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CASE REPORT PEER REVIEWED | OPEN ACCESS

Death during exercise testing in a patient with asymptomatic severe aortic stenosis

Mahek Shah, Anuraj Sudhakaran, Baburaj Aparna, Muhammad Qasim, Brijesh Patel, Lohit Garg, Bruce Feldman

ABSTRACT

Introduction: Patients with symptomatic severe aortic valve stenosis (AS) experience short and long-term survival benefit with aortic valve replacement (AVR). Among patients with asymptomatic severe AS (ASAS) current guidelines recommend exercise stress testing (ETT) as a safe and effective method to risk stratify patients and to assist with the timing of AVR. We discuss the course of disease in AS, review the role of ETT and express concerns about the safety of performing stress tests in asymptomatic patients with severe AS. Case Report: We describe the case of a 69-year-old male with left bundle branch block and ASAS who underwent ETT with echocardiographic imaging. We describe the details of the patient's clinical, ECG and echo doppler parameters prior, during and following the test. Patient developed pulseless electrical activity during early recovery with eventual resuscitation and mechanical support. The patient did not survive due to continued deterioration in clinical status. Conclusion: Despite being considered safe, ETT can unmask symptoms in ASAS and result in hemodynamic instability leading to death. A comprehensive registry of safety data is needed. Clinical vigilance and physician supervision during stress testing may minimize the risk of serious adverse events.

Keywords: Asymptomatic severe aortic stenosis, Exercise treadmill testing, Mortality, Safety

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INTRODUCTION

Exercise testing is contraindicated in symptomatic patients with severe AS [1]. However, for asymptomatic patients with severe aortic stenosis (ASAS), the 2014 AHA/ACC Valvular heart disease guidelines recommend six monthly assessment of exercise related physiological and hemodynamic changes to determine presence of symptoms and need for aortic valve replacement (Class IIa, LOE B) [1]. Exercise limiting symptoms on stress testing are strongly associated with spontaneous symptom development or sudden death over the next 12 months [2]. Stress testing helps to provide objective assessment of functional capacity, changes in Valvular or ventricular function and in addition to valve gradients and forward versus regurgitant flow.

Treadmill exercise or upright/supine bicycle ergometry is generally considered safe and low risk as a test when performed under medically supervision, however comprehensive safety data is lacking. In a meta-analysis by Rafiq et al, risk of sudden cardiac death in patients with an abnormal stress test was 5% compared to none with normal testing [3]. Sixty six percent of patients had an adverse cardiac event who had an abnormal stress test compared to 21% who had a normal stress test. We present a patient with ASAS who experienced cardiac arrest immediately following an exercise test and eventual death.

CASE REPORT

A 69-year-old male with severe calcific aortic valve stenosis presented for an elective clinical evaluation. He was a very active individual, performed moderate intensity exercise regularly and denied reduced activity tolerance, effort dyspnea, chest distress, light-headedness or syncope on careful history taking. There was no family history of sudden cardiac death. His physical exam revealed a harsh late-peaking systolic ejection murmur obscuring S2. His exam was otherwise normal. A resting electrocardiogram revealed sinus rhythm with left bundle branch block. The T waves in the lateral precordial leads were upright indicating primary abnormalities. Transthoracic echocardiography showed normal left ventricular systolic function with moderate left ventricular hypertrophy. The aortic valve was severely calcific with restricted leaflet motion. The peak trans-aortic velocity reached 4.1 m/s with mean Valvular gradient of 38 mmHg and calculated aortic valve area of 0.8 cm2. Patient was scheduled to undergo a symptom limited exercise stress echocardiogram to examine for exercise limitations and hemodynamic changes after an extensive discussion of the risks and benefit involved. He agreed to consider elective aortic valve replacement if there were high risk findings during the treadmill exercise stress test with immediate post exercise echo Doppler imaging.

Prior to starting the ETT, patient heart rate (HR) was 84 beats/min and resting blood pressure was 120/75mmHg. During the sixth minute of a Bruce protocol he reported "not feeling well". The test was promptly terminated. There was no angina like chest distress or faintness. His BP had increased from 120/75 to 140/68 mmHg. At peak exercise the ECG revealed sinus tachycardia at 170 bpm, persistent left bundle branch block (LBBB) with new ST-segment abnormalities including 2–3 mm ST segment depression Figure 1 (A and B). Within the first 30 seconds of recovery, frequent premature ventricular complexes were observed followed by acute loss of consciousness with pulseless electrical activity Figure 1 (A and B). Post stress echocardiographic or Doppler images could not be acquired. Following prolonged cardiopulmonary resuscitation, the patient developed profound shock. He was transferred to the cardiac catheterization laboratory emergently, which showed non-obstructive coronary artery disease. He required hemodynamic support, was started on three intravenous pressors and initiated on veno-arterial extracorporeal membrane oxygenation device. Unfortunately, the patient's condition continued to deteriorate with development of disseminated intravascular coagulation and diffuse alveolar hemorrhage. Following discussion with the family, care was withdrawn and the patient expired.

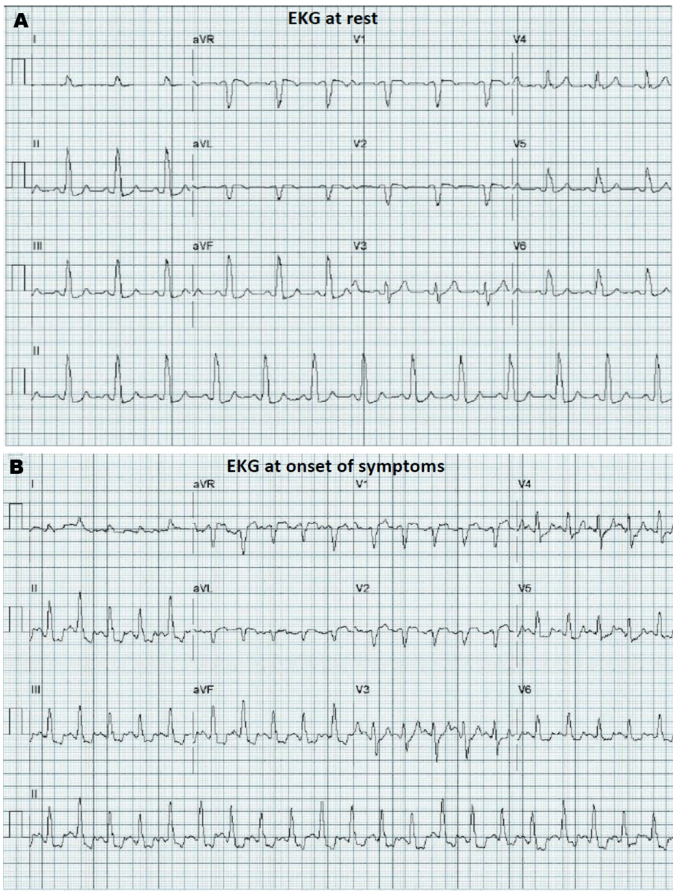


Figure 1 (A and B): Electrocardiographic changes obtain during treadmill exercise stress testing at baseline and symptom onset. A: Resting EKG shows normal sinus rhythm and baseline left bundle branch block with primary ST segment changes. Note upright T waves in the lateral precordial leads.

B. Exercise EKG shows sinus tachycardia with heart rate 126 bpm and new 2–3 mm ST segment depressions in the inferolateral leads.

DISCUSSION

The natural history of aortic stenosis traverses a protracted course. During the early period, patients are usually asymptomatic. Aortic valve area usually decreases by 0.1 cm^2 and V_{max} increases by 0.3 m/s per year, however this can be highly variable in

individual patients. With passage of time, the process of maintaining cardiac output against obstruction in form of aortic stenosis results in left ventricular hypertrophy and increased stress on ventricular wall and workload demands. Serial hemodynamic measurements in patients with severe aortic stenosis over years have revealed significant progression in most but all patients. Pellikka et al studied outcomes in 622 adults with asymptomatic hemodynamically significant AS and concluded that 67% of the patients developed symptoms within five years [4]. Relatively accelerated symptom onset has been noted with increased hemodynamically severe AS, the degree of aortic valvular calcification, abnormal stress test, ventricular hypertrophy, baseline functional status, and comorbidities. Chizner et al reported that the risk of sudden cardiac death was significantly lower (≈1%/yr.) among patients with asymptomatic aortic stenosis in comparison to symptomatic aortic stenosis (34%) in their study [5]. However, in another study, when a group of patients older than 70 years with ASAS were evaluated, event free survival was 73% and 23% at one and four years respectively [6]. Authors of the study proposed early consideration for elective AVR among the elderly with ASAS at lower surgical risk. The exact mechanism of syncope and sudden cardiac death in patients with aortic stenosis is not well elucidated. Fixed obstruction in the setting of high cardiac demand, tachy- or Brady arrhythmias, low cardiac output can lead to decompensation from severe AS. Additionally, an abnormal Bezold-Jarisch reflex as a consequence of stretch-induced baroreceptor response that results in inappropriate peripheral vasodilation during states of extreme fiber stimulation and increased left ventricular wall stress has been proposed [7].

An abnormal stress test is currently defined as development of symptoms such as dyspnea, angina, syncope or near syncope during exercise; a decrease in blood pressure or a <20 mm Hg increase in systolic blood pressure during exercise; <80% of normal exercise tolerance; or ≥ 2 mm horizontal or down slopping ST segment depression during exercise. The vitals are carefully monitored and stress testing is stopped if systolic blood pressure falls >10 mm Hg or patient develops symptoms or complex ventricular arrhythmia. Current European and ACC/AHA guidelines both strongly recommend serial stress testing for asymptomatic severe aortic stenosis. Treatment decision in aortic stenosis is largely based on symptoms and degree of aortic stenosis. The management of asymptomatic patients still is debated. Improper selection of patients for AVR carries the risk of surgical complications and long-term complications secondary to anticoagulation without significant benefit [8]. Delayed AVR risks the patient for sudden cardiac death and poor outcomes. In a majority of these patients, there is under estimation of severity of functional impairment. Among the elderly, symptoms might be masked as patients limit their activities and attribute the symptoms to physical deconditioning. Recent studies postulate that elderly patients may actually benefit from early elective surgery than watchful waiting [9]. Although the rate of progression of aortic stenosis is hard to predict in individual patients, the onset of symptoms significantly changes the prognosis with an average survival rate of 60% at one year. Identifying at risk patients would allow optimal timing for AVR and reduce the risks involved with inadvertent aortic valve replacements. Several predictors have been proposed to identify symptom onset, outcome and operative mortality in patients with asymptomatic severe aortic stenosis. These include abnormal stress testing, severity of AS, rapid hemodynamic progression of AS, elevated left atrial pressure assessed using tissue Doppler, atrial natriuretic peptide, low stroke volume, reduced ejection fraction, left ventricular hypertrophy and pulmonary hypertension among others as shown in Figure 2 [10, 11].

Stress testing remains the most validated tool to identify patients who might benefit from AVR. Stress testing in low to moderate risk patients is rarely associated with serious adverse events. In a national survey of over 500,000 procedures, the incidence of serious arrhythmias, acute myocardial infarction or death after exercise stress testing was estimated to be 9 per 10,000 procedures [12]. The incidence of serious complications with maximal exercise stress testing within a low risk population, performed at a single center (70,000) was noted to be 0.8 per 10,000 [13]. A meta-analysis of seven studies involving 491 patients with asymptomatic severe AS undergoing exercise stress testing revealed no serious complications suggesting that the procedure was relatively safe [3]. Despite the safety data available, a recently published case report has described sustained ventricular tachycardia and loss of consciousness early in recovery in patient with asymptomatic severe AS and widened QRS complex (107 ms) undergoing supine bicycle exercise testing [14]. This report in combination with our case indicates stress testing in some patients

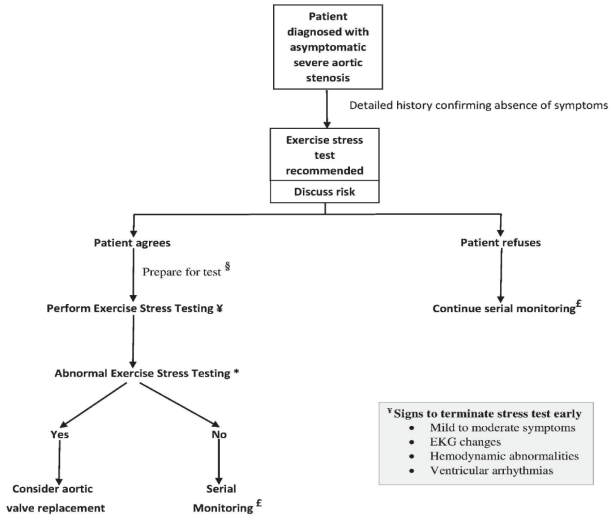
Markers for worse prognosis in asymptomatic severe aortic stenosis
Abnormal stress test
Development of symptoms
Peak transaortic velocity
Increased transaortic mean pressure gradient
Low aortic valve area
Rapid progression of aortic stenosis (≥0.3 m/s per year)
Low flow state (reduced stroke volume index <35 ml/m^2)
Elevated left atrial pressure / Left atrial dilation
Left ventricular systolic dysfunction (Ejection Fraction <50%)
High Valvuloarterial impedance
Left ventricular hypertrophy
Pulmonary hypertension
Poor baseline functional status
Multiple comorbid conditions
Elevated BNP ≥130 pg/mL or Nt-BNP ≥80 pmol/L
Resting to peak exercise mean aortic transvalvular gradient (>18 mm Hg)
Aortic valve calcification by electron beam computed tomography

Figure 2: Markers for worse prognosis among patients with asymptomatic severe aortic stenosis.

with asymptomatic severe AS can be associated with serious adverse events.

Our patient's death prompted us to evaluate options to reduce the risk of adverse events during stress testing. We proposed critical screening for symptoms immediately prior to testing. We recognized that confirming a lack of symptoms can be challenging because they may be hesitant to report or may not recognize reduced activity tolerance or mild shortness of breath as a significant symptom. Early termination of the test in response to mild to moderate symptoms, use of a modified Bruce protocol may reduce risk. Termination in response to pre-specified ECG changes such as new ST depression >0.5 mm or any fall in systolic blood pressure may reduce risk without compromising the prognostic value of the procedure. However, isolated ST-segment depression is rarely a reason to stop the test [15]. Identifying echo Doppler variables during exercise including an increase in mean aortic valve gradient >20 mmHg, systolic pulmonary arterial pressure >60 mm Hg or absence of improvement in left ventricular function is feasible and may enhance safety but requires semi supine bicycle exercise [16]. The safety of stress testing in patients with LBBB and asymptomatic severe AS is not well defined. The presence of LBBB with primary T wave changes, as occurred in our case, may be a marker of high risk for adverse events during stress testing.

There is an unmet need for standardization of stress exercise protocols in ASAS, and additional research on yield and safety for treadmill versus semi-supine or upright bicycle stress testing. Prior data on exercise stress testing used higher cut-offs for aortic valve area thus including mild or moderate AS who presumably have lower risk as it is. Based on current available data, it is appropriate to discuss with the patient the potential for adverse events including life threatening arrhythmias and death. We advocate confirming the absence of symptoms by a repeat detailed and well-directed history immediately before proceeding with a stress test by an experienced physician or exercise technician. In Figure 3, we propose a simplified algorithm that may be useful in guiding exercise testing among patients with severe asymptomatic AS. We recommend a low threshold for discontinuation in response to a patient's report of distress, ECG changes or hemodynamic findings associated with a poor prognosis. A systematic study of the safety of stress testing in patients with LBBB and asymptomatic severe AS would be valuable. We propose that assessment of severe aortic stenosis with exercise be performed in an appropriate environment. That environment should include testing only in a hospital facility that is prepared to treat cardiac arrest and perform ACLS, a hospital facility that staff's cardiothoracic surgeons capable of performing valve replacement surgery, performing test in presence of a cardiologist.



§ Perform stress test at hospital facility prepared to treat cardiac arrest and perform ACLS, a hospital facility that staff's cardiothoracic surgeons capable of performing valve replacement surgery, performing testing with a cardiologist present. Repeat history should be taken to confirm absence of symptoms prior to performing stress test.

* Abnormal exercise stress test is defined as development of symptoms such as dyspnea, angina, syncope or near syncope during exercise; a decrease in blood pressure or a <20mm Hg decrease in systolic blood pressure during exercise; <80% of normal exercise tolerance; or ≥ 2mm horizontal or down slopping ST segment depression during exercise.

£ Consider six monthly exercise stress testing if remains asymptomatic.

Figure 3: Simplified algorithm in guiding exercise testing among patients with severe asymptomatic aortic stenosis.

CONCLUSION

Despite being considered safe, ETT can unmask symptoms in ASAS and result in hemodynamic instability leading to death. Clinical vigilance and physician supervision during stress testing may minimize the risk of serious adverse events. A comprehensive registry of safety data is needed for a large population of patients with asymptomatic severe AS undergoing stress testing.

REFERENCES

1. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: Executive summary: A report of the American college of cardiology/American heart association task force on practice guidelines. Circulation 2014 Jun 10;129(23):2440–92.
2. Amato MC, Moffa PJ, Werner KE, Ramires JA. Treatment decision in asymptomatic aortic valve stenosis: Role of exercise testing. Heart 2001 Oct;86(4):381–6.
3. Rafique AM, Biner S, Ray I, Forrester JS, Tolstrup K, Siegel RJ. Meta-analysis of prognostic value of stress testing in patients with asymptomatic severe aortic stenosis. Am J Cardiol 2009 Oct 1;104(7):972–7.
4. Pellikka PA, Sarano ME, Nishimura RA, et al. Outcome of 622 adults with asymptomatic, hemodynamically significant aortic stenosis during prolonged follow-up. Circulation 2005 Jun 21;111(24):3290–5.

5. Chizner MA, Pearle DL, deLeon AC Jr. The natural history of aortic stenosis in adults. Am Heart J 1980 Apr;99(4):419–24.
6. Zilberszac R, Gabriel H, Schemper M, Laufer G, Maurer G, Rosenhek R. Asymptomatic severe aortic stenosis in the elderly. JACC Cardiovasc Imaging 2017 Jan;10(1):43–50.
7. Myerburg RJ, Castellanos A. Cardiac Arrest and sudden cardiac death. In: Braunwald E, Mann DL, editors. 10ed. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 10ed. Philadelphia: Elsevier/Saunder; 2015.
8. Dimarakis I, Rehman SM, Grant SW, et al. Conventional aortic valve replacement for high-risk aortic stenosis patients not suitable for trans-catheter aortic valve implantation: Feasibility and outcome. Eur J Cardiothorac Surg 2011 Sep;40(3):743–8.
9. Kang DH, Park SJ, Rim JH, et al. Early surgery versus conventional treatment in asymptomatic very severe aortic stenosis. Circulation 2010 Apr 6;121(13):1502–9.
10. Dal-Bianco JP, Khandheria BK, Mookadam F, Gentile F, Sengupta PP. Management of asymptomatic severe aortic stenosis. J Am Coll Cardiol 2008 Oct 14;52(16):1279–92.
11. Stewart RL, Chan KL. Management of asymptomatic severe aortic stenosis. Curr Cardiol Rev 2009 Jan;5(1):29–35.
12. Stuart RJ Jr, Ellestad MH. National survey of exercise stress testing facilities. Chest 1980 Jan;77(1):94–7.
13. Gibbons L, Blair SN, Kohl HW, Cooper K. The safety of maximal exercise testing. Circulation 1989 Oct;80(4):846–52.
14. Christensen NL, Carter-Storch R, Bakkestrøm R, Dahl JS. Sudden cardiac death in asymptomatic aortic stenosis: Is the valve to blame? BMJ Case Rep 2016 Jan 7;2016. pii: bcr2015211473.
15. Magne J, Lancellotti P, Piérard LA. Exercise testing in asymptomatic severe aortic stenosis. JACC Cardiovasc Imaging 2014 Feb;7(2):188–99.
16. Lancellotti P, Magne J, Donal E, et al. Determinants and prognostic significance of exercise pulmonary hypertension in asymptomatic severe aortic stenosis. Circulation. 2012 Aug 14;126(7):851–9.

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Author Contributions

Mahek Shah – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Anuraj Sudhakaran – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Baburaj Aparna – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Muhammad Qasim – Acquisition of data, Drafting the article, Final approval of the version to be published

Brijesh Patel – Acquisition of data, Drafting the article, Final approval of the version to be published

Lohit Garg – Acquisition of data, Drafting the article, Final approval of the version to be published

Bruce Feldman – Substantial contributions to conception and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor of Submission

The corresponding author is the guarantor of submission.

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Consent Statement

Written informed consent was obtained from the patient for publication of this study.

Conflict of Interest

Authors declare no conflict of interest.