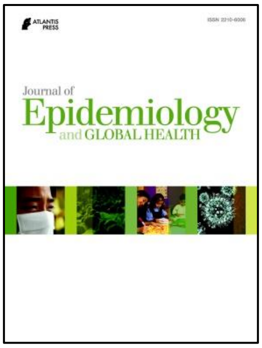

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Objective cardiac markers and cerebrovascular lesions in Indian seniors

Stephanie H. Charles [1], Amanda C. Tow [1], Joe Verghese *

Department of Neurology, Albert Einstein College of Medicine, 1165 Morris Park Avenue, Room 301, Bronx, NY 10461, USA
Department of Medicine, Albert Einstein College of Medicine, 1165 Morris Park Avenue, Room 301, Bronx, NY 10461, USA

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Abstract Cardiovascular risk factors are implicated in cerebrovascular disease, resulting in cognitive impairment. This study investigated the relationship between objective cardiac markers and cerebral changes in older Indian adults with and without dementia. Dementia patients with major electrocardiographic (EKG) abnormalities were 8.19 times more likely to have evidence of stroke on magnetic resonance imaging (MRI) compared with patients with no EKG abnormalities ($p < .05$). The relationship between major EKG abnormalities and stroke on MRI was not significant for patients without dementia. Objective cardiac markers may identify MRI cerebrovascular lesions in patients with dementia, and thus guide neuroimaging allocation in resource-poor areas.

1. Introduction

Cardiovascular risk factors are implicated in the pathogenesis of cerebrovascular disease with subsequent cognitive impairment [1]. The Kerala-Einstein Study (KES) previously reported that objective cardiac markers on electrocardiogram (EKG) and echocardiogram are associated with a clinical diagnosis of dementia, especially vascular dementia (VaD) [2]. Left ventricular hypertrophy (LVH) and atrial fibrillation are EKG markers that predict stroke [3,4]. Risk factors for stroke have been associated with white matter hyperintensities (WMHs) on magnetic resonance imaging (MRI) [5]. Building on the above findings, this study hypothesized that objective cardiac markers on an EKG and an echocardiogram may identify cerebrovascular pathology in patients with dementia.

Abbreviations: MRI; magnetic resonance imaging; EKG; electrocardiogram; LVH; left ventricular hypertrophy

* Corresponding author. Address: Division of Cognitive & Motor Aging, Department of Neurology, Albert Einstein College of Medicine, 1165 Morris Park Avenue, Room 301, Bronx, NY 10461, USA. Tel.: +1 718 430 3808; fax: +1 718 430 3829.
E-mail addresses: Stephanie.charles@med.einstein.yu.edu (S.H. Charles), Amanda.tow@med.einstein.yu.edu (A.C. Tow), Joe.verghese@einstein.yu.edu (J. Verghese).
[1] contributed equally as first authors.

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2. Methods

A cross-sectional study based at the Baby Memorial Hospital in Kerala, India as part of the KES was performed. Study design and methods have been reported [2]. Participants with dementia were recruited from neurology clinics; normal controls were recruited from relatives of patients and patients with non-cognitive complaints as previously described [2]. Dementia diagnosis followed Diagnostic and Statistical Manual (fourth edition) criteria and was assigned at consensus case conferences as previously described [2]. All participants were 55 and older and provided informed consent [2]. Exclusion criteria included severe audiovisual loss or presence of active medical or psychiatric illness. The study protocol was approved by the local institutional review board.

MRI, 12-lead EKG, and transthoracic 2D echocardiogram were obtained from all participants with dementia and 52 normal controls. Based on the previous study, major EKG abnormalities (any one of the following: Q—QS wave abnormalities, left ventricular hypertrophy, Wolff—Parkinson White syndrome, complete bundle branch block or intraventricular block, major ST—T changes, atrial fibrillation or atrial flutter) and ST—T changes were examined [2]. In addition, LVH was also examined on the echocardiogram. The EKG was read by a study clinician. The echocardiograms and MRIs were interpreted by physicians who were not on the KES team. These EKG and echocardiographic abnormalities were termed objective cardiac markers [2].

MRI scanning was performed with a 1.5 T Siemens Avanto (SQ Engine) MRI system equipped with a 12-channel parallel imaging capable head coil. MRI findings examined included large vessel strokes, lacunar infarctions, leukoaraiosis, and hippocampal atrophy. Other cerebrovascular markers like microbleeds were not available for the study. The diagnoses of dementia and subtypes were made at a consensus conference using established criteria [2]. Physicians interpreting EKG, echocardiogram, and MRI were blinded to dementia status.

Baseline characteristics of participants with and without dementia were compared using descriptive

Table 1 Association of EKG and echocardiographic markers with MRI lesions by dementia status. Results are shown as OR (95% CI), adjusted for age, gender, and education.

		Overall	Controls	Dementia
Sample size		102	41	61
MRI Stroke	Major EKG abnormalities	3.19* (1.17—8.68)	.87 (.16—4.65)	8.19* (1.58—42.41)
	EKG ST/T changes	2.55 (.74—8.83)	.95 (.14—6.32)	5.90 (.65—53.30)
	Echo LVH	4.17* (1.70—10.25)	2.86 (.71—11.60)	6.07* (1.65—22.39)
MRI Lacunes	Major EKG abnormalities	2.00 (.62—6.38)	.91 (.14—6.00)	4.01 (.67—24.01)
	EKG ST and T changes	1.73 (.42—7.10)	.81 (.10—6.87)	3.48 (.31—38.89)
	Echo LVH	3.01* (1.08—8.39)	2.02 (.42—9.81)	4.28 (.97—18.77)
MRI Leukoaraiosis	Major EKG abnormalities	1.83 (.70—4.76)	3.88* (1.07—14.15)	1.24 (.40—3.88)
	EKG ST and T changes	3.32* (1.03—10.73)	7.86* (1.95—31.76)	1.75 (.45—6.82)
	Echo LVH	1.86 (.76—4.55)	1.46 (.42—5.09)	2.46 (.83—7.30)
Any Cerebrovascular Disease (Stroke, Lacunes, or Leukoaraiosis)	Major EKG abnormalities	2.77 (.97—7.93)	1.08 (.21—5.40)	6.72* (1.25—36.07)
	EKG ST and T changes	2.76 (.70—10.85)	1.62 (.24—11.18)	4.34 (.47—39.87)
	Echo LVH	3.82* (1.49—9.78)	3.59 (.88—14.61)	4.24* (1.12—16.10)
MRI Hippocampal Atrophy	Major EKG abnormalities	0.99 (.36—2.79)	.63 (.05—8.11)	.79 (.24—2.64)
	EKG ST and T changes	.84 (.23—3.03)	1.08 (.07—16.21)	.56 (.12—2.71)
	Echo LVH	.92 (.36—2.33)	1.04 (.11—10.40)	.73 (.24—2.20)

* *p*-Value <.05.

statistics. Odds ratios (OR) with 95% confidence intervals were calculated using multivariate logistic regression for the association of objective cardiac markers with MRI findings adjusting for age, gender, and education. The analysis stratified by dementia status was also repeated to examine associations by diagnostic groups.

3. Results and discussion

Of the 113 participants (mean age 70.8 ± 7.2, 45.1% women) who underwent MRI, 61 had dementia (mean age 71.9 ± 7.4 y, 54.1% women, mean education 6.5 ± 0.43 y) and 41 were cognitively normal (mean age 68.9 ± 6.0 y, 34.1% women, mean education 10.4 ± 0.43 y). Eleven participants with mild cognitive impairment syndrome (MCI) were excluded; including them in the non-dementia group did not materially alter the findings.

3.1. Echocardiogram

LVH was associated with large vessel stroke on MRI (Table 1). The relationship between LVH and MRI stroke was significant for dementia but not for controls.

3.2. EKG

Major EKG abnormality was associated with MRI stroke only in dementia cases ($p < .05$). No objective cardiac markers were related to hippocampal atrophy (Table 1). Although lacunes and leukoaraiosis were not individually associated with objective cardiac markers, echocardiographic LVH and major EKG abnormalities were associated with the presence of any cerebrovascular disease (stroke, lacunes or leukoaraiosis) in dementia (Table 1).

4. Conclusions

These findings show that LVH on echocardiogram and major EKG abnormalities identify stroke pathology on MRI in older Indian adults with dementia. Previous studies have found that LVH is associated with stroke [3]. This investigation supports this finding, but found that the association was significant in dementia but not normal controls. Cerebrovascular disease on MRI is not only helpful in subtyping vascular dementia, but also is associated with faster cognitive decline; highlighting the importance of identifying these lesions. Objective cardiac markers identified leukoaraiosis (WMHs) but not other MRI vascular lesions in cognitively normal individuals. Unlike some previous studies [5], there was no association found between leukoaraiosis and cardiovascular disease in dementia cases.

The limitations of this study include a small sample size, failure to include other potential MRI markers of cerebrovascular disease such as microbleeds, and large confidence intervals. Because of limited power secondary to a small sample size, other cardiovascular risk factors such as hypertension, ischemic heart disease, and diabetes mellitus were not examined. As MRI is costly and less accessible than EKGs and echocardiograms, establishing the diagnostic utility of objective cardiac markers will be useful in identifying which patients will benefit from further neuroimaging in resource-poor areas.

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Conflict of interest

The authors declare that there is no conflict of interest.

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