This is the accepted manuscript of the article, which has been published in Annals of noninvasive electrocardiology, 2019, 24(3), e12607. https://doi.org/10.1111/anec.12607

**Upsloping ST depression: Is it acute ischemia?**

Mahboob Alam, MD[1]

Kjell Nikus, MD[2]

Miguel Fiol, MD[3]

Antoni Bayes de Luna, MD[4]

Yochai Birnbaum, MD[1]

1- The Section of Cardiology, Baylor College of Medicine and Texas Heart Institute, Baylor St Luke Medical Center, Houston, Texas, USA
2- The Heart Center, Tampere University Hospital and Faculty of Medicine and Life Sciences, University of Tampere, Finland
3- The Illes Balears Health Research Institute. Faculty of Medicine. Son Espases University Hospital. Palma. Spain.
4- Cardiovascular Research Foundation. Cardiovascular ICCC- Program, Research Institute Hospital de la Santa Creu i Sant Pau, IIB-Sant Pau, Barcelona, Spain.

**Running title:** Upsloping ST depression.

Financial Support: The John S. Dunn Chair in Cardiology Research and Education.

Address for reprints: Yochai Birnbaum, MD, FACC, FAHA, The Department of Medicine, Section of Cardiology, Baylor College of Medicine. One Baylor Plaza. MS: BCM620. Houston, TX 77030. Phone: 713-798-2735. Fax: 713-798-0270. Email: ybirnbau@bcm.edu

**Abstract:**

We describe a patient with acute coronary syndrome, presenting with upsloping ST depression in leads I, II, V3-V6 and ST elevation in lead aVR. Coronary angiography revealed spontaneous dissection in a big, dominant left circumflex artery. No other lesions identified. During stenting of the dissection site, the distal left circumflex, supplying a large posterior descending artery was occluded, resulting in ST elevation myocardial infarction with ST elevation in lead III and aVF, but not II. This pattern is considered to represent right coronary artery infarction, rather than left circumflex infarction.

**Key words:** acute coronary syndrome; aVR; Coronary artery dissection; Electrocardiogram; ST depression.

The electrocardiogram (ECG) is an essential part of the initial evaluation of patients presenting with chest pain. Here we describe a patient with atypical ECG pattern and discuss the differential diagnosis explaining the ECG findings.

**Case:**

A 50-year-old man with a history of smoking, hypertension, end stage renal disease on dialysis, diabetes mellitus and obstructive sleep apnea presented to the Emergency Department after an episode of substernal chest pressure that woke him from sleep. His presenting ECG is shown in Figure 1. Initial laboratory results showed serum creatinine 8.97 mg/dl; potassium 5.0 meq/L; sodium 136 meq/L; troponin-I 0.91 ng/ml (normal range 0.00-0.03 ng/ml). After initial treatment with aspirin, heparin and metoprolol, his symptoms subsided and as he was hemodynamically stable. He was scheduled for coronary angiography later the day and not for emergent angiography per the ST elevation -acute coronary syndrome (STE-ACS) protocol.

Bedside echo showed moderate concentric left ventricular hypertrophy and left ventricular enlargement. The distal anterolateral and apical segments were severely hypokinetic. Left ventricular ejection fraction was 40%. There was mild aortic stenosis. Coronary angiography showed a dissection flap in the mid left circumflex coronary (LCX) artery that was extended into a large obtuse marginal/posterolateral (OM/PL) branch (Figure 2a). The LCX also had a large posterior descending (PD) branch. No other lesions were identified. A stent was deployed into the LCX at the junction of the OM/PL branch. However, post-procedure flow was decreased in the PD branch. Attempts to open the artery failed, and the distal artery remained occluded (Figure 2b). A repeat ECG showed ST elevation in leads aVF and III (but not II) with reciprocal ST depression in I and aVL. In addition, horizontal ST depression is now seen in V2-V5. (Figure 3). The troponin I level rose up to 121.91 ng/ml the next day. Repeat echo showed akinesis of the basal and mid inferior segments without worsening of global left ventricular ejection fraction.

**Discussion:**

The patient presented with non-ST elevation myocardial infarction caused by acute dissection of the mid dominant LCX with involvement of a large OM, PD and PL branches. This is an atypical case, as spontaneous coronary artery dissection usually affects young female patients and often presents with ST elevation rather than with ST depression (Roig et al., 2003; Tweet et al., 2012). Moreover, the left anterior descending coronary artery (LAD) seems to be the most affected coronary artery (Roig et al., 2003). The ECG on presentation showed upsloping ST depression in 6 leads along with ST elevation in aVR.

The fact that upsloping ST depression has not been considered as a sign of myocardial ischemia is based on observations during the exercise stress test (Desai, Crugnale, Mondeau, Helin, & Mannting, 2002)). Newer study data has questioned this statement (Polizos & Ellestad, 2006). Upsloping ST depression with positive T waves is commonly seen in persons during tachycardia, even in persons without myocardial ischemia. However, the same pattern can be seen in patients with acute ischemia at slower heart rates and is increasingly recognized as a sign of regional subendocardial ischemia caused by a subtotal occlusion of an epicardial artery (Birnbaum et al., 2014; de Winter, Adams, Verouden, & de Winter, 2016). This pattern has been described in patients with subtotal or total occlusion of the LAD (de Winter et al., 2016) or the LCX (Birnbaum et al., 2014). Yet, the recent Fourth Universal Definition of

Myocardial Infarction (2018) document continues to include in the table of the electrocardiographic manifestations suggestive of ischemia only new horizontal or downsloping ST depression (Thygesen et al., 2018). However, in the discussion, they include upsloping ST depression in the precordial leads as one of several atypical presentation of ischemia induced by LAD artery occlusion. The current patient is an example illustrating that LCX ischemia can induce upsloping ST depression in the precordial leads.

ST elevation in lead aVR has been reported to represent subendocardial ischemia due to proximal LAD, left main coronary artery sub-occlusion or multivessel disease, especially when associated with concomitant diffuse ST depression in 6 or more leads (Birnbaum et al., 2014; Thygesen et al., 2018). The current patient presented with significant ST elevation in aVR along with ST depression in 6 leads. However, the ST depression is upsloping, whereas in left main sub-occlusion or ischemia due to multivessel disease, ST depression is usually horizontal or downsloping and associated with T wave inversion (Nikus et al., 2004). Moreover, diffuse ST depression with ST elevation in aVR can be seen in conditions other than left main sub-occlusion, proximal LAD occlusion or three vessel disease (Knotts, Wilson, Kim, Huang, & Birnbaum, 2013). Especially, severe aortic stenosis can cause such an ECG pattern (Huang, Lee, Lin, Lu, & Lee, 2015). Our patient had only mild aortic stenosis that is not expected to cause circumferential subendocardial ischemia.

During the percutaneous coronary intervention, the distal part of the LCX, including the PD branch, occluded. This caused ST elevation in the inferior leads III and aVF along with ST depression in I, aVL, and V2-V5. Our patient was treated with percutaneous coronary intervention. Tweet et al. suggested that better results could be obtained by initial conservative treatment or coronary bypass surgery (Tweet et al., 2012).

It is commonly believed that ST elevation in lead III more than in lead II is predictive of right coronary artery occlusion (Wagner et al., 2009). Yet, as the occlusion is distal, it is not possible to differentiate between ischemia caused by right and left PD occlusion (Hira, Wilson, & Birnbaum, 2011). Our patient developed ST elevation in leads III and aVF without ST elevation in lead II despite the fact that the culprit lesion was the LCX.

In the past, it was speculated that ST depression in the precordial leads V1-V4 in patients with inferior ST elevation myocardial infarction represent involvement of the basal inferior segment that is vertical and parallel to the anterior wall. More recently, using cardiac magnetic resonance imaging, it was demonstrated that ST depression in V1-V3 correlates with the size of the frontal plane projection of the inferior wall ischemic area at risk in relationship to the anterior/posterior chest wall rather than to a vertical basal inferior segment (Jia et al., 2018). Thus, they should be considered reciprocal changes to ischemia of the inferoseptal segments.

**References:**


Birnbaum, Y., Wilson, J. M., Fiol, M., de Luna, A. B., Eskola, M., & Nikus, K. (2014). ECG diagnosis and classification of acute coronary syndromes. *Ann Noninvasive Electrocardiol, 19*(1), 4-14. doi:10.1111/anec.12130

de Winter, R. W., Adams, R., Verouden, N. J., & de Winter, R. J. (2016). Precordial junctional ST-segment depression with tall symmetric T-waves signifying proximal LAD occlusion, case reports of STEMI equivalence. *J Electrocardiol, 49*(1), 76-80. doi:10.1016/j.jelectrocard.2015.10.005

Desai, M. Y., Crugnale, S., Mondeau, J., Helin, K., & Mannting, F. (2002). Slow upsloping ST-segment depression during exercise: does it really signify a positive stress test? *Am Heart J, 143*(3), 482-487.

Hira, R. S., Wilson, J. M., & Birnbaum, Y. (2011). Introducing a new algorithm in inferior ST-segment elevation myocardial infarction to predict the culprit artery and distinguish proximal versus distal lesions. *Coron Artery Dis, 22*(3), 165-170. doi:10.1097/MCA.0b013e328342c748

Huang, T. C., Lee, M. K., Lin, S. J., Lu, Y. H., & Lee, K. T. (2015). Diffuse ST-Segment Depression with ST-Segment Elevation in Lead aVR in 12-Lead Electrocardiography May Indicate Ischemic Change of Severe Aortic Stenosis. *Acta Cardiol Sin, 31*(5), 449-452.

Jia, X., Heiberg, E., Sejersten Ripa, M., Engblom, H., Carlsson, M., Halvorsen, S., . . . Birnbaum, Y. (2018). Cardiac Magnetic Resonance Evaluation of the Extent of Myocardial Injury in Patients with Inferior ST Elevation Myocardial Infarction and Concomitant ST Depression in Leads V1-V3: Analysis from the MITOCARE Study. *Cardiology, 140*(3), 178-186. doi:10.1159/000491745

Knotts, R. J., Wilson, J. M., Kim, E., Huang, H. D., & Birnbaum, Y. (2013). Diffuse ST depression with ST elevation in aVR: Is this pattern specific for global ischemia due to left main coronary artery disease? *J Electrocardiol, 46*(3), 240-248. doi:10.1016/j.jelectrocard.2012.12.016

Nikus, K. C., Eskola, M. J., Virtanen, V. K., Vikman, S., Niemela, K. O., Huhtala, H., & Sclarovsky, S. (2004). ST-depression with negative T waves in leads V4-V5--a marker of severe coronary artery disease in non-ST elevation acute coronary syndrome: a prospective study of Angina at rest, with troponin, clinical, electrocardiographic, and angiographic correlation. *Ann Noninvasive Electrocardiol, 9*(3), 207-214. doi:10.1111/j.1542-474X.2004.93545.x

Polizos, G., & Ellestad, M. H. (2006). The value of upsloping ST depression in diagnosing myocardial ischemia. *Ann Noninvasive Electrocardiol, 11*(3), 237-240. doi:10.1111/j.1542-474X.2006.00109.x

Roig, S., Gomez, J. A., Fiol, M., Guindo, J., Perez, J., Carrillo, A., . . . Bayes de Luna, A. (2003). Spontaneous coronary artery dissection causing acute coronary syndrome: an early diagnosis implies a good prognosis. *Am J Emerg Med, 21*(7), 549-551.

Thygesen, K., Alpert, J. S., Jaffe, A. S., Chaitman, B. R., Bax, J. J., Morrow, D. A., . . . Group, E. S. C. S. D. (2018). Fourth universal definition of myocardial infarction (2018). *Eur Heart J*. doi:10.1093/eurheartj/ehy462

Tweet, M. S., Hayes, S. N., Pitta, S. R., Simari, R. D., Lerman, A., Lennon, R. J., . . . Gulati, R. (2012). Clinical features, management, and prognosis of spontaneous coronary artery dissection. *Circulation, 126*(5), 579-588. doi:10.1161/CIRCULATIONAHA.112.105718

Wagner, G. S., Macfarlane, P., Wellens, H., Josephson, M., Gorgels, A., Mirvis, D. M., . . . Heart Rhythm, S. (2009). 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, 53*(11), 1003-1011. doi:10.1016/j.jacc.2008.12.016

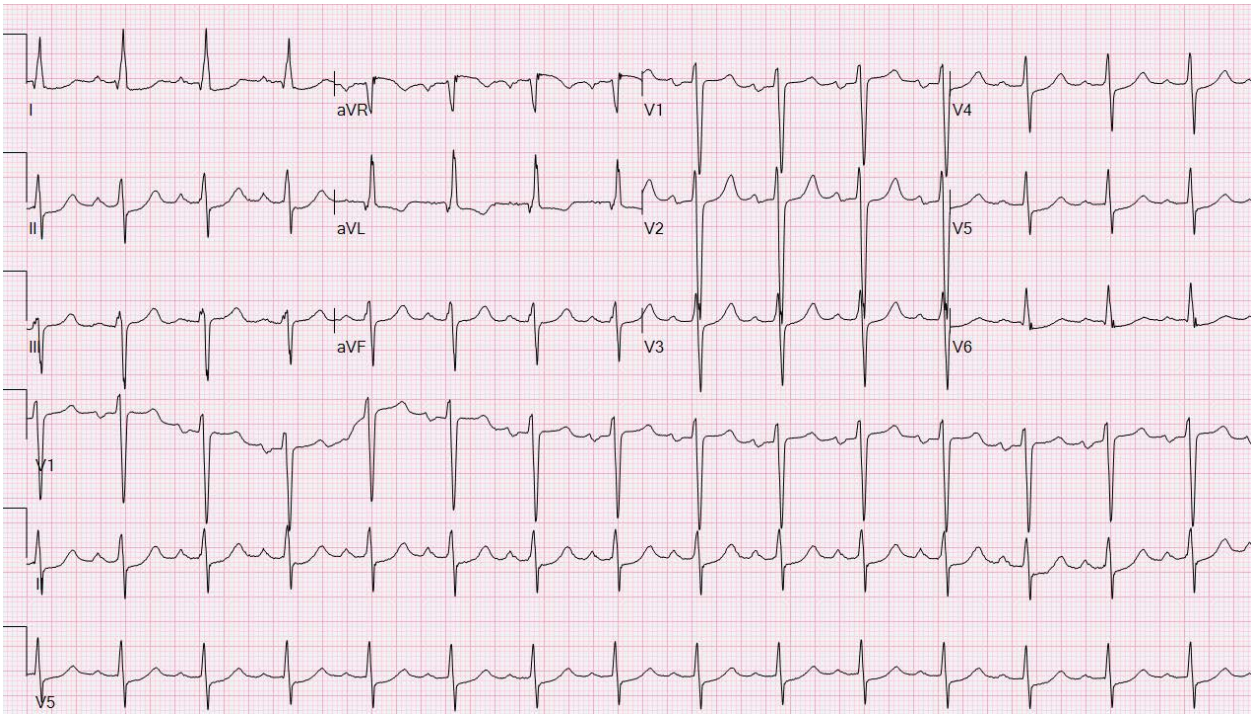


**Figure 1:** Presenting ECG showing sinus rhythm. There is upsloping ST depression in leads I, II, V3-V6. There is down-sloping ST depression and T wave inversion in aVL and ST elevation in lead aVR.

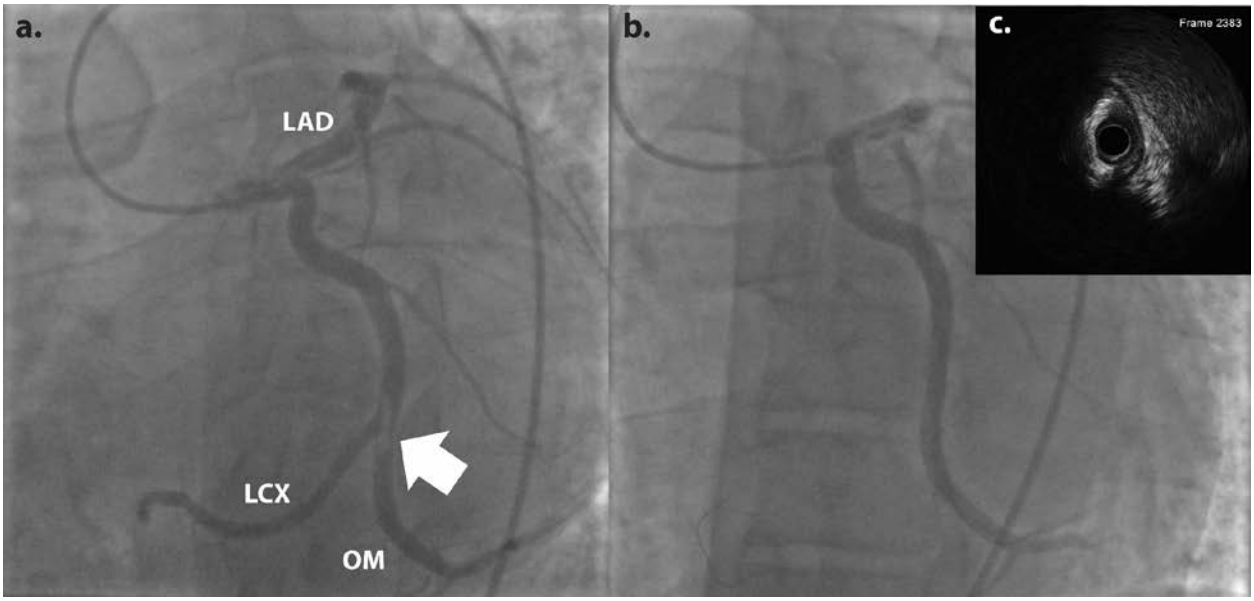


**Figure 2: a.** Initial left coronary artery angiogram in the left anterior oblique (LAO) caudal projection shows a filling defect (white arrow) concerning for a thrombotic plaque at the bifurcation point of a large distal obtuse marginal (OM) branch with the LCX in A-V groove that continues towards the left posterior descending artery (PDA). **b.** Post-PCI: Left coronary angiogram in the same projection shows a large OM branch with occlusion of the distal LCX and left PDA due to plaque shift into the distal LCX

artery. Black arrows- a wire in the PDA artery. **C.** Intravascular ultrasound study (IVUS): pre-PCI shows a large area of echolucent plaque with an overlying echodense flap. This is consistent with a plaque rupture resulting in dissection and thrombosis. When compared to the normal segment, there is significant narrowing of the lumen at the site of plaque rupture.

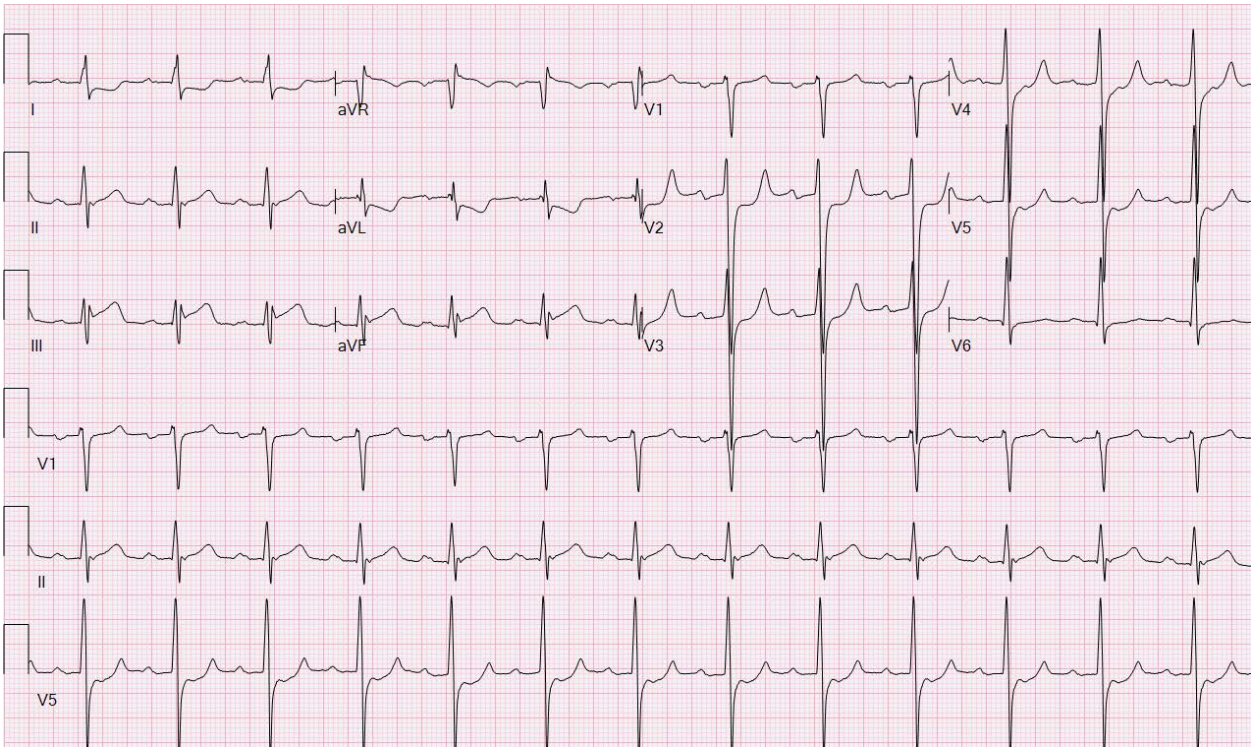


**Figure 3:** Post intervention, ECG shows sinus rhythm. There is ST elevation in leads aVF and III (but not II) with reciprocal ST depression in I and aVL. In addition, horizontal ST depression now seen in V2-V5.