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Electrocardiographic Changes Following Cerebrovascular Events: A Systematic Review

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Abstract

Background: Electrocardiographic (ECG) changes occurring after the onset of Cerebrovascular Accidents (CVA), including both ischemic and haemorrhagic stroke, have been demonstrated in numerous studies. These changes can be due to various causes. They could be a complication of the CVA or a concomitant Acute Myocardial Infarction (AMI). Meanwhile, ECG abnormalities including atrial fibrillation could reflect a cause of CVA or could be present prior to the stroke. These often present as clinical dilemmas as to whether urgent cardiac interventions should be prioritized over treatment for CVA. Therefore, the aim of this systematic review was to summarise the available evidence on the prevalence of various ECG abnormalities after different CVA subtypes, their effects on clinical outcomes as well as to give an overview on the pathogenesis of the ECG changes.

Methods: A systematic review was conducted on Pubmed, Embase and Cochrane Library. Two independent reviewers screened for studies based on the inclusion and exclusion criteria. Main findings extracted were the prevalence of ECG abnormalities and their associations with post-stroke complications and mortality. Statistical analyses were performed to obtain overall pooled proportions of ECG abnormalities and mortality and to conduct a subgroup analysis of ischemic versus haemorrhagic stroke. A total of 44 studies were included in the final review.

Results: There was considerable heterogeneity among studies. The most common ECG abnormalities reported were QTc prolongation, LVH and nonspecific ST changes. When comparing between stroke subtypes, sinus tachycardia and ST elevations were found to have statistically significant higher associations with haemorrhagic than ischemic stroke. Few studies examined the associations between ECG changes and outcomes. Several proposed mechanisms for the ECG abnormalities were given, particularly for cases of spontaneous subarachnoid haemorrhage.

Conclusion: Studies suggest that ECG abnormalities following intracranial haemorrhage were less likely to be due to myocardial disease than that following ischemic stroke. However, it was hard to draw firm conclusions due to the varied nature of the studies. This remains an interesting area for further research.

Keypointers

1. ECG abnormalities following CVA are varied and can be due to various causes.
2. The most common ECG abnormalities found were QTc prolongation, LVH and nonspecific ST changes. Fewer than 10 studies reported malignant arrhythmias like VT, VF and Torsades de Pointes.
3. Some of the postulations for the pathogenesis of ECG abnormalities after CVA were attributed to location of pathology, autonomic dysregulation, electrolyte abnormalities and effects of drugs.
4. ECG abnormalities in ischemic stroke patients are more likely from ongoing ischemic cardiac pathologies, which thus, warrant investigations to exclude clinically significant coronary artery disease. In haemorrhagic stroke patients, however, some studies concluded ECG abnormalities are mainly the direct consequence of haemorrhage while others suggested cardiac workup and constant monitoring.

Introduction

Electrocardiographic (ECG) changes occurring after the onset of Cerebrovascular Accidents

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(CVA), including both ischemic and haemorrhagic stroke, have been demonstrated in numerous studies. As an example, a study conducted by Christensen H et al., showed that ECG abnormalities were found in up to 60% of patients with cerebral infarction and the presence of Atrial Fibrillation (AF), ST elevations and depressions, T wave inversions and atrioventricular (AV) block were found to be predictive of 3-month mortality [1].

There are several postulations as to why these ECG changes happen. Repolarisation abnormalities such as QTc prolongation and changes suggestive of myocardial ischemia such as ST elevation, could be a direct result of the CVA or a concomitant Acute Myocardial Infarction (AMI), which can occur following a stroke [2-5]. On the other hand, ECG abnormalities such as arrhythmias including atrial fibrillation, may reflect the underlying cause of CVA [6,7]. Other ECG changes may have been present prior to the stroke and thus, reflect pre-existing cardiac issues. The ECG abnormalities detected following CVA has clinical implications. For instance, ST changes due to true myocardial ischemia would require prompt coronary reperfusion therapy while a false diagnosis of myocardial ischemia can potentially delay treatment for the CVA episode.

This systematic review will summarize the available evidence on the prevalence of various ECG abnormalities after different CVA subtypes, their effects on clinical outcomes as well as give an overview on the current understanding of the pathogenesis of the ECG changes.

Methodology

This review followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [8]. Figure 1 illustrates the steps taken in the literature search.

Search strategy

The databases Pubmed, Cochrane Library and Embase were systematically searched on 2 March 2020. The search strategy used “Cerebrovascular disorders”, “Cerebrovascular diseases”, “Electrocardiogram” and “Electrocardiography” as keywords. Two independent reviewers (J.N and N.N) screened titles and abstracts to select articles for full text review. Full texts were then analyzed based on the inclusion and exclusion criteria given below. Discrepancies between the two reviewers were resolved by review and discussion with the senior reviewer (F.L). The following Table 1 depicting the criteria.

The studies included in the systematic review are summarized in Table 2 [9-50].

Data extraction and analysis

The prevalence of ECG abnormalities following CVA and their associations with post-stroke complications and mortality were extracted independently.

Different studies utilized different definitions of ECG changes. Hence, specific ECG changes analyzed in this study followed a standardized set of definitions that included the following:

1. Sinus tachycardia (>100 bpm), sinus bradycardia (<60bpm), atrial flutter and atrial fibrillation were grouped together in this present review,

2. Left ventricular hypertrophy as defined by the Sokolow-Lyon Criteria, QTc prolongation (>440 ms for females and >420 ms for males), and

3. The rest of the ECG changes included: presence of U wave, ST elevations, ST depressions, non-specific ST changes, T wave inversions, flattened T waves, peaked T waves, nonspecific T wave abnormalities, pathological Q waves, Left Bundle Branch Block (LBBB), PR prolongation (>200 ms), Premature Ventricular Complexes (PVCs), Ventricular Tachycardia (VT), Ventricular Fibrillation (VF) and Torsade's de Pointes.

Statistical analyses for pooling of proportions of ECG changes and mortality were analysed with R version 4.0.0. A descriptive summary was done for associations of ECG changes with post-stroke complications and mortality, due to the small number of studies with data available. In the statistical analysis, a meta-analytic model was fitted in ‘meta for in R’. Effect sizes were transformed using log it transformation and pooled, based on the inverse variance method. Between-study variance estimates were generated *via* the random effect model using the DerSimonian-Laird estimator (DL). Subgroup analysis of ischemic against hemorrhagic stroke was also done *via* a mixed-effect model. A *p*-value<0.05 was considered statistically significant.

Results

The search strategy yielded 44 relevant articles that were included in the final review. A summary of the articles is shown in Table 2, of which 11 were on ischemic stroke and 33 studies looked at hemorrhagic stroke [9-50].

Prevalence of ECG abnormalities after CVA

A summary of the pooled proportions of specific ECG abnormalities following CVA is shown in Table 3. The most common ECG abnormalities reported are:

QTc prolongation (0.31, 95% CI 0.25- 0.38)

LVH (0.23, 95% CI 0.15-0.33), and

Non-specific ST changes (0.23, 95% CI 0.13-0.37).

When comparing between stroke subtypes, only sinus tachycardia ($P<0.001$) and ST elevations ($P=0.004$) were found to have statistically significant higher associations with haemorrhagic than ischemic stroke. Fewer than 10 studies reported malignant arrhythmias like VT, VF and Torsades de Pointes.

Associations of ECG abnormalities with mortality and post-stroke complications

The overall pooled proportion of mortality was 0.14 (95% CI 0.11-0.19). We defined mortality as that reported in the primary studies, which ranged from in-hospital mortality to 1-year follow-up. The proportion of mortality for ischemic stroke of 0.08 (95% CI 0.04-0.18) was lower than that of haemorrhagic stroke of 0.17 (95% CI 0.13-0.23), though they were not statistically significant.

Haemorrhagic stroke: Three studies examined the associations between specific ECG changes and mortality [14,23,51]. Nonspecific ST and T wave changes and bradycardia were found to be associated with higher mortality [14,23]. The other ECG abnormality associated with higher mortality included prolonged QTc [51]. Kawasaki et al., found that ST depression, T waves inversion and pathological Q waves were more common in non-survivors than survivors of subarachnoid haemorrhage [51].

Common post-stroke complications associated with specific ECG changes reported for haemorrhagic stroke included poor

Table 1: Analysis of the inclusion and exclusion criteria.

Selection criteria	Inclusion criteria	Exclusion criteria
Language of published article	English	All other languages
Type of literature	Published journal article	1. Editorials 2. Commentary 3. Conference abstracts
Accessibility of article	Only full-length articles	Abstract only articles and all other non-full-length articles
Study design	All other types of studies	1. Case reports or series 2. Review papers 3. Guidelines
Research subject	Only human studies	Non-human experimental studies
Timeframe between ECG recordings and CVA/ICH	Studies detecting ECG abnormalities after the onset of CVA/ICH	Studies detecting ECG abnormalities prior to onset of CVA/ICH
Reported research population	1. Disease subtype: Only spontaneous ischemic stroke, spontaneous subarachnoid hemorrhage and intracerebral hemorrhage	1. Disease subtype: Transient ischemic attack, traumatic brain injury

neurological outcome and cardiac wall motion abnormalities. ECG changes that were associated with a poor Glasgow Outcome Scale (GOS) included ST depression, as found by Sakr et al., on univariate analysis, and QTc prolongation [17]. T wave inversions were found to be associated with cardiac wall motion abnormalities in 3 studies while Sugimoto et al., also observed ST elevation and ST depression to be related [27,31,32]. Other complications examined included the following: Chen et al., found nonspecific ST or T waves changes and pathological Q waves to be associated with neurogenic pulmonary edema; whilst Schuling et al., found ST depression to be associated with delayed cerebral ischemia [12,19].

Ischemic stroke: Three studies examined the association between specific ECG abnormalities and mortality. ECG changes included: nonspecific T-waves and ST depressions, prolonged QTc and Q waves in more than 2 leads [37,40,47].

Post- ischemic stroke complications and their associations with ECG abnormalities were varied among the studies. Sorgun et al., found nonspecific T waves to be associated with raised troponin; Pirinen et al., found bundle branch blocks, P-terminal force, LVH and a wider QRS complex to be associated with recurrent cardiovascular events [45,46].

Pathogenesis of ECG abnormalities following CVA

Exactly how CVAs result in certain ECG changes is not very clear. However, there are some mechanisms that have been proposed by various authors; one of them being autonomic dysregulation [30,39,48,52-54]. The hypothalamus and insula are often suggested as a cause for sympathetic stimulation [17,22,37,54-57]. Decreased inhibition by the insula could lead to stimulation of the sympathetic system, and ischemic lesions of the hypothalamus after CVAs could also result in sympathetic stimulation [52]. Analysis of heart rate variability can reveal information about autonomic dysregulation and a study conducted by Colivicchi F et al., showed that all measures of HRV were decreased to a greater extent in patients who suffered acute stroke with right insular involvement [57]. These patients also tended to have more complex arrhythmias, such as SVT and non-sustained VT, than patients with strokes of different localization [57].

CVAs resulting in sympathetic stimulation either due to insular or hypothalamus involvement can also result in increased secretion of catecholamines and cortisol [18]. In SAH, local arteriolar spasm or haemorrhage near the basal cisterns could result in elevated secretion of catecholamines as the hypothalamus is located nearby [51]. Catecholamines could result in myocardial injury resulting in ECG

changes, either via adrenaline and noradrenaline or through afferent and efferent pathways of the sympathetic system [38]. The effects of catecholamines on the cardiovascular system include tachycardia, coronary artery spasm, increased intracellular calcium and myocyte injury [53,54]. Cortisol could potentiate this by increasing sensitivity to catecholamines [18]. Small areas of sub-endocardial haemorrhage and myocytolysis near nerves have been identified histologically [53]. Myocytolysis reflects acute stress on the cardiac muscle and this differs from the typical coagulation necrosis witnessed in coronary artery disease [53]. The presence of these results suggest that ECG changes may result from CVA and that autonomic dysregulation has a role to play [53].

However, evidence regarding myocardial damage caused by catecholamines is conflicting. Interestingly, Grad et al., conducted a study in which there was no increased frequency of ECG changes usually associated with SAH such as QT prolongation and U waves in patients with high concentration of norepinephrine [16]. Brouwers et al., also concluded that elevated norepinephrine concentrations were not a sufficient explanation for myocardial ischemia in SAH, as patients without SAH who also had elevated norepinephrine concentrations had drastically lower rates of cardiac ischemia [10].

Non-hypothalamic areas such as the cerebellum have also been implicated as the cerebellum also contains sympathetic and parasympathetic connections [39]. Injury to the cerebellum, therefore, could lead to stimulation of the cardiovascular system and result in ECG abnormalities. Kaya et al., reported significantly prolonged QRS durations in cerebellar infarcts; Troponin levels were also raised in patients with cerebellar lesions, potentially due to the role of the cerebellum in the autonomic control of the cardiovascular system [39].

Electrolyte abnormalities such as hypokalemia and hypoxia have also been proposed as a cause for the ECG changes [23]. A study by van der Bergh et al., demonstrated that hypomagnesemia is associated with severity of haemorrhage in SAH. Hypomagnesemia was associated with ECG changes such as prolonged PR interval and a shortened QTc interval [35]. Drugs such as antihistamines, anti-arrhythmic agents and antibiotics could also result in ECG changes, especially QTc prolongation [24].

Discussion

There was great heterogeneity in terms of patient selection, reporting of ECG abnormalities and differences in methodology of study outcomes in the available literature. This made comparison

Table 2: Summary of studies investigating ECG abnormalities in patients with cerebrovascular accidents (CVA).

Authors, year	Sample size	Time frame, hours	ECG abnormalities reported	Electrolyte abnormalities, cardiac enzymes and catecholamines	Conclusion of findings
SUBARACHNOID HEMORRHAGE					
Rudehill A. et al, 1982 ⁹	22	0-48	1. Atrial fibrillation 2. QTc prolongation 3. U wave 4. ST depressions 5. Flat, inverted, notched T waves 6. VF 7. VT	Hypocalcemia, hypokalemia	Biochemical evidence for myocardial damage could not be found and thus, ECG changes occurring after SAH may not be caused by myocardial injury.
Brouwers PJ. et al, 1995 ¹⁰	37	288	1. Non-specific ST changes 2. T wave inversions 3. Peaked T waves 4. Pathological Q waves	Elevated CK-MB, serum catecholamines	High plasma noradrenaline concentrations in patients with SAH do not fully explain cardiac ischaemia in SAH as cardiac ischemia was seen rarely in the control group who also had high plasma noradrenaline concentrations.
Brouwers PJ. et al, 1989 ¹¹	61	288	1. Sinus tachycardia 2. Sinus bradycardia 3. Atrial flutter 4. Atrial fibrillation 5. SVT 6. LVH 7. QTc prolongation 8. U wave 9. Non-specific ST changes 10. T wave inversions 11. Flattened T waves 12. Peaked T waves 13. Pathological Q waves 14. PR prolongation or 1 st degree heart block 15. PVC	NA	ECG changes indirectly depict adverse intracranial factors after SAH, rather than imminent cardiac disease. Therefore, they may be helpful as an independent factor in predicting poor outcome.
Chen WL., et al, 2016 ¹²	269	48	1. ST elevations 2. ST depressions 3. T wave inversions 4. Peaked T waves 5. Non-specific T wave abnormalities 6. Pathological Q waves	NA	Patients who had neurogenic pulmonary edema (NPE) had a higher percentage of ECG abnormalities, specifically non-specific ST or T wave changes. Abnormal Q or QS waves were also related with NPE.
Chia BL., et al, 1971 ¹³	6	NA	1. QTc prolongation 2. ST depressions 3. T wave inversions 4. Flattened T waves 5. Peaked T waves	Hypokalemia	ECG changes varied and ECG changes such as ST depression and inverted T waves were found in patients with SAH, meningitis and intracerebral space occupying lesions.
Coghlan LA., et al, 2009 ¹⁴	588	NA	1. Sinus tachycardia 2. Sinus bradycardia 3. Atrial fibrillation 4. QTc prolongation 5. ST elevations 6. ST depressions 7. Non-specific ST changes 8. T wave inversions 9. Peaked T waves 10. Pathological Q waves	NA	In SAH patients treated with surgical aneurysm clipping, pre-operative bradycardia (HR≤60 bpm), relative tachycardia (HR>80), and nonspecific ST segment and T wave abnormalities (NSSTWA) were linked to increased mortality.
Ibrahim, GM., & Macdonald, RL., 2012 ¹⁵	413	Before vasospasm (24 hours) and during angiographic vasospasm period (168-264 hours)	1. Sinus tachycardia 2. Sinus bradycardia 3. Atrial fibrillation 4. QTc prolongation 5. ST elevations 6. ST depressions 7. Non-specific ST changes 8. T wave inversions	NA	During the vasospasm risk period, QTc prolongation was the most prevalent ECG abnormality.
Grad A., et al, 1991 ¹⁶	40	0-24, 72 and 168	1. Sinus tachycardia 2. Atrial fibrillation 3. QTc prolongation 4. U wave 5. ST elevations 6. ST depressions 7. PVC 8. VT	Elevated plasma norepinephrine	QTc prolongation, U waves, ST depression and arrhythmias occurred to a similar extent in both groups of patients who had normal and high serum catecholamines. Other than sinus tachycardia and negative T waves, ECG changes in patients with SAH are not due to raised catecholamines.

Sakr YL., et al, 2004 ¹⁷	159	24	1. Sinus tachycardia 2. Sinus bradycardia 3. Atrial fibrillation 4. LVH 5. QTc prolongation 6. U wave 7. ST elevations 8. ST depressions 9. T wave inversions 10. Flattened T waves 11. Peaked T waves 12. Non-specific T wave abnormalities 13. Pathological Q waves 14. Left bundle branch block 15. PR prolongation or 1 st degree heart block PVCs	NA	Repolarisation abnormalities are the most frequently occurring ECG abnormalities and ST depression occurs more frequently in patients with poor prognosis.
Salvati M., et al, 1992 ¹⁸	70	72	1. Sinus tachycardia 2. Sinus bradycardia 3. Atrial fibrillation 4. QTc prolongation 5. U wave 6. ST elevations 7. ST depressions 8. T wave inversions 9. Left bundle branch block 10. VT	NA	Most frequent ECG abnormalities were T wave inversions, prolonged QTc interval and U waves.
Schuling WJ., et al, 2006 ¹⁹	121	0	1. QTc prolongation 2. U wave 3. ST elevations 4. ST depressions 5. T wave inversions 6. Peaked T waves 7. (No left bundle branch block)	NA	Only ST depression was associated with delayed cerebral ischemia. ECG abnormalities did not contribute to predicting delayed cerebral ischemia and are not particularly valuable in identifying poor prognosis.
Shuster S., 1960 ²⁰	12	0	1. ST depressions 2. Non-specific ST changes 3. T wave inversions 4. Flattened T waves 5. Peaked T waves 6. (No QTc prolongation)	NA	Striking ECG abnormalities include T wave inversion and ST segment displacement. Atrial arrhythmias were common too.
Sommargren CE., et al, 2002 ²¹	100	0	1. LVH 2. QTc prolongation 3. U wave 4. ST elevations 5. ST depressions 6. T wave inversion	Elevated troponins	Repolarisation abnormalities are common in SAH patients and some patients also have LVH. Prolongation of QTc interval is also associated with cardiac injury but not associated with mortality.
Szabo MD., et al, 1993 ²²	19	504	1. QTc prolongation 2. U wave 3. T wave inversions 4. Non-specific T wave abnormalities 5. Pathological Q waves	NA	Abnormal myocardial perfusion and possibly cardiac ischemia occur commonly after SAH. However, there are no particular ECG abnormalities that allows identification of patients with abnormal perfusion.
Huang CC., et al, 2012 ²³	222	NA	1. ST elevations 2. ST depressions 3. Non-specific ST changes 4. T wave inversions 5. Peaked T waves 6. Pathological Q waves	NA	Non-survivors had significantly slower heart rate and a longer QTc interval than survivors. Non-survivors also had a greater frequency of ECG abnormalities and non-specific ST or T wave changes.
Ichinomiya T., et al, 2010 ²⁴	71	NA	7. QTc prolongation	Elevated troponins	QTc interval continues to be prolonged in SAH patients with poor outcome and recovers in patients with favourable outcomes.
Zaroff JG, et al, 1999 ²⁵	313	72	1. Sinus bradycardia 2. ST elevations 3. ST depressions 4. T wave inversions 5. Pathological Q waves 6. (No VT, torsades de pointes, or VF)	Elevated CK-MB	ECG abnormalities are related to poorer neurological outcome but not independently associated with all-cause mortality.
Cruickshank JM., et al, 1974 ²⁶	40	NA	1. Sinus tachycardia 2. Sinus bradycardia 3. QTc prolongation 4. U wave 5. ST elevations 6. ST depressions 7. T wave inversions 8. Flattened T waves 9. Peaked T waves 10. Q waves	Hypokalemia	Urinary normetanephrins, metanephrins and plasma cortisol were elevated in 19 patients with abnormal ECGs compared to 8 patients with normal ECGs. There were no significant differences in serum potassium concentrations between patients with normal and abnormal ECGs.

Sugimoto K., et al, 201 ⁸²⁷	161	48	1. Sinus tachycardia 2. Sinus bradycardia 3. Atrial fibrillation 4. LVH 5. QTc prolongation 6. U wave 7. ST elevations 8. ST depressions 9. T wave inversions 10. Flattened T waves 11. Pathological Q waves 12. Left bundle branch block 13. PR prolongation 14. PVC	NA	ST elevation, ST depression and inverted T waves were predictors of wall motion abnormalities.
Kawahara E., et al, 2003 ²⁸	42	48	1. Sinus tachycardia 2. Sinus bradycardia 3. QTc prolongation 4. U wave 5. ST elevations 6. ST depressions 7. T wave inversions 8. Pathological Q waves	Elevated catecholamines	Patients with SAH had ECG abnormalities and increased concentrations of cardiac enzymes and plasma catecholamines. During the acute phase of SAH, both sympathetic and vagal activity are enhanced, resulting in ECG abnormalities and myocardial damage.
Kawasaki T., et al, 2002 ²⁹	122	NA	1. U wave 2. ST elevations 3. ST depressions 4. T wave inversions 5. Peaked T waves 6. Pathological Q waves	NA	In patients with SAH, the ECG score which comprises total number of ECG leads with ST depression, inverted T waves and pathological Q waves, was found to be a predictor of prognosis.
Lorsheyd A., et al, 2003 ³⁰	97	48	1. Sinus bradycardia 2. LVH 3. QTc prolongation 4. U wave 5. ST elevations 6. ST depressions 7. T wave inversions	Hypokalemia, hyponatremia	Prolonged QTc intervals were encountered more often in patients with severe haemorrhage. LVH was associated with aneurysm in the anterior communicating artery whilst a U wave was associated with the posterior communicating artery and the middle cerebral artery.
Pollick C., et al, 1988 ³¹	13	72	1. T wave inversions 2. Flattened T waves 3. Pathological Q waves	NA	Initial creatine kinase myocardial isoenzyme concentrations, neurologic grades and initial heart rates were higher in patients with wall motion abnormalities than in patients without wall motion abnormalities. T wave inversions were also more common in patients with wall motion abnormalities.
Mayer SA., et al, 1995 ³²	57	24	1. Sinus tachycardia 2. Sinus bradycardia 3. LVH 4. QTc prolongation 5. U wave 6. Non-specific ST changes 7. T wave inversions 8. Flattened T waves 9. Peaked T waves 10. Pathological Q waves 11. PR prolongation or 1 st degree heart block 12. PVCs	NA	Wall motion abnormalities on echocardiogram were associated with symmetrical T wave inversion and severe prolongation of QTc interval than normal echocardiograms.
Manninen PH., et al, 1995 ³³	70	96	1. Sinus tachycardia 2. Non-specific ST changes 3. Non-specific T wave abnormalities 4. Pathological Q waves 5. PVCs	NA	ECG abnormalities occurred more frequently in patients who had a larger amount of intracranial blood or intracerebral clot, as seen on CT scan. However, the amount of blood seen on CT scan and ECG abnormalities were not useful in predicting prognosis.
Zhang, L., & Qi, S., 2016 ³⁴	834	72	1. QTc prolongation 2. ST elevations 3. ST depressions 4. Non-specific ST changes 5. T wave inversions 6. Peaked T waves 7. Pathological Q waves	NA	ECG abnormalities 3 days following SAH are associated independently with poor outcomes in patients with SAH.
van den Bergh, WM., et al, 2004 ³⁵	62	72	1. Sinus bradycardia 2. LVH 3. QTc prolongation 4. U wave 5. Non-specific ST changes 6. Non-specific T wave abnormalities 7. PR prolongation 8. (No VF or torsades de pointes)	Hypokalemia, hypomagnesemia	Lower serum magnesium concentrations are associated with less marked increases in the QTc interval duration.

Stober T. & Kunze K., 1982 ³⁶	89	0-1152	1. Sinus tachycardia 2. Sinus bradycardia 3. LVH 4. QTc prolongation 5. U wave 6. ST elevations 7. ST depressions 8. T wave inversions 9. Flattened T waves 10. Peaked T waves 11. PVCs	Hypokalemia, elevated CK-MB	Common ECG abnormalities included ST depression and elevation, QTc prolongation, flattened T waves, inverted T waves, U waves and TU fusion waves, sinus tachycardia, bradycardia and extrasystoles (in order of decreasing frequency).
ISCHEMIC STROKE					
Tanaka M., et al, 2004 ³⁷	216	0	1. Atrial fibrillation 2. ST elevations 3. ST depressions 4. T wave inversions 5. Pathological Q waves 6. Left bundle branch block	NA	Q waves in more than 2 leads could predict mortality after acute ischemic stroke.
Adeoye A. et al, 2017 ³⁸	403	24	1. Atrial flutter 2. Atrial fibrillation 3. LVH 4. QTc prolongation	NA	Compared to hemorrhagic stroke patients, ischemic stroke patients were more likely to have atrial fibrillation but less likely to have left ventricular hypertrophy.
Kaya A. et al, 2018 ³⁹	241	24	1. LVH 2. QTc prolongation 3. ST depressions 4. PR prolongation or 1 st degree heart block	Elevated CK-MB, troponins	Most common abnormality was QTc prolongation. However, this was not related to severity or mortality.
Hromádka M., et al, 2016 ⁴⁰	69	48	1. QTc prolongation	NA	A prolonged QTc interval after 2 days was related to neurological outcome and 1-year mortality.
Pirinen J., et al, 2015 ⁴¹	690	24-336	1. Atrial flutter 2. Atrial fibrillation 3. LVH 4. QTc prolongation 5. T wave inversions 6. Pathological Q waves 7. Left bundle branch block 8. PR prolongation or 1 st degree heart block Complete or incomplete bundle branch block	NA	35% of patients had ECG abnormalities and T wave inversion, LVH, prolonged P wave and prolonged QTc interval were the most frequently observed.
Jensen JK., et al, 2008 ⁴²	185	120	1. Non-specific ST changes 2. Non-specific T wave abnormalities	NA	The frequency of ST segment and T wave abnormalities ranged from 13% to 16%.
Jiang B., et al, 2015 ⁴³	351	48 and 168	1. Non-specific ST changes 2. Non-specific T wave abnormalities 3. Pathological Q waves	NA	Incidence of ECG abnormalities were high in patients with acute ischemic stroke and was associated with poor prognosis.
Pasquini M., et al, 2006 ⁴⁴	208	48	1. Sinus tachycardia 2. Atrial fibrillation 3. Atrial flutter 4. QTc prolongation 5. ST depressions 6. T wave inversions 7. Left bundle branch block 8. PR prolongation or 1 st degree heart block	NA	There was no significant association between ECG abnormalities and strokes with or without insular infarcts or strokes with left or right insular infarcts.
Pirinen J., et al, 2016 ⁴⁵	690	336	1. Atrial fibrillation 2. Atrial flutter 3. LVH 4. QTc prolongation 5. T wave inversions 6. Pathological Q waves 7. PR prolongation or 1 st degree heart block	NA	Bundle branch blocks, P-terminal force, LVH and a wider QRS complex were associated with recurrent cardiovascular events. No ECG abnormalities were associated independently with recurrent stroke in young ischemic stroke patients.
Sorgun MH., et al, 2015 ⁴⁶	100	24	1. Atrial fibrillation 2. QTc prolongation 3. ST depressions 4. Non-specific T wave abnormalities 5. Pathological Q wave abnormalities	Elevated troponin	ECG abnormalities were more common in patients with coronary artery disease, severe stroke, and complications. T waves were independently associated with raised troponin and atrial fibrillation.
Fogelholm, R., & Aho, K., 1975 ⁴⁷	141	72	1. ST depressions 2. Non-specific T wave abnormalities	NA	ECG abnormalities were more common in the group of non-survivors, at least negative or isoelectric T-waves and ST depressions were associated with poor outcomes.

INTRACEREBRAL HEMORRHAGE					
Takeuchi S., et al, 2015 ⁴⁸	118	24	1. Sinus tachycardia 2. Sinus bradycardia 3. Atrial fibrillation 4. LVH 5. ST elevations 6. ST depressions 7. T wave inversions 8. PVCs 9. (No VT, torsades de pointes or VF)	NA	The most common ECG abnormality was ST depression, LVH, prolongation of QTc interval and inverted T waves. Involvement of the insula was an independent predictive factor of ST depression. Insular involvement and intraventricular haemorrhage were independent predictive factors of QTc prolongation whilst a deep hematoma location and haemorrhage volume of more than 30 ml were independent predictive factors of inverted T waves.
Adeoye A. et al, 2017 ³⁸	212	24	1. Atrial fibrillation 2. LVH 3. QTc prolongation 4. (No atrial flutter)	NA	Compared to hemorrhagic stroke patients, ischemic stroke patients were more likely to have atrial fibrillation but less likely to have left ventricular hypertrophy.
van Bree MD., et al, 2010 ⁴⁹	31	48	1. Sinus tachycardia 2. Sinus bradycardia 3. Atrial flutter 4. Atrial fibrillation 5. LVH 6. QTc prolongation 7. ST elevations 8. ST depressions 9. Non-specific ST changes 10. T wave inversions 11. Pathological Q waves 12. PR prolongation or 1 st degree heart block 13. (No torsades de pointes)	NA	Prolongation of the QTc interval seems to be related to insular cortex involvement, intraventricular haemorrhage and hydrocephalus.
Yamour BJ., et al, 1980 ⁵⁰	65	NA	1. Sinus tachycardia 2. Sinus bradycardia 3. Atrial fibrillation 4. QTc prolongation 5. U wave 6. Non-specific ST changes 7. Non-specific T wave abnormalities 8. Pathologic Q waves 9. PR prolongation or 1 st degree heart block 10. PVCs	NA	Hemorrhages of the frontal lobe are associated with QT prolongation and neurogenic T waves while hemorrhages of the brain stem are linked to non-cardiogenic pulmonary edema and sudden onset of atrial fibrillation.

between results difficult and hard to draw firm conclusions. Study designs varied considerably. Most studies did not include a baseline ECG prior to CVA; only a few studies included a control population or excluded patients with pre-existing heart disease. Hence, all study designs were included in this review. This is of note as not all ECG changes reported could be attributed to the CVA but could be a result of an earlier condition or due to other coexisting factors including electrolyte abnormalities or heart disease [58]. The onset between CVA and ECG recording varied among studies and therefore, the abnormalities picked up could potentially be different, due to the different time frames, especially for SAH where there is an initial period of risk of angiospasm. The type of ECG recording done, intermittent or continuous, also varied across the studies. This could also affect prevalence of abnormalities such as paroxysmal AF or other ECG changes that are transient or intermittent. In this review, the effect of time was excluded by analyzing the results in terms of prevalence and pooled proportions, as opposed to incidence rates. There is also a lack of a standardized measure to assess clinical outcomes following CVA. Hence, a suggestion is for future studies to use validated measurement tools to assess outcome for easier comparison with other studies, such as the Barthel Index (BI) and modified Rankin Scale (mRS) as a measurement of disability [59].

There was much more available data on ECG changes following haemorrhagic stroke, particularly after SAH, than on ischemic stroke. Many studies on ischemic stroke focused on detecting paroxysmal AF as a cause of ischemic stroke rather than ECG changes that occur because of stroke. Most common ECG abnormalities detected

following ischemic stroke included LVH, prolonged QTc and nonspecific T waves. It is unclear if they are due to existing heart disease or as a complication of stroke. Nevertheless, in studies that examined causes of death, it was found that many of the ischemic stroke patients who died, do so due to cardiac disease, mainly acute Myocardial Infarction (MI) [44-46]. Hence, ECG changes like T waves abnormalities in ischemic stroke patients are more likely to be due to ongoing ischemic cardiac pathologies, which warrant investigations to exclude clinically significant coronary artery disease. Meanwhile, for haemorrhagic stroke, only a few studies in this review reported a small number of patients who had cardiac-related pathologies, as detected by wall motion abnormalities, raised cardiac enzymes or on autopsy findings [21,25,31,32]. An existing review found that ECG changes following SAH seemed to be the direct consequence of haemorrhage and were not accompanied by extensive myocardial damage [60]. Nevertheless, other reviews commented on occurrence of myocardial injury and recommended cardiac workup and constant monitoring [62,63].

There was scant data on the use of medications in treating arrhythmias following CVA. 4 studies in this review reported the use of vasopressors following subarachnoid haemorrhage [22,24,25,32]. However, they were used mainly to support systemic blood pressure due to hypotension, while Szabo et al., concluded that the use of vasopressors or vasodilators could not explain abnormal myocardial perfusion leading to abnormal ECG changes [22,32]. It has been suggested that use of anti-adrenergic medication can limit the effect of sympathetic hyperstimulation which could prevent arrhythmias

Table 3: Prevalence of ECG abnormalities among patients with cerebrovascular accident (CVA)^a.

ECG abnormalities	Number of articles	All CVA patients (95% CI)	Ischemic stroke, (95% CI)	Intra-cranial haemorrhage, (95% CI)	P value
Sinus tachycardia	18	0.11 (0.07-0.17)	0.02 (0.01- 0.05)	0.12 (0.08-0.18)	<0.01
Sinus bradycardia	18	0.11 (0.07-0.17)	NA	0.11 (0.07-0.16)	-
Atrial flutter/ Atrial fibrillation	22	0.05 (0.03-0.08)	0.09 (0.04- 0.18)	0.04 (0.02-0.06)	0.07
LVH ^b	16	0.23 (0.15-0.33)	0.27 (0.09- 0.56)	0.22 (0.15-0.31)	0.70
QTc prolongation	37	0.31 (0.25-0.38)	0.21 (0.10- 0.39)	0.34 (0.28-0.41)	0.17
U wave	17	0.22 (0.14-0.31)	NA	0.22 (0.15-0.32)	-
ST elevations	20	0.08 (0.06-0.11)	0.02 (0.01- 0.05)	0.08 (0.06-0.11)	0.004
ST depressions	27	0.12 (0.09-0.17)	0.17 (0.10-0.26)	0.12 (0.08-0.17)	0.25
Nonspecific ST changes	16	0.23 (0.13-0.37)	0.19 (0.11-0.30)	0.26 (0.12-0.47)	0.45
T wave inversions	30	0.16 (0.13-0.20)	0.15 (0.11-0.19)	0.17 (0.13-0.22)	0.49
Flat T waves	9	0.18 (0.08-0.34)	NA	0.18 (0.08-0.34)	-
Peaked T waves	14	0.07 (0.04-0.12)	NA	0.07 (0.04-0.12)	-
Non-specific T wave changes	12	0.18 (0.13-0.26)	0.22 (0.15-0.31)	0.17 (0.09-0.31)	0.54
Pathological Q waves	21	0.07 (0.05-0.10)	0.06 (0.04-0.09)	0.08 (0.05-0.11)	0.50
Left Bundle branch block	7	0.01 (0.01-0.03)	0.02 (0.00-0.06)	0.01 (0.00-0.02)	0.62
PR prolongation	11	0.06 (0.04-0.08)	0.06 (0.03-0.10)	0.05 (0.02-0.10)	0.80
Premature Ventricular Complexes (PVCs)	6	0.09 (0.05-0.16)	NA	0.09 (0.05-0.16)	-
Ventricular tachycardia	7	0.02 (0.01-0.07)	NA	0.04 (0.02-0.07)	-
Ventricular fibrillation	4	0.00 (0.00-0.02)	NA	0.01 (0.00-0.05)	-
Torsades de Pointes	4	0.01 (0.00-0.02)	NA	0.01 (0.00-0.03)	-

^a Reported as pooled proportions^b Left ventricular hypertrophy as defined by the Sokolow-Lyon Criteria

from occurring [63,64]. It may thus be useful for large, prospective trials to be carried out to examine the effects of these medications.

Conclusion

In conclusion, there are various ECG changes following CVA. However, the causes and the clinical implications of these ECG abnormalities remain to be further assessed. The possibility of using medications to prevent life threatening arrhythmias can be also be studied in future randomized controlled trials.

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