

## Stress induced global ischemia in severe aortic stenosis: Electrocardiographic and echocardiographic documentation of a perfect storm

Fabio M Leonelli, MD<sup>1</sup>; Daniel Lumpy, MD<sup>2</sup>; Maqsood Siddique, MD<sup>1</sup>

**\*Corresponding Author: Fabio M Leonelli, MD**

Department of Cardiology, James A. Haley Veterans' Hospital, USA.

Email: Fabio.Leonelli@va.gov

### Abstract

A 12 lead ECG pattern of V1-V6 and inferior ST depression with ST elevation in aVR associated with chest pain is considered to represent diffuse sub-endocardial ischemia due to LM or LME 3 Vessel disease critical stenosis. We present the case of a 48-year-old man with severe AS and normal coronary anatomy who, during a stress echo, developed angina and this ECG pattern. Echocardiographic images taken at the same time showed global hypokinesis. Within 15 minutes both ECG and echo abnormalities were fully resolved.

### Keywords

Global ischemia; aortic stenosis; echocardiography; electrocardiography.

### Abbreviations

EKG/ECG: Electrocardiogram; LM: Left Main; LME: Left main equivalent; AS: Aortic Stenosis; LV: left ventricle; ACC: American College of Cardiology; AHA: America Heart Association; ESE: Exercise Stress Echo; LMCA: Left Main Coronary Artery; VD: Vessel disease; LVEDP: Left ventricular end diastolic pressure; LVDEV: Left ventricular end diastolic volume; ATP: Adenosine Triphosphate; LVH: Left ventricular hypertrophy

### Introduction

Global ischemia is a pathology characterized by a general oxygen supply/demand mismatch in the majority of the left ventricle. Critical disease of the LM or LME 3 vessel disease is a frequent culprit of this global ischemia and has characterized electrocardiographically extensively [1]. This condition, modeled in animal studies [2], can be clinically observed during severe LM or LME coronary artery stenosis [3]. The ECG appearance is fairly typical with marked ST depression in the inferior and the chest leads and ST elevation in aVR. A myocardial infarction or sudden cardiac death is the usual outcome if this condition is not

promptly relieved.

Theoretically, global ischemia could be caused by other circumstances inducing the same widespread LV imbalance between oxygen demand and supply. One of these situations could be severe AS where a number of altered coronary compensatory mechanisms accompany a fixed oxygen supply. A patient with AS could, during exercise, reach such a point and induce global LV ischemia. The following case documents electrical, mechanical and hemodynamic events of reversible global ischemia during an echo-stress in a 48-year-old man with severe AS due to congenital bicuspid valve.

## Case Presentation

In October 2018, a 48-year-old gentleman was referred to our Institution for further management of a possible pre syncope episode. Prior investigations carried out at a different Hospital demonstrated a normal cardiac function with non-obstructive coronary artery disease and a moderate to severe bicuspid AS.

Co-morbidities included hypertension, hyperlipidemia, and tobacco use. Physical exam was unremarkable except for a “crescendo-decrescendo” late peaking systolic murmur in the right upper sternal border. To further investigate his presenting symptoms of pre syncope and assess the functional severity of his AS in view of a potential employment, a symptom limited stress test was ordered. As per ACC/AHA guidelines an exercise stress test in these situations has IIa recommendation level and can add significant prognostic information in patients with severe AS [4].

The baseline resting electrocardiogram and the echocardiogram showed respectively normal Sinus Rhythm without ST-T changes (Figure 1) and severe AS with an aortic valve area of 0.8 cm<sup>2</sup>, peak velocity of 419 cm/s mean peak gradient of 40 mmHg and normal LV systolic function (Figure 2). Mild LVH: IVSd: 1.3 cm LVPWd: 1.2 cm LV Relative wall thickness: 0.45 {ratio}LV mass: 273.9 grams LV mass index: 137.7 grams/m<sup>2</sup>.

During the Exercise Stress Echo, the ECG became abnormal at stage 3 of the Bruce protocol after 8:50 min of exercise (Figure 3); shortly thereafter at 9:20 min patient developed severe SOB, presyncope and chest pain and the test was stopped, with peak stress EKG (Figure 4). The first recovery ECG shows sinus tachycardia with a rate of 115 beats per minute, BP 77/62 mmHg, ST depression in V4-V6 and ST elevation in V1 and aVR, ST depression extends to the inferior leads (Figure 5). At 7 min into the recovery, the down sloping ST depression was followed by marked T wave inversions. The ECG normalized at 16 min into recovery with complete resolution of symptoms. The echo images paralleled the electrocardiographic changes showing a marked global decrease in LV function with minimal LV dilatation immediate post stress (Figure 6, Figure 7 and Figure 8). LV function recovered fully in recovery phase as the ECG normalized.

**Outcome:** The patient was referred for Aortic Valve replacement which was performed uneventfully 2 weeks after the test. He is now asymptomatic and gainfully employed.

## Discussion

Clinical acute LV global ischemia has been described during a profound decrease of coronary blood flow to the majority of the LV [3]. This is characteristically accompanied by ECG changes consisting of infero lateral ST depression with aVR and V1 elevation. These changes in the presence of angina are considered highly predictive of occlusion or high-grade stenosis of LMCA or 3 vessel disease [1]. Global ischemia in this setting rapidly decreases the level of intracellular ATP followed by a swift and dramatic loss of LV contractility. Ischemia also alters the diastolic properties of the LV causing incomplete ventricular relaxation and a reduction in LV distensibility. These changes in the elastic properties of the myocardium, will increase the LVEDP without marked changes in the LVEDV. The subendocardial diastolic flow is severely compromised by these high levels of LVEDP further exacerbating the circumferential ischemia of this sub endocardial myocardial layer [5]. At the same time, the shift in pressure-volume relationship to the right alters the optimal Frank-Starling dynamics which, in turn, should contribute to the decrease in of contractility with a inversely proportional increase in myocardial stiffening initiated by ATP deficiency. As such, these finding have been able to be produced in anesthetized dogs [6].

The ECG changes occurring during severe circumferential global ischemia are more evident during repolarization as the major electrical vector shifts from the epicardium toward the sub-endocardium, resulting in diffuse ST depression with inverted T waves in all the precordial leads [7]. Characteristically, the aVR lead which explores the LV cavity, will record this right superior axis as an elevated ST with positive T wave, which represents a mirror image of apical leads V5 and V6 [8]. Symptoms, echocardiogram and ECG findings in our patient at peak exercise, were typical of global ischemia, yet our patient had normal coronary anatomy. Circumferential sub endocardial ischemia during the stress test must, in this case, have been induced by a different mechanism and it can be seen as a perfect storm developing on the background of a number of physio pathological abnormalities induced by the fixed cardiac output from aortic valvular stenosis.

Other three major factors that induce this degree of ischemia in our patient include, the first being the marked increased in LVEDP [9] induced by effort, which, together with the omnipresent Left ventricular Hypertrophy (LVH) in chronic AS, will raise intramyocardial pressure opposing coronary flow [10]. Secondly, coronary anatomy in AS is insufficiently developed to match the increase in LV mass with a resultant decrease in relative capillary density [11]. This together with the physical deformation of the coronary vessels due to increased LVEDP and LV hypertrophy will increase baseline coronary flow resistance and impair coronary autoregulation [12]. Thirdly, this compromised blood supply it is sufficient at rest, but rapidly becomes critically curtailed during physical exercise because of the increase in heart rate reducing the duration of diastole when coronary flow occurs. Furthermore, the decrease in coronary circulation is non-homogeneous with subendocardial circulation being particularly impacted on by the increase in LVEDP and the alteration in coronary autoregulation.

The perfect storm of global ischemia, in our patient, was the result of an increased oxygen demand met by a fixed cardiac output and a combination of hypertrophy induced coronary anomalies, elevated end

diastolic pressure due to LVH and outflow obstruction and physiologic tachycardia shortening diastolic filling. Other reports have documented the occurrence of this typical ECG pattern in patients with normal coronary anatomy [13] and speculated, as we have done, a supply/demand imbalance to explain the findings. Therefore, in agreement with other authors [14], we believe that the ECG pattern considered to be highly predictive of ischemia induced by severe CAD should, instead, be recognized to represent a nonspecific picture of “circumferential subendocardial ischemia”. The ischemia is triggered by either a decrease in supply or an unbalance in supply/demand exacerbated by coexistent abnormalities (i.e. increased LVEDP and deficient coronary autoregulation in AS) induced by specific pathologies. This is particularly relevant when confronted with a patient presenting with angina and electrocardiographic changes considered highly predictive of severe coronary obstruction and a baseline normal ECG. Clinical exam and a confirmatory echocardiogram would promptly lead to the correct diagnosis. Furthermore, the complete functional and electrocardiographic recovery of our patient following 10-15 minutes of rest would have been inconsistent with global ischemia due to LM/LME where ischemia will evolve into a myocardial infarction of variable dimension.

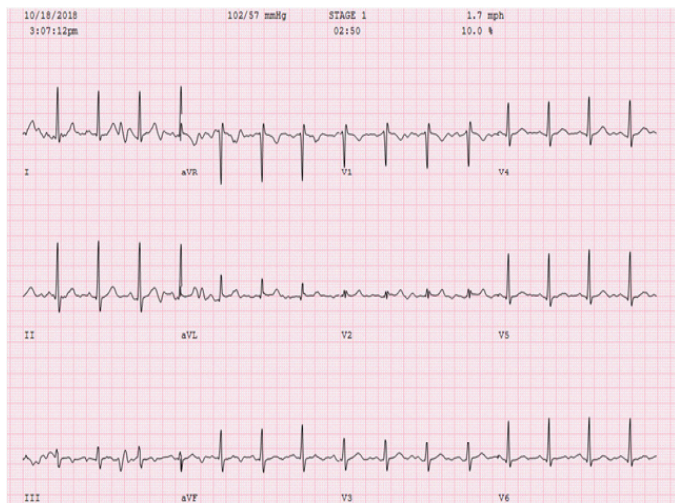


Figure 1: Baseline EKG prior to stress.

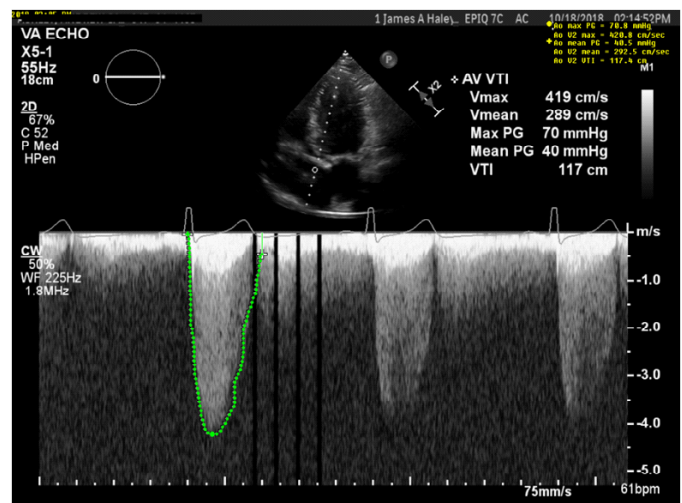


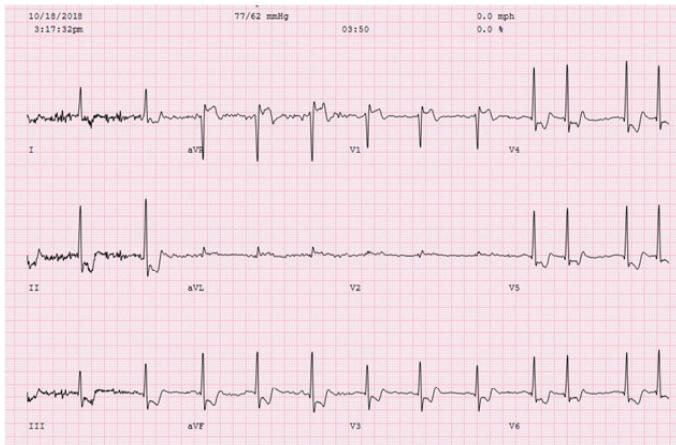
Figure 2: Resting aortic valve gradients.



Figure 3: 8:50 into Bruce protocol.



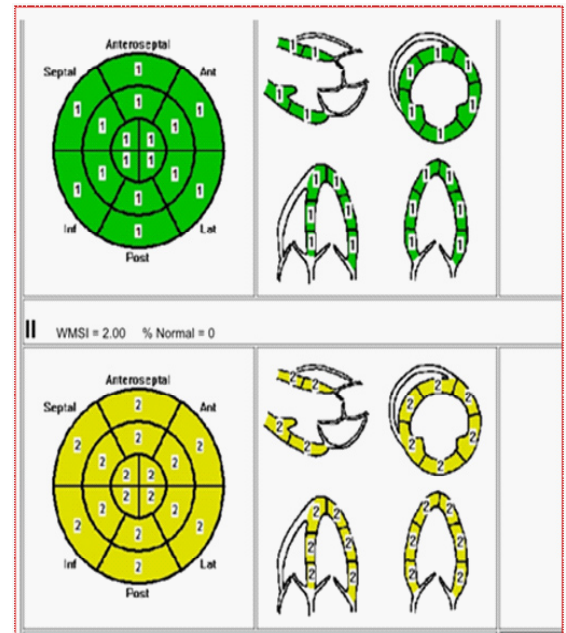
Figure 4: 9:20 min at Stage 4 of the Bruce protocol. Patient is at peak stress and symptomatic with dyspnea, dizziness and chest pain.



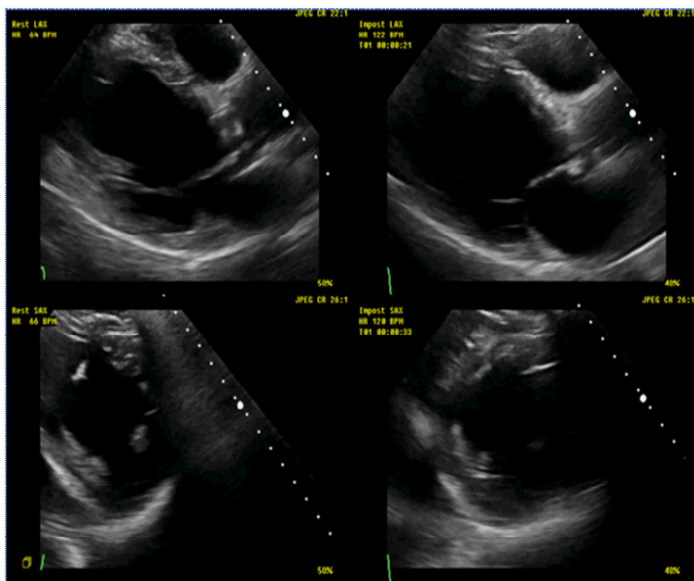
**Figure 5:** Patient is in immediate recovery phase. Diffuse T wave inversions now present.

Rest

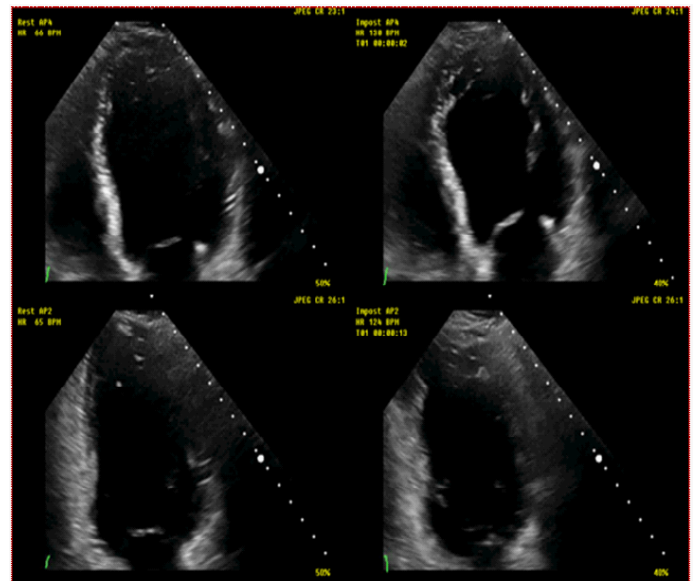
Immediate Post Stress



**Figure 6:** Global reduction in ventricular function at peak stress.



**Figure 7:** Parasternal views. Left side reflects baseline, right side reflects Immediate Post peak stress.



**Figure 8:** Apical views. Left side reflects baseline, right side reflects Immediate post peak stress.

## References

1. Wagner GS, Macfarlane P, Wellens H, Josephson M, Gorgels A, Mirvis DM, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: Part VI: Acute ischemia/infarction: A scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. J Am Coll Cardiol. 2009; 53: 1003-1011.
2. Apstien CS, Deckelbaum L, Mueller, Hagopian L, Hood WB. Graded Global Ischemia and Reperfusion Cardiac Function and Lactate Metabolism. Circulation. 197; 55: 864-872.

3. Wellens HJJ, Gorgels AM, Doevendans PAFM. The ECG in Acute Myocardial Infarction and Unstable Angina: Diagnosis and Risk Stratification. Boston, MA: Kluwer Academic Publishers, 2004.
4. Redfors B, Pibarot P, Gillam LD, Burkhoff D, Bax JJ, Lindman BR, et al. Stress Testing in Asymptomatic Aortic Stenosis. *Circulation*. 2017; 135: 1956-1976.
5. Palacios I, Johnson RA, Newell JB, Powel WJ. Left ventricle end diastolic pressure volume relationship with experimental global ischemia. *Circulation* 1976; 39: 744-755.
6. Edwards CH, Rankin JS, McHale PA, Ling D, Anderson RW: Effects of ischemia on left ventricular regional function in the conscious dog. *Am J Physiol*. 1981; 240: 413-420.
7. Li D, Li CY, Yong AC, Kilpatrick D. Source of electrocardiographic ST changes in subendocardial ischemia. *Circ Res*. 1988; 82; 957-970.
8. Gorgels APM, Engelen DJM, Wellens HJJ. Lead aVR, a Mostly Ignored But Very Valuable Lead in Clinical Electrocardiography. *J Am Coll Cardiol*. 2001; 28: 1355-1356.
9. Dunn RB, Griggs DM. Ventricular filling pressure as a determinant of coronary blood flow during ischemia. *Am J Physiol Heart Circ Physiol*. 1983; 244: 429-436.
10. Marcus ML, Mueller TM, Gascho JA, Kerber RE. Effects of hypertrophy secondary to cardiac hypertension on the coronary circulation. *Am J Cardiol*. 1979; 44: 1023-1028.
11. Duncker DJ, Koller A, Merkus D, Canty JM. Regulation of Coronary Blood Flow in Health and Ischemic Heart Disease *Prog Cardiovasc Dis*. 2015; 57: 409-422.
12. Marcus ML, Doty DB, Hiratzka LF, Wright CB, Eastham CL. Decreased coronary reserve: a mechanism for angina pectoris in patients with aortic stenosis and normal coronary arteries. *N Engl J Med*. 1982; 307: 1362-1366.
13. Kim E, Birnbaum Y. Acute coronary syndromes presenting with transient diffuse ST segment depression and ST segment elevation in lead aVR not caused by "acute left main coronary artery occlusion": Description of two cases. *Ann Noninvasive Electrocardiol*. 2013; 18: 204-209
14. KnottsRJ, Wilson JM, Kim E, . Huang HD, Birnbaum Y. Diffuse ST depression with ST elevation in aVR: Is this pattern specific for global ischemia due to left main coronary artery disease? *J Electrocardiol*. 2013; 46: 240-248.

**Manuscript Information:** Received: February 10, 2021; Accepted: May 27, 2021; Published: May 31, 2021

**Authors Information:** Fabio M Leonelli, MD<sup>1</sup>; Daniel Lumpy, MD<sup>2</sup>; Maqsood Siddique, MD<sup>1</sup>

<sup>1</sup>Department of Cardiology, James A. Haley Veterans' Hospital, USA.

<sup>2</sup>Department of Internal Medicine, University of South Florida, USA.

**Citation:** Leonelli FM, Lumpy D, Siddique M. Stress induced global ischemia in severe aortic stenosis: Electrocardiographic and echocardiographic documentation of a perfect storm. *Open J Clin Med Case Rep*. 2021; 1755.

**Copy right statement:** Content published in the journal follows Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>). © Leonelli FM (2021)

**About the Journal:** Open Journal of Clinical and Medical Case Reports is an international, open access, peer reviewed Journal focusing exclusively on case reports covering all areas of clinical & medical sciences.

Visit the journal website at [www.jclinmedcasereports.com](http://www.jclinmedcasereports.com)

For reprints and other information, contact [info@jclinmedcasereports.com](mailto:info@jclinmedcasereports.com)