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Culprit Artery Identification of Patients with Lead AVR ST Segment Elevation in Acute Coronary Syndrome

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I. INTRODUCTION

Myocardial ischemia is characterized by an imbalance between myocardial oxygen supply and demand. MI is defined as myocardial cell death due to prolonged ischemia. The condition is diagnosed when blood levels of biochemical markers of cell death are increased in the clinical setting of acute myocardial ischemia [1].

While patients with ongoing chest discomfort and persistent ST-segment elevation are classified as STE-ACS, NSTE-ACS patients are, in turn, classified as having either non-ST-segment elevation MI (NSTEMI) or unstable angina pectoris (UA), based on the presence or absence of biomarkers of myocardial necrosis [1]. The most common cause of NSTE-ACS is reduced myocardial perfusion that results from coronary artery narrowing caused by a nonocclusive thrombus that has developed on a disrupted atherosclerotic plaque.

MI may occur with atypical symptoms or even without symptoms, being detectable only by the ECG, biomarkers or cardiac imaging [1].

Lead aVR is a mostly ignored but veryvaluable lead in ACS [2,3,4]. Lead aVR, an augmented and unipolar limb lead, wasconstructed to obtain specific information from the rightupper portion of the heart, including the outflow tractof the right ventricle and the basal portion of the interventricularseptumand LV cavity. ST-segment elevation in lead aVRin patients with ACS can be caused by

(1) transmural ischemia in the basalpart of the interventricular septum caused by impairedcoronary blood flow of the first major branch originatingfrom the left anterior descending coronary artery;

(2) transmural ischemia in the right ventricular outflowtract caused by impaired coronary blood flow of thelarge conal branch originating from the right coronaryartery;

(3) in some cases of circumflex branch occlusion, with ischemia, most pronounced in the posterobasal area, ST-elevation in lead aVR, but not in lead V1, may occur.

(4) reciprocal changes opposite to ischemicor non-ischemic ST-segment depression in the laterallimb and precordial leads

The current evidence suggests that in patients withNSTE-ACS, ST-segment elevation in lead aVR is associatedwith LMT or 3-vessel disease and increased adverseevents. Considering the location of lead aVR, globalsubendomyocardial ischemia can produce ST-segmentelevation in lead aVR.

Therefore, it is reasonable that STsegmentelevation in lead aVR is associated with LMT or3-vessel disease in NSTE-ACS.

avR ST elevaion has also been noted with proximal LAD and LCx occlusion in patients with ACS.

So we took 32 patients with ACS presenting with avR ST elevation,who underwent coronary angiogram within 48 hours ,and looked for clues in ECG which can help in localization of culprit artery.

AIMS AND OBJECTIVES

Aim was to identify culprit artery in patients of ACS presenting with aVR ST elevation

II. MATERIALS AND METHODS

TYPE OF STUDY

Descriptive

STUDY SETTING & STUDY PERIOD

From October 2016 to September 2017, we studied 32 consecutive patients who were admitted to the coronary care unit of our institute "AMALA INSTITUTE OF MEDICAL SCIENCES"with a diagnosis of ACS.

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INCLUSION CRITERIA

All consecutiveACS presenting with ST elevation in lead aVR in CCU of AMALA INSTITUTE OF MEDICAL SCIENCESand undergoing CAG when ST elevation was persistent.

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EXCLUSION CRITERIA
Patients with a previous history of CAD,Chronic kidney disease and with electrolyte abnormalities.

SAMPLE SIZE : 32

DATA COLLECTION
All32studied patients had the following investigations on admission including 12-lead EKGs, chest X-ray, troponin T, creatine phosphokinase (CPK), creatine kinase MB fraction (CK MB) and blood chemistry including fasting blood sugar, renal function test (BUN and creatinine), electrolytes and lipid pro-files.CAG was performed in all within 48 hours after admission**.**

Definition
Acute coronary syndrome includes acute STelevation myocardial infarction (STEMI),acute non-STelevation myocardial infarction (NSTEMI) and unstableangina (UAP).
Culprit lesion was the coronary artery lesionwhich was totally occluded or showed severe stenosis(flow delay-TIMI flow grade 1 or local dissection orthrombosis or more than 75% stenosis).
• ECG: The 12-lead EKGs recorded on admissionwere analyzed (averaged 5 consecutive beats)and ST segment elevation were measured.
• A ST segment deviation either elevation ordepression was determined as the mean value of 5 consecutivebeats measured at 60 milliseconds after the Jpoint of the QRS complex. ST segment elevation wasdefined as present when ST segment elevation was> 0.05 mV or 0.5 mm in the limb leads and aVR lead andST segment elevation was > 0.1 mV or 1 mm in thepre-cordial leads.

Statistical Analysis
• Descriptive data were expressed as mean +SD
• The incidence of ST segment elevation inaVR and all leads were analyzed and compared
• p value < 0.05 was considered statistically significant

III. REVIEW OF LITERATURE

Myocardial ischemia can occur during two pathophysiologic processes: decreased blood supply, in which a coronary artery has been acutely occluded by a thrombus or vasospasm, or increased myocardial demand in which there has been acutely increased cardiac work by exercise or other stress in the presence of coronary artery disease (CAD).

Patients with myocardial ischemia as a result of decreased supply typically present with two types of electrocardiogram (ECG) patterns:
a) predominant ST-segment elevation acute coronary syndrome (STE-ACS), and are classified as having either "aborted myocardial infarction (MI)" or ST-elevation MI (STEMI) based on the presence or absence of biomarkers of myocardial necrosis; and
b) patients without predominant STsegment elevation on the 12-lead ECG - non-ST elevation ACS (NSTE-ACS) [1].

STE-ACS has homogeneous etiology of transmural ischemia typically caused by fibrin-rich (red) thrombus occluding the infarct-related artery, except in cases of cardiac spasm. NSTE-ACS has heterogeneous etiologies of predominantly subendocardial ischemia, frequently caused by a platelet-rich (white) thrombus [5]. The majority of patients presenting with a clinical syndrome compatible with STE-ACS progress into the evolving stages of STEMI, and a minority have aborted MI [6]. Patients presenting with NSTE-ACS represent a wide spectrum of severity of CAD and, therefore, have major differences in the outcome. Urgent reperfusion with thrombolytic therapy has been proven to be beneficial only in patients presenting with ST-segment elevation, whereas in the general group without ST-segment elevation, including those with ST-segment depression, flat or negative T wave and even normal or unchanged ECG, it may be harmful [7]. Moreover, studies have shown a superiority of an invasive strategy over a conservative one in high-risk patients with NSTE-ACS [8].

Rapid risk stratification of patients with NSTE-ACS is crucial for appropriate management of these patients and for targeting more potent and invasive therapies for higher-risk patients. The ECG remains the most immediately accessible and widely used diagnostic tool for guiding emergent treatment strategies. The ECG recorded during acute myocardial ischemia is of diagnostic, therapeutic and prognostic significance. There is clearly a need to determine subgroups of patients having anatomically or functionally severe coronary obstruction based on standard 12- lead ECG interpretation. It was recently been pointed out that there are overlooked subgroups with NSTE-ACS who may potentially benefit from emergent reperfusion therapy [9].

When ischemia is confined primarily to the subendocardium, the overall ST vector typically faces the inner ventricular layer and the ventricular cavity such that the surface ECG leads show ST-

segment depression. This subendocardial ischemic pattern is a frequent finding during spontaneous episodes of rest angina. In cases of severe extensive subendocardial ischemia, as in acute subtotal or even total occlusion of the left main coronary artery (LM), the injury vector may be seen as ST-segment depression in the majority of the ECG leads but as ST-segment elevation in lead aVR [10].

Localization of subendocardial ischemia from the ECG changes is not as straight-forward as in the case of regional transmural ischemia due to total vessel occlusion. Reproducing subendocardial ischemia in animal models has proven difficult [11]. It is partly due to this that the ECG manifestations of subendocardial ischemia are not well-defined in the literature. It is especially important to identify patients with severe CAD, including LM disease, since these are associated with high mortality, conceivably by means of non-invasive methods.

Accordingly, ST-segment depression and lead aVR ST-segment elevation have been established as ECG markers of poor outcome in NSTE-ACS [12,13,14,15]. The ECG pattern with widespread ST-segment depression and inverted T waves maximally in leads V4-V5 has been described by Sclarovsky as circumferential subendocardial ischemia (CSI) [16].

PATHOPHYSIOLOGY OF ECG CHNAGES IN NON-ST ELEVATION ACUTE CORONARY SYNDROME

In coronary artery occlusion, oxygen tension within the myocardium falls to almost zero within a minute after complete cessation of blood flow. The ischemic myocardial cells consume all the available oxygen within a few minutes after the myocardium loses its blood supply; as a result, oxidative phosphorylation comes to a complete halt. The large amounts of phosphate released from hydrolysis of adenosine triphosphate in the ischemic heart cause calcium to be trapped within the sarcoplasmic reticulum. Phosphate pours out into the extracellular space, and to maintain electrical neutrality, these anions are accompanied by potassium, the major intracellular cation. This causes a large potassium efflux, which results in depolarization of the ischemic myocardial cells [17].

Myocardial cell death begins 15 to 40 minutes after the heart's blood supply is cut off completely, and about 6 hours later, few viable cells remain in the ischemic region. This progression resembles a wave of necrosis that begins in the endocardium, where energy requirements are greatest, and spreads outward through the wall of the left ventricle toward the epicardium [18]. The timetable depends on the level of myocardial protection. Depolarization of ischemic myocardial cells establishes differences in resting potential that allow current to flow between the normally perfused and ischemic regions of the heart. These currents, called injury currents, cause diagnostic ST-segment shifts on the surface ECG that help to distinguish between subendocardial ischemia, which depresses the ST segment and transmural ischemia, which in turn results in ST-segment elevation.

POSSIBLE MECHANISMS OF ST SEGMENT ELEVATION IN LEAD AVR

The augmented limb leads were developed to derive more localized information than the bipolar leads I, II and III could offer. For this purpose from the existing limb electrodes, new leads aVR, aVF and aVL were constructed, being unipolar leads looking at the right, left and lower part of the heart with the reference electrode constructed from the other limb electrodes. Thus, the purpose of lead aVR was to obtain specific information from the right upper side of the heart, such as the outflow tract of the right ventricle and the basal part of the septum. In practice, however, most electrocardiographers consider lead aVR as giving reciprocal information from the left lateral side, being already covered by the leads aVL, II, V5 and V6. This has been the reason that lead aVR has become largely ignored.

Lead aVR ST segment elevation in acute, proximal LAD occlusion is the result of transmural ischemia of the basal part of the septum, where the injury's electric current is directed toward the right shoulder. It is certainly reasonable to theorize that acute LMCA obstruction also causes ischemia of the basal part of the septum through disturbance of the major septal branch blood flow—that is, interruption of the proximal LAD blood flow. This would account for lead aVR ST segment elevation associated with acute LMCA obstruction.

ST segment elevation in lead aVR versus lead V1. Acute LMCA obstruction, but not LAD obstruction, ordinarily causes ischemia of the posterior wall through disturbance of LCx blood flow. It is reasonable to assume that the electrical force in posterior wall ischemia counterbalances the ischemia-induced electrical force in the anterior wall. In fact, several reports have shown reciprocal changes in the precordial leads (V1 and V2) induced by posterior wall ischemia that was caused by LCxobstruction . The most likely interpretation of less ST segment elevation in lead V1 in the LMCA group compared with the LAD group is that

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it is the result of the electrical force induced by posterior wall ischemia, associated with LMCA obstruction counterbalancing the ischemia-induced electrical force in the anterior wall.

The classical electrocardiographic (ECG) pattern of LMCA disease includes STE in lead aVR in the presence of extensive ST depression (most prominent in leads I, II, and V4–6) with the STE in aVR ≥ V1 . Patients with these findings may potentially require early coronary angiography and coronary bypass surgery.

Since lead aVR is electrically opposite to the left-sided leads I, II, aVL, and V4–6; ST depression in these leads will produce reciprocal ST elevation in aVR.

In some cases of circumflex branch occlusion, with ischemia, most pronounced in the posterobasal area, ST-elevation in lead aVR, but not in lead V1, may occur.

Ischemia of the basal part of the septum might be caused by blood flow disturbance in interventricular branches, arising from the well-developed RCA, thus resulting in lead aVR ST segment elevation.

IV. RESULTS

Patient' s characterstics n=32	values
Mean age	57
Male : female	19:13
Dm	15
HTN	18
DM and HTN	9
SMOKERS	7
Family history of CAD	8
DLP	11

	LM/TVD	OTHERS	TOTAL
AVR≥V1	24	5	29
AVR<V1	0	3(LAD)	3
TOTAL	24	8	32

	OTHERS (5)
LAD	2 (de winter sign)
LCx (non dominant or codominant)	2(lead 1 and avL discordance)
LCx (Dominant)	1 (lead 1 and avLConcordance,ST depression in both 1 and avL)

	LEFT MAIN	TVD	LAD	LCx
ST elevation in lead avR(mm)	1.32	1.3	1.12	1.16

There were 32 studied patients with the mean age around 57 years old, ranging from 36 to 77. Malewere predominant(59%). Diabetes mellitus and hypertension was found in 47% and 56% respectively.Current cigarette smokingand family history of CVD was 22% and 25% respectively.About 34% of patients had dyslipidemia.

Out of 32 patients,14 (44%) had left main disease, 10 (31%) had triple vessel disease,5 had double vessel disease (16%,LAD culprit artery in 2

and LCx in 2) and 3 had SVD (9%,LAD culprit artery in 2 and LCx in 1).
3 had ST elevation in V1>aVR,and culprit artery in all the 3 was LAD. 29 had ST elevation in avR>= V1,and out of these29,28 had aVR ST>= 1mm .23 had left main or triple vessel disease,2 had LAD as a culprit artery (de winter sign) and remaining 3 had LCx as a culprit artery. Out of three, 2 had non dominant or co-dominant LCxWith ST depression in lead I but upright ST in aVL, lead I and aVLdiscordance). One had dominant LCx with ECG features of posterior wall MI with ST depression in both I and aVL(lead I and aVL Concordance).
One patient with aVR ST > V1 BUT < 1 mm,had triple vessel disease.
24 patients were plan for CABG and 8 underwent PTCA.2 patients with left main disease were not willing for CABG,so were taken up for PCI. One patient with distal left main 90% occlusion died before he could be taken up for CABG.
Degree of ST segment elevation in lead aVR was comparable in all subgroups.

V. DISCUSSION

Lead aVR ST segment elevation with less ST segment elevation in V1 in patients with acute coronarysyndrome are considered to relate with culprit left main coronary artery disease. Lead aVR ST segmentelevation determines severe coronary artery disease such as acute left main occlusion[4] and three-vessel coronary artery disease[19].

In the present study patients with ST elevation in aVR, 75 % had left main or triple vessel disease which is comparable to findings in other studies.

Kosugeet al[20]analyzed ECGs of 310 patients with NSTE-ACS undergoingcoronary arteriography and found that ST-segmentelevation ≥ 0.05 mV in lead aVR was the strongest predictorof LMT or 3-vessel disease, with 78% sensitivity and86% specificity.

In another study, Kosugeet al[21] examined 572 patients with NSTE-ACS undergoing coronary arteriography and showed that ST-segment elevation ≥ 0.1 mV in lead aVR identified severe LMT or 3-vessel disease (≥ 75% stenosis of LMT and/or 3-vessel disease with ≥ 90% stenosis in ≥ 2 proximal lesions of the LAD and other major epicardial arteries), with 80% sensitivity and 93% specificity.

In another study, Kosugeet al[22] examinedthe prognostic value of ST-segment elevation ≥ 0.05 mVin lead aVR in 333 patients with NSTE-ACS undergoingcoronary arteriography and showed that ST-segment elevation≥ 0.05 mV in lead aVR as well as serum troponin Tlevel ≥ 0.1 ng/mL were independent predictors of 90-day adverse outcomes, including death, myocardial infarction(MI), or urgent revascularization.

Barrabés et al[23] examined the association between ST-segment shift in lead aVR and in-hospital mortality in 775 patients with a first non ST-segment elevation myocardial infarction (NSTEMI) and found that the rates of in-hospital mortality were 1.3% in 525 patients without ST-segmentelevation in lead aVR, 8.6% in 116 patients with 0.05 mV to 0.1 mV of ST-segment elevation in lead aVR, and 19.4% in 134 patients with ST-segment elevation ≥ 0.1 mV in lead aVR. After adjusting for clinical variables, the odds ratios (ORs) for in-hospital mortality in the last 2 groups were 4.2 (95%CI: 1.5-12.2) and 6.6 (95%CI: 2.5-17.6), respectively. In 437 patients who underwent coronary arteriography within 6 mo of the onset of symptoms, the prevalence of LMT or 3-vessel disease among the 3 groups was 22.0%, 42.6%, and 66.3%, respectively.They concluded that in NSTEMI, ST-segment elevation in lead aVR is independently associated with increased in-hospital mortality probably because of severecoronary artery disease.

Taglieri et al[15] showed that ST-segment depression ≥ 0.05 mV in any lead plus ST-segment elevation ≥ 0.1 mV in lead aVR was independently associated with culprit LMT disease and increased in-hospital and 1-year cardiovascular deaths in 1042 patients with NSTE-ACS.

The current evidence suggests that in patients withNSTE-ACS, ST-segment elevation in lead aVR is associatedwith LMT or 3-vessel disease and increased adverseevents.

ST-segment elevation ≥1.0 mm in lead aVR on admission electrocardiogram is highly suggestive of severe LM/3VD in patients with NSTE-ACS.

Patients with aVR ST elevation may have severe proximal left coronary artery disease as the basal septum (which the lead aVR faces) receives blood supply either from the proximal septalbranches of the left anterior descending artery or from the posterior descending branch of the right coronary artery in those with prior proximal left coronary artery occlusions.

Lead aVR also helps in differentiating between LMCA and proximal left anterior descending artery (LAD) disease. the magnitude of STsegment elevation in lead aVR greater than or equal tothat of ST-segment elevation in lead V1 was found to have 81% sensitivity and 80% specificity for differentiating acute LMT occlusion

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from acute LAD occlusion. In our study all 3 patients with ST elevation in V1 >aVR had LAD as the culprit artery.

We also had 2 patients with de winter sign, occlusion of proximal LAD,with ECG findings of 1-2 mm ST elevation in .lead aVR and 1- 3 mm upsloping ST segement depression at the J point in lead V1 to V6 that continued into tall, positive symmetrical T waves [24].The electrophysiological explanation of the observed ECG pattern remains elusive[24].

Three patients had LCx as a culprit artery.Out of three, two had non dominant or co-dominantLCx With ST depression in lead I but upright ST in aVL lead I and aVL discordance. One had dominant LCx with ECG features of posterior wall MI with ST depression in both I and aVL.

Usually in LMCA occlusion, aVR> V1 ST segment elevation is associated with ST depression in both lead aVL and lead I along with other leads.

In general, the current of injury resulting from occlusion of the LCx has a mean vector that forms an obtuse angle with the axis of aVR, ie towards leads I and aVL. Therefore, we would expect ST -segment depression in aVR with LCx occlusion. Gorgels et al [3] had showed that in some cases of circumflex occlusion, with ischaemia in the posterobasal area, the current of injury is directed towards the right shoulder, hence aVR may be elevated.

We suggest that ST segment discordance between the adjacent leads aVL and LI can be an electrocardiographic clue to differentiate isolated LCx from LMCA occlusion. This may due to a greater basal involvement of the high lateral infarction. Thisvariation may be due to short left main (LMCA), Type II LAD, and early origin of circumflex artery.

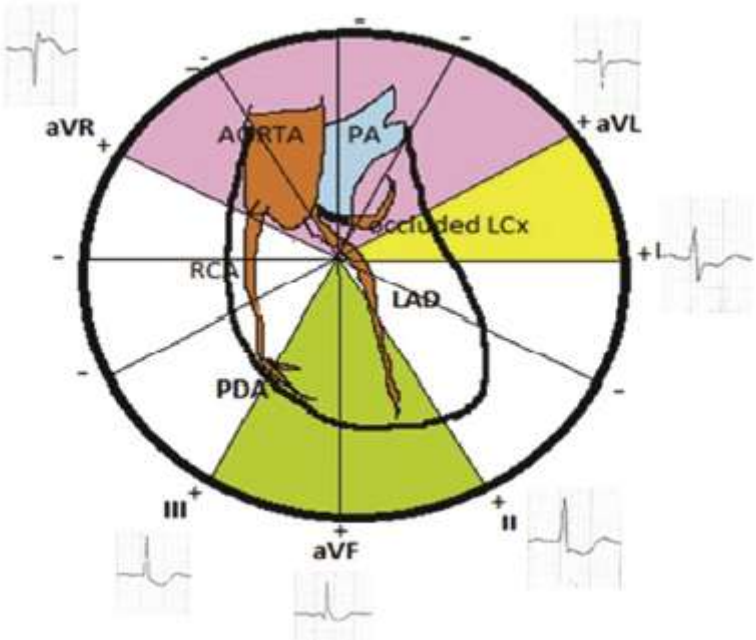
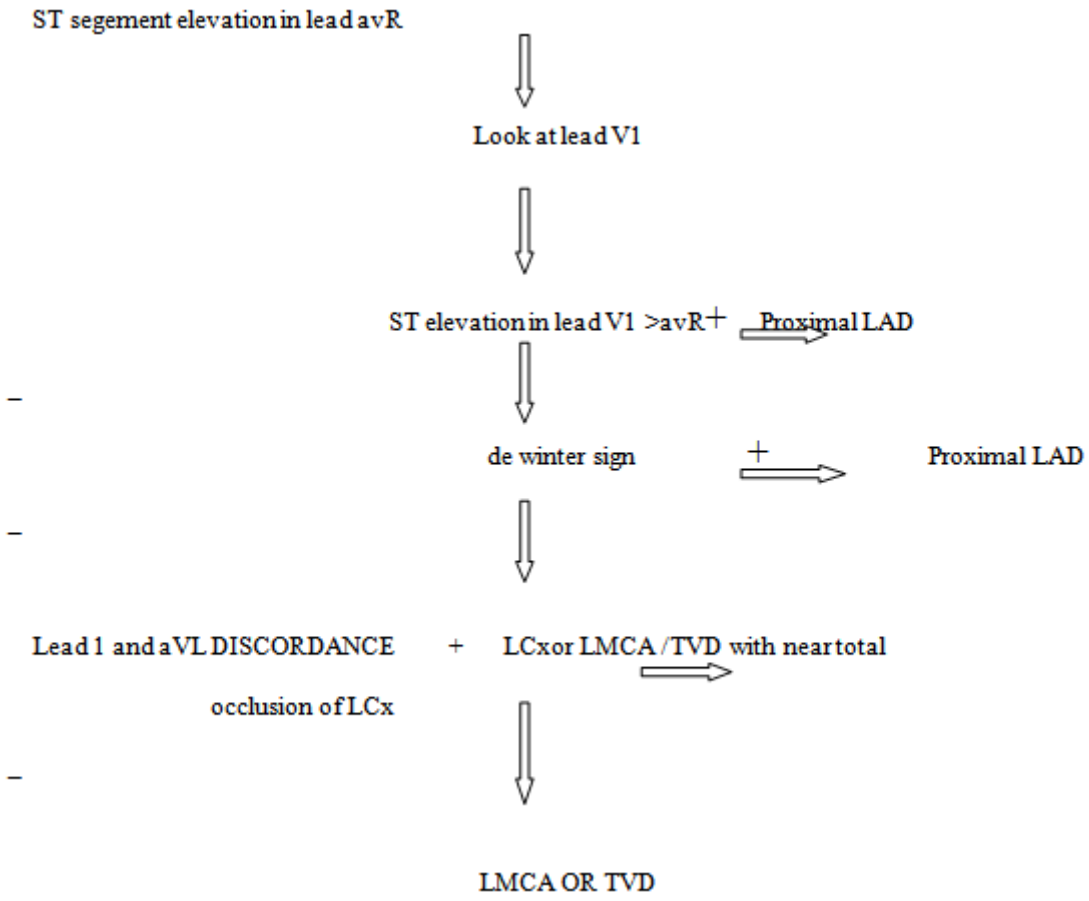


FIGURE 1

Thus we can localize the culprit arteryof patients with Lead aVR ST Segment Elevation in Acute Coronary Syndrome with the following algorithm :



In our study 24 patients were plan for CABG and 8 underwent PTCA. Out of the 8 patients undergoing PTCA, 2 had ST elevation in V1 >aVRand 2 had de winter sign in ECG. Two patients with left main disease were not willing for CABG,so were taken up for PCI.

avRST elevation patients presenting with NSTEMI should be considered in high risk ACS group.These group of patients will benefit from promptly undergoing angiography and revascularization by PTCA or CABG.

VI. CONCLUSION

We can localize the culprit arteryof patients with Lead aVR ST Segment Elevation in Acute Coronary Syndrome with the help of ECG. ST elevation in lead V1 morethen lead avR or de winter's sign is suggestive of proximal LAD occlusion. ST segment discordance between the adjacent leads aVL and LI can be an electrocardiographic clue to differentiate isolated LCx from LMCA or triple vessel disease in patients with ST elevation in lead avR more then or equal to lead V1.These patients should promptly undergo angiography and revascularization .

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ABBREVIATIONS

ACS acute coronary syndrome
CABG coronary artery bypass grafting
CAD coronary artery disease
CS I circumferential subendocardial ischemia
ECG electrocardiogram
LAD left anterior descending coronary artery
LCx left circumflex coronary artery
LM left main
LV left ventricle
MI myocardial infarction
NSTE non-ST-elevation
NSTE-ACS non-ST elevation acute coronary syndrome
NSTEMI non-ST-elevation myocardial infarction

PCI percutaneous coronary intervention
RCA right coronary artery
STE-ACS ST-segment elevation acute coronary syndrome
STEMI ST-segment elevation myocardial infarction
TIMI Thrombolysis in Myocardial Infarction
UA unstable angina pectoris