

Prevalence of electrocardiographic changes in patients with acute aneurysmal subarachnoid hemorrhage and their relationship with outcome

Saktheeswaran Mahesh Kumar, Dinesh Choudhary, Ajeet Arulkumar, Thajudeen Anees, Suresh Nair¹, Jaganmohan A. Tharakan

Departments of Cardiology and ¹Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India

ABSTRACT

Background: Electrocardiographic (ECG) alterations occurring after subarachnoid hemorrhage (SAH) have been described frequently, but the prognostic significance of these changes has not been well characterized. **Aim and Objectives:** To report the prevalence and patterns of ECG alterations in patients with acute aneurysmal SAH and to study the relationship between ECG alterations and the neurological outcome, if any. **Materials and Methods:** Records of consecutive patients admitted to the neurosurgical intensive care unit of the SCTIMST, Trivandrum between January 1999 and January 2011 with acute aneurysmal SAH were retrospectively analyzed. **Results:** Of the 321 patients with SAH, 190 (59.2%) had abnormal ECGs. Repolarization abnormalities were the most common, with T wave inversion in the anterolateral leads occurring in 155 (48.3%) patients. By univariate analysis, female sex, Glasgow Coma Score (GCS) at admission of <15, World Federation of Neurological Surgeons (WFNS) grade >I, ST segment depression or T inversion in anterolateral leads, prolonged corrected QT interval, and sinus bradycardia were associated with increased risk of death. By multivariate analysis, only GCS and WFNS grade independently predicted mortality and none of the ECG changes predicted the same. Presence of tall T waves in anterior leads, T inversion in anterolateral leads, sinus bradycardia, and WFNS grade >1 were independently associated with GCS <15 and poor outcome at discharge. **Conclusions:** In patients with acute aneurysmal SAH, repolarization abnormalities are the commonest ECG alterations. ECG alterations do not independently predict death, but independently predict poor discharge neurological status.

Key words: Electrocardiographic changes, neurological outcome, subarachnoid hemorrhage

INTRODUCTION

Subarachnoid hemorrhage (SAH) is a catastrophic neurological event that occurs primarily during young to mid-adulthood in both sexes.^[1] The most common cause of SAH is rupture of an aneurysm arising from the blood vessels at the base of the brain. A less common source of hemorrhage is the rupture of an aneurysm that is traumatic or infectious in origin or rupture of an arteriovenous malformation.

In addition to the classic clinical signs and symptoms of

SAH, electrocardiographic (ECG) abnormalities often occur. Although these ECG alterations are associated with a wide variety of neurological events, (including cerebrovascular accidents, head injury, meningitis and tumors) the highest prevalence and most pronounced changes occur after SAH.^[2] Upto 10% of the patients with SAH are known to have potentially lethal arrhythmias, such as ventricular tachycardia (particularly torsades de pointes) associated with a prolonged corrected QT (QTc) interval and ventricular fibrillation.^[3]

ECG changes in SAH commonly mimic those seen in ischemic heart disease; thus, ST-segment elevation and T wave inversion are not uncommon. Therapeutic thrombolytic therapy and anticoagulation as well as withholding of life-saving neurosurgery in such cases may endanger the life of the patient concerned. These ECG changes are not the result of underlying cardiac disease, but reflect intracranial factors. They may have an independent value in predicting poor outcome.^[4]

| Access this article online | |
|---|----------------------------------|
| Quick Response Code: | Website: www.ijns.in |
|  | DOI: 10.4103/2277-9167.110219 |

Address for correspondence: Dr. Saktheeswaran Mahesh Kumar, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India. E-mail: maheshpaed@yahoo.co.in

The aim of this study was to report the prevalence and patterns of ECG alterations in patients with acute aneurysmal SAH and to study the relationship between ECG alterations and neurological outcome in a tertiary referral center.

MATERIALS AND METHODS

Study population

The records of all patients admitted to the neurosurgical intensive care department of the SCTIMST, Trivandrum with a diagnosis of aneurysmal SAH confirmed by cerebral angiography or by computed tomography (CT) scan between January 1999 and January 2011, were retrospectively reviewed. Patient records that had an ECG which had not faded, that had been performed before any surgical intervention or drug administration (that could have affected the ECG) were included in the study. If more than one ECG was recorded during the first 24 hours of admission, the most abnormal ECG was considered for the purpose of this study. Of the 392 patients admitted with aneurysmal SAH to the neurosurgical intensive care unit, a total of 71 (18.1%) patients were excluded: 12 (3.1%) patients had no ECGs and the ECGs of 59 patients (15.0%) had faded. A total of 321 patients were analyzed in the study. In 254 of these patients, intra arterial cerebral angiography had been performed prior to surgery. All patients were treated according to standard intensive care guidelines during their hospitalization.

Data collection

Patient details were retrieved from the hospital records retrospectively. Interpretation of ECG is shown in Table 1. The outcomes of interest were in hospital death or the Glasgow Coma Score (GCS) at discharge.

Data analysis

Statistical analyses were done using SPSS 14.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to report the number and type of ECG abnormalities. We related the outcomes to baseline characteristics and to the individual ECG abnormalities (ST depression or elevation, a peaked T or T wave inversion, and a U wave) of admission ECG. A $P < 0.05$ was considered to be statistically significant. Univariate and multivariate analyses were performed by logistic regression analysis. 95% confidence intervals were provided for the odds ratios.

RESULTS

Patient demographics are shown in Figure 1. Hypertension was present in 41.7% and diabetes in 13.7% of the study population. Investigations performed and the outcome characteristics of the patients are shown in Figure 2.

Table 1: Interpretation of electrocardiographic changes

| Category | Abnormality | Finding |
|------------------------------|--|---|
| Rhythm abnormalities | Sinus bradycardia | HR<60/min |
| | Sinus tachycardia | HR>100/min |
| | Atrioventricular nodal rhythm | |
| | Atrial premature contractions | |
| | Ventricular premature contractions | |
| | Atrial fibrillation or flutter | |
| Conduction abnormalities | Ventricular tachycardia | ≥3 consecutive VPCs |
| | 1 st degree AV block | >0.20 s |
| | Short PR interval | <0.12 s |
| | Higher grades of AV block | 2 nd or 3 rd degree |
| Repolarization abnormalities | Right or left bundle branch block | QRS≥0.12 s+characteristic morphology |
| | QTc segment prolongation | ≥0.44 s |
| | ST-segment elevation | ≥0.1 mV with upward convexity |
| | ST-segment depression | ≥0.1 mV, flat or downsloping |
| | Peaked T wave | >66% of R amplitude in the same lead |
| | Isoelectric or diphasic T wave | Negative component<3 mm |
| Others | Inverted T wave | Negative component≥0.3 mV in two contiguous leads |
| | U wave | >0.1 mV |
| | Pathological Q waves | >0.04 s duration/ amplitude>25% of R wave |
| | Right ventricular hypertrophy | R/S ratio>1 in V1 and R≥0.5 mV |
| | Left ventricular hypertrophy | S in V1 and R in V5,6≥3.5 mV |
| | Peaked P wave | P≥0.25 mV in II |
| Left atrial enlargement | ≥2.5 mV wide notched P wave in II or>0.1 mV negative in V1 | |

HR – Heart rate; AV – Atrioventricular; VPC – Ventricular premature contraction

Echocardiography was normal in 90.3% of the subjects. ECG changes noted in study population are shown in Figure 3. Overall, abnormal ECGs were noted in 190 (59.2%) patients. Repolarization abnormalities were the most common abnormalities. T wave inversion in the anterolateral leads was noted in 48.3% of patients. QTc prolongation was noted in 40 (12.5%) patients. Among arrhythmias, sinus bradycardia was the most common and was noted in 16.8% of the study population. Ventricular tachycardia was noted in 6 (1.8%) patients. All the observed ventricular tachycardias were polymorphic and were successfully terminated by electrical cardioversion. There were no deaths directly attributable to arrhythmias. Table 2 shows the odds ratio for death based on ECG findings. ST depression or T inversion in anterolateral

leads, prolonged QTc interval, and sinus bradycardia had higher odds ratio for death based on univariate analysis. Similarly, odds ratio of GCS less than 15 at discharge based on ECG changes by univariate analysis showed that ST depression or T inversion in anterolateral leads, prolonged QTc, and sinus bradycardia were associated with GCS <15 at discharge.

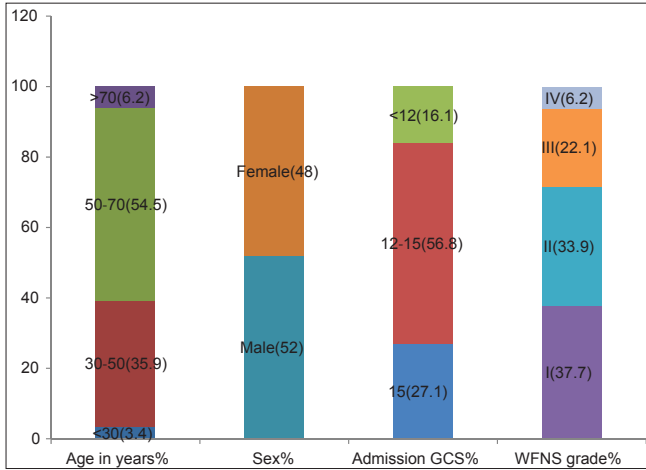


Figure 1: Patient demographics. GCS – Glasgow coma score; WFNS – World Federation of Neurological Surgeons

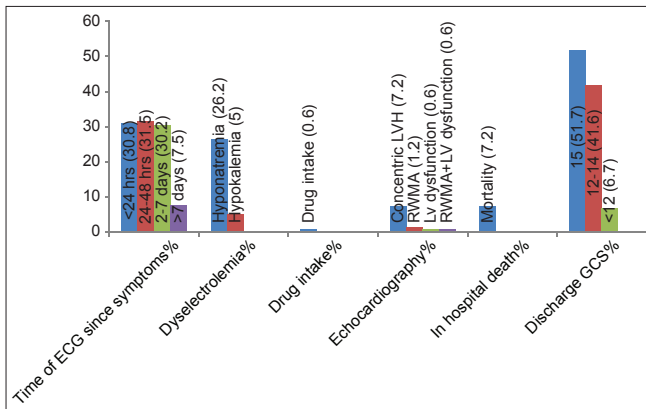


Figure 2: Investigations and outcome characteristics. RWMA – Regional wall motion abnormality; GCS – Glasgow coma score

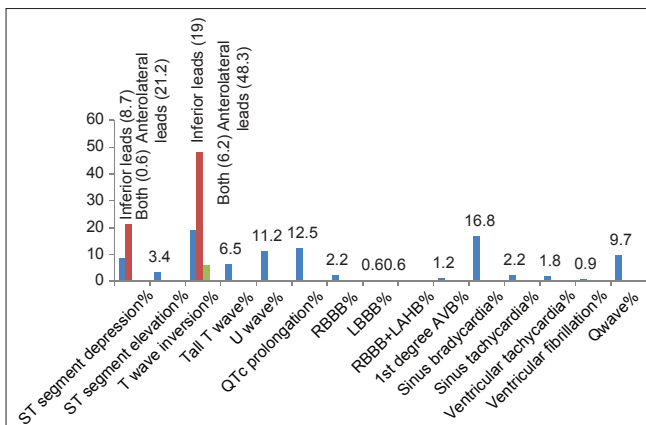


Figure 3: Electrocardiographic features in study population

By multiple regression analysis [Table 3], the only independent predictors of mortality were GCS at admission less than 15 and World Federation of Neurological Surgeons (WFNS) grade worse than 1. None of the ECG variables were an independent predictor of death. However, four variables – presence of tall T waves in anterior leads, T inversion in anterolateral leads, sinus bradycardia, and WFNS grade >1 were independently associated with GCS <15 at discharge based on multiple regression analysis. As shown in Table 4, presence of 2 of the 3 independent variables (T inversion or tall T in anterior leads, sinus bradycardia, and WFNS grade ≥2) is associated with 90.6% risk of GCS <15 at discharge and presence of all 3 variables is associated with 100% risk of poor outcome.

Table 2: Univariate analysis of risk of death based on electrocardiographic findings

| | Death | | P value | Odds (CI*) |
|---|------------|-----------|---------|-------------------------|
| | No | Yes | | |
| ST depression in anterolateral leads | | | | |
| Yes | 55 (80.9) | 13 (19.1) | 68 | <0.01 5.74 (2.40-13.78) |
| No | 243 (96) | 10 (4) | 253 | 1 |
| ST-segment elevation | | | | |
| Yes | 9 (81.8) | 2 (18.2) | 11 | 0.149 3.06 (0.62-15.07) |
| No | 289 (93.2) | 21 (6.8) | 310 | 1 |
| T inversion in anterolateral leads | | | | |
| Yes | 139 (89.7) | 16 (10.3) | 155 | 0.034 2.62 (1.05-6.54) |
| No | 159 (95.8) | 7 (4.2) | 166 | 1 |
| Arrhythmias | | | | |
| Yes | 10 (83.3) | 2 (16.7) | 12 | 0.193 2.74 (0.56-13.33) |
| No | 288 (93.2) | 21 (6.8) | 309 | 1 |
| Prolonged QTc | | | | |
| Yes | 33 (82.5) | 7 (17.5) | 40 | 0.007 3.51 (1.35-9.17) |
| No | 265 (94.3) | 16 (5.7) | 281 | 1 |
| Sinus bradycardia | | | | |
| Yes | 44 (81.5) | 10 (18.5) | 54 | <0.01 4.44 (1.83-10.75) |
| No | 254 (95.1) | 13 (4.9) | 267 | 1 |

*Confidence interval

Table 3: Independent predictors of death by multiple regression

| | B | S | Odds (CI) |
|---------------------------|------|-------|-----------------------|
| GCS admission (15) | | | |
| 12-14 | 1.28 | 0.440 | 3.61 (1.04-93.45) |
| <12 | 1.87 | 0.042 | 6.49 (1.07-39.33) |
| WFNS grade (I) | | | |
| II | 1.51 | 0.308 | 4.54 (0.25-83.07) |
| III | 6.49 | 0.000 | 658.37 (51.33-844.27) |
| IV | 6.62 | 0.000 | 748.77 (46.8-1197.14) |

B – Beta coefficient; S – Sigma error; GCS – Glasgow coma score; WFNS – World Federation of Neurological Surgeons; CI – Confidence Interval

Table 4: Prediction of Glasgow coma score at discharge <15 based on the presence of three independent predictors

| | GCS at discharge | | | |
|---|------------------|---------|-------|---------|
| | 15 | | <15 | |
| | Count | Percent | Count | Percent |
| 0 | 117 | 70.9 | 48 | 29.1 |
| 1 | 34 | 34.3 | 65 | 65.7 |
| 2 | 3 | 9.4 | 29 | 90.6 |
| 3 | 0 | 0.0 | 2 | 100.0 |

GCS – Glasgow coma score; (T inversion or tall T in anterior leads, sinus bradycardia, and World Federation of Neurological Surgeons ≥ 2)

DISCUSSION

The cardiac effects of intracranial hemorrhage were initially described in 1903 by Cushing. Byer and collaborators first described ECG changes in a patient with SAH in 1947. ECG changes commonly experienced by patients with SAH can mimic changes associated with coronary ischemia or infarction, and therefore, healthcare professionals must anticipate and recognize these changes. Evidence from a number of studies indicates that patients with SAH are at high risk for malignant ventricular arrhythmias if the QTc interval is prolonged.^[4-6] A decrease in cardiac output due to alterations in heart rate associated with SAH, such as sinus bradycardia, sinus tachycardia, or rapid atrial fibrillation, can also adversely affect patients' clinical status.

Originally, the cause of ECG changes in SAH patients was thought to be pre-existing coronary artery disease exacerbated by the physiological demands of critical illness. However, a previous study reported that both coronary angiography and autopsy revealed normal coronary vasculature in patients with SAH who had marked ECG changes.^[7] Cardiac injury due to elevated myocardial wall stress associated with tachycardia and hypertension has also been suggested as a causative factor. Yuki *et al.*^[8] proposed that coronary vasospasm and reversible post-ischemic "stunned myocardium" may cause the development of ECG changes in patients with SAH. Increasingly, evidence indicates a neurogenic etiology for ECG abnormalities in SAH. Studies in animals and humans have indicated that injury to the insula, an area of the cortex thought to be involved in arrhythmogenesis, might be implicated in both abnormal cardiac rhythm and focal myocardial necrosis that occurs after SAH.^[9] Currently, the release of catecholamines, either systemically or within the myocardium, as a cause of ECG abnormalities is the subject of much research. Autopsies have revealed areas of characteristic subendocardial ischemic lesions, contraction band necrosis, in the hearts of patients who died of SAH.^[10] The characteristic pattern and

distribution of myocardial lesions in these patients suggests that the damaging catecholamines are probably released from intramyocardial nerve endings rather than from the general circulation. Parekh *et al.*^[11] found that patients with elevations in cardiac troponin I were more likely than patients without elevations in the biomarker to have ECG abnormalities. Factors that may influence the development of arrhythmias in patients with SAH include hypoxia, electrolyte imbalance or cerebral vasospasm, and sudden increase in intracranial pressure due to compression of cerebral structures triggering a sympathetic or vagal discharge.^[5,12]

In this study, of the 321 patients who were reviewed, ECG changes were noted in 190 (59.2%) patients. This is in contrast to a prospective study of 406 patients with SAH, in which Rudehill *et al.*^[13] found that 82% of patients had ECG alterations regardless of the presence of underlying heart disease. Timing of the ECGs (only 60% ECGs taken within 48 h) in this study could have influenced the prevalence and specific ECG abnormalities. In this study, repolarization abnormalities were the most common abnormalities with T inversion in anterolateral leads present in 48.3% of patients. T wave abnormalities have been reported to occur in 59-72% in various studies.^[4,5] Rhythm abnormalities were noted in 22.7% of this study population with sinus bradycardia constituting 16.8%. The prevalence of rhythm abnormalities reported by various studies also varies between 10% and 65%.^[4,5]

Regarding prediction of outcomes in this study, though several variables were associated with odds ratio of >1 for poor outcome by univariate analysis, only four variables, namely, presence of tall T waves in anterolateral leads, T inversion in anterolateral leads, sinus bradycardia, and WFNS grade >1 were independently associated with GCS <15 at discharge based on multiple regression analysis. This is consistent with the results of Brouwers *et al.*,^[14] who found that ECG changes were related to the initial level of consciousness, subsequent events and outcome after 3 months, though cardiac disease did not contribute directly to morbidity or mortality. By multivariate analysis, the only independent predictors of mortality were GCS at admission less than 15 and WFNS grade of more than I. ECG changes may simply be a marker of more severe disease already reflected by the other variables.^[15] In contrast in a retrospective study by Kawasaki *et al.*,^[16] ECG changes were powerful predictor of death.

Echocardiographic or cardiac enzyme evidence of neurogenic myocardial damage may be more likely than ECG changes to show a relationship with outcome, although studies provide conflicting data. In this study,

the time course of alterations in the ECG changes was not studied due to its retrospective nature.

This study is limited by its retrospective nature and the introduction of selection bias by the exclusion of 71 (18.1%) patients with SAH with no interpretable ECGs. In addition, assessment of arrhythmias based on a 12-lead ECG is likely to be less sensitive than Holter monitoring, and the results may thus have underestimated the true incidence of arrhythmias. Also, neurogenic ECG changes may evolve over time. Cardiac enzyme release which occurs with myocardial damage may be more likely to show a relationship with outcome than ECG changes and was not evaluated in this study.

In conclusion, ECG changes are noticed in about 60% of patients with SAH. Repolarization abnormalities are the most common ECG alterations with T inversion in anterolateral leads being the most frequent. Sinus bradycardia is the most common rhythm abnormality and right bundle branch block the most common conduction abnormality. By univariate analysis, ECG alterations are associated with death and poor discharge neurological status, whereas by multivariate analysis, none of the ECG alterations independently predict death but they independently predict poor discharge neurological status.

REFERENCES

1. Kotila M. Declining incidence and mortality of stroke? *Stroke* 1984;15:255-9.
2. Burch GE, Meyers R, Abildskov JA. A new electrocardiographic pattern observed in cerebrovascular accidents. *Circulation* 1954;9:719-23.
3. Yamour BJ, Sridharan MR, Rice JF, Flowers NC. Electrocardiographic changes in cerebrovascular hemorrhage. *Am Heart J* 1980;99:294-300.
4. Brouwers PJ, Wijdicks EF, Hasan D, Vermeulen M, Wever EF, Frericks H, *et al.* Serial electrocardiographic recording in aneurysmal subarachnoid hemorrhage. *Stroke* 1989;20:1162-7.
5. Di Pasquale G, Pinelli G, Andreoli A, Manini G, Grazi P, Tognetti F. Holter detection of cardiac arrhythmias in intracranial subarachnoid hemorrhage. *Am J Cardiol* 1987;59:596-600.
6. Carruth JE, Silverman ME. Torsade de pointe atypical ventricular tachycardia complicating subarachnoid hemorrhage. *Chest* 1980;78:886-8.
7. Kuroiwa T, Morita H, Tanabe H, Ohta T. Significance of ST segment elevation in electrocardiograms in patients with ruptured cerebral aneurysms. *Acta Neurochir (Wien)* 1995;133:141-6.
8. Yuki K, Kodama Y, Onda J, Emoto K, Morimoto T, Uozumi T. Coronary vasospasm following subarachnoid hemorrhage as a cause of stunned myocardium. Case report. *J Neurosurg* 1991;75:308-11.
9. Svigelj V, Grad A, Tekavcic I, Kiauta T. Cardiac arrhythmia associated with reversible damage to insula in a patients with subarachnoid hemorrhage. *Stroke* 1994;25:1053-5.
10. Doshi R, Neil-Dwyer G. Hypothalamic and myocardial lesions after subarachnoid haemorrhage. *J Neurol Neurosurg Psychiatry* 1977;40:821-6.
11. Parekh N, Venkatesh B, Cross D, Leditschke A, Atherton J, Miles W, *et al.* Cardiac troponin I predicts myocardial dysfunction in aneurysmal subarachnoid hemorrhage. *J Am Coll Cardiol* 2000;36:1328-35.
12. Lorscheid A, Simmers TA, Robles De Medina EO. The relationship between electrocardiographic abnormalities and location of the intracranial aneurysm in subarachnoid hemorrhage. *Pacing Clin Electrophysiol* 2003;26:1722-8.
13. Rudehill A, Olsson GL, Sundqvist K, Gordon E. ECG abnormalities in patients with subarachnoid haemorrhage and intracranial tumours. *J Neurol Neurosurg Psychiatry* 1987;50:1375-81.
14. Brouwers PJ, Wijdicks EF, Hasan D, Vermeulen M, Wever EF, Frericks H, *et al.* Serial electrocardiographic recording in aneurysmal subarachnoid hemorrhage. *Stroke* 1989;20:1162-7.
15. Solenski NJ, Haley EC Jr, Kassell NF, Kongable G, Germanson T, Truskowski L, *et al.* Medical complications of aneurysmal subarachnoid hemorrhage: A report of the multicenter, cooperative aneurysm study. Participants of the Multicenter Cooperative Aneurysm Study. *Crit Care Med* 1995;23:1007-17.
16. Kawasaki T, Azuma A, Sawada T, Sugihara H, Kuribayashi T, Satoh M, *et al.* Electrocardiographic score as a predictor of mortality after subarachnoid hemorrhage. *Circ J* 2002;66:567-70.

How to cite this article: Kumar SM, Choudhary D, Arulkumar A, Anees T, Nair S, Tharakan JA. Prevalence of electrocardiographic changes in patients with acute aneurysmal subarachnoid hemorrhage and their relationship with outcome. *Indian J Neurosurg* 2013;2:52-6.

Source of Support: Nil, **Conflict of Interest:** None declared.