

SHORT-TERM OUTCOME OF CARDIOEMBOLIC STROKE IN DIFFERENT AGE GROUPS

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ABSTRACT

Background: The heart is established as an important source of cerebral embolism. Cardioembolic stroke (CES) accounts for about 20% of all ischaemic strokes. Various cardiac conditions either major or minor sources have been clearly associated with an increased risk of ischaemic stroke. Outcome and prognosis in cardioembolic ischaemic stroke are affected by different demographic, clinical, laboratory, and radiological parameters.

Objectives: The aim of this work was to study short-term neurological outcome of cardioembolic ischaemic stroke patients during the first six weeks following stroke onset in different age groups.

Methods: Forty patients with first-ever cardioembolic ischaemic stroke (23 males and 17 females) divided according to their ages into four groups (group I less than 20 years, group II 20-<40 years, group III 40-<60 years and group IV >60 years). Those were included in a hospital-based follow up prospective study and were subjected to clinical assessment, cardiological evaluation, CT/MRI measurement of brain infarction, patients were followed up for 6 weeks. Stroke severity was assessed by mNIHSS, GCS and CANS and functional outcome as assessed by mRS. Also sensitivity and specificity of these scales were assessed. The results were compared in different age groups.

Results: A highly statistically significant improvement in mean scores of mRS between the first and fifth visit were only recorded in young age groups I, II and III of CES patients denoting improvement of functional outcome during the follow up visits of study period ($p < 0.001$), while the old age group IV (60-80 years) didn't show any statistical difference in mean values of mRS during follow up visits. A highly statistical significant increase of vascular comorbidity in older age groups than younger ones (100%, 100% in group III, IV vs 0.0%, 10% in group I, II, $p = 0.001$) was recorded. Patients with AF and IHD had statistically significant more severe strokes as assessed by CANS and mNIHSS than those with RVHD (77.3% of AF and 78.6% of IHD had CANS score < 6.5 Vs 38.5% of RVHD, $P = 0.03$), (72.7% of AF, 71.4% of IHD had mNIHSS score ≥ 12 Vs 30.8% of RVHD, $P = 0.03$). Regarding functional outcome, death (mRS = 6) was significantly higher in AF patients (36.4% in AF, 35.7% in IHD, and 0.0% in RVHD, $P = 0.04$). A significant positive correlation between initial neurological severity as assessed by mNIHSS and functional outcome by mRS at the end of the study period in CES patients. ($p = 0.01$). GCS was found to be the most accurate stroke severity scale in predicting outcome (50% sensitivity, 100% specificity with positive predictive value of 100.0 and accuracy of 85.0%).

Conclusion: the overall short-term functional outcome of CES patients; in terms of (improvement, disability and death) was significantly better in younger than older age groups reflecting the negative impact of age, difference in underlying cardiac source of cerebral embolism, comorbidity with other vascular risk factors and the complications between the two age groups on the functional outcome.

Key words: Cardioembolic, stroke, short-term outcome, age, scores.

INTRODUCTION

The heart is established as an important source of cerebral embolism. Cardioembolic stroke (CES) accounts for about 20% of all ischaemic strokes⁽¹⁾. Various cardiac conditions either major or minor sources have been clearly associated with an increased risk of ischaemic stroke⁽²⁾. Cardiac factors that independently increase the risk of stroke include atrial fibrillation (AF), valvular heart disease, myocardial infarction, coronary artery disease, congestive heart failure^(1,2). Improved cardiac imaging has led to increased detection of potential predisposing conditions, such as patent foramen ovale (PFO), atrial septal aneurysms, aortic arch atherosclerotic disease, mitral annular calcification, left atrial appendage, spontaneous echo contrast and valvular strands^(2,3).

Clinical features that have been reported to support cardioembolism as a mechanism for ischaemic stroke have included documented cardiac source of embolism, maximal neurological

deficit at onset, multiple cerebrovascular territories involved, enhanced tendency toward haemorrhagic transformation, enhanced risk of syncope or seizure associated with presentation, and lower likelihood of premonitory transient ischaemic attacks^(1,3). Features that tend to make cardioembolic stroke less likely include significant cerebral atherosclerosis, stepwise progression of the neurological deficit within a definite period of time, vascular distribution such as entire internal carotid artery territory with combined middle cerebral artery and anterior cerebral artery involvement or watershed distribution, and premonitory transient ischaemic attacks⁽⁴⁾.

Cardioembolic stroke is associated with a poorer outcome compared with other types of ischaemic stroke. While this is related in part to large artery occlusion and underlying heart disease⁽⁵⁾. Stroke progression is one of the important contributors to poor outcome. The infarct in CES is typically larger than that in

atherothrombotic stroke so the outcome is poorer. In addition, cardioembolic stroke carries increased risk of haemorrhagic transformation (HT). Stroke progression is also among the most common serious adverse events and is significantly associated with a poor outcome^(4,5). Stroke progression is likely multifactorial, with brain edema, clot propagation, reocclusion of the parent vessel, recurrent emboli to the same territory, and haemodynamic fluctuations accounting for most cases⁽⁶⁾. Outcome and prognosis in cardioembolic ischaemic stroke are affected by different demographic, clinical, laboratory, and radiological parameters^(5,6,7).

Cardioembolic stroke is largely preventable, warranting efforts at primary prevention for major-risk cardioembolic sources. Once stroke due to cardiac embolism has occurred, the likelihood of recurrence is relatively high for most cardioembolic sources, and consequently, secondary prevention is also important⁽⁸⁾.

This study was done to evaluate short-term neurological outcome of cardioembolic ischaemic stroke patients during the first six weeks following stroke onset in different age groups. This may throw light on this type of ischaemic stroke, their pattern of presentation and the importance of different co-morbid risk factors. This may help in paving the way to better outcome and improving prevention strategies in these patients.

PATIENTS AND METHODS

This prospective follow up study included 40 patients with first-ever cardioembolic ischaemic stroke collected from neurology, cardiology, cardiothoracic and internal medicine ICUs of Zagazig university hospitals. The follow up cohort of CES patients included 23 males with mean ages(\pm SD) of 40.9 \pm 24 years, and 17 females with mean ages(\pm SD) of 41.2 \pm 17.7 years. The studied patients were divided into four age groups.

Patient groups:

The patients in the cohort will be classified according to their age limit into four groups:

Group I: CES patients with ages less than 20year:

This group included ten patients; (8) males and (2) females, their ages ranged from 3-19 years (Mean age: 16. 2 \pm 5.3 years).

Group II: CES patients with ages ranged from 20- <40years:

This group included ten patients; (4) males and (6) females, their ages ranged from 22-38 years (Mean age : of 27 \pm 5.0 years).

Group III: CES patients with ages ranged from 40-<60 years:

This group included ten patients; (3) males and (7) females, with ages ranged from 44-60 years (Mean age: 51.4 \pm 5.9 years).

Group IV: CES patients with ages ranged from 60-80 years:

This group included ten patients; (8) males and (2) females, with ages ranged from 62-75 years (Mean age: 68.7 \pm 5.2 years).

Stroke will be diagnosed as rapidly developing signs of focal or global neurological dysfunction lasting > 24 hours with no apparent aetiology other than of vascular origin⁽⁶⁾.

***Enrollment criteria:**

All patients have fulfilled the following Enrollment criteria:

The patients were chosen consecutively with the following inclusion criteria:

[I] Inclusion criteria: Focal or global neurological deficit lasting > 24 hours on initial neurological evaluation, first ever stroke, CT scan and/or MRI of the brain show evidence of cerebral ischaemia and stroke patients of presumed cardioembolic origin, and those with cryptogenic stroke who were proved with other investigations to have cardioembolic source.

[II] Exclusion criteria: Patients with any of the following criteria were excluded from the study: Intracerebral haemorrhage, atherothromboembolic stroke, lacunar strokes "small vessel disease, recurrent stroke, hypercoagulable haematological disorders, demyelinating and vasculitic disorders, other causes of cerebral and spinal hemiplegia, space-occupying lesion, other neurological causes of acute focal cerebral dysfunction such as head trauma, infection, and neurovasculopathy, organ failure (e.g., hepatic failure, renal failure, heart failure and hypoglycemia) and patients with diseased carotid artery: stenosis (\geq 50%) or plaques.

METHODS

After taking written consent, all patients in the study cohort were subjected to the following:

Initial general and clinical examination, CT and MRI, carotid doppler, echocardiography and laboratory investigations.

[A] On admission:

(1) Clinical assessment: including

(I) Detailed history taking with paying special attention to past medical history obtained from the patients or their relatives to establish the presence of any stroke risk factor: hypertension, diabetes mellitus, dyslipidaemia. And smoking.

- Cardiac diseases were determined as those having previous clinical diagnosis with ECG and/or Echo abnormalities.

- Those with cryptogenic stroke who were proved after investigations to have cardioembolic source

II) Full general examination:

Routine general examination of stroke patients including careful cardiac auscultation.

(III) Thorough neurological examination including evaluation of stroke severity on admission using:

- Glasgow coma scale (GCS)**, for assessment of the level of consciousness⁽⁹⁾.
- The Canadian neurological scale (CANS)**⁽¹⁰⁾. Stroke severity was categorized into mild severity if CANS score >6.5 and severe stroke if CANS score ≤6.5⁽¹¹⁾.
- The modified National Institute Of Health Stroke Scale (mNIHSS)**. (mNIHSS) is a quantitative measure of stroke-related neurological deficit that was developed for prospective clinical research. It is a test that widely used in clinical trials and practice to assess neurological outcome and degree of recovery⁽¹²⁾.

-The clinical assessment was repeated for every patient along the 5 visits of the study period.

I) Routine laboratory investigations:

Complete blood count, erythrocyte sedimentation rate, blood glucose level, lipid profile, liver and kidney function tests, prothrombin time, concentration and international normalized ratio (PT, PC and INR) and activated partial thromboplastin time (aPTT), Cardiac enzymes(LDH ,CK-MB). Protein C, S, lupus anticoagulants and other coagulation protein when indicated.

(3) Cardiac investigations:

- Twelve- lead eletrocardiography** (12-lead ECG) .

b- Echocardiography:

* Transthoracic echocardiography (TTE)

* Transesophageal echocardiography (TEE) provides more information about the atria than TTE in case of atrial septal aneurysm, PFO, atrial myxoma atrial appendage thrombus, mitral valve vegetations, infective endocarditis and nonbacterial thrombotic endocarditis.

(4) Carotid doppler ultrasonography

(5) Neuro-imaging study:

The patients in the study will have CT scan and/or MRI of the brain done to prove the diagnosis and to determine site, size of brain infarction. The size of the infarct was estimated according to the rules used by **Castillo et al.**⁽¹³⁾.

Size = $0.5 \times a \times b \times c$, as a and b represented the largest perpendicular diameters measured on CT

and c = Slice thickness which is 9 mm. The size of brain infarct on CT was classified as follow⁽¹⁴⁾ .:

1. Large infarct: 3 cm or more.
2. Medium-sized infarct: less than 3 cm and more than 1.5 cm.
3. Small infarct: less than 1.5 cm.

[B] Follow-up assessment of the patients:

The patients in the study were followed-up for 6 weeks from the date of admission and throughout 5 visits: clinical neurological, general, use of the previously mentioned scales in addition to modified Rankin scale (mRS) to assess the functional outcome. The (mRS) ranging from 0(no symptoms at all to 6 (Dead). outcome was defined as independence or good (mRS =0-2); poor (bad) outcome was defined as dependence (mRS = 3 - 5) and death (mRS = 6)⁽¹⁵⁾.

Statistical analysis

The data were tabulated and statistically analyzed using **Epi-INFO** and **SPSS** Version 15 software package, data were expressed as mean ±SD. Student 't' test, chi square "X" and correlation coefficient "r" were used for analysis of the results, logistic regression models were also used to assess independent predictors of outcome⁽¹⁶⁾.

RESULTS

This prospective follow up study was conducted on 40 patients with first-ever cardioembolic ischaemic stroke. They included 23 males with mean ages(±SD)of 40.9±24 years ,and 17 females with mean ages (±SD) of 41.2± 17.7 years. They were subdivided into four groups according to their ages, their mean age in different groups were (16.2±5.3, 27±5.5, 51.4±5.9, 68.7±5.2) years in group I, II, III and IV respectively

We found The vascular risk factors including hypertension,diabetes mellitus, hypercholesterolemia and smoking were significantly higher in older age groups (group III and IV) than younger one (group I and II) of CES as percentage of hypertension was (0.0%, 10%, 70% and 100% in group I, II, III and IV respectively, p=0.001), diabetes mellitus represented (0.0%, 0.0%, 50%, 60% in group I, II, III and IV respectively, p=0.001), hypercholesterolemia was shown in (0.0%, 0.0%, 40%, 50% in group I, II, III and IV respectively, p=0.007) and smoking was found in (0.0%, 0.0%, 20% and 50% in group I, II, III and IV respectively, p=0.008) (**table2**).

Regarding the distribution of major and minor cardioembolic sources of cerebral embolism in the studied CES groups we found that AF was significantly higher in (group IV and III 100% and 90% respectively than group II and I 30% and

0.0% respectively, $p=0.001$), RHD was significantly higher in (group II 70% than other groups, $p=0.01$), IHD was significantly higher in group IV and III 80% and 60% respectively whereas absent in other group, $p=0.001$) and MVP were found to be significantly higher in group I (50%) than other groups 20% in group II and 0.0% in both group III and IV, $p=0.008$) (**table 3**).

Statistically significant higher percentages of pneumonia, bed sores and recurrent stroke were recorded in older age groups than younger ones, pneumonia {80%, 60%, 20% and 10% in groups IV, III, II and I, respectively, $p=0.003$ }, bed sores {50%, 20%, 0.0%, 0.0% in groups IV, III, II and I respectively, $p=0.001$ }. Recurrent stroke during the period of follow-up were higher in the 4th group: 40% in the 4th group, 10% in the 3rd group whereas the 2nd and 1st group showed no recurrent stroke ($p=0.012$) (**table 4**).

On studying the functional outcome as assessed by mRS in the studied CES groups during follow up visits of study period (**table 5**), a highly statistically significant difference in mean scores of mRS between the first and fifth visit were only recorded in groups I, II and III of CES patients denoting improvement of functional outcome during the follow up visits of study period ($p<0.001$), while the old age group IV (60-80 years) didn't show any statistical difference in mean values of mRS during follow up visits.

On doing a comparison between AF, IHD and RVHD regarding initial stroke severity and functional outcome among CES patients (**table 6**), the results showed that patients with AF and IHD had statistically significant more severe strokes as assessed by CANS and mNIHSS than those with

RVHD (77.3% of AF and 78.6% of IHD had CANS score <6.5 Vs 38.5% of RVHD, $P=0.03$), (72.7% of AF, 71.4% of IHD had mNIHSS score ≥ 12 Vs 30.8% of RVHD, $P=0.03$). Regarding functional outcome, death (mRS =6) was significantly higher in AF patients (36.4% in AF, 35.7% in IHD, and 0.0% in RVHD, $P=0.04$).

Multiple logistic regression analyses for independent significant predictors of 45-day functional outcome in patients with first-ever CES (**Table 7**) showed factors associated with poor functional outcome. Old age, hypertension, AF, initial stroke severity, large infarction size, haemorrhagic transformation, length of hospital stay, and elevated serum glucose level were found to be associated with significant increase of OR of poor functional outcome among the studied CES patients.

There was a significant positive correlation between initial neurological severity as assessed by mNIHSS and functional outcome by mRS at the end of the study period in CES patients. ($p=0.01$) (**table 8**) and **fig. (1)**.

On comparing different stroke severity scales (GCS, CANS and mNIHSS) regarding their sensitivity and specificity in predicting outcome in CES patients (**table 9**). GCS had (50% sensitivity, 100% specificity with positive predictive value of 100.0 and accuracy of 85.0%), CANS had (100% sensitivity, 64.3% specificity with positive predictive value of 54.5 and accuracy 75.0%) and mNIHSS had (75.0% sensitivity, 75.0% specificity with positive predictive value of 56.3 and accuracy of 75.0%). GCS was the most accurate stroke severity scale in predicting outcome.

Table (1): demographic data in different age groups of cardioembolic ischaemic stroke patients (CES).

Groups	Group I (n = 10)		Group II (n = 10)		Group III (n = 10)		Group IV (n = 10)		Test	P
Variable	Age <20 y		20-<40 y		40-<60		60-80			
Age										
Range	3-19		22-28		44-60		62-75			
X±SD	16.2±5.3		27±5.5		51.4±5.9		86.7±5.2			
Sex										
	N	%	N	%	N	%	N	%	χ^2	
Male	8	80.0	4	40.0	3	30.0	8	80.0	8.49	0.13
Female	2	20.0	6	60.0	7	70.0	2	20.0		
Residence										
									χ^2	
Rural	8	80.0	7	70.0	6	60.0	7	70.0	0.95	NS
Urban	2	20.0	3	30.0	4	40.0	3	30.0	0.8	NS

Table (2): risk factors distribution among different groups of cardioembolic ischaemic stroke.

Risk factors	Group I		Group II		Group III		Group IV		Test χ^2	P
	Age <20 y		Age (20-<40)		Age (40-<60)y		Age (60-80)y			
	N	%	N	%	N	%	N	%		
Hypertension	0	0.0	1	10.0	7 ⁺	70.0	10 ⁺	100.0	27.8	0.001**
Diabetes mellitus	0	0.0	0	0.0	5 ⁺	50.0	6 ⁺	60.0	15.4	0.001**
Hypercholesterolemia	0	0.0	0	0.0	4 ⁺	40.0	5 ⁺	50.0	11.9	0.007**
Smoking	0	0.0	0	0.0	2	20.0	5 ⁺	50.0	11.6	0.008**

+ P<0.05 when compared with other groups.

Table (3): distribution of high- and low-cardiac sources of embolism in different age groups of cardioembolic stroke.

Cardiac Source of embolism	Group I		Group II		Group III		Group IV		Test χ^2	P-value
	Age <20 ys (n=10)		Age 20-<40 (n=10)		Age 40-<60 ys(n=10)		Age 60-80 ys (n=10)			
	No	%	No	%	No	%	No	%		
I- High risk										
-Atrial fibrillation	0	0.0	3	30.0	9	90.0 ⁺	10	100.0 ⁺	27.8	0.001**
Non-valvular (NVAf)	0	0.0	1	10.0	6	60.0 ⁺	10	100.0 ⁺	26.5	0.001**
Valvular AF (VAF)	0	0.0	2	20.0	3	30.0	0	0.0	9.83	0.12
-Rheumatic heart disease	3	30.0	7	70.0 ⁺	3	30.0	0	0.0	11.28	0.01*
-Ischaemic heart disease	0	0.0	0	0.0	6	60.0 ⁺	8	80.0 ⁺	22.42	0.001**
-Prosthetic valve	1	10.0	5	50.0	0	0.0	0	0.0	6.67	0.08
-Infective Endocarditis	1	10.0	1	10.0	0	0.0	0	0.0	2.11	0.55
-Dilated cardio-myopathy	0	0.0	1	10.0	1	10.0	0	10.0	2.11	0.55
II- Low risk										
-Mitral valve prolapse	5	50.0 ⁺	2	20.0	0	0.0	0	0.0	11.6	0.008**
-Patent foramen ovale	0	0.0	1	10.0	0	0.0	0	0.0	3.08	0.37
-PFO +ASA	1	10.0	0	0.0	0	0.0	0	0.00	3.08	0.37
-Papillary fibroblastoma	1	10.0	0	0.0	0	0.0	0	0.0	3.08	0.37

+ P<0.05 when compared with other groups.

Table (4): complications in different age groups of CES during study period.

Complication	Group	Group I (<20 y)		Group II (20-<40 y)		Group III (40-<60 y)		Group IV (60-80 y)		Test χ^2	P-value
		N	%	N	%	N	%	N	%		
Systemic											
*Pneumonia		1	10.0	2	20.0	6	60.0 ⁺	8	80.0 ⁺	13.4	0.003**
* Urinary tract infection		0	0.0	2	20.0	4	40.0	5	50.0	7.4	0.06
* Bed sores		0	0.0	0	0.0	2	20.0	5	50.0 ⁺	11.6	0.001**
*Heart failure		1	10.0	1	10.0	1	10.0	3	30.0	2.35	0.5
- Neurological											
* Recurrent stroke		0	0.0	0	0.0	1	10.0	4	40.0 ⁺	9.83	0.021*

+ P<0.05 when compared with other groups.

Table (5): functional outcome as assessed by mRS in different age groups of CES patients during follow up visits of study period

Outcome mRS	Follow up visitis					Test F	P
	1 st visit (2 nd day)	2 nd visit (7 th day)	3 rd visit (15 th day)	4 th visit (30 th day)	5 th visit (45 th day)		
Group I (<20y)							
Range	2 - 5	1 - 5	1 - 5	0 - 6	0 - 1		
X±SD	3.2±1.0	2.7±1.1 ⁺	2.0±1.1 ⁺	1.8±1.6 ⁺	0.44±0.5 ⁺	8.83	0.001**
Group II (20-40y)							
Range	4 - 5	3 - 6	2 - 4	1 - 3	0 - 2		
X±SD	4.1±0.3	3.7±0.94	2.7±0.8 ⁺	1.8±0.6 ⁺	1.33±0.7 ⁺	27.2	0.001**
Group III (40-60y)							
Range	3 - 5	3 - 5	2 - 5	2 - 6	0 - 3		
X±SD	4.5±0.7	4.2±0.8	3.5±0.85 ⁺	3.3±1.3 ⁺	2.7±0.9 ⁺	6.07	0.001**
Group IV (60-60y)							
Range	4 - 5	2 - 5	1 - 5	1 - 6	0 - 6		0.62
X±SD	4.5±0.7	4.2±1.0	3.9±1.4	3.9±1.96	3.5±2.0	1.38	NS

+ P<0.05 by paired analysis, there was a significant change from the first visit.

Table (6): comparison between AF, IHD and RVHD regarding initial stroke severity and functional outcome among CES patients.

Cardiac risk factors	AF (n = 22)		IHD (n = 14)		RHD (n = 13)		test X ²	P-value
	N	%	N	%	N	%		
Initial stroke severity								
- CANS ≥6.5	5	22.7	3	21.4	8	61.5 ⁺	6.72	0.03*
- CANS < 6.5	17	77.3	11	78.6	5	38.5		
- mNIHSS ≥ 12	16	72.7	10	71.4	4	30.8 ⁺	6.92	0.03
- mNIHSS < 12	6	27.3	4	28.6	9	69.2		
Functional outcome								
Good (mRS 0-2)	11	50.0	7	50.0	1	84.6	4.7	0.09
Poor (mRS 3-5)	3	13.6	2	14.3	2	15.4	0.34	0.84
- Death (mRS 6)	8	36.4	5	35.7	0	0.0 ⁺	6.39	0.04*

+ P<0.05 when compared with other groups.

Table (7): multiple logistic regression analyses for independent significant predictors of 45-day functional outcome in patients with first-ever CES.

Variable	OR (CI 95%)	P-value
*Old age	1.91(1.05-3.49)	0.001**
Hypertension	1.63 (0.89-2.96)	0.02
AF	1.83 (1.01-3.35)	0.01
m NIHSS> 6	2.67(1.45-4.39)	0.04
*CANS <6.5	2.55(1.39-4.71)	0.001**
large infarction size>3cm	2.07(1.13-3.79)	0.01
Haemorrhagic transformation	1.07(1.02-3.79)	0.021
Random blood glucose	1.99(1.09-3.63)	0.02
* Length of hospital stay	2.16(1.18-3.95)	0.002**

OR: Odds ratio. CI: Confidence interval

Table (8): correlation between initial neurological severity as assessed by mNIHSS and functional outcome by mRS at the end of the study period in CES patients.

r	P-value
0.56	<0.001**

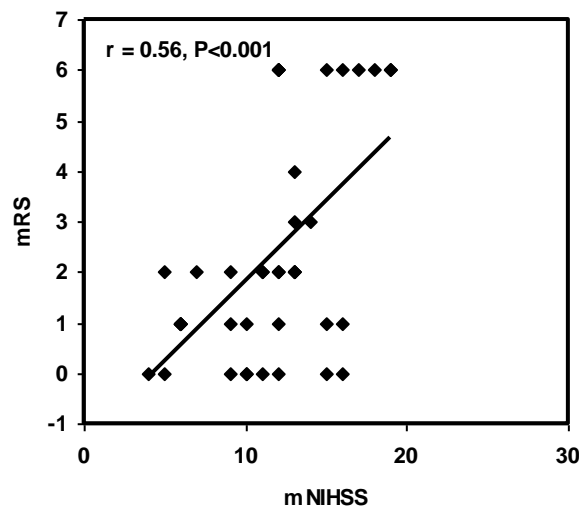


Fig. (1): correlation between initial neurological severity as assessed by mNIHSS and functional outcome by mRS at the end of the study period in CES patients.

Table (9): comparison between different stroke severity scales (GCS, CANS and m NIHSS) regarding their sensitivity and specificity in predicting outcome in CES patients.

	Sensitivity	Specificity	Predictive value		Accuracy
			+ve	-ve	
GCS	50.0	100.0	100.0	82.4	85.0
CANS	100.0	64.3	54.5	100	75.0
nNIHSS	75	75	56.3	87.5	75.0

* >70% accuracy (valid test)

DISCUSSION

Cardioembolic stroke (CES) accounts for about 20% of all ischaemic strokes. Various cardiac conditions either major or minor sources

have been clearly associated with an increased risk of ischaemic stroke. The high- risk cardiac factors that independently increase the risk of stroke include AF, rheumatic valvular heart disease,

myocardial infarction, coronary artery disease, congestive heart failure^(2,3).

In the current study, concerning the distribution of underlying vascular risk factors in different age groups of our CES patients, it was noticed that hypertension, diabetes mellitus, hypercholesterolemia and smoking were significantly higher in older age groups than younger age groups of CES patients, hypertension was (100%, 70%, 10% and 0.0% in group IV, III, II, I of CES respectively, $p=0.001$), diabetes mellitus was detected in (60%, 50%, 0.0%, 0.0% in group IV, III, II, I of CES respectively, $P=0.001$), hypercholesterolemia (50%, 40%, 0.0%, 0.0% in group IV, III, II, I of CES respectively, $p=0.007$) and finally smoking was found in (50%, 20%, 0.0%, 0.0% in group IV, III, II, I of CES respectively, $p=0.008$), these data were in accordance with the results of the study done by **Essa et al.**⁽¹⁷⁾ on risk factors and outcome of stroke where they found that the prevalence of hypertension is increasing with age 42.9% of their patients below the age of 45 had hypertension, this prevalence increased to (95.1%) in the age group 45-65, and increased more to (96.2%) in the age group >65 years and this was statistically significant. The same finding regarding increased prevalence of diabetes mellitus, hypercholesterolemia and smoking in older age groups > 65 years was also reported by **Essa et al.**⁽¹⁷⁾.

In the present study, on studying the distribution of both high and low cardiac sources of brain embolism in different age groups of CES patients, we founded that the presence of AF was significantly higher in older age groups than younger groups, (percentage of AF was 100% in group IV: ages 60-80 years, 90% in group III: ages 40-<60 years vs 30% in group II: ages 20-<40 years, 0.0% in group I: ages <20 years, $p=0.001$), our finding was supported by results of the study of **Arbiox and Alio**⁽¹⁸⁾ who showed that the prevalence of AF increases with age, and the attributable risk of ischaemic stroke due to AF rises from 1.5% at the age of 50 years to 24% at the age of 80 years, moreover the incidence of cardioembolic stroke in patients with NVAF was estimated to be 2-7 times higher than in people without AF and those with VAF. Our finding about increased percentage of AF in older age groups was also confirmed by results of **Yasaka et al.**⁽¹⁹⁾ who studied the pathophysiology of CES in different age groups and concluded that AF; specifically NVAF was the most common cardiac source of cerebral embolism in older age of 65-85 years. As regards the distribution of IHD in

different ages of our study groups, significantly higher percentage of IHD were reported in older age groups than younger ones (80%, 60% in group IV and group III vs 0.0% in group I and group II respectively, $p=0.001$), a finding which was in accordance with data obtained by studies of **Marini et al.**⁽⁷⁾ and **Giacalone et al.**⁽⁴⁾ who reported higher prevalence of coronary heart disease in older age groups of cardioembolic ischaemic stroke. In explanation for that significant atio-pathogenic association between IHD and CES in older age groups, **Giacalone et al.**⁽⁴⁾ postulated that older age groups with IHD have more AF, transmural thrombus, thus increasing their embolic risk of developing stroke in this age group

Rheumatic valvular heart disease was significantly reported to be higher in group II cardioembolic stroke patients with ages ranging from 20-40 years (70% in group II, 30% in group I, III, while 0.0% in group IV, $p=0.001$), these results were in agreement with **Ghandehari and Moud**⁽²⁰⁾ who studied the aetiology of cardioembolic stroke in 60 Iranian patients and found that rheumatic heart disease was constituting 32.8% of stroke aetiologies in young adult patients ages 15-45 years. Our finding concerning this issue was also consistent with results of the study done by **Spengos and Vemmos**⁽²¹⁾ on the aetiology and outcome of cardioembolic stroke in young adults and concluded that that rheumatic valvular heart disease and prosthetic valves were the most common aetiology of CES in young adults aged from 20-49 years, and more common in developing countries due to less effective eradication of streptococcal infection in these countries. The documented rates of cardioembolism in two studies from Iran and Tunisia reported cardioembolic stroke as the most frequent stroke subtype among young individuals with rheumatic valvular heart disease and prosthetic valves^(22,23). As far as minor cardiac sources of cerebral embolism were concerned in this study, we noticed statistically significant higher ratio of mitral valve prolapse in young age groups of cardioembolic stroke patients in ages less than 20 years (50% in group I ages less than 20 years, 20% in group II ages from 20-<40 years vs 0.0% in groups III and IV ages from 40-<60 and 60-80 years respectively, $p=0.008$), a finding which was in agreement with **Ghandehari and Moud**⁽²³⁾ who showed in their study that MVP was reported to be an important potential minor cardioembolic source in younger age groups. Moreover **Avierinos et al.**⁽²⁴⁾ in their study found that up to one third of patients under the age of 45 years with cerebral infarction had MVP and added that mitral leaflet regurg resulting from MVP

plays an important role in causing cerebral infarction. When studying the distribution of other minor cardiac sources of brain embolism among different age groups of our CES patients, patent foramen ovale was found to cause ischaemic stroke in only one case in age group from 20-<40 years (10% of group II and 2.5% of total patients), combined patent foramen ovale and atrial septal aneurysm caused ischaemic stroke in one case of age group I less than 20 years (10% of this age group and 2.5% of total patients), while papillary fibroblastoma was detected in one patient under age 20 years (10% of this age group and 2.5% of total patients), but this difference was not statistically significant in different age groups, may be due to few numbers of PFO cases detected during study period and also due to rare prevalence of cardioembolic stroke under age of 20 years. Our finding was matching to the study of **Spengos and Vemmos**⁽²¹⁾ who studied the aetiology of cardioembolic stroke in Greek patients aged 15-45 years and found that nearly half of the cases (48.5%) were attributed to congenital interatrial septal defects (PFO and ASA), this probably due to better and more diagnostic techniques and work up in search for potential cardiac risk factors in this group of patients who were previously accused as cryptogenic stroke.

In the current study, on studying the frequency of complications in different age groups of CES patients during study period, pneumonia and bed sores, recurrent stroke were found to be significantly higher in older age groups of CES than in younger patients (pneumonia occurred in 80%, 60% in a age group IV and III Vs 20%, 10% in group II and I respectively, $p=0.003$), (Bed sores were reported in 50% in group IV vs 20% in group III and 0.0% in group I and II, $p=0.001$), these findings were in agreement with results of **Yasaka et al.**⁽¹⁹⁾ and **Arboix and Alió**⁽²⁵⁾ who stated that the complications of CES were more evident in older patients, this because old patients usually had a major cardioembolic source of cerebral embolism, had more severe strokes on admission, more large infarction, least rate of functional recovery and longer in-hospital stay and hence suffering more complications than younger age groups.

In the current study, CES patients were prospectively followed up and different types of outcomes among the studied patients were recorded; recovery (mRS score was 0-2), moderate to severe disability (mRS score was 3-5), death (mRS score 6), and recurrent stroke. As far as the clinical outcome at the end of the study period in different age groups of CES patients were

concerned, we compared functional outcome as assessed by mRS in different age groups and found that improvement (mRS 0-2) was significantly higher in younger age groups of CES (ages less than 20 years and ages from 20-<40 years) than in older ones (ages 40-<60 years and ages 60-80 years). Improved patients represented (90%, 90%, 60%, 30% in group I, II, III and IV respectively, $p=0.01$). On the other hand, mortality (mRS 6) was reported to be significantly higher in older age groups (60-80 years) than in younger age groups of the studied patients, mortality was present in (60% in group IV 60- vs 20%, 10%, 10% in group I, II, III respectively, $p=0.02$), also recurrent stroke was significantly higher in older age groups than younger ages (40% in group IV age 60-80 years vs 10% in group III and 0.0% in CES groups I, II respectively, $p=0.012$). These findings were in accordance to the results obtained by **Bagg et al.**⁽²⁶⁾ who studied the effect of age on functional outcome after stroke and concluded that advancing age had negative impact on functional outcome when assessed at discharge and explained that significant negative association between age and outcome by the direct effect of age itself and by an indirect effect through age-related comorbidities such as hypertension, diabetes mellitus and AF, IHD which in turn affect negatively the outcome in such age group. Our results were also supported by the recent study of **Spengos and Vemmos**⁽²¹⁾ on aetiology and outcome of cardioembolic stroke in young adults that overall outcome in this specific patient group is surprisingly good. The probability of recurrent vascular events was very low and the probability of 10-year survival was almost 90%. Moreover young patients with cardioembolic stroke due to atrial fibrillation showed mild neurological deficits and remarkably good courses compared to older individuals, who are known to present more severe clinical syndromes and permanent handicaps. In explanation for that **Spengos and Vemmos**⁽²¹⁾ showed that causes of cardioembolism and clinical outcome in young adults differ significantly from those in the elderly due to difference in underlying cardiac source of cerebral embolism between the two age groups. Similarly, **Gaintin et al.**⁽¹⁵⁾ studied the effect of age on the outcome of ischaemic stroke and found that death occurred in old ages (90% over 85 years), moreover, among the patients who died cardioembolic cerebral infarction was more prevalent than in the surviving group (55.6% vs 21.4%). It was found also in the current study that mortality was associated with stroke progression and embolic recurrence as 5 (2.5%) cases of the dead patients were having recurrent stroke with the first 14 days of first stroke onset, a finding which

was in agreement with data obtained from the study of **Arboix et al.**⁽²⁷⁾ regarding embolic recurrence in CES, who postulated that the risk of early embolic recurrence in cardioembolic stroke varies between 1% and 22%, adding that old ages with CES were more liable to embolic recurrence than younger ages.

As far as short-term outcome in different age groups of CES patients was concerned in this study, functional outcome as measured by mRS was assessed on admission and during follow up visits in each age group of CES patients separately, we reported significant improvement of functional outcome in younger age groups I, II, III during follow up visits while old age group IV ages 60-80 years didn't show any functional improvement at the end of study period. These findings were confirmed by **Spengos and Vemmos**⁽²¹⁾ who noticed in their study on aetiology and outcome of cardioembolic stroke in young adults that overall outcome in this specific patient group is surprisingly good. The probability of recurrent vascular events was very low and the probability of 10-year survival was almost 90%. Moreover young patients with cardioembolic stroke due to atrial fibrillation showed mild neurological deficits and remarkably good courses compared to older individuals, who are known to present more severe clinical syndromes and permanent handicaps. In explanation for that **Spengos and Vemmos**⁽²¹⁾ showed that causes of cardioembolism and clinical outcome in young adults differ significantly from those in the elderly as congenital defects of the atrial septum, such as PFO and ASA seem to be the leading cause of cardioembolic strokes and the severity of strokes due to PFO and/or ASA is considered to be low, moreover outcome was excellent, with no permanent disability, stroke recurrence or deaths in young patients, on the other hand and in agreement with other studies, cardioembolic strokes in elderly usually caused by major sources of cerebral embolism like AF and IHD, suffered more severe strokes, liable to more complications and longer in hospital stay and hence show poor functional outcome.

In the current study, on doing a comparison between AF, IHD and RVHD regarding initial stroke severity and functional outcome, we reported that CES patients with AF and IHD had statistically significant more severe strokes as assessed by CANS and mNIHSS than those with RVHD (77.3% with AF and 78.6% with IHD had CANS score < 6.5 Vs 38.5% with RVHD, $P=0.03$), (72.7% with AF, 71.4% with IHD had mNIHSS score ≥ 12 Vs 30.8% of RVHD, $P=0.03$). Regarding functional outcome, death (mRS =6) was significantly higher in CES

patients with AF and IHD (36.4% in AF, 35.7% in IHD, and 0.0% in RVHD, $P=0.04$). These findings were in agreement to results of **Winter et al.**⁽²⁸⁾ who showed in their study on the relationship between different cardiac sources of cerebral embolism and functional outcome that cardiac conditions that predispose to ischaemic stroke (such as extensive acute myocardial infarction, chronic myocardial injury with left ventricular aneurysm formation, and nonvalvular atrial fibrillation) are themselves associated with severe strokes, poor outcome and increased mortality. In explanation, old age, other vascular comorbidities such as diabetes and hypertension that may underlie such heart diseases may also increase risk for poor outcome following stroke. Moreover Stroke patients with AF more often have large cortical infarct and less frequently lacunar infarction, compared with patients without AF and hence suffered more severe stroke than patients with other cardiac risk factors⁽²⁹⁾. On the other hand **Ruttmann et al.**⁽³⁰⁾ in their study showed that CES with RVHD had less severe strokes and better functional outcome and attributed that for relatively young age of patients, beside their benefit from anticoagulation without feared side effects as in older age groups with AF or IHD.

On doing multiple logistic regression models to demonstrate the most important and independent factors that affect functional outcome of CES patients at the end of study period which were old age, HTN, AF, initial stroke severity, large infarction, haemorrhagic transformation, length of hospital stay, the presence of complications as bed sores, pneumonia, recurrent stroke and elevated serum levels of glucose. These findings were supported by many studies^(17,25,31) that showed that old age, history of HTN, DM, AF, initial stroke severity, large infarction size and haemorrhagic transformation were strongly linked to poor outcome and dependency in stroke patients. **Aslanyan et al.**⁽³²⁾ in their study found also that 65% of ischaemic stroke patients with good recovery were younger, had lower rates of atrial fibrillation, hypertension, and total anterior circulation infarction, and had higher rates of lacunar stroke compared with patients without recovery who were older, having higher rates of AF, hypertension, higher levels of blood glucose, had higher mNIHSS scores at baseline, at 7 and 90 days, suffered more from TACS.

On doing a correlation between the initial stroke severity as assessed by mNIHSS and final functional outcome as measured by mRS in the studied patients, a significant positive correlation was demonstrated between initial mNIHSS scores and functional outcome by mRS at the end of

study period ($r = 0.41$, $p < 0.01$), and this significant positive correlation was supported by the study of **Meyer et al.**⁽³³⁾ who stated that mNIHSS has very good sensitivity, specificity and accuracy in predicting clinical outcome as assessed by mRS. Several studies investigated the relationship between stroke severity and outcome and concluded that the NIHSS score strongly predicts the likelihood of a patient's recovery after stroke. A score of ≥ 16 forecasts a high probability of death or severe disability whereas a score of < 6 forecasts a good recovery^(34,35,36).

In the current study, on comparing different stroke severity scales (GCS, CANS and mNIHSS) regarding their sensitivity and specificity in predicting outcome in the studied CES patients, we found that GCS had (50% sensitivity, 100% specificity with positive predictive value of 100.0 and accuracy of 85.0%), CANS had (100% sensitivity, 64.3 % specificity with positive predictive value of 54.5 and accuracy 75.0%) and NIHSS had (75.0% sensitivity, 75.0% specificity with positive predictive value of 56.3 and accuracy of 75.0%). GCS was the most accurate stroke severity scale in predicting outcome (accuracy of 85%). Our results concerning that issue were matching to that of **Grote et al.**⁽³⁷⁾ who reported that the diagnostic value of $GCS \leq 8$ had a sensitivity of (56.1%) but higher specificity (82.2%). In addition, the GCS score predicts both 2 week mortality and 3 month placement after stroke⁽³⁸⁾. In contrast to the results of our study, **Muir et al.**⁽³⁹⁾ postulated that the mNIHSS provided the most prognostic information: sensitivity to poor outcome (71), specificity, (90) and overall accuracy, (83), moreover logistic regression showed that the mNIHSS added significantly to the predictive value of all other scores, while baseline measurements on the CANS predict functional outcome 6 months after stroke.

CONCLUSION

Our results support the hypothesis that the overall short-term functional outcome of CES patients; in terms of (improvement, disability and death) was significantly better in younger than older age groups who had major sources of cerebral embolism like AF and IHD, had severe neurological deficits on admission, more large sizeable brain infarcts, more liable to in-hospital complications (pneumonia, bedsores and recurrent stroke), reflecting the negative impact of age on the functional outcome or could be attributed to difference in underlying cardiac source of cerebral embolism between the two age groups and the comorbid risk factors in elderly. Furthermore, old age, AF, the initial stroke severity as well as long

hospitalization and large infarction size in patients with CES and haemorrhagic transformation were considered to be the main predictors of high mortality and poor short-term functional outcome.

From this study, we can say that early recognition of cardiac diseases in different age groups, detection of other comorbid risk factors, good clinical, neurological and general care and thorough follow up and trials to avoid complications can help to improve outcome in different age groups. Evidence-based recommendations with more researches can improve the diagnostic and therapeutic strategies and thus improve survival and functional outcome in these patients.

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المآل قصير المدى في السكتة الدماغية الإحتشائية الناتجة عن اعتلال القلب في مختلف الأعمار

يعد القلب احد أهم المصادر الرئيسي للسدات المسببه للاحتشاء المخي حيث تشكل السكتات الدماغية الإحتشائية الناتجة عن أمراض القلب المختلفة ما يقارب ٢٠%. فهناك العديد من أمراض القلب المختلفة سواء الكبرى أو الصغرى و التي ترتبط بشكل وطيد بزيادة نسبه الخطر لحدوث السكتة الدماغية الإحتشائية. ان مآل و عواقب السكتة الدماغية الإحتشائية الناتجة عن اعتلال القلب تتأثر بالعديد من العوامل الديموجرافية و الاكلينيكية.

تهدف هذه الدراسة الى تقييم المآل قصير المدى في مرضى السكتة الدماغية الإحتشائية الناتجة عن اعتلال القلب وذلك في المراحل العمرية المختلفة خلال الست اسابيع الاولى من بدء الأعراض.

وقد أجريت هذه الدراسة على ٤٠ مريض يعانون لأول مرة من جلطة المخ الناتجة عن السدات القادمة من القلب وذلك خلال ٤٨ ساعة من بداية الأعراض [٢٣ ذكر تراوحت اعمارهم من ٣-٧٥ سنة ومتوسط العمر (٩,٤٠±٢٤) سنة و ١٧ انثى تراوحت اعمارهم من ١٤-٧٠ سنة ومتوسط العمر (٢,٤١±١٧) سنة] وتم تقسيم مجموعات المرضى إلى أربع مجموعات عمرية: **المجموعة الأولى:** اشتملت على ١٠ مرضى أعمارهم اقل من ٢٠ سنة ومتوسط أعمارهم ٢,٣±١٦,٢ سنة، **المجموعة الثانية:** اشتملت على ١٠ مرضى تراوحت اعمارهم من ٢٠-٤٠ أقل من ٤٠ سنة ومتوسط اعمارهم ٥,٥±٢٧ سنة، **المجموعة الثالثة:** اشتملت على ١٠ مرضى تراوحت اعمارهم من ٤٠-٦٠ أقل من ٦٠ سنة ومتوسط اعمارهم ٥,٩±٥١,٤ سنة، **والمجموعة الرابعة:** اشتملت على ١٠ مرضى تراوحت اعمارهم من ٦٠-٨٠ سنة ومتوسط اعمارهم ٥,٢±٦٨,٧ سنة. وقد أجرى لهم فحص اكلينيكي عام وفحص عصبي كامل وفحوصات معملية وفحوصات القلب المختلفة و اشعات مقطعية و رنين مغناطيسى و تم قياس شدة السكتة الدماغية بقياس جلاسجو للغيوبه و القياس الكندى العصبى و مقياس m NIHSS كما تم تتبع المرضى و تقييم المآل قصير المدى خلال ٦ اسابيع باستخدام مقياس رانكن المعدل.

وقد سجلت نسبه تحسن على مقياس رانكن المعدل ذات قيمة احصائية عالية في المجموعات العمرية الاصغر سنا (الاقل من ٢٠ سنة والذين تتراوح اعمارهم من ٢٠-٤٠ أقل من ٤٠ سنة) من مرضى السكتة الدماغية الناتجة عن اعتلال القلب، بينما كانت نسبه الوفيات والتكرار المبكر للسكتة الدماغية اعلى احصائيا في كبار السن (الذين تتراوح اعمارهم من ٤٠-٦٠ أقل من ٦٠ سنة ومن ٦٠-٨٠ سنة).

وجود فرق احصائي واضح في متوسط نتائج مقياس رانكن المعدل اثناء الخمس زيارات التي تم متابعة المرضى خلالها حيث كان متوسط النتائج في الزياره الخامسه في المرضى الذين اظهروا تحسن اقل احصائيا منه في الزياره الاولى عند الدخول وقد لوحظ هذا الفرق الاحصائي الواضح في المجموعات العمرية (الاقل من ٢٠ سنة، من ٢٠-٤٠ أقل من ٤٠ سنة و من ٤٠-٦٠ أقل من ٦٠ سنة) بينما اختفى هذا الفرق في المجموعة العمرية الاكبر (الذين تتراوح اعمارهم من ٦٠-٨٠ سنة) والذين لم يظهروا اى تحسن احصائي ملحوظ في مقياس رانكن المعدل خلال زيارت المتابعة الخمس.

-كان المرضى الذين يعانون من الرجفان الأذيني و احتشاء عضله القلب يعانون من سكتات دماغية أكثر حدة و نسب تحسن اقل من هؤلاء الذين يعانون من أمراض صمامات القلب الروماتيزمى.

سجلت علاقه طرديه ذات قيمة احصائية عالية بين حدة السكتة الدماغية للمرضى عند الدخول بمقياس (NIHSS المعدل) ودرجه التحسن (بقياس رانكن المعدل) في نهايه مدة الدراسة وأثبت ان مقياس جلاسجو لقياس شدة السكتة الدماغية كان أكثر المقاييس المستخدمه دقة وحساسيه و صلاحية للتنبؤ بالمآل قصير المدى في مرضى الدراسة.

ان المآل قصير المدى بشكل عام (متضمنا التحسن والاعاقه السريرييه والوفاة) خلال الست اسابيع الاولى من بدء الأعراض في مرضى السكتة الدماغية الإحتشائية الحادة الناتجة عن اعتلال القلب كان أفضل في المرضى صغار السن مقارنة بالمرضى الاكبر سنا والذين يعانون بنسبه أكبر من سكتات دماغية شديدة ويظهرون نسب إعاقه ووفاه أكبر، بالإضافة الى ذلك كان تقدم السن والرجفان الاذيني وشدة السكتة الدماغية وحجم الاحتشاء المخي والنزيف به وطول فترة البقاء في المستشفى و حدوث مضاعفات للمريض مثل الالتهاب الرئوى وقرح الفراش وتكرر الجلطات من بين عوامل التنبؤ بين المرضى.