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Serum endocan and carotid intima-media thickness as markers of atherosclerosis in acute ischemic stroke

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Abstract

Stroke, a kind of cerebrovascular event, affects a large percentage of the population and is a leading cause of death and disability. Ischemic and hemorrhagic strokes are two different types of strokes. In the lungs and kidneys, active endothelial cells produce and release endocan, a dermatan sulphate proteoglycan that is soluble in water. Pro-inflammatory cytokines regulate its production. TNF-, IL-1, LPS, and angiogenic agents such as vascular endothelial growth factor (VEGF) increase endocan synthesis and secretion, whereas interferon- decreases endocan synthesis and secretion. To predict stroke and coronary heart disease (CHD), a noninvasive intermediate measure is the carotid intima–media thickness (IMT). IMT is also an indicator of cardiovascular risk factors and atherosclerosis in the carotidartery Risk factors for stroke and brain haemorrhage include common carotid artery plaque and an IMT of >0.9mm in the whole carotid artery. CCA plaque was linked to an increased risk of cerebrovascular illness.. The purpose of this research is to see whether carotid Doppler may help in the diagnosis of acute ischemic stroke. It is important for us to better understand the role of intima-media thickness (IMT) as an early and reliable measure of atherosclerosis in the study of ischemic cerebrovascular stroke (CVS) and subclinical atherosclerosis (CCA). Detection of patients at high risk of developing cerebrovascular symptoms will be improved by the use of IMT assessment in primary prevention. To find out whether stroke severity and intima-media thickness are linked. Cerebrovascular stroke patients' serum endocan levels should be measured as an atherosclerosis marker. Patients at high risk of cerebrovascular stroke may be identified early on by measuring their serum endocan levels. In this section, you will learn about the research methods and findings. Cerebral vascular stroke patients and control volunteers of the same age and gender were included in the research. All of the participants had their common carotid artery intima-media thickness and serum endocan tested. The NIHSS was administered to all participants as part of a comprehensive history-taking, as well as a general and detailed neurological assessment. This study found that higher intima media thickness (IMT) of the common carotid artery (CCA) is related with increased risk of stroke and increased stroke severity (p 0.0001). IMT of CCA increases with age (P 0.0001). The increased risk of cerebrovascular stroke occurrence and increased stroke severity is associated with increased IMT of the common carotid artery, which is a sign of atherosclerosis, as well as increased serum endocan, which is a sign of atherosclerosis and endothelial dysfunction. Combined with early preventive measures, non-invasive CIMT and endocan measurements could significantly reduce the risk of stroke.

Key words: intima-media thickness, common carotid artery, cerebrovascular stroke.

1.Introduction

This chronic inflammatory disease of the arteries, known as atherosclerosis, is responsible for nearly half of all fatalities in Westernized culture. When low-density lipoprotein (LDL) builds up and activates inflammation in certain arteries, it's known as atherosclerotic cardiovascular disease (ASCVD), which may lead to heart attacks, strokes, and other types of vascular problems [1].

Stroke, a cerebrovascular event, is a common cause of both morbidity and death in patients of all ages. ischemic and hemorrhagic strokes are both types of stroke [2].

In the lungs and kidneys, active endothelial cells produce and release endocan, a dermatan sulphate proteoglycan that is soluble in water. Pro-inflammatory cytokines regulate its production. Tumor necrosis factor- (TNF-), interleukin-1 (IL-1), lipopolysaccharide, and angiogenic agents like vascular endothelial growth factor (VEGF) increase endocan production and secretion, whereas interferon- decreases it [3].

2. Patients and Methods

This is a comparative cross sectional case control study conducted on 60 patients presented by cerebrovascular ischemic stroke and 60 healthy control with matching age and sex, recruited from neuropsychiatry department in benha university hospital. Both genders aged 50 – 85 years and diagnosed with acute cerebrovascular ischemic stroke were included, while excluding stubor or coma, previous ischemic stroke, cerebral hge, embolic infarction Pre-existing neurological, psychiatric, or other illnesses that would confound the neurological evaluations. Severe concomitant medical condition (e.g. metastatic cancer, AIDS, renal failure, liver failure…etc.)., study subjects were informed of the possibility of using the data obtained for academic purpose.

2.1. Tools:

All participants (cases & control) were subjected to the following:

1. Medical history taking.
2. Full general and neurological examination.
3. Patients' initial stroke severity will be assessed on admission by the National Institutes of Health Stroke Scale
4. Ct scan of the brain.
5. *Extracranial carotid artery duplex and sonography*
6. *serum endocan level*

Ethical consideration:

An informed written consent was obtained from patients and control subjects before their participation in the current study. It included data about aim of the study,

site of the study, study procedure and their acceptance for publication of anonymous data obtained. It was explained to both groups that they can withdraw from the study at any time without any consequences and it will not affect the type and quality of care they are receiving from the facility. It was also assured to all participants regarding the confidentiality of results

Statistical analysis

The collected data was revised, coded and tabulated using Statistical package for Social Science **(4).** Shapiro test, Mean Standard deviation (± SD), Student T Test, Mann Whitney Test (U test), The Kruskal-Wallis test, Chi-Square test, Fisher's exact test, Correlation analysis: and Regression analysis was used. All reported *p* values were two-tailed and $p < 0.05$ was considered to be significant **(5, 6,7).**

3. Results

Table (1) Comparison of demographic data between studied groups.

			Group				*P*
			Control	**n=60**	**AIS**	**n=60**	
Age (years)		**Mean ± SD**	62	±10	62	±11	0.931
		min-max	30	83	30	83	
Sex	**Male**	**N, %**	32	53.3%	33	55.0%	0.855
	Female	**N, %**	28	46.7%	27	45.0%	

Table (2) risk factors among study cases.

	AIS	**n=60**
	N	**%**
Smoking	21	35.0%
DM	40	66.7%
Hypertension	48	80.0%

Table (3) association of IMT with demographics and risk factors among studied cases.

		Normal mean IMT	**n=19**	**Abnormal mean IMT**	**n=41**	***p***
Age (years)	**mean±SD**	56.8	±14	64.5	±7.6	**0.008**
Male	**N, %**	10	52.6%	23	56.1%	0.802
Female	**N, %**	9	47.4%	18	43.9%	
Smoking	**N, %**	7	36.8%	14	34.1%	0.839
DM	**N, %**	12	63.2%	28	68.3%	0.695
Hypertension	**N, %**	16	84.2%	32	78.0%	0.735

Table (4) acute ischemic stroke features of studied cases.

				AIS	**n=60**
NIHSS		**Median**	**Min-max**	5	1-16
Stroke severity	**minor stroke**	**N,%**		23	38.3%
	moderate stroke	**N,%**		35	58.3%
	moderate to severe stroke	**N,%**		2	3.3%
Stroke size (cm)	**<1.5**	**N,%**		31	51.7%
	1.5-3	**N,%**		18	30.0%
	>3	**N,%**		11	18.3%
Plaque	**Absent**	**N,%**		47	78.3%
	Present	**N,%**		13	21.7%

Table (5) comparison of serum endocan according to risk factors.

	Cases n=60		***p***
	Serum endocan		
	median	**range**	
Non smoker	162.9	96.5-845.1	0.810
Smoker	226.9	99.6-610.5	
Non DM	158.15	96.5-611	0.371
DM	182.05	119.7-845.1	
No hypertension	161.3	96.5-611	0.631
Hypertension	178.85	99.6-845.1	

Table (1) : The present study was conducted on 60 AIS cases. Their mean age was 62 years, ranged from 50 to 83 years. They were 33 males (55%) and 27 females (45%). In addition to 60 healthy control subjects of matched age and gender ($p>0.05$ for age and gender). .
Table (2) Among all studied cases, 35% were smokers, 66.7% were diabetics and 80% were hypertensives. .
From table (3) . Abnormal mean IMT was significantly associated with older age, but not with gender, smoking, DM or hypertension.
Table (4) Median NIHSS was 5, ranged from 1 to 16, 38.3% had minor stroke severity (NIHSS : 1-4), 58.3% had moderate stroke severity(NIHSS:5-15) and 3.3% had moderate to severe stroke(16 – 20) 3.3%.
Regarding stroke size, 51.7% had stroke size < 3 cm in large axis, 30% had stroke size of > 3cm and 18.3% had stroke size involve multiple cerebral lobes.
Plaque was found in 21.7% of all studied cases..
Table (5). Serum endocan level was not affected significantly by smoking, DM, hypertension ($p>0.05$ for each).

4. Discussion

A total of 60 AIS patients participated in this investigation. Their ages varied from 50 to 83, with the average being 62. There were 33 men and 27 females in the group (45 percent). 60 healthy control volunteers of a similar age and gender were also included in the study. According to Chaudhary et al, who reported that the research cohort comprised 8561 consecutive patients with ischemic stroke, their mean age was 70.1 13.9 years, men were 51.6 percent and women were 49.4 percent, 35% of the cases were smokers, 66.7% were diabetics, and 80% were hypertensive. There was a 75.2 percent prevalence of hypertension, followed by dyslipidemia (62.2 percent), and diabetes in the study population (32.4 percent). Some 9.5 percent of the patients had ischemic stroke, atrial fibrillation, or flutter, and some 1.3 percent had hypercoagulable condition [8]. The median NIHSS score was 5, which was consistent with Majidi et al., who found that among 121 patients with a median age of 65 and 63 percent of them were women, their NIHSS score was 3 on the NIHSS scale [9]. In addition, 38.3% of patients had a small stroke, 58.3% had a moderate stroke, and 3.3% had a severe stroke, out of the total patients we examined. Mathew et al. discovered that stroke severity was moderate in 61.3 percent of patients, mild in 20.9 percent of patients, and severe in 17.7 percent of patients in their research, which is in agreement with our findings [10]. AIS patients were found to have bigger IMT on the right and left sides (1 vs 0.6), as well as a larger mean IMT on both sides (1 versus 0.59) when compared to the control group. However, the average IMT in the sick group was 0.798 mm, whereas in the control group, it was just 0.6 mm. There was a substantial difference in IMT between individuals with carotid plaque and those who did not. There was a statistically significant difference in the mean IMT between the various age groups in the patient group, and the IMT was connected with increasing age and the presence of carotid plaques [11]. The prevalence of aberrant IMT on the right side, left side, and mean IMT on both sides was substantially greater in AIS patients than in the control group. Age, but not gender, smoking, diabetes mellitus, or hypertension, were shown to be significant predictors of abnormal mean IMT. However, a cardiovascular specialist manually demarcated the IMT for the normal and CVD groups, whereas Loizou et al discovered that. There was no significant difference between the CCA left-side IMT and the right-side IMT when compared to normal values [12]. According to Touboul et al., aberrant IMT was related with increased stroke severity and bigger stroke size, which is consistent with our findings. For 470 stroke patients and 463 control groups, the mean CCA IMT values were 0.797-9.35 mm, respectively. They also found a correlation between greater IMT and an increased risk of stroke [13]. As Meenakshisundaram et al. reported in their study, Mean IMT was not substantially connected with risk factors such as diabetes or high blood pressure; however it did have a significant connection with age and dyslipidemia. In addition, there was no link between the severity of coronary artery disease and the degree of IMT (14). IMT was substantially greater in moderate to severe strokes than in small strokes, according to our findings. A greater proportion of bigger strokes were related with a greater proportion of increased IMT. Sun et al. observed that individuals with greater cIMT levels were older, had higher SBP, fasting glucose, were more likely to smoke and drink, had a lower estimated GFR, and were more likely to have a first stroke in patients with hypertension. It was revealed that individuals with greater MAP or DBP levels had a stronger link between cIMT and their first stroke. The MAP and DBP were both significant impact modifiers [15]. Researchers observed that median serum endocan levels were considerably greater in patients with acute ischemic stroke (AIS) than in the control group, which was in agreement with previous research by He et al [16]. Endocan levels were significantly higher in those with abnormal mean IMT, but were not affected significantly by smoking, diabetes mellitus (DM), or hypertension. Zhao et al. found that endocan levels in patients with hypertension, coronary artery disease, and coronary slow flow were higher than those in the control group. The mean endocan concentration difference across the three groups was 0.53. Further investigation revealed that individuals with hypertension and coronary artery disease had greater levels of serum endocan than those with hypertension alone [17].

5. Conclusion

Atherosclerosis and endothelial dysfunction are associated with increased cerebrovascular stroke occurrence and increased stroke severity, and non-invasive investigations such as measuring IMT and endocan levels could significantly reduce morbidity by identifying atherosclerosis and endothelial dysfunction early enough to implement preventative measures.

6. Limitations

Since there were just a few patients enrolled, the study's statistical power to detect a meaningful link may have been inadequate. Restrictions on who may participate and who can't participate. and lacked the necessary sample size to assess the potential impact of some of the risk variables. A hazard ratio based on IMT values was not possible in our investigation. IMT progression could not be tracked.

7. Recommendation

Considering the study's limitations, serum endocan levels should be monitored in patients with cerebral vascular stroke, measuring IMT in patients at risk of developing cerebral vascular stroke, and measuring CIMT and endocan levels (non-invasive investigations) could significantly reduce mortality and morbidity.

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Controversial relationships

There aren't any potential entanglements.

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