar systolic heart murmurs ranging from grade II/VI to V/VI. All puppies are screened via echocardiography and diagnosed with equivocal-to-severe SAS.

Your Choice's Implications

The initial outcome of breeding and ovariohysterectomy was successful; however, the increased risk for endocarditis was overlooked. If the diagnosis of SAS had been known prior to anesthesia, peri- and postoperative antibiotics likely would have been used (based on clinician preference and common clinical practice) and may have prevented the patient from developing endocarditis. There is no clinical evidence to support the use of postoperative antibiotics in addition to perioperative antibiotics; however, it is common practice.

Although this patient was outwardly healthy and able to conceive, tolerate pregnancy, and give birth to a litter of puppies, the puppies had varying severity of this defect, and at least one had severe SAS, which carries a worse prognosis and increased risk for sudden cardiac death. SAS is a documented familial/hereditary defect in golden retrievers, and affected individuals should be removed from the breeding pool.

SAS = subaortic stenosis

entyce[®]
(capromorelin oral solution)

30 mg/mL

BRIEF SUMMARY: Before using this product, please consult the full product insert for more information.

For oral use in dogs only

Appetite Stimulant

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description: ENTYCE[®] (capromorelin oral solution) is a selective ghrelin receptor agonist that binds to receptors and affects signaling in the hypothalamus to cause appetite stimulation and binds to the growth hormone secretagogue receptor in the pituitary gland to increase growth hormone secretion.

Indication: ENTYCE (capromorelin oral solution) is indicated for appetite stimulation in dogs.

Contraindications: ENTYCE should not be used in dogs that have a hypersensitivity to capromorelin.

Warnings: Not for use in humans. Keep this and all medications out of reach of children and pets. Consult a physician in case of accidental ingestion by humans. **For use in dogs only**

Precautions: Use with caution in dogs with hepatic dysfunction. ENTYCE is metabolized by CYP3A4 and CYP3A5 enzymes (See Clinical Pharmacology). Use with caution in dogs with renal insufficiency. ENTYCE is excreted approximately 37% in urine and 62% in feces (See Adverse Reactions and Clinical Pharmacology).

The safe use of ENTYCE has not been evaluated in dogs used for breeding or pregnant or lactating bitches.

Adverse Reactions: Field safety was evaluated in 244 dogs. The most common adverse reactions were diarrhea and vomiting. Of the dogs that received ENTYCE (n = 171), 12 experienced diarrhea and 11 experienced vomiting. Of the dogs treated with placebo (n = 73), 5 experienced diarrhea and 4 experienced vomiting.

To report suspected adverse drug events and/or obtain a copy of the Safety Data Sheet (SDS) or for technical assistance, call Aratana Therapeutics at 1-844-640-5500.

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NADA 141-457, Approved by FDA

US Patent: 6,673,929

US Patent: 9,700,591

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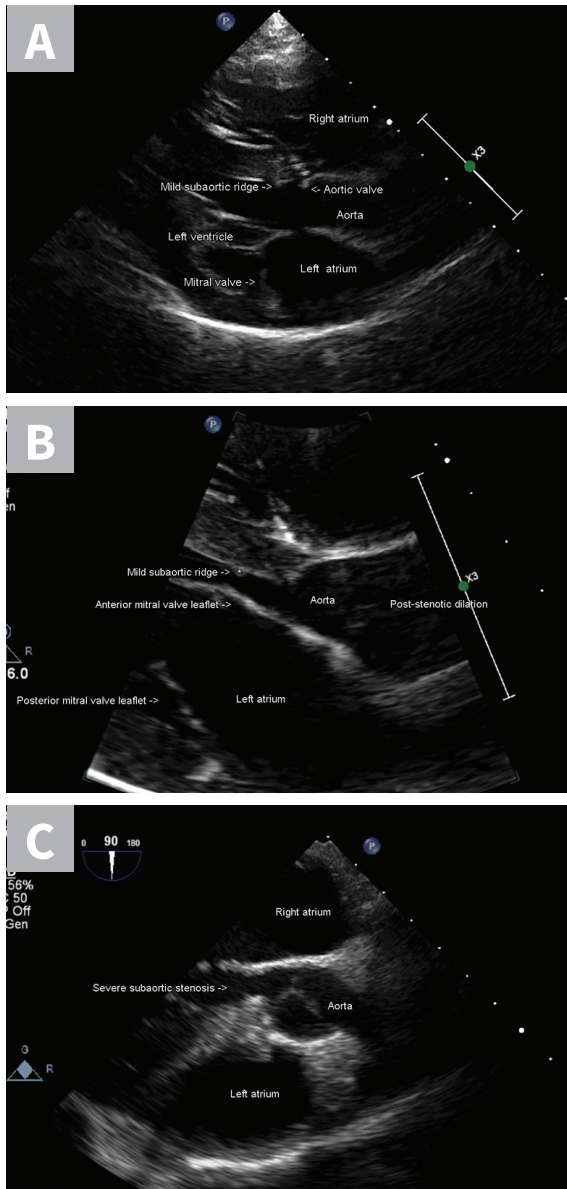
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▲ **FIGURE 1** Echocardiographic image from the right parasternal long-axis left ventricular outflow tract (LVOT) view (A). A small subaortic ridge can be visualized in the LVOT view under the aortic valve. Zoomed-in image of the mild subaortic ridge (B). Echocardiographic image from the right parasternal long-axis LVOT view (C). A tunneling defect resulting in significant narrowing of the subaortic region (below the aortic valve and within the left ventricular outflow tract) in a different dog is shown for comparison.

CHF = congestive heart failure
 LVOT = left ventricular outflow tract
 SAS = subaortic stenosis

CASE ROUTE 2

Because of concern about a potential congenital heart defect, you strongly recommend echocardiography with a cardiologist despite the low grade of the heart murmur. You avoid providing additional recommendations regarding breeding to the owner until a diagnostic investigation with a cardiologist has been pursued.

Case Progression

The owner is reluctant to spend additional money for further diagnostic investigation of the heart murmur. It is explained to the owner that although the murmur is soft and that severe SAS is less likely (unless in the presence of severe systolic dysfunction, which can result in a softer murmur in cases of severe SAS), this congenital defect can be passed to offspring. In addition, if heart disease is present, a safer anesthetic protocol can be made based on the results of the cardiac investigation. The owner thus decides to make an appointment with a cardiologist.

A subcostal continuous-wave Doppler aortic velocity of 2.4 m/sec, equivocal hypertrophy of the left ventricular walls, trace aortic insufficiency, and a small subvalvular aortic ridge are visualized on an echocardiogram (Figures 1-3). The left atrium and left ventricular cavities are normal in size, and there is good contractile function. These findings are consistent with mild SAS and appropriate cardiac function.

You elect to have a more detailed discussion with the owner about breeding and recommend pursuing ovariectomy.

Clinical Considerations

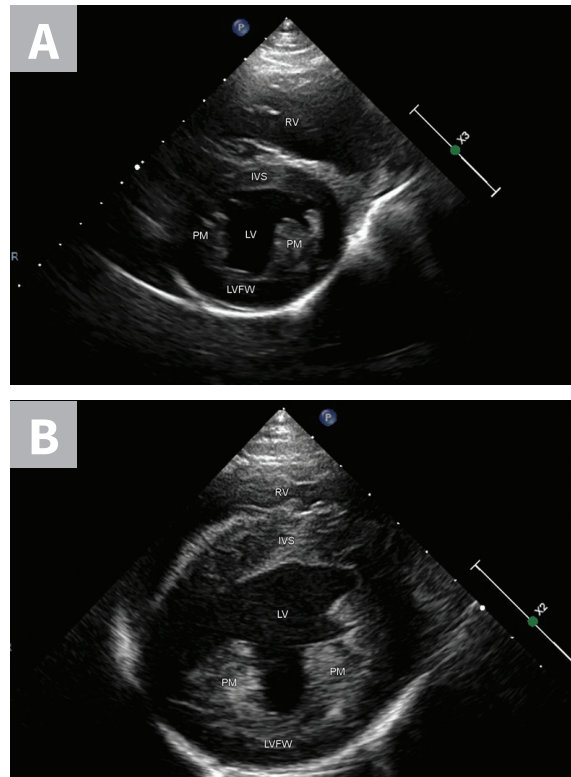
An echocardiogram in patients with a left systolic basilar murmur may reveal congenital heart

defects such as aortic stenosis or pulmonic stenosis. However, an echocardiogram may alternatively reveal a flow murmur that is benign and nonpathologic in nature, in which case the owner may consider echocardiography to be a superfluous diagnostic test and the associated cost to be unjustified.

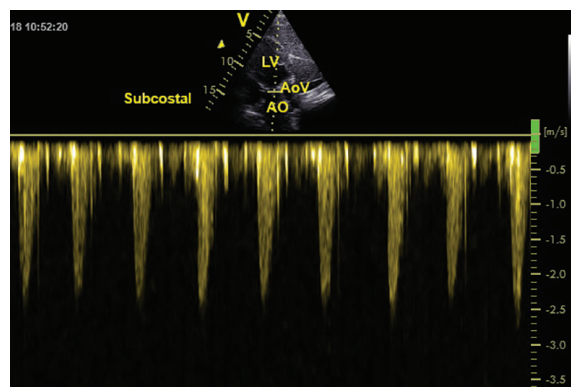
SAS is a common congenital heart defect in golden retrievers and large-breed dogs and is suspected to have an autosomal recessive inheritance pattern. Other breeds predisposed to SAS include Newfoundlands, boxers, rottweilers, German shepherd dogs, and Dogues de Bordeaux.^{5,6} The prevalence of SAS in the United States is 15%, with a male predominance.¹³

Echocardiography is recommended to further evaluate dogs with heart murmurs, particularly those with breed predisposition for congenital heart defects. Echocardiography can screen for congenital heart defects and determine the severity of the cardiovascular lesion, although it can be challenging to differentiate between equivocal and mild SAS. Equivocal SAS is characterized by aortic velocity (2.1-2.4 m/sec) with no overt structural abnormalities in the left ventricular outflow tract visualized on echocardiogram. It can be more difficult to advise owners of dogs with equivocal SAS regarding breeding, as these patients may have a mild variant of SAS with an uncertain risk for passing on this defect. Currently, the gold standard for diagnosis of mild SAS is necropsy.⁵⁻⁸

Most patients with mild SAS (ie, minimal left ventricular hypertrophy and pressure gradient of <50 mm Hg) will have a normal lifespan and only rarely exhibit clinical signs, with a minimal risk for development of arrhythmias, sudden death, and/or CHF.^{5,6} The clinical implications of mild SAS relate to breeding concerns. In general, patients with SAS are at an increased risk for endocarditis, albeit a lower risk in patients with mild SAS. A median survival time of 19 months has been reported in dogs with severe SAS that do not receive treatment, with sudden death typically



▲ FIGURE 2 Echocardiographic image from the right parasternal short-axis view at the level of the left ventricle and papillary muscles. Equivocal concentric left ventricular hypertrophy is evident (A). Moderate-to-severe concentric left ventricular hypertrophy in a different dog is shown for comparison (B). LV = left ventricular cavity, LVFW = left ventricular free wall, IVS = interventricular septum, PM = papillary muscles, RV = right ventricle



▲ FIGURE 3 Echocardiographic Doppler image from a transdiaphragmatic approach to assess the subcostal aortic velocity. Subcostal aortic velocity is 2.4 m/sec, which in conjunction with visualization of a subaortic ridge is consistent with mild subaortic stenosis.

occurring in the first 3 years of life. In addition, dogs with severe SAS typically have clinical signs (eg, exercise intolerance, syncope, coughing, dyspnea/tachypnea if CHF is present) and a reduced quality of life.⁵ With treatment options such as β blockers (eg, atenolol) and balloon valvuloplasty procedures, the median survival time in dogs with severe SAS has been reported to be approximately 55 months, although the risk for sudden cardiac death remains high.¹⁴ The prognosis for patients with SAS can vary, depending on disease severity.

Outcome

Because of the concern for passing on the genes for a congenital heart defect, the owner elected not to breed the dog and pursued ovariohysterectomy. A cardiac-safe anesthetic protocol was followed, and a perioperative antibiotic (ie, cefazolin [20 mg/kg IV at the start of the procedure and an additional dose every 90-120 minutes during the procedure]) was administered due to the increased risk for endocarditis with SAS. Antibiotics are not indicated for every patient with a heart murmur and should be used judiciously and administered based on the degree of concern for development of endocarditis. The patient recovered uneventfully.

Your Choice's Implications

The patient had mild heart disease that did not affect lifespan and only a mildly increased anesthetic risk. Although the cost of echocardiography was an owner concern, further diagnostic testing allowed the owner to make an informed decision about breeding, as well as allowed for an appropriate anesthetic protocol to be tailored to the patient. The cost of an initial cardiac investigation is less expensive than screening all offspring for congenital heart disease and for treatment of endocarditis in the alternative scenario in Case Route 1. In patients with a murmur that is secondary to an innocent flow murmur, the cost of echocardiography may also be worthwhile for peace of mind. ■

CHF = congestive heart failure

SAS = subaortic stenosis

See page 66 for references.

VETORYL® CAPSULES (trilostane)

5 mg, 10 mg, 30 mg, 60 mg and 120 mg strengths
Adrenocortical suppressant for oral use in dogs only.

BRIEF SUMMARY (For Full Prescribing Information, see package insert.)

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: VETORYL Capsules are an orally active synthetic steroid analogue that blocks production of hormones produced in the adrenal cortex of dogs.

INDICATION: VETORYL Capsules are indicated for the treatment of pituitary- and adrenal-dependent hyperadrenocorticism in dogs.

CONTRAINDICATIONS: The use of VETORYL Capsules is contraindicated in dogs that have demonstrated hypersensitivity to trilostane. Do not use VETORYL Capsules in animals with primary hepatic disease or renal insufficiency. Do not use in pregnant dogs. Studies conducted with trilostane in laboratory animals have shown teratogenic effects and early pregnancy loss.

WARNINGS: In case of overdosage, symptomatic treatment of hypoadrenocorticism with corticosteroids, mineralocorticoids and intravenous fluids may be required. Angiotensin converting enzyme (ACE) inhibitors should be used with caution with VETORYL Capsules, as both drugs have aldosterone-lowering effects which may be additive, impairing the patient's ability to maintain normal electrolytes, blood volume and renal perfusion. Potassium sparing diuretics (e.g. spironolactone) should not be used with VETORYL Capsules as both drugs have the potential to inhibit aldosterone, increasing the likelihood of hyperkalemia.

HUMAN WARNINGS: Keep out of reach of children. Not for human use. Wash hands after use. Do not empty capsule contents and do not attempt to divide the capsules. Do not handle the capsules if pregnant or if trying to conceive. Trilostane is associated with teratogenic effects and early pregnancy loss in laboratory animals. In the event of accidental ingestion/overdose, seek medical advice immediately and take the labeled container with you.

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ADVERSE REACTIONS: The most common adverse reactions reported are poor/reduced appetite, vomiting, lethargy/dullness, diarrhea, elevated liver enzymes, elevated potassium with or without decreased sodium, elevated BUN, decreased Na/K ratio, weakness, elevated creatinine, shaking, and renal insufficiency. Occasionally, more serious reactions, including severe depression, hemorrhagic diarrhea, collapse, hypoadrenocortical crisis or adrenal necrosis/rupture may occur, and may result in death.


VETORYL® CAPSULES
(trilostane)

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NADA 141-291, Approved by FDA


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CASE ROUTES ► CONTINUED FROM PAGE 34

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