REVIEW ARTICLE

Clinical Utility of aVR—The Neglected Electrocardiographic Lead

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Background: Several studies suggest that electrocardiographers tend to neglect lead aVR during the reading of electrocardiograms (ECGs). Our objective was to provide a systematic review of the most important diagnostic and prognostic uses of lead aVR.

Methods: We performed a thorough review of the literature about the lead aVR using PubMed, MEDLINE and the archives of the University at Buffalo libraries.

Results: We found that lead aVR may provide important additional information in the diagnosis of coronary artery disease. It may provide a clue to the location of a lesion as well as the possibility of three vessel disease during an acute coronary syndrome. Lead aVR was found useful in the locus of arrhythmias and in differentiation of narrow and wide QRS complex tachycardias. It provides useful prognostic information for patients with the Brugada syndrome and tricyclic antidepressant toxicity. Lead aVR provides alternative criteria for the electrocardiographic diagnosis of left ventricular hypertrophy and left anterior fascicular block.

Conclusion: Lead aVR provides very important additional diagnostic and prognostic information in multiple cardiac conditions and can be used either alone or in conjunction with other electrocardiographic leads.

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lead aVR; coronary artery disease; narrow complex tachycardias, wide complex tachycardias;
Brugada syndrome; tricyclic antidepressant toxicity

Lead aVR has been frequently neglected in the past during electrocardiogram (ECG) interpretation.^{1,2} This was probably due to the unusual configuration and direction of all recorded elements in lead aVR, which seemed to have little correlation with other easily useful and diagnostic frontal leads. More recent demonstrations of the diagnostic value of lead aVR have been attributed by some to the unique view directly into left ventricle provided by this lead. In this article, we discuss the most important diagnostic and prognostic information that can be discovered through a careful literature review.

LEAD AVR AIDING IN THE DIAGNOSIS OF ACUTE CORONARY SYNDROMES

Myocardial ischemic manifestations are commonly seen in lead aVR. Multiple studies have demonstrated that ST segment elevation in lead aVR is commonly seen in left main, left anterior descending and 3-vessel coronary disease.^{3–10} Analysis of the results of the Global Registry of Acute Coronary Events (GRACE) showed a significant correlation between ST segment elevation in aVR and left main or 3-vessel disease coronary artery

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disease.³ The prevalence of left main or three vessel disease increased by 10.1% with minor (0.5–1 mm) and by 29.6% with major (>1 mm) ST elevation in lead aVR.³ Several studies have attempted to distinguish between left main and left anterior descending coronary disease. ST segment elevation in lead aVR which is taller than that in V₁ is seen more often in left main coronary as opposed to left anterior descending coronary artery disease.⁴ ST elevation in lead aVR, right bundle branch block, ST depression in lead V₅, and ST elevation of more than 2.5 mm in lead V₁ were found to be predictive of a left anterior descending lesion prior to the major septal perforator.^{5,6} A prospective study of 950 consecutive patients presenting with ST elevation myocardial infarction was performed by Aygul et al.⁸ ST segment elevation in lead aVR of more than 0.5 mm was found to be the strongest of all ECG diagnostic parameters corresponding to acute left anterior descending coronary artery occlusion proximal to the first septal perforator artery in anterior myocardial infarctions. This finding was also associated with lower systolic blood pressure, ejection fraction, and higher Killip class at admission. ST segment elevation in lead aVR, Killip class, and systolic blood pressure at presentation were found to be an independent predictor of fatal outcome during admission. Patients considered at high risk of left main, proximal left anterior descending or 3-vessel coronary artery disease based on these criteria may be more effectively triaged.

The Role of Lead aVR in Stress Testing

Multiple studies have evaluated the significance of ST elevation in lead aVR during exercise stress tests.^{11–14} ST elevation in lead aVR and in lead V₁ was found to be 85.7% sensitive and 81.6% specific for left main coronary artery disease.¹¹ Rostoff et al. reported a similar sensitivity in the isolated use of lead aVR.¹² In a study by Michaelides et al., the combination of ST segment elevation in lead aVR with ST depression in lead V₅ was found to be predictive of a left anterior descending lesion.¹³

Lead aVR as a Prognostic Tool

Several research groups have shown the usefulness of T-wave analysis in contributing to true prognosis of myocardial disease. A retrospective cohort study including 24,270 male veterans evaluated the diagnostic value of an upright T wave in

lead aVR.¹⁵ Patients with atrial fibrillation, bundle branch blocks, paced rhythm, and Wolf-Parkinson-White syndrome were excluded. The average patient follow-up was 7.5 years. An upright T wave in lead aVR had a prevalence of 7.3%. Cox survival analysis showed that T-wave amplitude in lead aVR superseded cardiac infarction injury and Selvester score, left ventricular hypertrophy (by Romhilt-Estes criteria), Q waves, QRS duration, QT prolongation, and ST depression for predicting cardiovascular death. This was demonstrated both with the presence and absence of other ECG abnormalities. The relative risk for cardiovascular mortality was also calculated using T-wave amplitudes in lead aVR of <–2 mm (taken as a reference), –2 to –1 mm, –1 to 0 mm and >0 mm. Relative risks came out to be 1, 1.5, 3, and 5. The annual mortality rate in the last group was 3.4% versus 0.4% in the reference group. Kaplan-Meier survival curves showed a similar trend for the subgroup analysis of patients with normal ECG, left ventricular hypertrophy, pathological Q waves, prolonged QRS, prolonged QT, and ST depression. These data clearly show that lead aVR is the strongest predictor of cardiovascular mortality by electrocardiographic criteria alone. An upright T wave in lead aVR in the absence of left bundle branch block was found to be highly predictive of underlying myocardial disease as defined by the presence of left ventricular systolic dysfunction, right ventricular systolic dysfunction or left ventricular hypertrophy with preserved left ventricular function.¹⁶ Out of 255 patients with an upright T wave in lead aVR (11% of the total study population) 91% were found to have underlying myocardial disease.

Electrophysiology

The unique position of lead aVR makes it very useful in ECG analysis. It may simplify differentiation between supraventricular tachycardias, wide QRS complex tachycardias, and the location of origin of electrical pathways and impulses.

Narrow QRS Complex Tachycardias

Focal atrial tachycardias are uncommon supraventricular tachycardias. They may be treated with radiofrequency ablation. A review of the morphology and polarity of the P wave in lead aVR helps to differentiate the origin of the

tachycardia.^{17–19} A combination of three features: 1—a negative P wave in lead aVR; 2—a positive P wave in leads I and II, and 3—either bi-phasic or positive during both tachycardia and sinus rhythm in lead V₁ localizes the focus of the tachycardia to the crista terminalis with 93% sensitivity and 95% specificity.¹⁷ Right atrial tachycardia originating in the crista terminalis may be differentiated from other foci by review of the P wave morphology in lead aVR.¹⁸

Differentiation of narrow complex tachycardias is sometimes a challenging task. ST segment elevation in lead aVR was found to be 70–71% sensitive and 70–83% specific for the diagnosis of atrioventricular reentry tachycardias.^{20,21} Analysis of retrograde P waves during atrioventricular reentry tachycardia can be used for determining the location of accessory pathways.^{22,23}

Wide QRS Complex Tachycardias

Wide QRS tachycardias are frequently encountered in clinical practice. Despite several previously published protocols (Kindwall et al., Brugada et al., etc) their differentiation remains one of the most challenging tasks for physicians.^{24,25} Differentiation between supraventricular and ventricular tachycardias has important prognostic and treatment implications. Lead aVR has a unique view of the heart with a 210° angle in the frontal axis. The QRS complex is usually negative in this lead. A positive QRS complex in lead aVR indicates that the origin of the impulse is close to the apex of the left ventricle with depolarization progressing toward the base.²⁶ Verecke et al. proposed an algorithm of differentiation of monomorphic wide QRS tachycardias.²⁷ It consists of four criteria: (1) The presence of A-V dissociation which favors a ventricular origin of the tachycardia; (2) The presence of an initial R wave in lead aVR; (3) a QRS morphology that is different from bundle branch block or fascicular block; and (4) The ratio of the sum of voltage changes of the initial over the final 40 ms of QRS complex being less than or equal to one. This algorithm has a better sensitivity and specificity than the Brugada criteria. A new protocol using lead aVR as the sole lead for differentiation of monomorphic wide QRS tachycardias was introduced in 2008 by Verecke et al.²⁸ It consists of four criteria: (1) The presence of an initial R wave; (2) The presence of initial q or r waves of >40 ms duration; (3) The pres-

ence of a notch on the descending limb of a negative onset and predominantly negative QRS complex; (4) The ratio of the sum of voltage changes of the initial over the final 40 ms of the QRS complex being less than or equal to one. Interestingly enough, this protocol omitted AV dissociation criteria used as a first step in their previous protocol as it did not change the accuracy. Using a single lead and avoiding QRS morphology identification makes this protocol potentially easier to use when compared to the previous one. However, given the fact that up to 10% of wide QRS tachycardias are not diagnosed correctly by the use of any single protocol, the use of any protocol with additional criteria from others and the pretest probability of having VT might further improve the diagnostics.²⁸ Lead aVR is useful in location of origin and optimal ablation site of right ventricular outflow tract ventricular tachycardia.^{29–31}

The Brugada Syndrome

The stratification of asymptomatic patients with the Brugada syndrome might be important for referral of high-risk patients for ICD implantation prior to full disease manifestation. Babai et al. proposed using lead aVR as a predictive tool. In a small study involving 24 patients with the Brugada ECG pattern and 24 healthy controls, the presence of an aVR sign (R-wave amplitude of ≥ 0.3 mV or $R/q \geq 0.75$) correlated with a higher risk of recurrent arrhythmias.³² The presence of an aVR sign was found to correlate with a 57% increase of the events during the follow-up.

Tricyclic Antidepressants

Sinus tachycardia, right-axis deviation of 130–170°, QRS widening of greater than 100 ms, PR and QT interval prolongations and characteristic R wave changes in lead aVR could be seen early in tricyclic antidepressants toxicity.^{33–35} Characteristic R wave changes in lead aVR include an increase in the amplitude of the R wave and an increase of R wave to S wave ratio.³⁶ In a prospective cohort study by Liebelt et al., an amplitude of the terminal R wave in lead aVR of 3 mm or more was found to be the only significant predictor of arrhythmias and/or seizures with a sensitivity of 81% and a positive predictive value of 43%.³⁵ An R wave in lead

aVR of 5 mm or greater predicted events with 50% sensitivity and 97% specificity.

Other Useful ECG Criteria Involving Lead aVR

Warner et al. proposed alternative electrocardiographic criteria for left anterior fascicular block. These are very helpful since they introduce a vector approach to the diagnosis, increasing the specificity over the use of left axis alone. A terminal R wave must be present in both aVR and aVL and the peak of the R wave in aVL must precede the peak of the R wave in aVR.³⁷ Left anterior fascicular block is characterized by initial r-waves in leads II, III, and aVF. Inferior myocardial infarction is characterized by Q waves in exactly the same leads. The simultaneous occurrence of both conditions creates diagnostic difficulties. Warner et al. proposed a combination of a terminal R wave in leads aVR and aVL and the presence of a Q-wave in lead II, to diagnose left anterior fascicular block in the setting of inferior myocardial infarction.³⁸ Lead aVR may have a role in the diagnosis of right ventricular myocardial infarction.³⁹

The clinical utility of lead aVR has been demonstrated in many varied circumstances which are referenced below. An S wave in lead aVR of more than 14 mm is a criterion for left ventricular hypertrophy.⁴⁰ A positive QRS complex in lead aVR is a manifestation of dextrocardia or dextrocardia with situs inversus.^{41–43} Acute pericarditis is manifested by PR segment elevation and ST segment depression in lead aVR.⁴⁴ Since the early report of the S1Q3T3 finding by McGinn and White, the quest for sensitive and specific ECG signs of pulmonary embolism continues.⁴⁵ In a review of 245 patients by Petrozelli et al. a late R-wave amplitude of more than 1.5 mm in lead aVR, S1Q3T3 combination, P-R displacement, slurred S waves, and T wave inversion in leads V₁ or V₂ were noticed to be more commonly present in patients with pulmonary embolism than without.⁴⁶ ST-elevation in lead aVR was also described in association with massive pulmonary embolus.⁴⁷ PR segment depression in lead aVR combined with PR segment elevation in the inferior leads was described in association with tension pneumothorax.⁴⁸ We found a case report of Takotsubo cardiomyopathy presenting with transient ST segment elevation in lead aVR.⁴⁹

Lead aVR has a close and well-defined electrical relationship to each of the other leads in the hexaxial reference system. Unfortunately, this is not recognized in many articles concerning lead aVR. The voltage in lead aVR (pointing at -150°) can be calculated as half of the algebraic sum of leads I and II. One might speculate that use of an inverted lead aVR would make it easier for people to incorporate this valuable tool in their review of electrocardiograms. One of the possibilities is to use an inverted lead aVR which has an axis of $+30^\circ$ in the frontal plane. The use of "panoramic" or sequential displays in which an inverted lead aVR is used may aid its better understanding by interpreters and decreased probability of systematic lead aVR neglect.^{2,50,51}

CONCLUSION

Lead aVR may be helpful in diagnosing left main, left anterior descending, or triple vessel coronary artery disease on initial presentation of an acute coronary syndrome. It is very useful in diagnosing atrioventricular reentry tachycardia, the location of accessory pathways, the origin of focal atrial tachycardias, and the differentiation of wide QRS complex tachycardias. Lead aVR is also useful in the detection of patients with the Brugada syndrome at higher risk of fatal outcomes. Lead aVR may help diagnose tricyclic antidepressant toxicity and predict which patients are more prone to seizures and arrhythmias. The presence of upright T waves in lead aVR was found to be the most powerful electrocardiographic predictor of overall cardiovascular mortality in men.

An obvious question inevitably arises regarding the clinical relevance of lead aVR. Does this lead have independent predictive value in association with other leads, or perhaps only supplemental value? As discussed, it can be used as a sole source of information for differentiation of wide QRS complex tachycardias, risk stratification of patients with The Brugada Syndrome, tricyclic antidepressant overdose, and some other clinical scenarios. However, lead aVR should be viewed in conjunction with other electrocardiographic leads to increase its prognostic value in clarifying other cardiac conditions.

Lead aVR evaluation may be helpful in the following situations:

Detection of coronary artery lesion location in acute coronary syndromes
 Diagnosis of left anterior fascicular block in the setting of inferior myocardial infarction
 Diagnosis of right ventricular myocardial infarction
 Diagnosis of left main and left anterior descending coronary artery lesions during stress tests
 Mortality and morbidity prognostification
 Location of origin of focal atrial tachycardias
 Differentiation of narrow QRS complex tachycardias
 Differentiation of wide QRS complex tachycardias
 Location of origins and optimal ablation sited of right ventricular outflow tract ventricular tachycardias
 Risk assessment for asymptomatic patients with brugada syndrome
 Diagnosis of tricyclic antidepressant toxicity and risk stratification for associated arrhythmias and seizures
 Diagnosis of lead misplacement
 Alternative criteria of LAFB
 LVH criterion
 P wave morphology in dextrocardia and sinus inversus
 Diagnosis of pericarditis
 Diagnosis of pulmonary embolism and tension pneumothorax

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