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Resting 12-lead electrocardiogram reveals high-risk sources of cardioembolism in young adult ischemic stroke☆

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ABSTRACT

Background: The diagnostic work-up to reveal etiology in a young ischemic stroke (IS) patient includes evaluation for high-risk source of cardioembolism (HRCE), since this subtype associates with high early recurrence rate and mortality. We investigated the association of ECG findings with a final etiologic subgroup of HRCE in a cohort of young patients with first-ever IS.

Methods: The Helsinki Young Stroke Registry includes IS patients aged 15 to 49 years admitted between 1994 and 2007. Blinded to other clinical data, we analyzed a 12-lead resting ECG obtained 1–14 days after the onset of stroke symptoms in 690 patients. We then compared the ECG findings between a final diagnosis of HRCE (n = 78) and other/undetermined causes (n = 612). We used multivariate logistic regression to study the association between ECG parameters and HRCE.

Results: Of our cohort (63% male), 35% showed ECG abnormality, the most common being T-wave inversion (16%), left ventricular hypertrophy (14%), prolonged P-wave (13%), and prolonged QTc (12%). 3% had atrial fibrillation (AF), and 4% P-terminal force (PTF). Of the continuous parameters, longer QRS-duration, QTc, and wider QRS-T-angle independently associated with HRCE. After AF, PTF had the strongest independent association with HRCE (odds ratio = 44.32, 95% confidence interval = [10.51–186.83]), followed by a QRS-T angle >110° (8.29 [3.55–19.32]), T-wave inversion (5.06, 2.54–10.05), and prolonged QTc (3.02 [1.39–6.56]).

Conclusion: Routine ECG provides useful information for directing the work-up of a young IS patient. In addition to AF, PTF in particular showed a strong association with etiology of HRCE.

1. Introduction

Ischemic stroke (IS) is a multifactorial disease that, in the young differs considerably from IS in the elderly in terms of its distinct risk factor profile, its more diverse etiological spectrum and its larger proportion of cases with unknown cause [1,2]. Therefore, revealing the underlying pathophysiology in these conditions remains a major challenge. Of special interest here is cardioembolism, as this subtype associates with high early recurrence rate and mortality [3].

ECG is a routine investigation in stroke patients that provides essential information about underlying stroke etiology. In fact, ECG abnormalities are fairly common in elderly patients with acute stroke, even without any history of cardiac disease. According to such studies, the most common ECG abnormalities after stroke are QT-prolongation, cardiac ischemic changes (T-wave inversion and ST-segment depression) and non-hyperkalemia-dependent U-waves [4,5]. Furthermore, arrhythmias — particularly atrial fibrillation (AF), which also is as a causal etiology for ischemic stroke — were frequent [4,5].

To the best of our knowledge, no prior study has systematically analyzed ECG findings in young patients with ischemic stroke. In one small study (55 cases, 23 controls) interatrial block (IAB), defined as a P-wave duration >110 ms, was more common in young adult stroke patients than in healthy controls [6]. We hypothesized that ECG obtained in the subacute phase would provide relevant hints to guide a subsequent challenging search of the underlying etiology of young ischemic stroke. Our aims were (1) to characterize ECG changes broadly in a large database of consecutive patients with ischemic stroke at the age of 15 to 49 years and (2) to assess whether these changes correlate with the underlying cause of stroke, especially high-risk source of cardioembolism (HRCE).

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2. Patients and methods

The relevant authorities approved the study, which we carried out at the Departments of Neurology and Cardiology, Helsinki University Hospital. The retrospective study examined data from the Helsinki Young Stroke Registry (HYSR) [1], on 1008 consecutive young adult patients aged 15–49 years with the first-ever ischemic stroke admitted to our hospital between 1994 and 2007.

2.1. Study population

The patients were examined according to a standard protocol [1], which involved taking a 12-lead ECG on admission and, in most cases, also within two weeks from stroke onset, during the patient's hospital stay. To exclude changes related to an acute phase of stroke and to obtain an ECG close to baseline, the ECG analyzed was one taken 1 to 14 days after the onset of stroke symptoms and at least 1 day after admission. We excluded patients with a poor quality ECG and those with an initially false primary diagnosis (stroke mimic) (Fig. 1).

2.2. Comorbidities

Comorbidities considered and analyzed in this study were: obesity, hypertension, cigarette smoking, dyslipidemia, congestive heart failure, preexisting AF, diabetes mellitus type 1, diabetes mellitus type 2, and a composite of cardiovascular disease (any of pre-existing coronary heart disease, congestive heart failure, prior myocardial infarction, or peripheral artery occlusive disease) (online data supplement, supplemental methods).

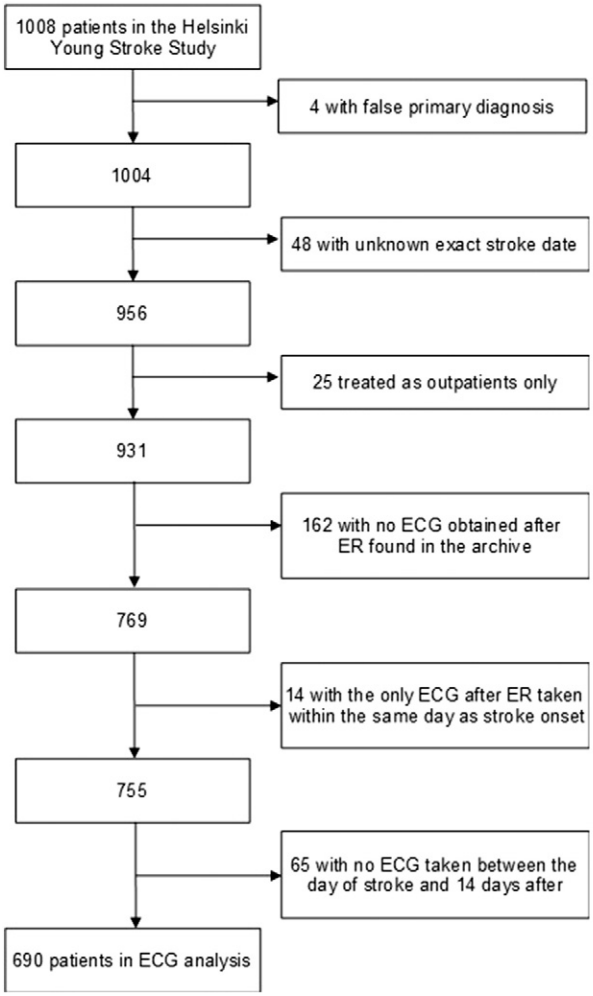

Fig. 1. Patient flow in the study.

2.3. Stroke etiology and characteristics

We used the TOAST classification [7] for subtyping stroke etiology, with specific modifications, to properly address the different etiological profiles of young stroke. We formed a separate group of dissections (including both vertebral artery dissection and internal carotid artery dissection) and separate groups for cardioembolism from a low-risk or uncertain source and a high-risk source. The low-risk or uncertain sources consisted of patent foramen ovale, with or without atrial septal aneurysm, or sole atrial septal aneurysm. The high-risk sources included all other documented sources of cardioembolism with a high primary annual risk (>2%) for stroke [8]. The etiologic subgroups were therefore large artery atherosclerosis (LAA), HRCE, cardioembolism from a low-risk source (LRCE), small-vessel disease (SVD), dissection, other non-dissection and undetermined. Stroke severity was assessed with the NIH Stroke Scale (NIHSS) [9]. Lesion size based on documented templates, with slight modifications [10].

2.4. ECG analysis

One investigator (J.Pi.) blinded to the clinical data analyzed the ECG strips: in uncertain cases J.Pi. and two senior cardiologists (M.L. and A.A.) reached a consensus judgment.

From the ECG recordings we measured heart rate, P-wave duration, P-wave axis, PR-interval, QRS-complex duration, QRS frontal axis, T-wave frontal axis, and QT-interval. If measurements automatically performed by the ECG-device were available, we used them [11]. We also calculated the angle between the QRS frontal axis and the T-wave frontal axis for each patient (QRS-T angle). We applied the ECG criteria by Sokolow–Lyon (SV1 + RV5 / 6 ≥ 3.5 mV) to define left ventricular hypertrophy [12]. P-terminal force (PTF) was defined as the terminal negative part of the P-wave in lead V1 having an amplitude deeper than −0.1 mV and a duration of at least 40 ms [13,14] (See Fig. 2). A P-wave duration of >120 ms was considered prolonged. We measured Q-waves in the frontal leads I, II, III, aVF and aVL, as well as in the precordial leads V2–V6. We set pathological Q-wave criteria as ≥1 mm deep and >30 ms wide in two adjacent frontal leads (I, aVL or II, aVF, III) or ≥1 mm deep and 20 ms wide in any precordial lead V2–V6. We measured T-wave inversions in leads V2–V6 and aVL, I, II and aVF. The presence of any T-inversion greater than 1 mm in depth was considered pathological. We defined the presence of a J-wave (early repolarization) as a >1 mm notch or slur in at least 2 adjacent leads: an inferior J-wave in II, aVF and III, and a lateral J-wave in I, aVL or V4–V6. We used the American Heart Association's (AHA) standard criteria to investigate the presence of left bundle branch block (LBBB), right bundle branch block (RBBB) and partial right bundle branch block (pRBBB) [15]. Subjects with a QRS-duration >120 ms in the absence of any specific block, we diagnosed with non-specific intraventricular conduction delay (IVCD). We used standard criteria to determine the presence of a second- or third-degree atrioventricular block (AV-block). After confirming the presence of any atrial or ventricular extrasystoles on the ECG strip, we classed them present or absent. We used Bazett's method QTc = QT/(√RR-interval) to calculate the corrected QT-interval (QTc) [16]. We defined a prolonged QTc as >450 ms in men and >470 ms in women. Subjects with a pathological Q-wave, T-inversions, LBBB, RBBB, IVCD, prolonged QTc, non-sinus rhythm, P-terminal force, LVH or a QRS-T angle >110°, were diagnosed with a major ECG abnormality.