Risk factors of Silent Cerebral Infarcts in Patients with Acute Coronary Syndrome Based on MRI Findings

Hazem K.elhewag[1], Alaaeldin S.bekhit[1], Mohamed A.tarek[1], Gharib F.mohamed[1], Sharaf .E.D Mahmoud [2].

1. Department of neurology, faculty of medicine, Sohag University, Sohag, Egypt.
2. Department of cardiology, faculty of medicine, Sohag University, Sohag, Egypt.

sharaf003@gmail.com

Abstract :

Introduction The presence of silent brain infarcts increases the risk of subsequent stroke by two to four times in the general population, independent of cardiovascular risk factors. The presence of silent brain infarcts doubles the risk of dementia, including Alzheimer's disease**.** **Aim Of The work** the degree of existence and the risk factors associated with silent cerebral infarcts (CSI) in patient with acute coronary syndrome (ACS) younger than 55 years old. Early detection might be helpful in optimizing treatment and prevention of further complications. **Patients and Methods**: This study was prospective cross -sectional study included 40 patients <55 years with ACS admitted at Sohag university hospitals: - with a definite diagnosis of ACS. MRI (1.5 Tesla) were done for all patients. Single cerebral infarction or more (and or) evidence of chronic white matter ischemia CWMI were considered as abnormal MRI findings. **RESULTS**: Patients were divided into two groups according to MRI findings: Group 1:- eight out of 40 patients (20%) with normal MRI. Group 2:- 32/40 patients (80%) with MRI findings of SCI and or chronic white matter ischemia. There was non-significant difference between two groups as regards-age, sex, and ACS presentation, but there was significant difference as regards-body mass index (BMI and family history (FH) of vascular events. Incidence of hypertension and dyslipidemia were significantly higher in abnormal MRI group. There was a non-significant difference between 2 groups as regards Montreal cognitive score (MOCA). Abnormal MRI group had significant higher TG and LDL. There was non-significant difference between 2 groups as regard echocardiographic criteria, coronary angiographic parameters and carotid Doppler findings. **Conclusion**: More than two-third of patients with ACS present an abnormal MRI suggestive of atherosclerosis and ischemia. Risk factors include BMI, FH, dyslipidemia and hypertension.

Key Words

Acute coronary syndrome, silent brain infarctions, risk factors, Dementia.

Receive Date : 23/5/2022	Accept Date: 1/6/2022	Publish Date : 1/6/2022

INTRODUCTION

The National Institute of Neurological Disorders and Stroke defines silent cerebrovascular disease (infarction and hemorrhage), which is detected by computed tomography or nuclear magnetic resonance imaging (MRI) by chance, as a predisposing condition of clinical cerebrovascular disease. (1) The presence of silent brain infarcts increases the risk of subsequent stroke by two to four times in the general population, independent of cardiovascular risk factors. (2) The

presence of silent brain infarcts doubles the risk of dementia, including Alzheimer's disease. (3) Acute stroke showed marked decrease in incidence due to Improvements in anticoagulation therapy however, silent cerebral infarcts (SCIs) are increasingly observed and may be more prevalent than symptomatic one. (4) Add to the absence of standardized screening, SBIs lack an immediate functional impact on patients, so physicians may be uncertain about its diagnostic significance, potentially leading to inconsistent reporting and counselling of patients with this condition (5)Advancements in MRI have resulted in increased detection and awareness of such lesions. (4) So, continuous efforts are needed to enhance the diagnosis of SBI and to reduce the misclassification bias. In addition, appropriate identification of the underlying risk factors and treating them may be useful in preventing recurrent stroke and dementia.

Aim Of The work

The aim of the study was focused on the degree of existence and the risk factors associated with silent cerebral infarcts (CSI) in patient with acute coronary syndrome younger than 55 years old and ? Early detection might be helpful in optimizing treatment and prevention of further complications.

SUBJECT AND METHODS

Cross sectional prospective study, done at coronary care unit of Sohag University Hospitals. We started to recruit the cases after CCU admission and diagnostic angiography was done. They were divided into two groups according to MRI findings either normal or abnormal. Patients with a single cerebral infarction or more and or evidence of chronic white matter ischemia CWMI will be considered as abnormal.nThis study included the first 40 patients <55 years with ACS admitted in CCU at Sohag university hospitals.

Inclusion Criteria:

Patients had a definite diagnosis of ACS established by cardiologist. Acute coronary syndrome represents a spectrum of diseases, including ST-elevation myocardial infarction (STEMI), non–ST-elevation myocardial infarction (NSTEMI) and unstable angina (UA) with its criteria defined by American heart association.(6)

Exclusion Criteria: Patients with atrial fibrillation and rheumatic heart disease will be excluded. Patients with definite previous or current stroke will not be included, also those with a definite history of transient ischemic attack.

Published by : NILES
Print ISSN 2636-3224
Online ISSN 2636-3232

Ethical consideration: The study approved by scientific and ethical committees at Sohag faculty of medicine, an informed written consent obtained from all participants in accordance with the Declaration of Helsinki.

Method of the study: The study was done in the department of neurology, sohag university hospital, for each patient the following will be done: 1-MRI brain (1.5 tesla) for all patients within 1 week from enrolment including diffusion, Flair, T1 and T2. 2- Complete physical examination, cardiac and neurologic examination. 3- Electrocardiogram and reporting the presence of ECG findings of ST segment elevation or depression, and the presence of atrial fibrillation. 4- Echocardiography:- The protocol will include the acquisition of 1) 2D images in parasternal axis long and short axis; 2) 2D and Doppler tissue images in the apical planes of 4, 2 and 3 chambers; 3) Pulsed, continuous and color Doppler M of transmitral LV flow and LV ejection. 5-Cardiac catheterization at time of admission for patients with STEMI and high risk non STEMI or after 24 hours in patients with low risk NSTEMI or UA. The operator reports the degree of stenosis in different coronary arteries. 6-Laboratory investigations include (complete blood picture, liver function tests, renal function tests, cardiac Enzymes (Troponin and CK-MB) , lipid profile.
7- Complete Assessment of Extracranial Carotid artery bilaterally by Doppler ultrasound (US) within 1 week for enrollment. The interpretation of the Doppler US reports was done according to Society of Radiologists in Ultrasound (SRU) consensus. (1) Normal. (2)<50% internal carotid artery (ICA) stenosis. (3) 50-69% ICA stenosis.(4) ≥70% ICA stenosis but less than near occlusion. (5) Near occlusion of the ICA. (6) Total occlusion of the ICA. (7) 8-Montreal cognitive assessment MoCA test “Arabic form” The Montreal Cognitive Assessment (MoCA), developed in Canada in 1996, was intended to be a means of accurately detecting levels of cognitive impairment. There are 11 sections of the assessment, with a total of 30 possible points. The patients were graded into 5 grades: (1) No dementia: MoCA >26/30. (2) Mild cognitive impairment “MCI”: MoCA 18-26/30. (3) Mild dementia: MoCA 11-17/30. (4) Moderate dementia: MoCA 6-10/30. (5) Severe dementia: <6/30. (8)

Statistical analysis:
Data was analyzed using STATA intercooled version 12.1, quantitative data was represented as mean, standard deviation, median, and range. Data was analyzed using student t test to compare means of two. When the data was not conclusive Mann-Whitney test was used. Qualitative data presented as percentage and compared using either Chi square test or fisher exact test. Graphs were produced by using Excel or STATA program. P value considered significant if less than 0.05.

Published by : NILES
Print ISSN 2636-3224
Online ISSN 2636-3232

RESULTS

Our study included 40 patients <55 years old. They were divided into two groups according to MRI findings: Group 1:- eight out of 40 patients (20%) with normal MRI means no silent cerebral infarction (SCI) or chronic white matter ischemia. Group 2:- 32/40 patients (80%) with MRI findings of SCI and or chronic white matter ischemia. (Figure1) and (Figure 2)

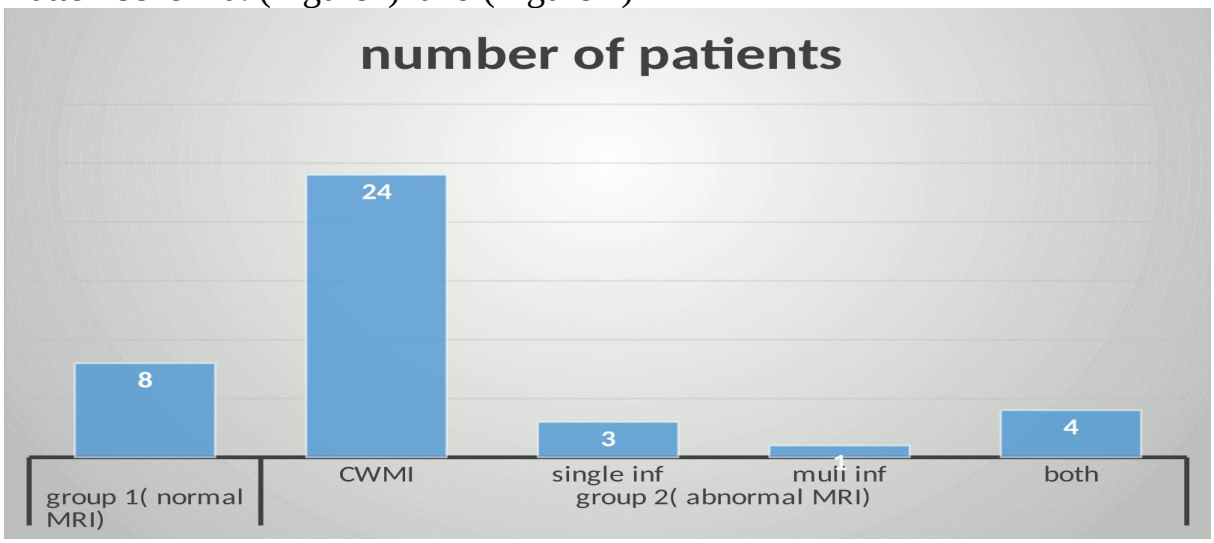


Figure (1) MRI results
Group 1 Normal MRI
Group 2 Abnormal MRI in the form of chronic white matter ischemia (CWMI), single infarction, multiple infarctions and both CWMI and infarctions

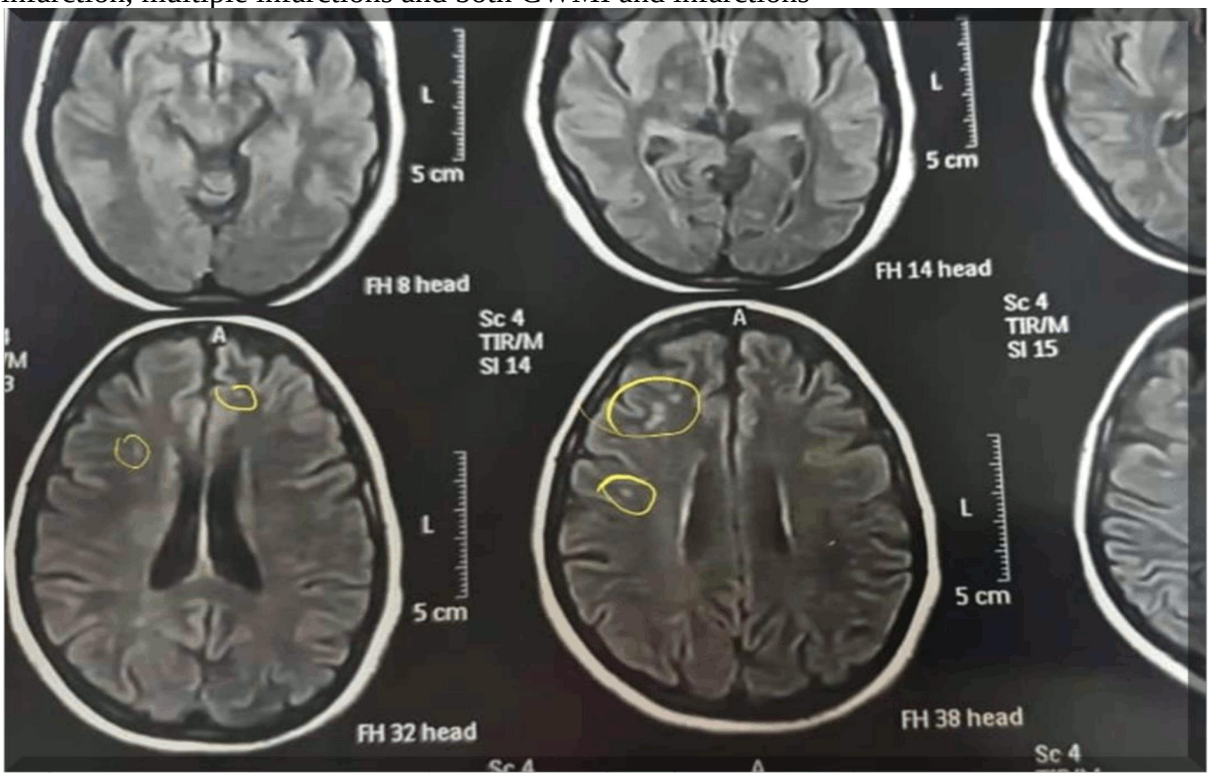


Figure (2) MRI of 51 and 49 years old patients presented by NSTEMI (red arrows highlights different sized infarctions)

Published by : NILES
Print ISSN 2636-3224
Online ISSN 2636-3232

By comparison between 2 groups, we found that there was non-significant difference between them as regards age, sex, and ACS presentation, but there was a significant difference as regards BMI and family history of vascular events (coronary heart disease and cerebrovascular stroke) (p=0.004, 0.04 respectively) as patients with SCI in MRI had higher BMI than MRI of patients without SCI and 59.4% of patients with SCI in MRI had family history of vascular events. Table (1)

Table (1). Comparison between Normal and abnormal MRI groups

		Patients without SCI in MRI	**Patients with SCI in MRI**	**P value**
Age (yrs)	**Mean±S.D**	46.63±6.63	47.56±5.88	0.712 (NS)
BMI	**Mean±S.D**	25.09±2.78	28.00±2.00	**0.004 (S)**
Sex	**Male**	4 (50%)	21 (65.6%)	0.444 (NS)
Family History of vascular events		1 (12.5%)	19 (59.4%)	**0.04 (S)**
ACS Dx	STEMI	3 (37.5%)	12 (37.5%)	0.935 (NS)
	NSTEMI	0 (0%)	1 (3.1%)	
	UA	5 (62.5%)	19 (59.4%)	

SCI indicates Silent cerebral infarctions; **MRI**, magnetic resonance imaging; **S.D**, Standard deviation; **S**, Significant; **BMI**, body mass index; **ACS Dx** , acute coronary syndrome diagnosis and **NS**, non-significant

As regards risk factors, incidence of hypertension and dyslipidemia were significantly higher in patients with SCI in MRI respectively than those without SCI in MRI. Table (2)

Table (2). Modifiable risk factors in the study groups

		Patients without SCI in MRI	**Patients with SCI in MRI**	**P value**
DM		3 (37.5%)	9 (28.1%)	0.677(NS)
Medications	Oral	3 (100%)	3 (33.3%)	0.182 (NS)
	insulin	0 (0%)	6 (66.7%)	
Hypertension		2 (25%)	21 (65.6%)	**0.053 (S)**
Dyslipidaemia		5 (62.5%)	30 (93.8%)	**0.04 (S)**
smoking		4 (50%)	21 (65.6%)	0.444 (NS)
Drug abuse		0 (0%)	6 (18.8%)	0.318 (NS)

SCI indicates Silent cerebral infarctions; **MRI**, magnetic resonance imaging**; DM**, Diabetes mellitus; **S**, Significant and **NS**, non-significant

There was non-significant difference between 2 groups as regards Montreal cognitive score (MOCA) as majority of patients in normal group had mild

Published by : NILES
Print ISSN 2636-3224
Online ISSN 2636-3232

cognitive impairment (87.5%) and 100% of abnormal group had mild cognitive impairment, on the other hand, 9/40 of patients in our study were illiterate and 3/40 of patients refused to do the test. Table (3)

Table (3). Montreal cognitive score (MOCA)

	Patients without SCI in MRI	Patients with SCI in MRI
Mild cognitive impairment	87.5%	100.0%
Normal MOCA score	12.5%	00.0%
Total	100%	100%

SCI indicates Silent cerebral infarctions; **MRI**, magnetic resonance imaging**; DM**; **S**, Significant and **NS**, non-significant
P value = 0.286 (NS)

There was non-significant difference between 2 groups as regard echocardiographic criteria as (segmental wall motion abnormalities, left ventricular function or thrombi) also the coronary angiographic parameters.
Also, there was a non-significant difference between the 2 groups as regard carotid Doppler findings of ICA stenosis. (Table 4)

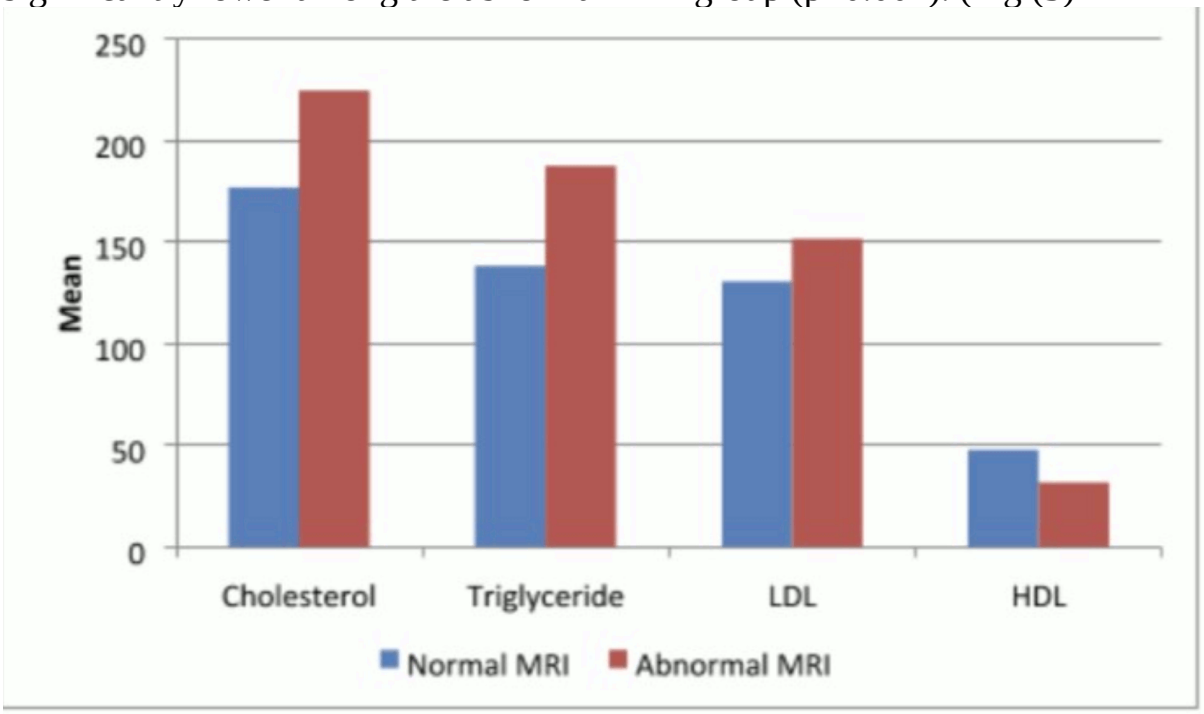
Table (4). Comparison between Patients with and without SCI in MRI regarding investigations

Echocardiography		Normal MRI	Abnormal MRI	P value
Ejection Fraction	**Mean±S.D**	58.25±7.90	53.78±10.41	0.265 (NS)
Dilated LV		2 (25%)	6 (18.7%)	0.356 (NS)
Dilated LA		1 (12.5%)	4 (12.5%)	
Valve lesion		1 (12.5%)	1 (12.5%)	
Coronary angiography				
3 Vessel disease for CABG		1 (12.5%)	10 (31.3%)	0.279(NS)
Left main disease		0 (0%)	2 (6.3%)	0.636(NS)
Proximal segment subtotal occlusion		2 (25%)	5 (15.6%)	0.611(NS)
total occlusion of LAD		0 (0%)	1 (3.1%)	0.800(NS)
mild diffuse atherosclerosis		2 (25%)	5 (15.6%)	0.200(NS)
Carotid doppler				
Normal		2 (25%)	9 (28.1%)	0.951 (NS)
<50% ICA stenosis		4 (50%)	14 (43.8%)	
50-69%ICA stenosis		2 (25%)	9 (28.1%)	
Near occlusion of ICA		0 (0%)	0 (0%)	
Total occlusion of ICA		0 (0%)	0 (0%)	

LV indicates Left ventricle; **LA**, Left atrium; **ICA**, Internal Carotid Artery; **CABG**, coronary artery bypass grafting ;**LAD**, left anterior descending artery; **S**, Significant and **NS**, non-significant

Published by : NILES
Print ISSN 2636-3224
Online ISSN 2636-3232

There was a non-significant difference between the 2 groups as regards laboratory investigations except lipid profile as abnormal MRI group had significantly higher TG and LDL than normal group (p=0.006, 0.024 respectively). HDL levels were significantly lower among the abnormal MRI group (p<0.001). (Fig (3)



Regarding the site of lesion, the majority had parietal (50%), then frontal (34.3%), then occipital (21.8%), then cerebellar and brain stem (12.5%), and no temporal lesions. Regarding the site of lesion as well, the majority had subcortical (65.6%) then periventricular (56.2%), and cortical (9.3%).

Discussion

Due to nearly similar risk factors coronary artery disease (CAD) and cerebrovascular diseases are usually coexist. In term: - a third of patients with ischemic stroke already have clinical manifestations of CAD and the reverse patients with established CAD are at higher risk of cerebrovascular events than those without. (9) The incidence of stroke was perhaps higher than previously estimated because of the occurrence of asymptomatic cerebral infarcts (aCI), which could be easily missed by clinicians. (10)

The advances in magnetic resonance imaging (MRI), such as diffusion-weighted imaging (DWI), have detected small and very recent ischemic stroke lesions, even in asymptomatic patients. (11) The mechanisms of cerebral infarcts are varied, atherosclerosis of the small arteries, microemboli from larger arteries or the heart may be involved. (12)

This cross sectional study was focused on the existence of silent infarcts in young patients (<55yrs) with ACS admitted in coronary care unit (CCU) at Sohag

Published by : NILES
Print ISSN 2636-3224
Online ISSN 2636-3232

university Hospital to allow for early detection and better optimization of treatment to prevent such consequences.

Each patient were subjected to MRI brain, complete physical, cardiological and neurologic examination, electrocardiogram, echocardiography, cardiac catheterization, laboratory investigations (complete blood picture , liver function tests , renal function tests , cardiac enzymes (Troponine and CK-MB), lipid profile and complete assessment of extracranial carotid artery bilaterally by Doppler ultrasound.

Surprisingly, in the current study among 40 patients with ACS, 32 patients (80%) had abnormal MRI findings SCIs and only 8 patients (20%) had normal MRI.

The Framingham study was established to improve understanding of the pidemiology of (CAD). A sample of patients with mean age of 62 years, the prevalence of silent multiple brain infarction was 10.7%, but it revealed that more three quarter of patients having a single infarct. (13) Similarly, the prevalence of multiple SCI (three or more infarcts per person) in patients with CAD was 46% in the study of Hoshide S. et al meanwhile, in patients with multi- (two- or three) vessel diseases (VD) a significantly higher prevalence of multiple SCI (68.1%) (12).

Lower incidence was reported in the Japanese brain check-up study by Kobayashi et al., among patients with obstructive sleep apnea and in a non-obese population who did MRI, they reported a prevalence of 10.6 %.(14) According to study by Tanaka et al., the prevalence of silent brain infarctions (SBI) in patients with ischemic heart disease was relatively high (28.2%) but still lower than current study. (15) (34.7%) of patients underwent primary percutaneous coronary intervention (p-PCI) had aCI approved by Cranial MRI as prescribed Murai et al.,2008 (16)

Another similar study by Nishino et al., who included patients with ACS reported that the incidence of SBIs was 30% (93% were of lacunar type). (17) Incidence variability between studies can be explained by different sample size and the ethnic differences. We included also patients with underling medical conditions making them at higher risk of cerebral infarctions.

There was no significant difference between two groups as regards age, sex, and ACS type (STEMI, NSTEMI &UA). Similarly, Weber et al., 2012 and Price et al., 1997 found that, there was no significant differences between patients with SCI and matched patients without SCI. (18,19) The majority of studies, however, did not support any gender disparity in SCI risk. (20) (21) In contrast , Das et al., found that, the prevalence of SCI increasing with age, and varied from (<8% in the group aged 30 to 49 years) to(>15% at age 70 to 89 years). (13)

In disagreement with the current study, Delgado et al., reported that, Prevalence of SCIs was gradually increased for both sexes with age, but they were more often in men than in women at any age category. (22) Longstreth et al.,

Published by : NILES
Print ISSN 2636-3224
Online ISSN 2636-3232

discovered that male gender to be protective against lacunar infarcts in an MRI study (23)

In the current study patients with abnormal MRI had significantly higher BMI and stronger family history of vascular events compared to patients without SCI. This result was supported by Dichgans et al., 2007, and this increased risk may be due to inherited predisposition for stroke and interactions between genes and environmental factors, (24) relation between higher BMI and risk of stroke was explained by Arboix, as weight and abdominal fat is associated with a higher in blood pressure, and may thereby increase the risk of stroke. (25)

As regards risk factors, the prevalence of hypertension and dyslipidemia were significantly higher in patients with abnormal MRI findings in comparison with those with normal MRI. On the other hand, the prevalence of other risk factors (DM, smoking, drug abuse & other medical conditions) were comparable with no significant difference between both groups.

In line with current study, Rotterdam Study concluded that blood pressure specially systolic one and cholesterol levels were important risk factors for SCI. (20) Also Takashima et al., and others found that hypertension was significant factor concerning SBI. (26,27,29) Similarly, Escudero-Martínez et al., showed that Hypertension was the most frequent risk factor (51.2%), and diabetes was the least common risk factor (5.6%) in SCI. (28)

In disagreement with the current study, Tanaka et al., reported that there was no significant difference noted in the incidence of hypertension, high serum cholesterol level, high serum triglycerides level, or low serum HDL cholesterol level between those with and without silent brain lesions. (15) In three studies, a strong association was sought between tobacco and SBI. (26, 27, 16)

There was no significant difference between the 2 groups as regards Montreal cognitive score (MOCA) and the majority of patients in the 2 groups had mild cognitive impairment. Similarly, Zhao et al., showed that MoCA scores were negatively associated with SCI risk and might be more valuable in predicting vascular cognitive impairment (VCI). (32)

Unlike our results, He et al., reported that: aACI has been associated with dementia or depression. (10)

In current study, there was non-significant difference between 2 groups in finding of carotid Doppler (grading according to society of Radiologists in Ultrasound consensus), coronary angiographic reports (need for CABG, degree & site of stenosis), Echo report (EF, dilated LA, dilated LV).

Our results were in harmony with Hoshide et al., who investigated the difference in the progression and the characteristics of SCI detected by brain MRI between patients with CAD. There was no association between the number of SCI with left ventricular function (ejection fraction) or with abnormal wall motion of either ventricular wall and SCIs. (12)

Published by : NILES
Print ISSN 2636-3224
Online ISSN 2636-3232

Furthermore, Büsing et al., and Murai et al., concluded that (the EF and the incidence of carotid stenosis) were statistically equivalent in both groups with either cerebral stroke or not. (33, 16)

In disagreement with previous studies, Das et al., reported that higher internal carotid artery (ICA) intimal medial thickness (IMT) as compared to patients with lower ICA IMT were significantly associated with SCI (13)Also univariate analysis by Escudero-Martínez et al., showed that, larger LA AP diameter (42 mm vs 39 mm) were associated with higher risk of SBI. (28) Controversially, Tanaka et al., reported that the severity of coronary stenosis was found to be positively correlated with the frequency of silent lesions. (15)

Regarding the site of lesion, the majority of our patients had parietal (50%), then frontal (34.3%), then occipital (21.8%), then cerebellar and brain stem (12.5%) and no temporal lesions. And as well, the majority had subcortical (65.6%) then periventricular (56.2%) and cortical (9.3%). We did not find a predominance of SCI in either of the hemispheres.

Davis et al., found that SCIs are common and usually small and affect the basal ganglia also did not find a predominance of SCI in either of the hemispheres. (34) Wessels et al., have demonstrated that the predominant lesions caused by stroke are located in subcortical regions. (35)

Limitation of the study

The current study had certain limitations; 1. There were relatively very few number of patients especially in the normal MRI arm 2. The possibility of misclassification of silent infarcts and CWMI. This may have occurred in 2 ways. First, we did not have pathological information to confirm the infarcts on the MRIs. In addition, to determine whether the infarcts were silent, we relied heavily on patient's self-reports of their history of TIA or stroke. Because of doubts concerning the specificity of the questions about past TIA, history of TIA was checked by reviewing medical letters of the patients who reported any of these symptoms. Therefore, some patients may have been incorrectly included in this study, and some infarcts may have been misjudged as silent. We did not include a control group with a similar number of patients without acute coronary syndrome as refused by the ethical committee.

Conclusion

According to our results, MRI could be a useful screening tool in screening high risk patients with ACS, since we know that more than two-third of those patients will present an abnormal MRI suggestive of atherosclerosis and ischemia. MRI is an expensive but highly sensitive technique to detect ischemic lesions. Hypertension, obesity, family history of vascular events and dyslipidemia were considered to be the risk factors for SCI.

Published by : NILES
Print ISSN 2636-3224
Online ISSN 2636-3232

Recommendations:-

More studies on larger sample size and multiple centers are required. Control group with no ischemic heart disease history should be included. Extended follow-up of those patients with SCIs for more evaluation of the associated risk factors, the late coronary and neurological outcome that's to establish strategies to modify, diagnose and treat.

REFERENCES

1.Smith EE, Saposnik G, Biessels GJ, Doubal FN, Fornage M, Gorelick PB et al.,(2017) Prevention of Stroke in Patients With Silent Cerebrovascular Disease: A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke.
2. Roy MP (2019) Stroke burden in India and strategies for mitigation. BMJ 365:l4243.
3. Simmatis LER, Scott SH, Jin AY (2019). The Impact of Transient Ischemic Attack (TIA) on Brain and Behavior. Front Behav Neurosci 13:44.
4. Bendszus, M. & Stoll, G. Silent cerebral ischaemia: hidden fingerprints of invasive medical procedures. Lancet Neurol. 5, 364–372 (2006).
5.Leung, L. Y., Han, P. K. J., Lundquist, C., Weinstein, G., Thaler, D. E., & Kent, D. M. (2018). Clinicians' perspectives on incidentally discovered silent brain infarcts – A qualitative study. PLoS One, 13, e0194971.
6. Ezra A. Amsterdam, MD, FACC, Chair ; Nanette K. Wenger, MD, MACC, FAHA, Vice Chair; Ralph G. 2014 AHA/ACC Guideline for the management of patients with non-ST-elevation acute coronary syndromes: A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. Circulation, e344-426.
7. Von Reutern GM, Goertler MW, Bornstein NM et-al. Grading carotid stenosis using ultrasonic methods. Stroke. 2012;43 (3): 916-21.
8. Julayanont P., Phillips N., Chertkow H., Nasreddine Z.S. (2013) Montreal Cognitive Assessment (MoCA): Concept and Clinical Review. In: Larner A. (eds) Cognitive Screening Instruments. Springer, London. https://doi.org/10.1007/978-1-4471-2452-8_6.
9. Manolis AJ, Kallistratos MS, Vlahakos DV, et al. (2016) Comorbidities Often Associated with Brain Damage in Hypertension: Diabetes, Coronary Artery Disease, Chronic Kidney Disease and Obstructive Sleep Apnoea. Hypertension and Brain Damage. Springer,35-46.
10. He L-j, Zhang J-w, Yang Q, et al. (2014) The Incidence and Risk Factors of Acute Asymptomatic Brain Infarcts After Percutaneous Coronary Intervention in Patients with Acute Myocardial Infarction. International Journal of Gerontology 8: 70-73.
11. Bang OY and Li W. (2019) Applications of diffusion-weighted imaging in diagnosis, evaluation, and treatment of acute ischemic stroke. Precision and Future Medicine 3:69-76.
12.Hoshide S, Kario K, Mitsuhashi T, et al. (2001) Different patterns of silent cerebral infarct in patients with coronary artery disease or hypertension. American journal of hypertension 14: 509-515.
13. Das RR, Seshadri S, Beiser AS, et al. (2008) Prevalence and correlates of silent cerebral infarcts in the Framingham offspring study. Stroke 39: 2929-2935.
14.Kobayashi S, Okada K, Koide H, et al. (1997) Subcortical silent brain infarction as a risk factor for clinical stroke. Stroke 28: 1932-1939.
15.Tanaka H, Sueyoshi K, Nishino M, et al. (1993) Silent Brain Infarction and Coronary Artery Disease in Japanese Patients. Archives of neurology 50: 706-709.

Published by : NILES
Print ISSN 2636-3224
Online ISSN 2636-3232

16.Murai M, Hazui H, Sugie A, et al. (2008) Asymptomatic acute ischemic stroke after primary percutaneous coronary intervention in patients with acute coronary syndrome might be caused mainly by manipulating catheters or devices in the ascending aorta,regardless of the approach to the coronary artery. Circulation Journal 72: 51-55.
17.Nishino M, Sueyoshi K, Yasuno M, et al. (1993) Risk factors for carotid atherosclerosis and silent cerebral infarction in patients with coronary heart disease. Angiology 44: 432-440.
18. Weber R, Weimar C, Wanke I, et al. (2012) Risk of recurrent stroke in patients with silent brain infarction in the Prevention Regimen for Effectively Avoiding Second Strokes (PRoFESS) imaging substudy. Stroke 43: 350-355.
19. Price TR, Manolio TA, Kronmal RA, et al. (1997) Silent brain infarction on magnetic resonance imaging and neurological abnormalities in community-dwelling older adults:the Cardiovascular Health Study. Stroke 28: 1158-1164.
20. Vermeer SE, den Heijer T, Koudstaal PJ, et al. (2003) Incidence and risk factors of silent brain infarcts in the population-based Rotterdam Scan Study. Stroke 34: 392-396.
21.Rauch A, Wiklund J, Lumpkin GT, et al. (2009) Entrepreneurial orientation and business performance: An assessment of past research and suggestions for the future. Entrepreneurship theory and practice 33: 761-787.
22.Delgado P, Riba-Llena I, Tovar JL, et al. (2014) Prevalence and associated factors of silent brain infarcts in a Mediterranean cohort of hypertensives. Hypertension 64:658-663.
23.Longstreth W, Bernick C, Manolio TA, et al. (1998) Lacunar infarcts defined by magnetic resonance imaging of 3660 elderly people: the Cardiovascular Health Study.Archives of neurology 55: 1217-1225.
24. Dichgans M. (2007) Genetics of ischaemic stroke. The Lancet Neurology 6: 149-161.
25. Arboix A. (2015) Cardiovascular risk factors for acute stroke: Risk profiles in the different subtypes of ischemic stroke. World Journal of Clinical Cases: WJCC 3: 418.
26. Takashima Y, Miwa Y, Mori T, et al. (2010) Sex differences in the risk profile and male predominance in silent brain infarction in community-dwelling elderly subjects: the Sefuri brain MRI study. Hypertension Research 33: 748-752.
27. Masuda J, Nabika T and Notsu Y. (2001) Silent stroke: pathogenesis, genetic factors and clinical implications as a risk factor. Current opinion in neurology 14: 77-82.
28.Escudero-Martínez I, Ocete RF, Mancha F, et al. (2020) Prevalence and risk factors of silent brain infarcts in patients with AF detected by 3T-MRI. Journal of neurology.
29.Goldstein LB, Adams R, Alberts MJ, et al. (2006) Primary prevention of ischemic stroke: A guideline from the American heart association/American stroke association stroke council: Cosponsored by the atherosclerotic peripheral vascular disease interdisciplinary working group; cardiovascular nursing council; clinical cardiology council; nutrition, physical activity, and metabolism council; and the quality of care and outcomes research interdisciplinary working group: The American academy of neurology affirms the value of this guideline. Stroke 37: 1583-1633.
30.Howard G, Wagenknecht LE, Cai J, et al. (1998) Cigarette smoking and other risk factors for silent cerebral infarction in the general population. Stroke 29: 913-917.
31.Dhital R, Poudel DR, Tachamo N, et al. (2017) Ischemic stroke and impact of thyroid profile at presentation: a systematic review and meta-analysis of observational studies. Journal of stroke and cerebrovascular diseases 26: 2926-2934.
32. Zhao J, Tang H, Sun J, et al. (2012) Analysis of cognitive dysfunction with silent cerebral infarction: a prospective study in Chinese patients. Metabolic brain disease 27:17-22.
33.Büsing KA, Schulte-Sasse C, Flüchter S, et al. (2005) Cerebral infarction: incidence and risk factors after diagnostic and interventional cardiac catheterization—prospective evaluation at diffusion-weighted MR imaging. Radiology 235: 177-183.

Published by : NILES
Print ISSN 2636-3224
Online ISSN 2636-3232

34. Davis P, Bendixen B, Adams H, et al. (1996) Silent cerebral infarction in patientsenrolled in the TOAST study. Neurology 46: 942-948.
35. Wessels T, Wessels C, Ellsiepen A, et al. (2006) Contribution of diffusion-weighted imaging in determination of stroke etiology. American Journal of Neuroradiology 27: 35-39.

Published by : N I L E S
Print ISSN 2636-3224
Online ISSN 2636-3232