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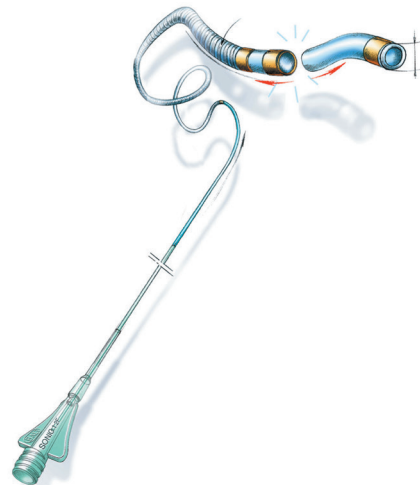Victor Erwin D. Jocson (Philippines) - *The Medical City*
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NOVEL TREATMENT OF DIRECT CAROTID CAVERNOUS FISTULA WITH XCALIBUR ANEURYSM OCCLUSION DEVICE: A CASE REPORT

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ABSTRACT

To report a case of post-traumatic direct carotid-cavernous fistula (CCF) treated with Merlin's XCalibur as a standalone treatment. XCalibur is a balloon mounted flow diverter covered with polymer biostable membrane. A single device was deployed across the rent which resulted in the complete exclusion of fistula. This is the second case of its kind to be reported for the treatment of post-traumatic direct CCF with an XCalibur device. The device proved to be effective and safe and did not require any additional coiling, thus this paper has immense value and benefit for the medical community at large as it displays a new technique being successfully used.

Key Words: Traumatic, Fistula, Direct, Sstent, Endovascular, High flow

INTRODUCTION

The idea behind treating a direct CCF is to occlude an arteriovenous shunt while preserving the patency of the concerned internal carotid artery (ICA)

Numerous strategies in the endovascular realm have been attempted in the last thirty years in a bid to gear the size and location of fistulous points while simultaneously ensuring venous outflow patterns.

In the past strategies included transvenous or transarterial access routes with detachable balloons, covered stents, coils, and liquid embolic agents. (1)

Transarterial embolization with flow diversion presents an alternative option that is possible and can be used in conjunction with coiling or even potentially standalone treatment method. (2)

In this case, we endeavor to evaluate the experience we had using membrane coated /covered stent (XCalibur Merlin MD) for endovascular treatment of direct CCF. To the best of the author's knowledge, this is just the second publication using XCalibur alone for the treatment of a direct CCF.

CASE DESCRIPTION

A 36-year-old man was referred to our institution complaining of pain in the right eye and displaying redness and swelling for over 2 months. There was no history given of nausea or vomiting but he did complain of having mild blurring of vision, double vision, and severe headaches in the past 2 weeks. A detailed history showed he had suffered a traumatic injury. An electrician by profession he had been electrocuted, receiving a head injury in the process that involved frontal skull fractures,

and resulted in an epidural hematoma with intracerebral hemorrhage. Additionally, he suffered burns and bone injuries on his extremities.

The patient got traditional treatment and was discharged from the local medical clinic following the relief of symptoms. He later developed further symptoms in his right eye 2 months later; this included redness, swelling, a blurring of vision, and visual decline in the right eye. There was no associated history of hypertension, diabetes, or any other infectious disease.

On examination, his visual equity was counting fingers in the right eye and 6/6 in the left. The intraocular pressure in the affected eye was 26mmHg and in the contralateral eye was 16mmHg. On physical examination, the right eye exhibited proptosis up to 23mm, mild ptosis, chemosis, eyelid swelling, and corkscrew hyperemia centered around the cornea. Left eye proptosis was 18mm. Furthermore, there was a slight restriction of movements in abduction and elevation. However, depression and adduction were normal. The left eye was unremarkable. Corneal reflex was intact in both eyes. The vitreous and lenses were clear. Fundoscopic examination showed there was no disc swelling or hemorrhages in either eye. Glaucoma was also ruled out.

INVESTIGATIONS

The MRI of the periorbital locale uncovered a dilatation of the right superior ophthalmic vein, slight thickening of the right lateral rectus muscle, and preseptal swelling. The neurological assessment was unremarkable aside from a periorbital bruit on the affected eye. The diagnosis of traumatic direct type of CCF was made and the patient was sent to the neuro-interventional department.

Investigation included MRI with orbital protocol which showed the right superior ophthalmic vein dilatation with preseptal swelling and thickening of the right lateral rectus muscle. Neurological examination did not reveal anything new except a periorbital bruit on the right side. Thus, a tentative diagnosis of right CCF was made and the patient was sent to a neuro-interventionalist. Digital subtraction angiography

was done to identify venous drainage patterns and to plan treatment. The DSA revealed a right direct (post-traumatic) CCF with a fistulous hole involving the anterior genu of the cavernous segment of ICA. The fistula was draining superiorly to the superior ophthalmic vein, angular vein, and common facial vein system, to pterygoid plexus inferiorly and reflux to cortical veins through the superior and inferior petrosal sinuses. Manual cross compression was performed which shows significant contralateral filling. Keeping in view the young age of the patient, we decided to use a membrane-based flow diverter stent, to preserve the parent vessel.

EMBOLIZATION TECHNIQUE

It was decided to treat the CCF with the deployment of XCalibur across the fistula. It is a balloon-expandable device pre-mounted on a balloon delivery catheter. The frame is coated with a porous ultra-thin polymeric film. The film serves to permanently occlude the neck of the aneurysm after deployment.

The patient was premedicated with a daily dose of aspirin 150mg and clopidogrel 75mg for 7 days. The right femoral artery access was made with a 6Fr long sheath Neuron MAX 088 (Penumbra USA) which was navigated up to the cervical segment of the right ICU. A 6Fr distal access catheter Navien (Medtronic USA) was navigated through the Neuron MAX catheter over a 035 guidewire and placed above the fistula at the cerebral segment of the right ICA.

The balloon-expandable stent of size (4.5mm x 15mm) was navigated through the 6 Fr guider over a Trexxas 014 microwire (Microvention) and deployed across the fistulous hole covering the rent with inflation of the balloon. The non-compliant balloon attached at the distal end of the catheter is designed to inflate the device to a controlled diameter at a given pressure.

After deployment, angiography showed significant device opening but an incomplete wall approximation at the inferior aspect causing an endoleak. Further, device expansion was done using an NChant rapid exchange balloon of size (4.75mm x 7mm). It was a non-compliant post-dilatation balloon used for post-deployment dilation of XCalibur AOD. Control angiogram

after post-deployment dilation with the balloon showed complete obliteration of the fistula.

Position of neuron guiding catheter and long 6 Fr sheath, Traxcess microwire visualized at right MCA distally, deployment balloon over which the flow diverter is mounted showing proximal and distal markers, flow diverter is also showing proximal and distal marker, post balloon angioplasty image showing complete expansion of device with no endoleak.

Immediate angiogram after deployment of XCalibur AOD in arterial and venous phase showing complete obliteration of fistula with delayed stasis in venous phase

OUTCOME AND FOLLOW UP

The patient was discharged on the third postoperative day and was continued with dual antiplatelets. A Follow-up angiogram to be performed after 6 months of the initial procedure showed complete exclusion of the fistula due to flow diversion. Clinically there was complete resolution of symptoms and the bruit had disappeared. The proptosis was 18mm in both eyes. The vision was improved from counting fingers. The eye movements were normal in all dimensions in the affected eye. Clopidogrel was stopped at 6 months and oral aspirin was prescribed for life.

DISCUSSION

Endovascular treatment of direct CCF has undergone an evolution over the past few years. The aim of treatment in direct CCFs is occlusion of tear between the ICA and the cavernous sinus while simultaneously keeping the ICA patent. (2)

The ideal method of occlusion of a fistula in the early days used to be arterial embolization using detachable balloons or the sacrificing of the parent artery if a defect was too large. (3) Balloons gained popularity in the early days but were unexpectedly withdrawn from the market in 2004. The transvenous or transarterial access routes used covered stents, coils, and liquid embolic agents and evolved as newer modalities came to the forefront. (1) Flow Diverting devices are intended for the treatment of complex cerebral aneurysms yet strategies and indications for FD keeps on advancing. As of late published case reports indicated promising outcomes for the treatment of

direct CCF with FD. (1) Over time its off-label indications have extended to incorporate carotid-cavernous fistulas (CCFs). (4) Case reports being published these days show promise with varied treatment modalities of diCCF with the use of flow diverters. (1)

Mahendran Nadarajah et al in their work described the first-ever case of a direct CCF treated solely with flow-diverting stents in 2012. (5) There are several cases described in the publications where direct CCF are treated with FD stent deployed inside the injured internal carotid artery and coils set inside the large sinus. (6) Various cases have in literature pointed to a direct CCF being treated with FD stent placement within the injured region of the carotid artery and coils being placed on the cavernous sinus. (6). Other studies demonstrate the intraprocedural direct CCF that developed immediately after flow diversion for the treatment of asymptomatic paraclinoid right internal carotid artery aneurysm and the use of another FD to close the fistula. (7) Further studies show that intraprocedural direct CCF were developed immediately after the flow diversion technique took hold and asymptomatic paraclinoid right internal carotid artery aneurysms were being treated with another FD to close the fistula. (7) The flow diverter is also used in those cases of Barrow type 'B' CCFs that have no vascular access (neither venous nor arterial). (8) Flow diverters have better flexibility and are easy to navigate in tortuous anatomy, hence they can be deployed easily. However, theoretically high flow fistulas cannot be treated alone by flow diverters due to patency of side branches, therefore several FD layers, additional venous coil occlusion, and embolization with liquid embolic agents is needed as adjuncts. Complete obliteration of a direct CCF may take a long time and long-term double antiplatelet therapy is mandatory. (1) On the contrary, XCalibur is a single device treatment, there is no need for coiling support. The point is to build metallic coverage and limit porosity in tear at the ICA segment with fistulous communication. The XCalibur AOD has a metallic coverage of roughly 65% (9) (10) in comparison to 10-20% of others, and hence it works properly.

Additionally, the device contains a biocompatible polymer membrane, and does not get absorbed but instead endothelized. The

fundamental downside to this strategy, as other FD stents, is the requirement for double antiplatelet treatment because of the danger of in-

stent thrombosis. This should be adjusted against the danger of further hemorrhage with regards to a CCF.

DECLARATION OF CONFLICT OF INTEREST

The author(s) declare that they do not have any potential conflicts of interest concerning the research, authorship, and/or publication of this article with Merlin MD Pte Ltd.

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FIGURE LEGENDS

Figure 1: Pre and post-procedure images demonstrating the reduction in redness and swelling of the right eye.
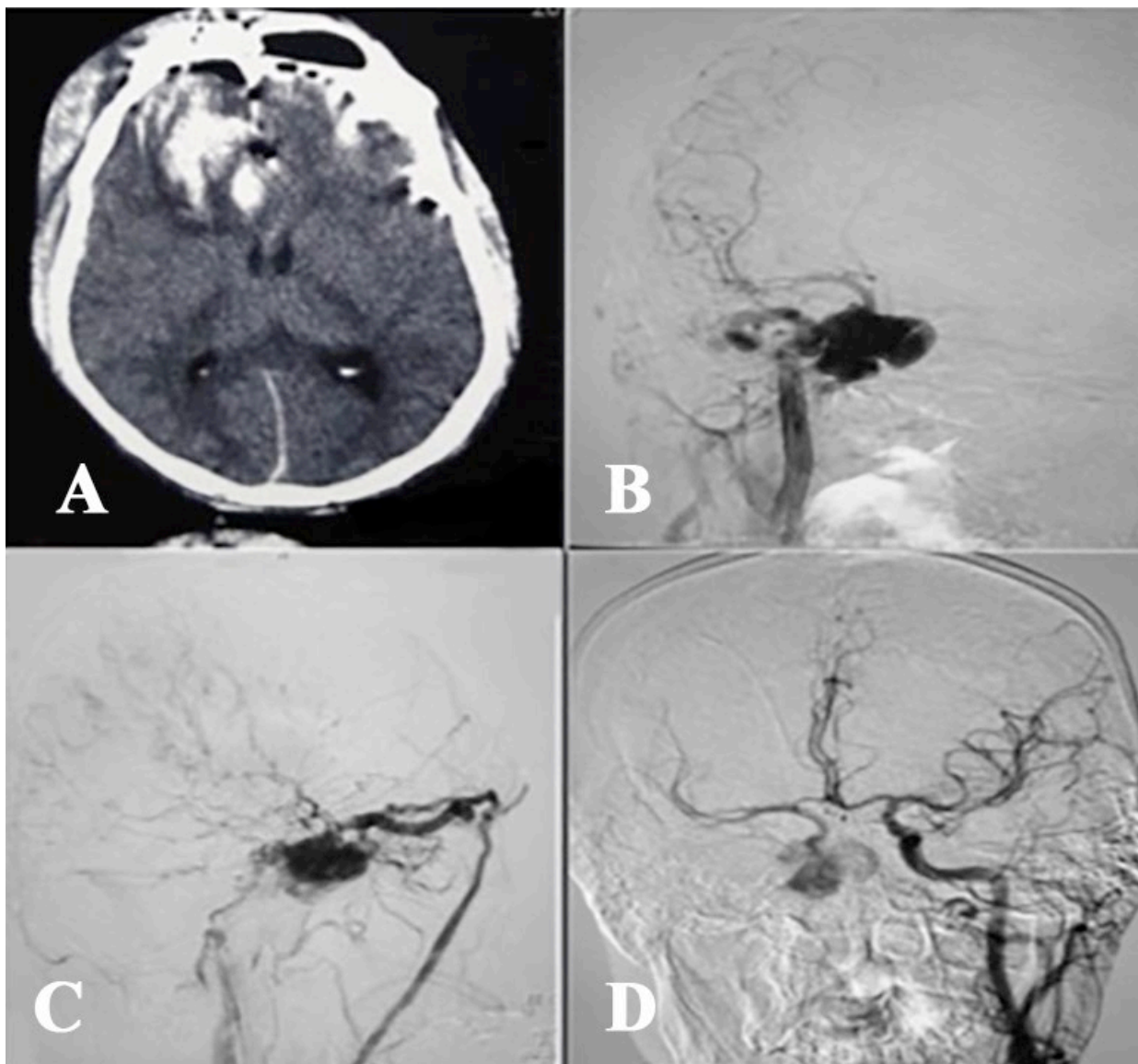
Figure 2: A) NCCT head axial section showing right frontotemporal epidural hematoma and intraparenchymal hemorrhage done 2 months before endovascular treatment. B-C) Diagnostic angiogram of right ICA showing right high flow CCF draining into superior ophthalmic vein and facial vein system. D) Diagnostic angiogram of left ICA (cross compression) showing filling of fistula from contralateral ICA.
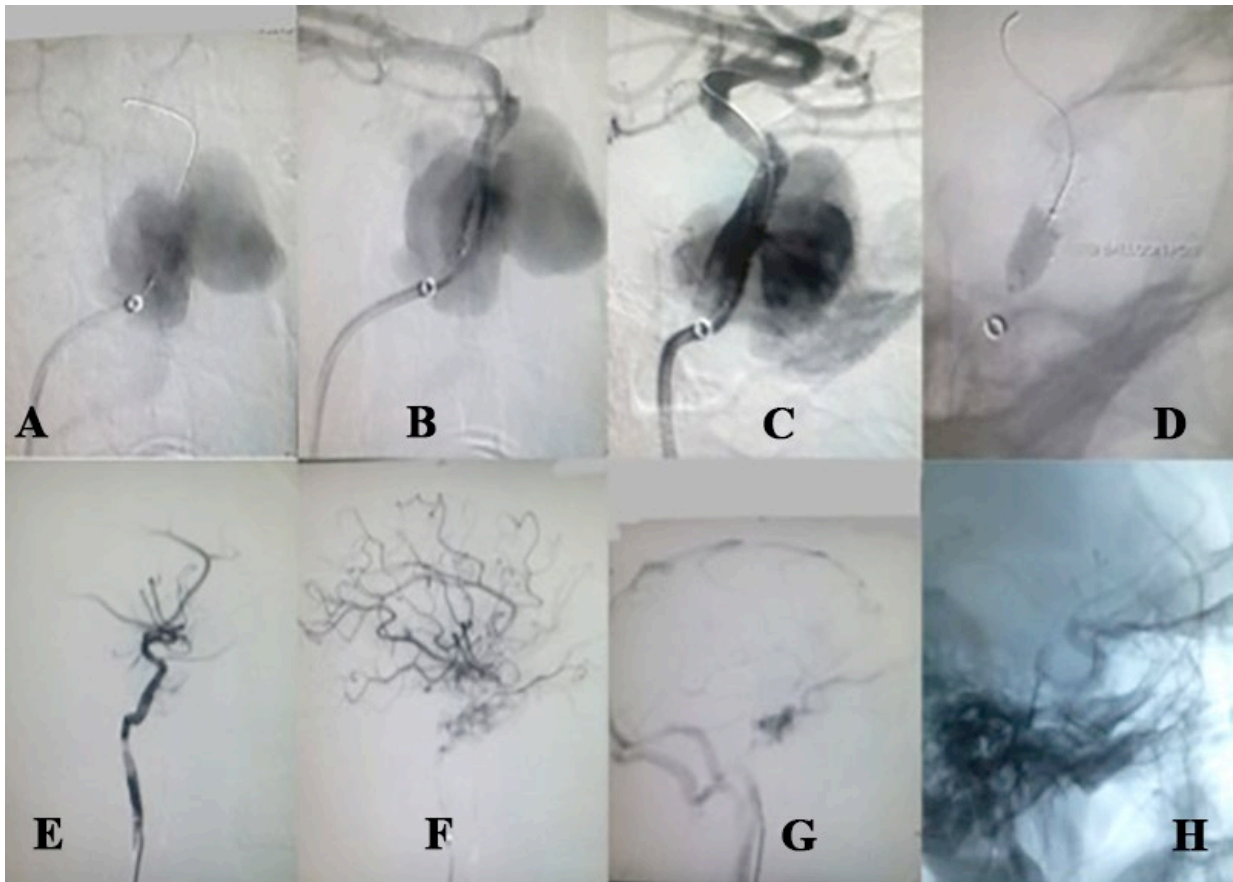
Figure 3: (A-B-C-D) Intraprocedural and post procedural (E-F–G-H) angiograms
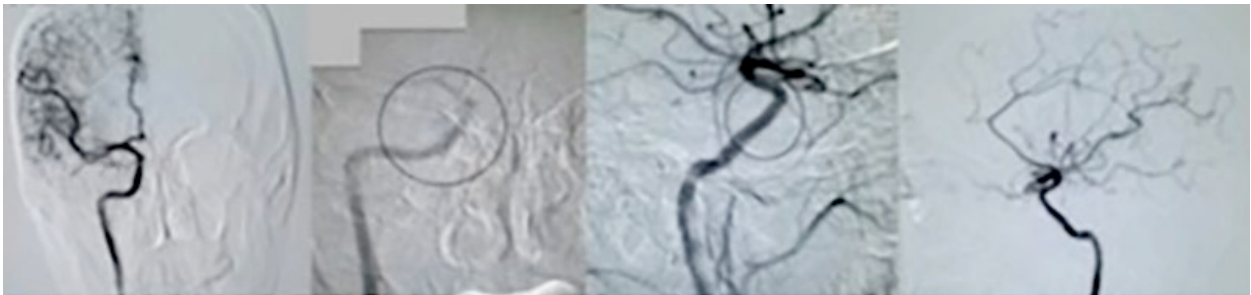
Figure 4: Follow up angiogram (right ICA, left ICA) after 6 months interval showing complete obliteration of fistula with no evidence of in-stent thrombosis
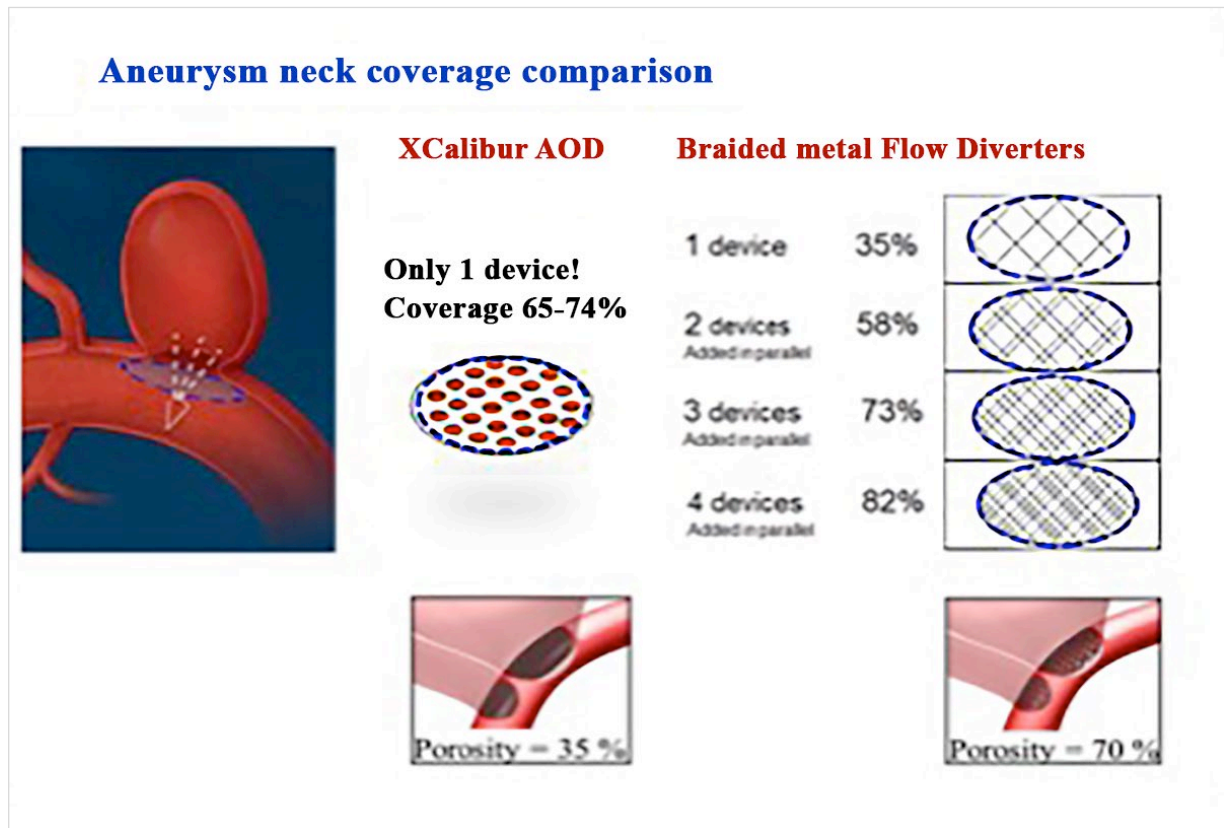
Figure 5: Demonstrating the coverage pattern of XCalibur in comparison to other Flow Diverter (Courtesy of Merlin MD)

THE IMPACT OF SOCIODEMOGRAPHIC VARIABLES ON RISK FACTORS ASSOCIATED WITH ISCHAEMIC STROKE PATIENTS BY AGE GROUP

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ABSTRACT
This study aims to identify the relevant risk factors based on different sociodemographic backgrounds among ischaemic stroke patients in relation to age. We included all adult ischaemic stroke patients from 1st January 2013 to 31st December 2019 who presented to Hospital Seberang Jaya. The study utilized data that were collected from medical records and were presented with descriptive and inferential statistics. Hypertension was common in male ($p=0.009$), female ($p<0.001$), Chinese ($p<0.001$), married ($p=0.006$), or single ($p=0.006$) ischaemic stroke patients with advancing age. Ischaemic stroke patients in their 50s who were female ($p=0.043$) or Indian ($p=0.005$) and Chinese patients ≥ 60 ($p=0.025$) more often presented with diabetes. Dyslipidaemia was predominant in ischaemic stroke patients who were male between 50 and 59 ($p=0.017$) or Chinese ≥ 60 ($p=0.041$). Male ($p=0.037$), female ($p=0.005$), Chinese ($p<0.001$), Indian ($p=0.022$), or married ($p=0.037$) ischaemic stroke patients with advancing age were more likely to be associated with at least two risk factors. There was a declining proportion of fewer than two risk factors among ischaemic stroke patients with the same sociodemographic background in progressing age. Risk factors had a specific age and sociodemographic distribution pattern in ischaemic stroke patients. Public health preventive programmes targeting certain age groups with different sociodemographic backgrounds could be useful to reduce the burden of stroke.

Keywords: impact, sociodemographic, variables, risk factors, ischaemic stroke, patients, age, stroke

1. INTRODUCTION

A 6-year stroke study conducted at Hospital Seberang Jaya, Penang showed that nearly 82% of the patients were ischaemic stroke (IS) patients.[1] There are modifiable and non-modifiable risk factors (RFs) associated with IS. Non-modifiable RFs include age, sex, ethnicity, and genetic factors. While these non-modifiable RFs cannot be altered, they still serve as imperative identifiers of stroke-risk patients.[2] On top of that, modifiable RFs such as hypertension, atrial fibrillation (AF), and ischaemic heart disease (IHD) may further influence the aetiology and outcomes of stroke.[3] As evidenced in the literature, the substantial impact of these RFs varied in combination with other variables such as sex and age.[4] Identification of these precipitating factors is essential in order to implement preventive measures that target patients at increased risk for stroke. Because RFs are frequently interrelated, clustering patterns of several RFs should be investigated. Understanding the association might be useful in creating interventions that target

numerous regularly co-occurring RFs in certain population groups.[5]

There were several studies in the past such as the Framingham Heart Study,[6] the Atherosclerosis Risk in Communities study,[7] and the Cardiovascular Health Study[8] that identified the RFs for stroke. Despite the fact that there have been stroke epidemiological studies worldwide, sometimes with inconsistent results, there are no studies done locally in Malaysia to identify the RFs of stroke. The RFs among different socioeconomic groups have also not been extensively studied. The lack of Malaysian stroke-related data is hampering evidence-based efforts to improve patient care and to provide and plan for a better healthcare policy. Therefore, we performed this 7-year observational study at a local stroke-ready hospital in order to identify the relevant RFs and to determine disparities in the co-occurrence of these various RFs based on sociodemographic backgrounds among IS patients in relation to age.

2. METHODS

This single-centre, hospital-based study was registered with the local National Medical Research Register (NMRR-20-1476-55732) and obtained ethical approval from the Medical Research and Ethics Committee, Ministry of Health Malaysia.

Hospital Seberang Jaya (HSJ) has an acute stroke care facility that provides 24/7 intravenous thrombolysis service to patients from Penang and nearby states.[9] We included all adult patients (above 18 years old) from 1st January 2013 to 31st December 2019 who presented to HSJ within 14 days of IS symptoms onset. Based on stroke subtypes as defined by the World Health Organization classification system, patients with other types of strokes, such as intracerebral haemorrhage, and subarachnoid haemorrhage, were excluded from this study.[10] The identification of stroke cases was based on clinical assessment by a neurologist and confirmed using computed tomography or magnetic resonance imaging of the brain. We collected relevant data from medical case notes obtained from the medical record office. The information was verified by a neurology stroke expert prior to data extraction and analysis.

Variables for analysis that were retrieved include the IS patients' sociodemographic data (age, sex, ethnicity, and marital status), and five major RFs (hypertension, diabetes, dyslipidaemia, IHD, and AF) that were identified via medical records. Hypertension was demarcated as a mean systolic blood pressure of ≥140 mmHg or a mean diastolic blood pressure of ≥90 mmHg in repeated measures, or use of antihypertensive medications, as documented in medical records.[11] Diabetes was demarcated as a fasting plasma glucose level ≥7 mmol/L or being prescribed with oral hypoglycaemic agents or an insulin regiment, as documented in medical records.[12] Hyperlipidaemia was defined as total cholesterol >5.2 mmol/L, high-density-lipoprotein cholesterol <1.0 mmol/L for male, and <1.2 mmol/L for female, triglyceride >1.7 mmol/L, and low-density-lipoprotein cholesterol >2.6 mmol/L with cardiac RFs or currently on statins, as documented in medical records.[13] IHD was demarcated as a self-reported physician diagnosis for angina pectoris or myocardial infarction, or with a history of angioplasty, stenting procedures or coronary artery bypass graft surgery.[4] AF was demarcated as a self-reported physician diagnosis with abnormal electrocardiogram findings, history of antiarrhythmic drugs or with anticoagulant therapy, as documented in medical records.[14]

All data analyses were performed using the Statistical Package of Social Sciences software, version 20.0. Descriptive statistics were employed for all variables in the study. The chi-square test or Fisher's exact test was used to assess the major RFs and the number of RFs by different age groups in the overall sample, in both male and female, in Malay, Chinese, and Indian, as well as in married and single patients. All probability values are two-sided, and a level of significance (p-value < 0.05) was considered statistically significant.

3. RESULTS
3.1 Ischaemic Stroke by Overall Sample

We included 1,280 IS patients with the mean age (SD) of 62.3 (12.1) years. Our study showed that hypertension was the most common RF of IS, followed by diabetes, dyslipidaemia, IHD, and AF. The five major RFs of IS was stratified into different age groups, ranging from 20 to ≥60 years

old. Overall, we found statistically significant association for all five major RFs, namely hypertension (p<0.001), diabetes (p=0.025), dyslipidaemia (p=0.006), IHD (p=0.040) and AF (p=0.006) with age. Hypertension was the most frequent RF across all age groups, present in 50% to 80% of the patients with IS. AF was the least common RF, hardly seen in patients aged below 60. (Figure 1A; Table 1)

We found significant association between number of RFs and age (p<0.001). Of the five major RFs assessed, 473 (37.0%) patients had two RFs, 20% to 30% of the patients had either no or one RF. The least number of patients, 31 (2.4%), had four RFs. In the youngest age group of 20 to 29 years, half had a single RF and the other half of them developed IS without having any RFs. As the age increased, the proportion of patients with either no or only one RF declined while the number of patients with two or more RFs of IS became greater. (Figure 2A; Table 2)

3.2 Ischaemic Stroke by Sex
Among the 815 (63.7%) male patients, association between age and hypertension (p=0.009) as well as dyslipidaemia (p=0.017) were found to be statistically significant (Table 1). The proportion of hypertension declined slightly in patients aged 40 to 49 years and rose thereafter in the subsequent elder age groups. Dyslipidaemia was found most often in male patients aged 50 to 59 years (18.2%), and least often in those aged 30 to 39 years (3.3%) (Figure 1B). In the female group, one patient aged between 20 and 29 with young IS had hypertension. The proportion of diabetes increased up to the age of 50s and declined thereafter (Figure 1C).

There was a statistically significant association between number of RFs and age in both male (p<0.037) and female (p=0.005) patients (Table 2). In male patients aged 30 to 39 years, a majority of them (46.7%) had only one RF whereas most of the females (66.7%) in the same age group did not have any RFs. The proportion of patients with at least two RFs increased steadily from age 30 to ≥60 in both male and female patients. More than 50% of the male and female patients who were ≥60 years had at least two RFs (Figures 2B and 2C).

3.3 Ischaemic Stroke by Ethnic Group
Although Malays accounted for more than half of the patients, we did not observe significant association between RFs and age (Table 1; Figure 1D). Among 405 (31.6%) Chinese patients, three major RFs, hypertension (p<0.001), diabetes (p=0.025) and dyslipidaemia (p=0.041) were significantly associated with increasing age (Table 1). Starting at the age of 30, both the proportion of hypertension and diabetes were seen in advancing age. The proportion of hypertension in Chinese patients aged ≥60 almost tripled as compared to younger patients in their 30s. There was also a marked increase in the proportion of dyslipidaemia from 4% to more than 20% as the age increased from 40 to ≥60 (Figure 1E). Meanwhile in the Indian group (14.9%), diabetes was the only RF showing significant association with varying age groups (p=0.005) (Table 1). A 10% decrease was first observed in the younger age group in the proportion of diabetes. However, it rose to approximately 60% as the age increased to ≥50 years (Figure 1F).

Statistically significant association was observed between the number of RFs and age in Chinese (p<0.001) and Indian (p=0.022) patients (Table 2). All Chinese patients aged below 40 years had either no or only one RF. As the age increased, patients with at least two RFs gradually predominated in the population (Figure 2E). Most Indian patients aged ≥60 had two RFs, whereas approximately 40% of those aged below 50 years had only one RF (Figure 2F).

3.4 Ischaemic Stroke by Marital Status
We found a statistically significant association between hypertension and age in both married (p=0.006) and single (p=0.006) patients (Table 1). Proportion of hypertension in married patients varied across all age groups, being highest in the 20 to 29 age group and lowest in the 30 to 39 age group (Figure 1G). Among patients who were single, the proportion of hypertension increased progressively from the age of 30 to ≥60 (Figure 1H). In patients aged below 60, hypertension was more often reported by those who were married in comparison with those who were single (Figures 1G and IH).

There was a significant association between the number of RFs and age in married

patients (p=0.037) (Table 2). In married patients aged 30 to 39 years, 25% had at least two RFs and the frequency then increased to about 40% in the ≥60 age group (Figure 2G).

The association between the number of RFs and age in single patients was not statistically significant (Figure 2H).

Table 1: Prevalence of major risk factors by different age groups (in overall sample; in male and female; in Malay, Chinese, and Indian; in married and single patients)

Major risk factors	Age groups (years)					Total	P-value
	20-29	30-39	40-49	50-59	≥ 60		
Overall sample, n (%)							
Hypertension	1 (50.0)	23 (54.8)	90 (62.9)	236 (67.0)	571 (77.1)	921 (72.0)	< 0.001
Diabetes	0 (0.0)	13 (31.0)	59 (41.3)	168 (47.7)	372 (50.2)	612 (47.8)	0.025
Dyslipidaemia	0 (0.0)	1 (2.4)	16 (11.2)	60 (17.0)	142 (19.2)	219 (17.1)	0.006
Ischaemic heart disease	0 (0.0)	0 (0.0)	14 (9.8)	27 (7.7)	85 (11.5)	126 (9.8)	0.040
Atrial fibrillation	0 (0.0)	0 (0.0)	1 (0.7)	3 (0.9)	31 (4.2)	35 (2.7)	0.006
Sex, n (%)							
a) Male (n=815, 63.7%)	**n = 1**	**n = 30**	**n = 107**	**n = 242**	**n = 435**	**n = 815**	
Hypertension	0 (0.0)	19 (63.3)	62 (57.9)	164 (67.8)	319 (73.3)	564 (69.2)	0.009
Diabetes	0 (0.0)	11 (36.7)	43 (40.2)	105 (43.4)	218 (50.1)	377 (46.3)	0.115
Dyslipidaemia	0 (0.0)	1 (3.3)	8 (7.5)	44 (18.2)	72 (16.6)	125 (15.3)	0.017
Ischaemic heart disease	0 (0.0)	0 (0.0)	14 (13.1)	20 (8.3)	55 (12.6)	89 (10.9)	0.075
Atrial fibrillation	0 (0.0)	0 (0.0)	1 (0.9)	2 (0.8)	14 (3.2)	17 (2.1)	0.185
b) Female (n=465, 36.3%)	**n = 1**	**n = 12**	**n = 36**	**n = 110**	**n = 306**	**n = 465**	
Hypertension	1 (100.0)	4 (33.3)	28 (77.8)	72 (65.5)	252 (82.4)	357 (76.8)	< 0.001
Diabetes	0 (0.0)	2 (16.7)	16 (44.4)	63 (57.3)	154 (50.3)	235 (50.5)	0.043
Dyslipidaemia	0 (0.0)	0 (0.0)	8 (22.2)	16 (14.5)	70 (22.9)	94 (20.2)	0.117
Ischaemic heart disease	0 (0.0)	0 (0.0)	0 (0.0)	7 (6.4)	30 (9.8)	37 (8.0)	0.201
Atrial fibrillation	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.9)	17 (5.6)	18 (3.9)	0.132
Ethnic group, n (%)							
a) Malay (n=684, 53.4%)	**n = 0**	**n = 19**	**n = 95**	**n = 185**	**n = 385**	**n = 684**	
Hypertension	0 (0.0)	13 (68.4)	65 (68.4)	131 (70.8)	295 (76.6)	504 (73.7)	0.248

Diabetes	0 (0.0)	8 (42.1)	46 (48.4)	88 (47.6)	195 (50.6)	337 (49.3)	0.819
Dyslipidaemia	0 (0.0)	1 (5.3)	13 (13.7)	30 (16.2)	64 (16.6)	108 (15.8)	0.547
Ischemic heart disease	0 (0.0)	0 (0.0)	11 (11.6)	13 (7.0)	41 (10.6)	65 (9.5)	0.243
Atrial fibrillation	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.6)	14 (3.6)	17 (2.5)	0.191
b) Chinese (n=405, 31.6%)	**n = 2**	**n = 11**	**n = 27**	**n = 97**	**n = 268**	**n = 405**	
Hypertension	1 (50.0)	3 (27.3)	12 (44.4)	59 (60.8)	205 (76.5)	280 (69.1)	< 0.001
Diabetes	0 (0.0)	1 (9.1)	8 (29.6)	37 (38.1)	124 (46.3)	170 (42.0)	0.025
Dyslipidaemia	0 (0.0)	0 (0.0)	1 (3.7)	19 (19.6)	62 (23.1)	82 (20.2)	0.041
Ischaemic heart disease	0 (0.0)	0 (0.0)	2 (7.4)	6 (6.2)	31 (11.6)	39 (9.6)	0.500
Atrial fibrillation	0 (0.0)	0 (0.0)	1 (3.7)	0 (0.0)	15 (5.6)	16 (4.0)	0.100
c) Indian (n=191, 14.9%)	**n = 0**	**n = 12**	**n = 21**	**n = 70**	**n = 88**	**n = 191**	
Hypertension	0 (0.0)	7 (58.3)	13 (61.9)	46 (65.7)	71 (80.7)	137 (71.7)	0.079
Diabetes	0 (0.0)	4 (33.3)	5 (23.8)	43 (61.4)	53 (60.2)	105 (55.0)	0.005
Dyslipidaemia	0 (0.0)	0 (0.0)	2 (9.5)	11 (15.7)	16 (18.2)	29 (15.2)	0.443
Ischaemic heart disease	0 (0.0)	0 (0.0)	1 (4.8)	8 (11.4)	13 (14.8)	22 (11.5)	0.475
Atrial fibrillation	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.3)	2 (1.0)	0.661
Marital status, n (%)							
a) Married (n=620, 78.2%)	**n = 1**	**n = 16**	**n = 61**	**n = 158**	**n = 384**	**n = 620**	
Hypertension	1 (100.0)	8 (50.0)	43 (70.5)	101 (63.9)	294 (76.6)	447 (72.1)	0.006
Diabetes	0 (0.0)	6 (37.5)	25 (41.0)	78 (49.4)	200 (52.1)	309 (49.8)	0.301
Dyslipidaemia	0 (0.0)	1 (6.3)	8 (13.1)	27 (17.1)	79 (20.6)	115 (18.5)	0.424
Ischaemic heart disease	0 (0.0)	0 (0.0)	3 (4.9)	13 (8.2)	52 (13.5)	68 (11.0)	0.087
Atrial fibrillation	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	18 (4.7)	19 (3.1)	0.060
b) Single (n=173, 21.8%)	**n = 0**	**n = 11**	**n = 25**	**n = 55**	**n = 82**	**n = 173**	
Hypertension	0 (0.0)	4 (36.4)	12 (48.0)	34 (61.8)	63 (76.8)	113 (65.3)	0.006
Diabetes	0 (0.0)	2 (18.2)	8 (32.0)	25 (45.5)	37 (45.1)	72 (41.6)	0.242

Dyslipidaemia	0 (0.0)	0 (0.0)	3 (12.0)	7 (12.7)	15 (18.3)	25 (14.5)	0.469
Ischaemic heart disease	0 (0.0)	0 (0.0)	1 (4.0)	2 (3.6)	10 (12.2)	13 (7.5)	0.248
Atrial fibrillation	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (0.6)	1.000

4. DISCUSSION

Generally, our data are comparable to Asian countries including developed countries such as Taiwan[15], Japan[16], Singapore[17], and South Korea[18] as well as developing countries such as China[19], India[20], Thailand[21], and Kuwait[22]. A previous study suggested that the average age of stroke patients in developing countries was younger than in the developed countries.[23] Compared to the four developing Asian countries mentioned above, our mean (SD) age of 62.3 (12.1) was the second highest after China, with an average age of 65. This likely means that the local burden of stroke contributed by young stroke patients may not be as significant, but further study is necessary to confirm this observation. Male IS patients are predominant in our setting and among all these countries. Males are reported to have more IS but females had more infarctions affecting the anterior circulation and more subarachnoid haemorrhages.[24, 25] In the general population, hypertension is the most significant RF for stroke and diabetes is second to hypertension as an RF for IS.[26, 27] Although AF was the least common RF, a study showed that there is a 5-fold increased risk of stroke for those with AF.[28]

4.1 Ischaemic Stroke by Overall Sample

The proportion of each RF increased with age, similar to previous studies. A hospital-based cohort in Taiwan showed that hypertension and diabetes were more common in older IS patients.[29] Furthermore, a China study indicated that classic vascular RFs such as IHD and AF were more common in elderly patients.[30] The proportion of at least two RFs increased with advancing age too. Aging is usually accompanied by other co-morbidities such as hypertension, diabetes, etc., which are also RFs for stroke, further contributing to the number of stroke and its aftermath.[31] We noticed that the proportion of hypertension in the younger age group i.e., 30-39 years old reaches 54.8%, which is significant and

unexpected. This calls for more intensive hypertension screening, including young adults, to examine whether the hypertension is essential or secondary. This measure helps patients to receive the appropriate treatment as early as possible, particularly young adults, in order to prevent or reduce the incidence of stroke events. In contrast with our finding, a past study found that dyslipidaemia was more common in the younger group.[32] Dyslipidaemia is common and plays a role in the development of atherosclerosis and cerebrovascular disease.[33] Given that the proportion of dyslipidaemia rises with age and that it is one of the five major modifiable RFs for cerebrovascular disease, it appears prudent to strive for more consistent and long-term monitoring and treatment of these frequent RF disorders.

4.2 Ischaemic Stroke by Sex

Studies have shown that the stroke rate doubles every 10 years after the age of 55 in both males and females.[34] A similar age pattern can be seen in our study with more than half of the IS patients in both sexes aged ≥60. On top of being the most prominent RF overall, the proportion of hypertension increased with age in both male and female IS patients. This indicates that the influence of hypertension on the risk of IS is the same in males and females. Previous study showed that males had somewhat higher rates of hypertension until they were around 50 years old, after which, between 50 and 70 years old, the incidence of hypertension was the same in both sexes. However, the number declined in both sexes between 70 and 80 years of age with a slightly steeper decrease in males.[35] It should be noted that the study was conducted in Denmark and the outcome could be affected by its local regional and socioeconomic differences. We also observed a disparity between the sexes. As the age of the patient progressed, the proportion of dyslipidaemia increased in males while the proportion of diabetes escalated in females.

Therefore, gender-specific approaches for optimal lipid or blood sugar management may be beneficial, but future studies are required to confirm the results. In addition, both RFs in males and females peaked when the patients were in their 50s with a slight decline thereafter, which may be due to mortality displacement in the elderly group. It is common to associate aging with at least two chronic illnesses.[36] Knowing the increased proportion of clustering of at least two RFs in both sexes with age in our stroke cohort, further study is warranted to investigate whether they function synergistically and enhance one another or whether they are just additive RFs for IS. The issue should be studied with consideration for hormonal, lifestyle, health behaviour, and other differences between males and females.

4.3 Ischaemic Stroke by Ethnic Group
Based on our study, the proportion of IS was the highest in Malay (53.4%) followed by Chinese (31.6%) and Indian (14.9%) patients. Despite the fact that more than half of the IS patients are Malay, only Chinese and Indian patients showed associations between RFs and age. Currently, there are only a few studies on ethnic variations in the Asian stroke population, mostly in Singapore, which has a more homogeneous population ethnically compared to Malaysia.[37, 38] Our study is the first that investigates RFs with ethnicity in relation to age among Malay, Chinese, and Indian IS patients. Even though our findings might not be definitive, socioeconomic, dietary patterns and lifestyles, as well as some hereditary variations are the factors to consider with the increased proportion of hypertension, and dyslipidaemia in Chinese and diabetes in both Chinese and Indian with age. Of note, one in two Chinese IS patients have hypertension in their 20s. Considering that younger stroke patients have a significantly higher risk of mortality than the general population, prompt treatment of stroke RFs, such as hypertension, particularly in the younger generation is critical.[39] We also observed that the proportion of Indian diabetic IS patients peaked in the 50s age range with a trivial drop afterwards. This may be due to mortality displacement which warrants further study to confirm. Another finding revealed that both Chinese and Indian IS patients had at least two RFs as they became older, with

Indians having a younger predisposition to multiple RFs, as early as in their 30s. The primary treatment approach for decreasing stroke-related morbidity and mortality is prevention.[40, 41] Given that the first-ever stroke was expected to occur under the age of 40 and the risk of stroke increased with having more RFs, it could be an advantage to target these RFs among young Indians. However, more evidence is needed to warrant the recommendation.

4.4 Ischaemic Stroke by Marital Status
Marriage as a way of life is not linked to a decreased risk of stroke in all studies.[42, 43] Our study also indicated that more than 75% of IS patients were married. It has been suggested that the association between marital status and risk of stroke were largely influenced by socioeconomic factors, unhealthy lifestyle behaviours and reduced social support.[44, 45] We also observed a similar age pattern in both married and single IS patients with hypertension. While the youngest single IS patients were in their 30s, it is noteworthy that the married IS patient with hypertension was in the 20s age range. According to a Chinese study, young IS patients with psychological symptoms had a greater proportion of married status, hypertension, infarct size, and family dysfunction when compared to those without psychological symptoms.[46] Young people's mental health may be unaffected, if not negatively affected, by early marriage, which is non-normative both statistically and culturally.[47] Lastly, our study showed that married IS patients have up to four RFs with increasing age. While marital status cannot be changed by medical intervention or therapy, knowing the mechanism may help in discovering potential strategies to lower the risk, a topic for future study. This also suggests early identification of RFs so that measures can be taken to increase awareness and public education about them which could, in the long run, reduce the prevalence of IS. Patients with hypertension had a 1.5 to 5.0 times higher risk of death or dependency/deterioration.[48] The proportion of both married and single IS patients with hypertension in their 60s was about the same (76%) in our study. Since previous research showed that individuals who live alone are more likely to die after a stroke,[49] elderly stroke

survivors who are single and living alone, particularly those with disabilities, may require extra attention for better post-stroke care management and long-term outcome.

5. LIMITATION

The study only represents a hospital-based study and may not represent the population in the whole of Malaysia. However, with over a thousand patients and general demographic variables that are comparable to both Malaysia and other Asian countries, our findings may provide insights that are relevant to a regional or international population. Our findings are exclusively based on marital status at the time of the stroke. The impact of changes in marital status on the risk of stroke is not taken into account in this study. Besides, we did not further investigate the type of hypertension (essential or secondary) among the patients. It is worthwhile to explore, especially among the group of patients 30-39 years old, if the high blood pressure is identified as essential or secondary hypertension. This is crucial since these findings could be attributed to metabolic syndrome, which is prevalent in our community and could become

more common among the younger age group. All of these warrant future studies so that more efficient public health measures can be introduced to target such communities. Lastly, this study is an observational retrospective study based on medical records, which may be subject to selection and information bias.

6. CONCLUSION

Young stroke is on the rise and the burden of IS is common in the elderly, with elderly stroke patients accounting for roughly a third of all healthcare visits with high mortality rates.[50, 51] The rising incidence of individuals with multiple RFs is also a serious public health problem that has gotten a lot of attention in recent years.[52] Our stroke study shows IS patients with different sociodemographic variables may have different RFs that vary in relation to age. The identification of these associations assists in developing more focused stroke prevention initiatives. Tailored public health preventive programmes targeting certain age groups with different sociodemographic backgrounds could be useful to reduce the burden of stroke.

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Supplement:

☐ Hypertension　▨ Diabetes　▨ Dyslipidaemia　▥ Ischaemic heart disease　■ Atrial fibrillation
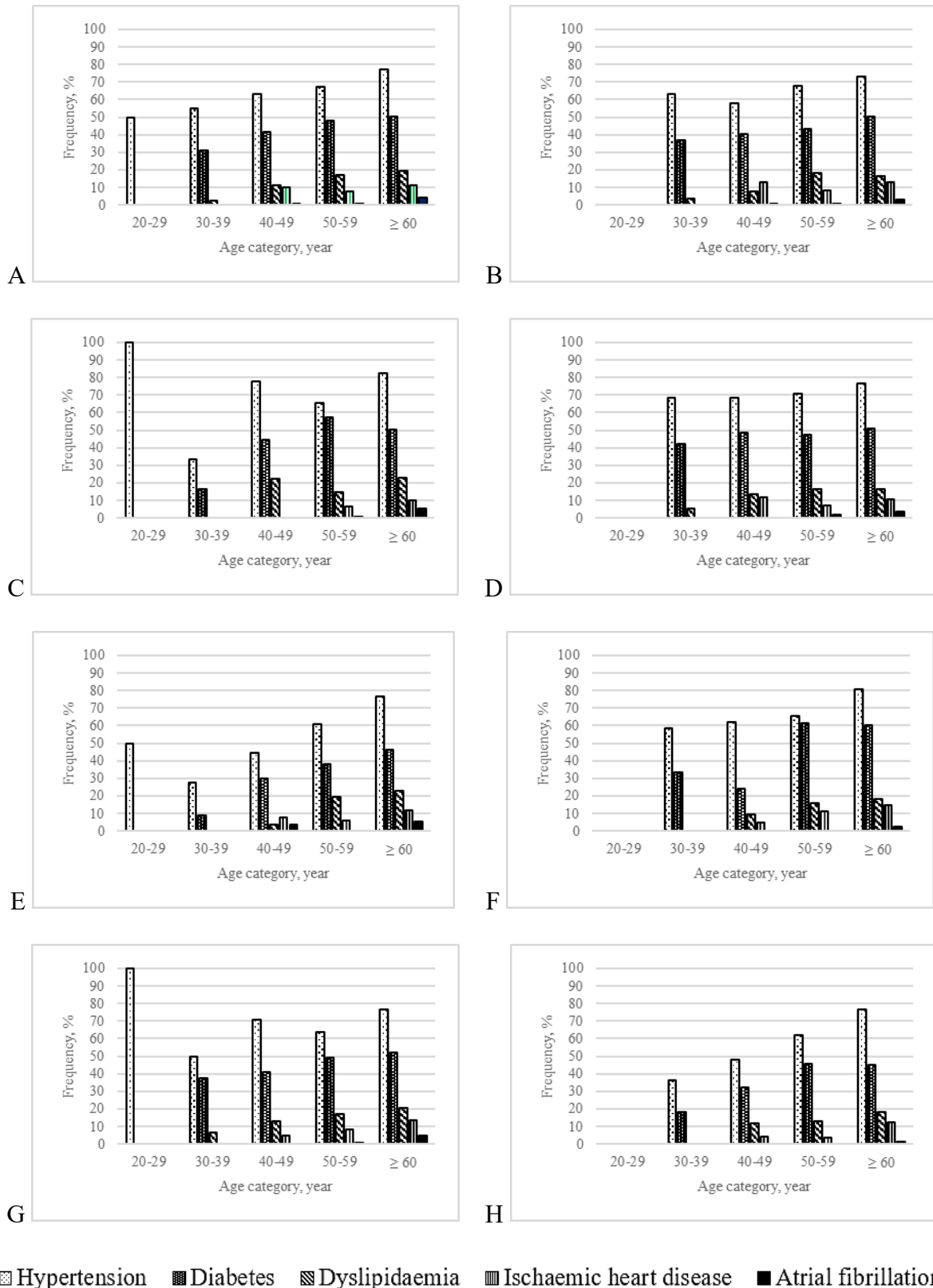
Figure 1: The five major RFs according to age group: (A) overall, (B) male, (C) female, (D) Malay, (E) Chinese, (F) Indian, (G) married, and (H) single.
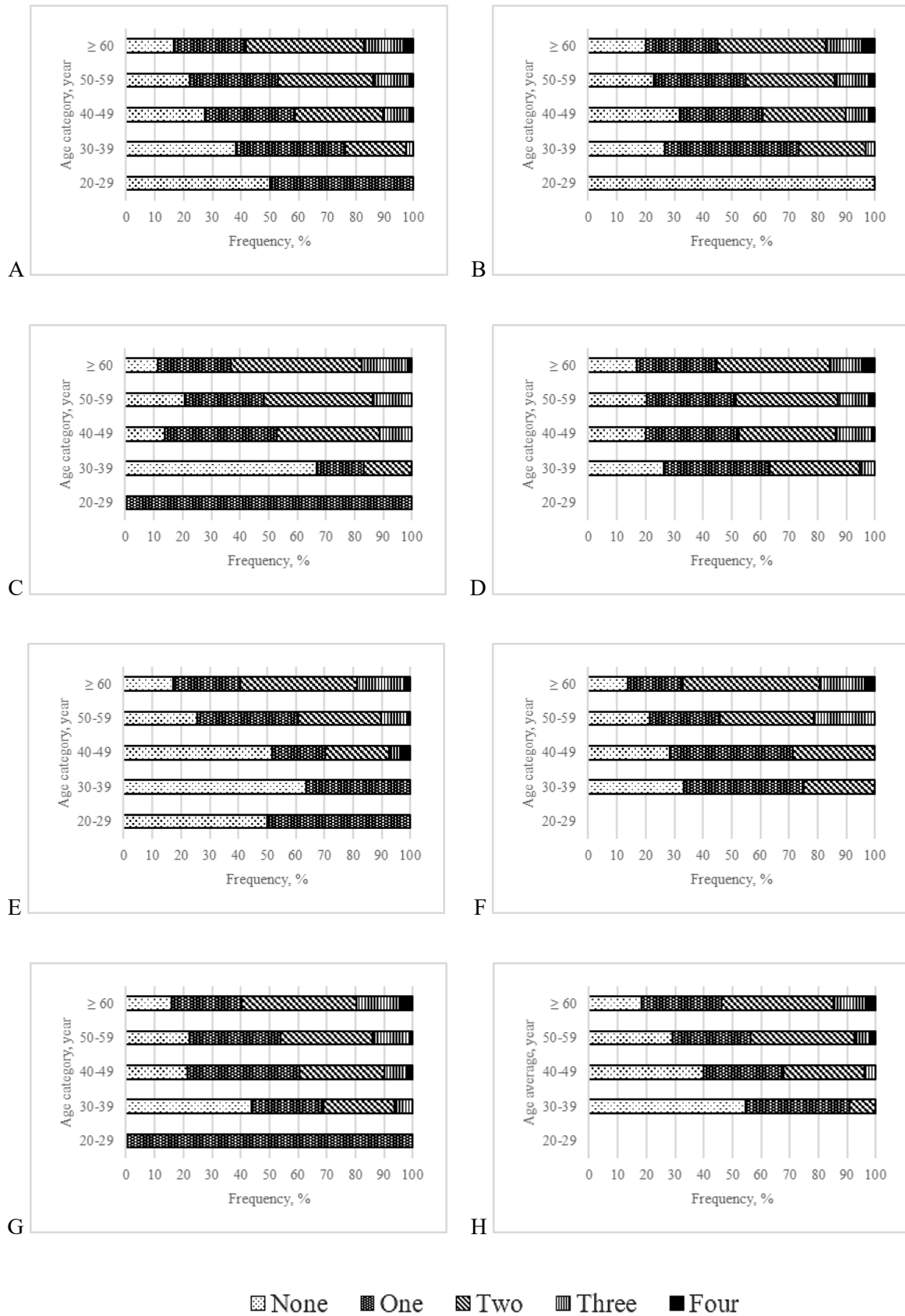
Figure 2: The number of five major RFs according to age group: (A) overall, (B) male, (C) female, (D) Malay, (E) Chinese, (F) Indian, (G) married, and (H) single.

Table 2: Prevalence of number of risk factors by different age groups (in overall sample; in male and female; in Malay, Chinese, and Indian; in married and single patients)

Characteristics	Age groups (years)					Total	P-value
	20-29	30-39	40-49	50-59	≥ 60		
Overall sample, n (%)	**n = 2**	**n = 42**	**n = 143**	**n = 352**	**n = 741**	**1280**	
None	1 (50.0)	16 (38.1)	39 (27.3)	78 (22.2)	123 (16.6)	257 (20.1)	< 0.001
One	1 (50.0)	16 (38.1)	45 (31.5)	108 (30.7)	187 (25.2)	357 (27.9)	
Two	0 (0.0)	9 (21.4)	44 (30.8)	117 (33.2)	303 (40.9)	473 (37.0)	
Three	0 (0.0)	1 (2.4)	13 (9.1)	44 (12.5)	104 (14.0)	162 (12.7)	
Four	0 (0.0)	0 (0.0)	2 (1.4)	5 (1.4)	24 (3.2)	31 (2.4)	
Sex, n (%)							
a) Male (n=815, 63.7%)	**n = 1**	**n = 30**	**n = 107**	**n = 242**	**n = 435**	**n = 815**	
None	1 (100.0)	8 (26.7)	34 (31.8)	55 (22.7)	88 (20.2)	186 (22.8)	< 0.037
One	0 (0.0)	14 (46.7)	31 (29.0)	78 (32.2)	109 (25.1)	232 (28.5)	
Two	0 (0.0)	7 (23.3)	31 (29.0)	75 (31.0)	164 (37.7)	277 (34.0)	
Three	0 (0.0)	1 (3.3)	9 (8.4)	29 (12.0)	55 (12.6)	94 (11.5)	
Four	0 (0.0)	0 (0.0)	2 (1.9)	5 (2.1)	19 (4.4)	26 (3.2)	
b) Female (n=465, 36.3%)	**n = 1**	**n = 12**	**n = 36**	**n = 110**	**n = 306**	**n = 465**	
None	0 (0.0)	8 (66.7)	5 (13.9)	23 (20.9)	35 (11.4)	71 (15.3)	0.005
One	1 (100.0)	2 (16.7)	14 (38.9)	30 (27.3)	78 (25.5)	125 (26.9)	
Two	0 (0.0)	2 (16.7)	13 (36.1)	42 (38.2)	139 (45.4)	196 (42.2)	
Three	0 (0.0)	0 (0.0)	4 (11.1)	15 (13.6)	49 (16.0)	68 (14.6)	
Four	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.6)	5 (1.1)	
Ethnic group, n (%)							
a) Malay (n=684, 53.4%)	**n = 0**	**n = 19**	**n = 95**	**n = 185**	**n = 385**	**n = 684**	
None	0 (0.0)	5 (26.3)	19 (20.0)	38 (20.5)	65 (16.9)	127 (18.6)	0.845
One	0 (0.0)	7 (36.8)	31 (32.6)	57 (30.8)	107 (27.8)	202 (29.5)	
Two	0 (0.0)	6 (31.6)	32 (33.7)	66 (35.7)	152 (39.5)	256 (37.4)	
Three	0 (0.0)	1 (5.3)	12 (12.6)	20 (10.8)	46 (11.9)	79 (11.5)	
Four	0 (0.0)	0 (0.0)	1 (1.1)	4 (2.2)	15 (3.9)	20 (2.9)	
b) Chinese (n=405, 31.6%)	**n = 2**	**n = 11**	**n = 27**	**n = 97**	**n = 268**	**n = 405**	
None	1 (50.0)	7 (63.6)	14 (51.9)	25 (25.8)	46 (17.2)	93 (23.0)	< 0.001
One	1 (50.0)	4 (36.4)	5 (18.5)	34 (35.1)	63 (23.5)	107 (26.4)	
Two	0 (0.0)	0 (0.0)	6 (22.2)	28 (28.9)	109 (40.7)	143 (35.3)	
Three	0 (0.0)	0 (0.0)	1 (3.7)	9 (9.3)	44 (16.4)	54 (13.3)	
Four	0 (0.0)	0 (0.0)	1 (3.7)	1 (1.0)	6 (2.2)	8 (2.0)	
c) Indian (n=191, 14.9%)	**n = 0**	**n = 12**	**n = 21**	**n = 70**	**n = 88**	**n = 191**	
None	0 (0.0)	4 (33.3)	6 (28.6)	15 (21.4)	12 (13.6)	37 (19.4)	0.022
One	0 (0.0)	5 (41.7)	9 (42.9)	17 (24.3)	17 (19.3)	48 (25.1)	
Two	0 (0.0)	3 (25.0)	6 (28.6)	23 (32.9)	42 (47.7)	74 (38.7)	
Three	0 (0.0)	0 (0.0)	0 (0.0)	15 (21.4)	14 (15.9)	29 (15.2)	
Four	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.4)	3 (1.6)	
Marital status, n (%)							
a) Married (n=620, 78.2%)	**n = 1**	**n = 16**	**n = 61**	**n = 158**	**n = 384**	**n = 620**	
None	0 (0.0)	7 (43.8)	13 (21.3)	35 (22.2)	61 (15.9)	116 (18.7)	0.037
One	1 (100.0)	4 (25.0)	24 (39.3)	50 (31.6)	94 (24.5)	173 (27.9)	
Two	0 (0.0)	4 (25.0)	18 (29.5)	51 (32.3)	154 (40.1)	227 (36.6)	
Three	0 (0.0)	1 (6.3)	5 (8.2)	20 (12.7)	59 (15.4)	85 (13.7)	
Four	0 (0.0)	0 (0.0)	1 (1.6)	2 (1.3)	16 (4.2)	19 (3.1)	
b) Single (n=173, 21.8%)	**n = 0**	**n = 11**	**n = 25**	**n = 55**	**n = 82**	**n = 173**	
None	0 (0.0)	6 (54.5)	10 (40.0)	16 (29.1)	15 (18.3)	47 (27.2)	0.307
One	0 (0.0)	4 (36.4)	7 (28.0)	15 (27.3)	23 (28.0)	49 (28.3)	
Two	0 (0.0)	1 (9.1)	7 (28.0)	20 (36.4)	32 (39.0)	60 (34.7)	
Three	0 (0.0)	0 (0.0)	1 (4.0)	3 (5.5)	9 (11.0)	13 (7.5)	
Four	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	3 (3.7)	4 (2.3)	

STATEMENTS

A REVIEW OF STRATEGIES TO IMPROVE STROKE CARE SERVICES IN LOW AND MIDDLE-INCOME COUNTRIES: THE INNOVATIVE EXPERIENCE OF LAHORE GENERAL HOSPITAL STROKE PROGRAMME

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ABSTRACT

Stroke, especially ischemic stroke, is the second leading cause of death and disability. The burden of stroke in low and middle-income countries is high and growing, putting already overburdened healthcare resources to the test. To combat the disease's enormous burden, innovative stroke treatment services are needed. This requires the advancement of a nationwide stroke plan in order to offer the right care to all patients who qualify for reperfusion therapy. High levels of coordination, close collaboration with crisis medicinal administrations for pre-emergency clinic evaluation, our comprehensive understanding of stroke singularity, the advancement of pre-assessment tools, a high level of responsibility of all stroke groups at stroke centres, the accessibility of a stroke-specific registry, and the local government to seize the initiative are all key components of success. In this study, we look at different systems in low and middle-income countries that deal with various aspects of stroke treatment. We can use the achievement of the Lahore General Hospital stroke programme as an indicator of progress. Reperfusion therapy has only recently started in Lahore General Hospital, and this paper describes a one-of-a-kind experience in Pakistan of using a limited number of resources to help the country's first stroke centre grow. The aim of this research is to compare and contrast the approaches to stroke care control and treatment in Pakistan, Thailand, and Egypt. While these countries have equal economic standings, Egypt and Thailand have stronger stroke-management healthcare networks than Pakistan. As a result, this paper investigates these disparities and proposes possible options for improving stroke care treatment in Pakistan. In addition, the present state of stroke treatment in Pakistan is examined. In conclusion, public and governmental awareness is more important as a first step as compared to structural stroke care establishment in developing countries such as Pakistan.

Keywords: Stroke Prevention; Acute Stroke Care; Stroke Unit; Low and Middle Income Countries

ABBREVIATIONS

AAFITN: Asian-Australasian Federation of Interventional and Therapeutic Neuroradiology
AIDS: Acquired Immunodeficiency Syndrome
CAST: Cardiac Arrhythmia Suppression Trial
CT : Computed Tomography
DALYs: Disability Adjusted Life Years
DWI: Diffusion Weighted Image
ED: Emergency Department
EMTs: Emergency Medical Technician
FAST: Face Arm Speech Test
FLAIR: Fluid-attenuated inversion recovery
HICs: High Income Countries
HIV: Human Immunodeficiency Virus
IST: International Stroke Trial
IV tPA: Intravenous tissue plasminogen activator
LMICs: Lower Middle Income Countries
MENA SINO: Middle East North Africa Stroke and Interventional Neurotherapies Organization
MSUs: Mobile Stroke Units
MRI: Magnetic Resonant Imaging
NRSP: NeuroRadiological Society of Pakistan
SU: Stroke Unit
TIA: Transient Ischemic Attack
PFO: Patent Foramen Ovale
WHO: World Health Organization

INTRODUCTION

Stroke, especially ischemic stroke, is the leading cause of death and disability worldwide. Stroke has become more common among both men and women around the world. Increased public understanding of early symptoms, accuracy of modern brain imaging, and the advancement of acute therapies help to reverse this pattern. Innovation in stroke-care systems is needed to remodel and train them to face this challenge. (1) Stroke mortality rates have decreased by half in high-income countries. Stroke victims in low- and middle-income countries are younger than people in high-income countries. According to Pakistan's 2017 Census, the country's population is 207 million people and the world's sixth-most populous country (2). Pakistan is classified as an emerging economy with a lower to middle financial benefit (3).

Aim: The aim of this study is to do a comparative analysis between Pakistan, Thailand and Egypt and their approaches to stroke care management

and treatment, which have been summarized in Table 1.

METHODS

A review of the literature was undertaken using PubMed and Google Scholar to find publications that detailed stroke treatment and developments in LMICs. We used the World Bank's 2019-2020 classification for this research. A country was categorised as "low income" if its total national income per capita for the previous year was less than USD 1,025; income between USD 1,026 and USD 4,035 was classified as "lower-middle income." (21)

Acute stroke, stroke care, stroke therapy, developed nations, low and middle-income countries were all included in a single search word. Articles on stroke treatment from low- and middle-income countries were included in this study and reports from high-income countries were excluded.

RESULTS

Current Resources in Stroke Prevention

Pre-medical service recognition, assessment, and evacuation, urgent stroke treatment (fast triaging in the emergency room), SU care and rehabilitation, and network assistance are all included in stroke care administrations. There are several roadblocks in the foundation of stroke treatment administrations in LMICs. A typical stroke pathway is depicted.

Prehospital Services

With rapid developments in prehospital stroke treatment mostly in high-income countries (HIC), it is critical to consider the conditions, difficulties, and applicability of these approaches in low and middle-income countries (LMIC). The strain of stroke is becoming more disparate between LMICs and HICs. LMICs account for over 75% of stroke deaths and about 80% of disability-adjusted life years (DALYs). In addition, there has been a 42 percent reduction in stroke occurrence in high-income countries and a 100 percent increase in LMICs over the last four decades. Regrettably, there is little data on the benefits of prehospital stroke treatment in these situations. (5)

Prehospital obstacles include inadequate transportation and a scarcity of qualified stroke

specialists. Ambulances are, for the most part, unprepared and lack trained personnel. Ambulances are often used to transport patients with burn wounds and obstetric emergencies in these conditions. (5)

Rescue 1122, a model of pre-clinical emergency management, was developed in Pakistan's Punjab province with a population of about 90 million people. In either situation, crisis management relies on decades-old crisis centres, no triage, no permanent doctor personnel, and virtually no pre-hospital emergency services. (6) The rescue1122 administration operates by a toll-free emergency code, 1122, which can be dialled on both landlines and mobile phones. This administration has provided emergency treatment to 498000 people while maintaining a regular and natural response time of 7 minutes in all locations. (6)

One driver and two EMTs make up the emergency vehicle crew. They have emergency care, bracing, basic life support in the event of heart failure, and transport of patients with immobilisation on the scene. Until now, they will only recommend the lack of discomfort and the use of sublingual glyceryl triturate if chest pain occurs. EMTs are instructed to spend the least amount of time on the scene and to transport patients to pre-assigned emergency departments as soon as possible. A 'scoop and chase' technique is used in the case of a large number of setbacks. The proximity of a pre-hospital set-up will likewise demonstrate to be useful in reinforcing crisis drug and further preparing of paramedics and cooperation programs for specialists. (6)

The Pakistan National Emergency Department Surveillance (Pak-NED) is another initiative. It was a pilot complex surveillance directed in seven notable tertiary care crisis divisions in six fundamental urban communities of Pakistan. Ambulance and patient care systems should be improved to save lives. Furthermore, the EDHI foundation, the country's largest volunteer ambulance organisation, has over 1800 vehicles and two air-ambulance planes. (7)
Early recognition of neurological symptom by ambulance paramedics utilizing FAST evaluation shows concurrence with neurologist evaluation. The high predominance and great understanding for forearm weakness recommends that early recognition is the most optimal method to identify early stroke and getting the proper treatment. (8)

Cost Effectiveness
Although the Mobile Stroke Unit's approach is an innovative way to cope with prehospital acute stroke, it is costly. A retrospective analysis was conducted in Siriraj Hospital in Bangkok in 2018. The study demonstrated that extremely low incidence of emergency medical services (EMS) use and the delay in referral of patients from other hospitals were two factors that greatly affected hospital arrival time after acute stroke in Thailand. (10) Since Thailand is classified as an LMIC, a study of stroke treatment approaches will aid in the development of improved models.

Acute Management Investigations and Imaging
Around 2005 and 2006, 464 patients with presumed acute stroke had their qualities, time intervals, and rtPA values tested. Consistent quality management is required to achieve the best results in each setting and to ensure that acute stroke patients in LMICs receive the best care possible. (11)

Emergency Department
Junaid et al conducted a pilot study in two districts of Pakistan where they collected data from rural and urban healthcare setups showing a high percentage of dissatisfaction (98%) among the community participants regarding emergency medical services. When it comes to the standard of treatment, 68 percent of those polled believe paramedics aren't well qualified to treat patients. Ambulances are usually only a means of transportation to and from the hospital, with a driver but no other paramedics. And if they are present, no additional management is provided before the patient arrives at a healthcare facility, resulting in a substantial delay in the provision of appropriate emergency services, leading to a rise in morbidity and mortality, particularly among stroke patients. (12)

Another research was conducted in India to determine the causes that contribute to the delay in the treatment of acute stroke. According to the findings, the average prehospital time delay for all clinically suspected stroke patients at the institute

was 716 minutes. The average cumulative in-hospital wait was 94.17 54.5 minutes. (14) Medical entry process delays, a lack of resources to move the patient, and the gap between the stroke unit and the CT room all contributed to the in-hospital delay. (14)

Stroke Unit

Since patients who are treated in SUs have improved results, all-district or primary government hospitals and teaching institutes should aspire to have at least one primary SU. If primary government hospitals operated by doctors are unable to establish autonomous SUs, they may be connected to SU-equipped tertiary teaching hospitals. The establishment of a telestroke system would be the next step in increasing stroke patients' access to superior medical services while also lowering the rate of thrombolysis. (15)

The use of protocols in different third-world countries is depicted in Figures 1,2, and 3. In Thailand, the average gross direct medical cost per admission to a tertiary level hospital is THB 42,400. In 2003, Khealani et al conducted a study on stroke and discovered that overall expenses on stroke services for a single patient was USD 1,179. (16)

In Egypt, about 1% of acute stroke patients receive alteplase (tPA) thrombolysis. They explain that there is such a poor incidence of reperfusion procedures and take steps to increase it. The inaccessibility of alteplase, the incorrect medication decision, the missing window when doing cerebral imaging, and the inaccessibility of bed were the main reasons for not giving thrombolytic treatment. (18)

Likewise, with the help of these models, we have developed our institutional stroke protocol in Pakistan in 2014 and started working on a pilot project, with minimum resources and without governmental support, in one of the eminent public hospitals.

Caregiver Burden and Support Systems
Secondary prevention

Secondary prevention includes reducing the risk of another stroke or TIA, as well as other vascular disease and other difficulties such as learning impairment, diabetes, and poor quality of life. Secondary prevention will reduce stroke recurrence by up to 80% of almost all patients who have had a stroke or TIA. Examination and recovery must occur in the hospital (stroke unit or stroke centre) and continue throughout the community throughout one's life. (19)

Investigations into stroke prevalence, aetiology, and risk factors should follow principle-based local guidelines, including rapid and effective cerebral imaging; repeated strokes should be investigated because the cause might not be the same as the initial. If MRI is performed, it should include T2, FLAIR, DWI and blood-sensitive sequences. On the unlikely possibility that there is no conspicuous explanation for stroke, distinguishing the heart causes like AF can still be checked out. (19)

Secondary prevention should include dietary counselling and blood pressure control; in patients with ischaemic episodes, antithrombotic therapy, a statin, and carotid endarterectomy (if appropriate) should all be used. Both health care professionals should have patient and attendant instruction on preventive measures at each level. (19)

Following the diagnosis of ischaemic stroke or transient ischemic attack (TIA), the aetiological cause should be determined. This approach allows for secondary prevention methods to be used in conjunction with the procedure. Surgical and radiological procedures such as carotid endarterectomy and stenting, as well as the closing of the PFO and the atrial appendage, are highly dependent on the operator. Success rates can be monitored, as they are dependent on proper preparation. (19)

According to available research, more than 60% of patients who present with a stroke are hypertensive; even though 80–90% of these patients are monitored on the first visit, less than 40% may have their blood pressure properly controlled. Essentially, despite the fact that any patient is given a statin upon release, long-term enforcement is low. Furthermore, many patients with AF are also not receiving oral anticoagulation. (19)

The medicines could be added to specific countries' WHO "lists of important medications" and made available in essential/local hospitals or government health centres in remote areas. They can be made available at a lower cost. The WHO's

(World Health Organization) strategy (Package of Essential Noncommunicable Disease Interventions) is as follows: This is a series of procedures, like dietary modifications, that can be easily communicated by a doctor or a health care assistant. (5)

Role of NRSP And Development of First Stroke Center Of Pakistan

The NeuroRadilogical Society of Pakistan (NRSP) is a non-profit medical association that works to develop and support standards for the training and practice of neuroradiologists and neuro interventionalists.

The first catheter-based treatment of ischemic stroke was performed in December 2014 at an international workshop organised by local experts from Lahore General Hospital, Alexandria University School of Medicine, Egypt, in partnership with MENA-SINO, AAFITN, and NRSP. Two cases of acute ischemic stroke were treated with mechanical thrombectomy for the first time in the country's history during this workshop, and a stroke treatment programme was developed. International seminars on stroke care are held every year at the hospital, with international speakers. Furthermore, the information campaign is disseminated on a wide scale by using the Quick protocol to distribute pamphlets.

DISCUSSION

Stroke is one of the leading causes of death and disability in South Asia. Fortunately, there is compelling evidence that stroke is strongly preventable, treatable, and manageable, and that the burden of stroke and its long-term consequences can be significantly reduced. This, however, necessitates collaboration between the government and healthcare experts. In the case of acute stroke treatment in LMICs, some countries can never be able to adopt complex healthcare services capable of successfully delivering time-sensitive treatments.

We emphasise two main focuses for development assistance in order to achieve long-term impacts and reduce the burden of stroke in LMICs. To begin, assistance should be provided to help, integrate, and organise both primary health and emergency care services in order to prevent stroke and improve stroke control, respectively. Second, aid should focus on community-based programmes that reduce stroke risk factors in an increasingly sustainable manner and increase stroke outcomes more efficiently. (20)

Governmental Based Approach to Prevent and Manage Stroke in LMCI's

In LMICs, ambulance services are available, but they are underutilised for stroke patients. Training EMTs (emergency medical technicians) to recognize a stroke, notify the ED, neurologists, and radiologists before the arrival of a stroke patient can reduce time lost in transit, ED and investigations. If the closest centre does not have an imaging service, patients may be transferred to one that does after being pre-notified. Establishing common stroke procedures that are specific to state and local requirements will also minimise time spent in the emergency room. (5)

In areas where the healthcare infrastructure is small, reserving 3–6 beds may initiate creating a minimum model of Stroke Units for stroke patients. Patients may be moved to advanced SU after initial management. More patients profit from SU services as a result of decentralising SUs and supplementing nursing care. (5)

Many facets of supportive care for acute ischemic stroke and acute intracerebral haemorrhage are the same, such as maintaining euglycemia and euthermia, providing proper hydration and nutrients, treating seizures, preventing aspiration, preventing deep vein thrombosis, and early patient mobilisation. (21)

Unless thrombolytic treatment is administered, blood pressure is often able to auto-regulate after an acute ischemic stroke. When a CT scan is unavailable, it might be prudent to recommend lowering all patients' systolic blood pressure to less than 180mmHg. Offer a bolus of intravenous saline to patients with unexplained aetiology strokes that intensify clinically when blood pressure is reduced and then enable them to self-regulate. (21)

Where CT is unavailable and IV tPA is not an option, the only antithrombotic agent available is aspirin. When neuroimaging is scarce, an

alternative to the risk-averse approach of refusing aspirin in all patients with acute stroke with uncertain aetiology is to giving aspirin to all of these patients. The probability of this technique is determined in part by the proportion of ischemic or hemorrhagic acute strokes. Thus, treating all patients with acute stroke with aspirin in the absence of CT could benefit at least two-thirds of the stroke population. There was little disparity between the results of the IST and CAST experiments, which looked at the effects of aspirin and placebo on a population of 40,000 people. Based on this research, it seems that giving aspirin to all patients who have had an acute stroke of uncertain aetiology can be helpful. Taking aspirin in reduced doses for 24 to 48 hours following a stroke of uncertain aetiology reduces the risk of ischemic stroke thus reducing the risk of haemorrhagic stroke. (21)

An expert panel should be convened to formulate consensus guidelines for the management of acute stroke of unknown etiology in settings where there is no rapid access to neuroimaging. (21)

Since tPA is not registered in our region, only a few private companies provide IV thrombolysis at a very high cost, and no figures are available at this time. The cost of tPA is also a limiting factor; however, medicine registration and government subsidies or free tPA in government hospitals can help to increase the thrombolysis rate.

In LMICs, smartphone use has risen dramatically in recent years. Improved enforcement can be achieved by creating web-based apps that notify patients of their prescriptions, investigations, and medical visits. Another approach is to create applications that warn patients and the general public about early stroke diagnosis using the Quick protocol, as well as apps to direct stroke victims to the closest primary or local health care centre that specialises in stroke treatment, including in rural parts of the world.

Community-Based Approach To Prevent And Manage Stroke In LMIC's
Given the concurrent existence of stroke, the most useful interventions for development assistance in LMICs should be centred at the level of the

population. Researchers have created a handful of important impact concepts and techniques that they can apply and repeat so that others can benefit after years of diligent study and experience. (20)

About 5 million people in Thailand stopped contracting HIV thanks to a highly successful influence technique devised by an influence genius. AIDS in Thailand have previously been limited to inmates who spread the disease by exchanging discarded needles. The illness was imprisoned with its hosts for many years. However, in 1988, King George VI granted amnesty to over 30,000 detainees. The AIDS virus, once free of its confinement, enjoyed its newfound liberation by wreaking havoc on a much wider intravenous drug patient population. In just a few months, over half of all users in the United States had been poisoned. (20)

Infectious disease specialists around the world watched with shock as the disease spread from one population to another month after month. Sex employees were targeted at the same time as IV opioid users. Within a year, one-third of the sex workers had fallen victim. In some provinces, up to one-third of sex workers tested positive for HIV within a year. Married men then took the scourge home to their unsuspecting wives, who then passed it on to newborn babies. HIV had affected an estimated 1 million Thais by 1993. Health researchers estimated that Thailand will lead the world in contagious per capita in just a few years, with one out of every four adults carrying the virus. (20)

But it never came to be. The virus reached a plateau after two years and then withdrew. By the late 1990s, new diseases had been reduced by 80%, thanks in large part to Dr. Wiwat's impressive influence policy. (20)

As AIDS was taking Thailand by surprise, Dr. Wiwat fought the disease alongside a few of his colleagues in the Ratchaburi province. His experience had shown him that the trick to combating the outbreak of any epidemic was in keeping the public aware of the danger. (20)

Dr. Wiwat took a job with Thailand's Ministry of Public Health with this notion in mind, and he addressed the challenge of educating an uninformed public in the same manner as business marketers aim to boost consistency, customer experience, or coordination. Wiwat's unit was in

charge of distributing flyers. They conducted classes for the public. They persuaded actors to air commercials on television and radio. (20)

Wiwat concluded that if he could convince 100 percent of the country's sex-workers to insist that their clients use contraceptives, he could nearly stop the spread of HIV in Thailand. That became his main plan of attack. He'd figure out a way to make any sex-worker follow the condom rule. And much to the dismay of the world's epidemiologists, Wiwat's scheme succeeded. (20)

Later, we'll look at how Dr. Wiwat was able to persuade sex workers to follow the plan. The point we want to emphasise right now is that by carefully looking for and targeting a critical behavior. Wiwat was able to break from conventional untested approaches and find one that really worked. It's no surprise that we need to concentrate on critical behaviours. Seeing the most important behaviour will help you solve a dilemma. The next step is to tailor the behaviours to the individual's local circumstances. (20)

Verbal manipulation is the most popular technique we use to influence people, but it does not always succeed. A personal experience with a great persuader. The mother of all perceptual map changers is personal knowledge. Vicarious experience serves as a stand-in for real-life experience. Indeed, when used effectively for social transformation over the last few decades, vicarious models have saved millions of lives and increased the quality of living for tens of millions more. (20)

We would potentially have the best stroke treatment by preventing as many strokes as possible. A shortage of qualified neurologists, mostly in urban areas, a high number of mostly rural patients, a lack of general education and information about stroke risk factors and treatment, and the prohibitive cost of stroke care are all challenges in stroke care. There is a lack of standardisation and uniformity in secondary and tertiary stroke care, and primary care is highly inadequate.

The goal of reducing stroke morbidity and mortality requires both community-based and government-based approaches to stroke recognition and care. This influencer model, in our view, can also be used to shift group attitudes toward stroke. We can recognise the critical behaviours that can be used to bring about a transformation in the community's thought habits by educating them by vicarious interactions, using tools such as TV, radio, and tablets, and positively propagandising. To carry out these activities, we must identify influencers from within our own society; these influencers include physicians, emergency personnel, and others.

In rural areas, we will recruit and train a few people from their provincial communities to serve as team leaders in their societies. Stroke plans, including those for communicable diseases, should be established at the national level to cope with a big disability. Many strokes are currently caused by modifiable risk factors like obesity, asthma, and smoking. It is important to raise visibility and reduce preventable strokes as soon as possible. The use of mass screening to identify individuals at high risk of stroke has been proposed as a way to reduce the burden of stroke. The current stroke services should be focused on successful execution, supervision, and assessment. A stroke that is reversed is much preferable to one that is treated. Furthermore, government-based approaches should look at strengthening health-care services related to stroke care, such as first-responder care, which is critical in the early stages of stroke management. Ambulances and first responders need to be updated, and staff need to be properly qualified in how to treat stroke patients. Furthermore, such advancements must take into account the economic, sociocultural, and financial conditions of LMICs, which are vastly different from those of high-income countries. As a result, advances in stroke treatment must consider these features in order to be effective in LMICs, as well as a rise in educational knowledge about these health problems such that patients obtain medical assistance as soon as possible, which is actually inadequate and one of the reasons why this disorder has such a high morbidity and mortality rate in Pakistan.

CONCLUSION

Several solutions that are cost-effective, practical, and repeatable were discovered in our research, but they have yet to be tried. Such advancements must take into account the LMICs' economic, sociocultural, and financial conditions, which are

vastly different from those of high-income countries. In LMICs, more studies into the introduction of regionally and geographically tailored stroke systems should be prioritised. The most critical thing is to raise public consciousness about these health problems so that patients seek medical treatment as soon as possible, which is still missing and one of the reasons why this disorder has such a high morbidity and mortality rate in Pakistan.

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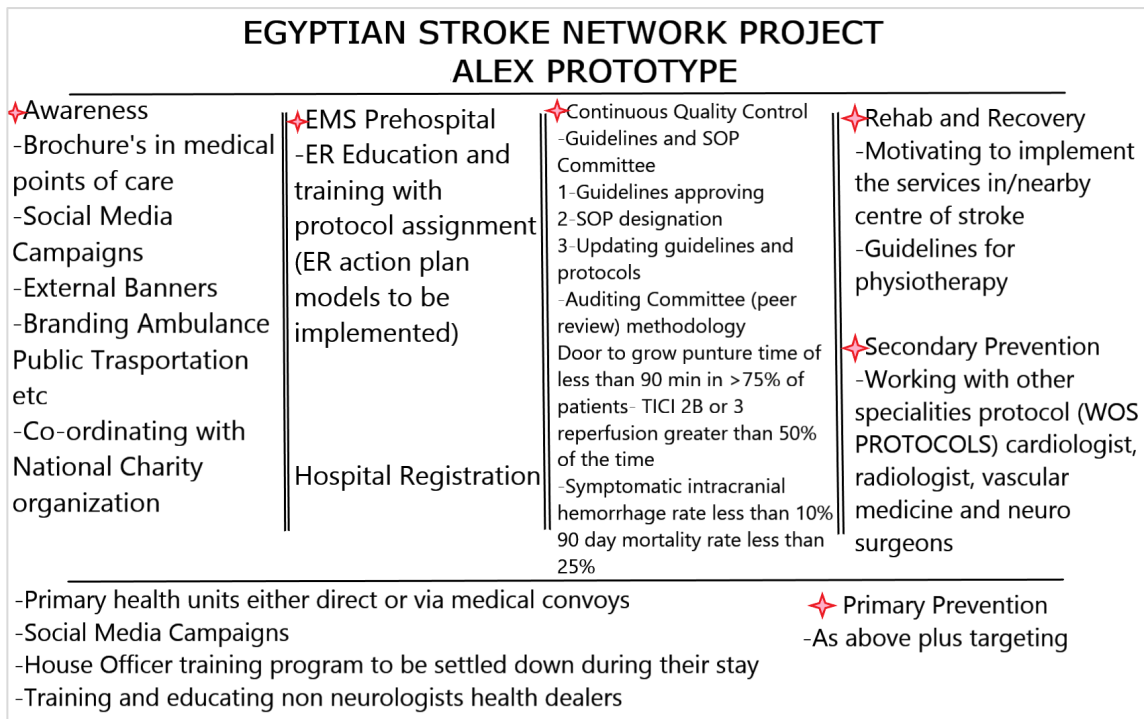
FIGURE LEGEND:

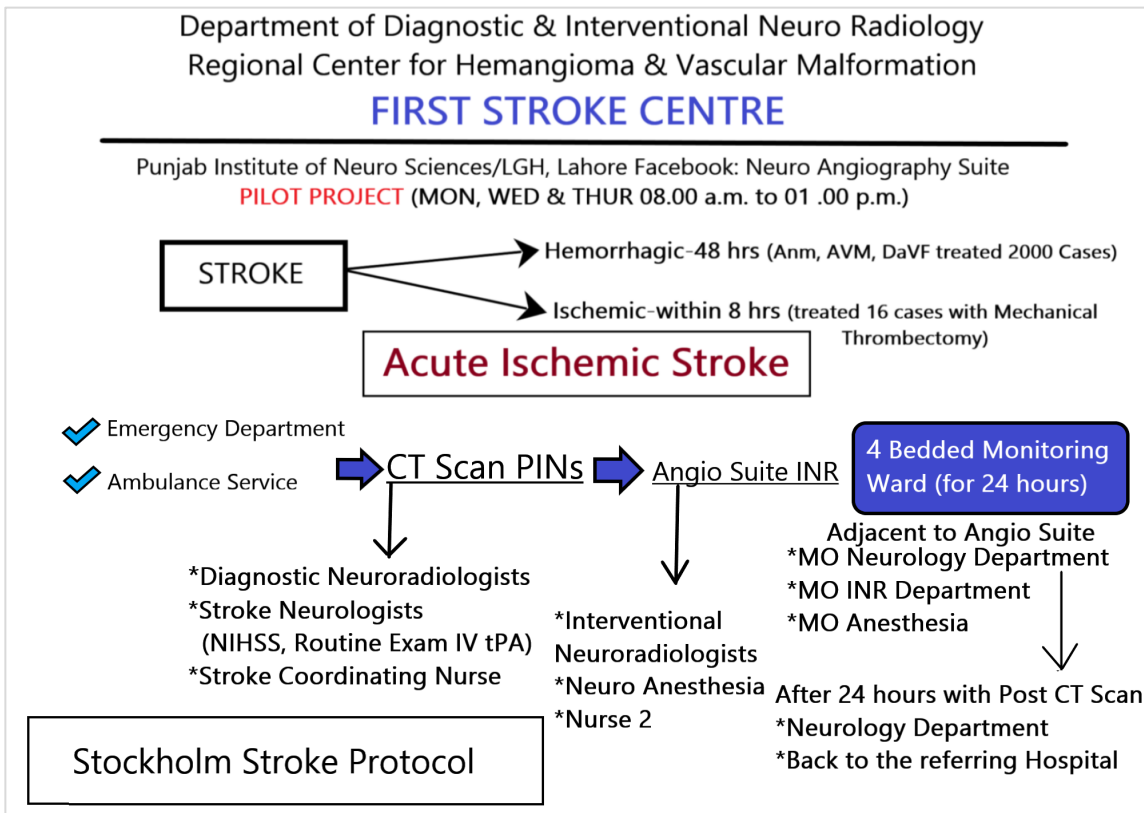**Figuire1:** Protocol used in stroke unit of Alexandria University Egypt.

Figure2: Protocol used in stroke unit of LGH Lahore

Suspected acute stroke at Siriraj Hospital

Tel. 99499

Radiology resident

Neuromed resident

INR resident

97021
โทรถามผู้ป่วย ซ้อมูล

ไปที่ ER ประเมินผู้ป่วยและพาผู้ป่วยไปยัง CT

ประสานงานผลลัพธ์ของ NCCT brain

NCCT brain fast track

+ve

-Onset <8hrs for Ant.Circulation
<12hrs for Post. Circulation
-NIHSS score >6 , No hemorrhage

Alert INR team

CTA/Multiphase CTA or CTP
MRI if suspected Post. Circulation

No Indication for MT

Postive indication for MT
ดูข้อบ่งชี้ในเอกสารประกอบ

Cancel INR team

Neuromed resident consult   ผู้สูงอายุ

INR resident confirm & set for MT

Neuro med
ดูแลผู้ป่วยต่อไป

INR team order
-Angiogram
-Inform consent & counseling

หากไม่ปฏิบัติตามแนวทางนี้ให้บันทึกเหตุผลในบันทึก
#REMARK# ทางการแพทย์ของผู้ป่วย
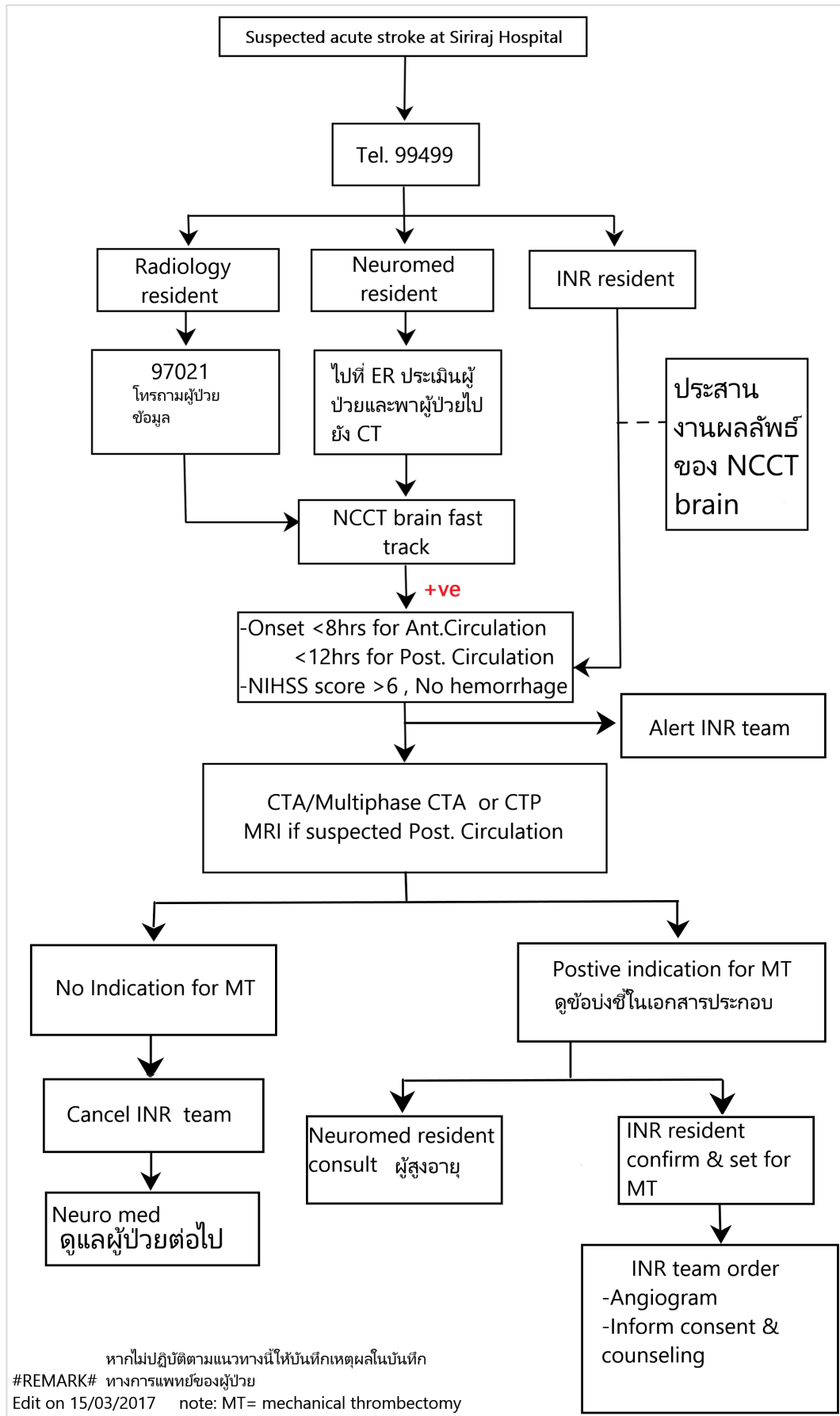Edit on 15/03/2017   note: MT= mechanical thrombectomy

Figure3: Protocol use in stroke unit of Siri Raj Hospital Thailand.

ASSOCIATION OF GLYCATED HAEMOGLOBIN LEVELS, LDL LEVELS, SYSTOLIC BLOOD PRESSURE, AND BMI WITH CAROTID ARTERY INTIMA-MEDIA THICKNESS (CIMT) IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT
Background: Hyperglycemia in type 2 Diabetes Mellitus patients causes glycated haemoglobin (HbA1C) transformed into AGEs, increasing oxidative stress and reduce nitric oxide activity. It lead to inflammation and endothelial dysfunction that triggers atherosclerosis. Changes in the vascular wall indicating atherosclerosis can be detected non-invasively using B-mode ultrasound.
Objective: To analyze the relationship between HbA1C levels, LDL levels, blood pressure, and BMI with the carotid artery intima-media thickness (CIMT) score in type 2 diabetes mellitus patients.
Methods: This was an observational analytic study consisted of 30 subjects with type 2 Diabetes Mellitus at the Endocrine Clinic Saiful Anwar Hospital, Malang, Indonesia from September 2018 to December 2019. Primary data were collected by CIMT examination using B mode ultrasound and measurement of other variables. Statistical analysis was done using SPSS 20.
Results: Statistical analysis showed a significant correlation between CIMT and HbA1C levels ($P<0.05$) with correlation coefficient P -0.441 and R 0.183, while the blood pressure, LDL levels, and BMI had a positive relationship to CIMT although they were not significant ($P > 0.05$).
Conclusion: There was a significant correlation between HbA1C levels and CIMT with an inverse relationship. The effectiveness of HbA1C predictor variable for CIMT was 18.3%.

Keywords: CIMT, type 2 diabetes mellitus, HbA1C, dyslipidemia, hypertension, obesity

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease characterized by an increased blood glucose levels (hyperglycemia) caused by insulin inadequacy. The most common cases in DM is type 2 diabetes.[1] According to data from the International Diabetes Federation (IDF) in 2015, the number of people with diabetes worldwide is around 415 million. Indonesia is the 6th country with highest number of diabetes patients in the world which is about 10.3 million people[2]. Diabetes with complications is the third leading cause of death after stroke and coronary heart disease, the percentage of deaths due to diabetes in Indonesia reaches 6.7%.

In type 2 diabetes mellitus, chronic hyperglycemia may transformed glycated haemoglobin (HbA1c) into advanced glycation end products (AGEs), increase oxidative stress and

reduce nitric oxide (NO) activity, then cause inflammation and endothelial dysfunction lead to atherosclerosis. Atherosclerotic plaque formation is a complex process involving many factors that play a role in the inflammatory response. This process takes a long time, progressively, slowly, and making it difficult to find the disease before the clinical symptoms occur[3].

Atherosclerosis commonly occurs in arterial branches, especially the common carotid artery which makes this artery as a sentinel vessel that describes the entire vascular condition. It is located in superficial and relatively easier to be examined than the aorta and femoral arteries. The carotid arteries are also being recognized as a valuable indicator for the status of coronary arteries. Atherosclerosis in the common carotid artery can be identified by measuring the intima-media thickness of the common carotid artery using carotid ultrasound examination. Sonographically, atherosclerotic plaque initially appears as an increased thickness of the intima and media layer then followed by ecogenic material lining the arterial lumen. B-mode ultrasound is a sensitive, noninvasive method for evaluating arterial walls and allows measurement of the carotid intima-media tunica thickness (CIMT) for the presence of stenosis and plaque. A thickening of the intima-media of the carotid artery by 0.1 mm is associated with an increased risk of developing myocardial infarction (10-15%) and stroke (13-18%). Carotid ultrasound is noninvasive, without ionizing radiation, is relatively inexpensive, and widely distributed so that it is easier to be reached [4].

A cross-sectional study that determines the correlation between levels of HbA1C and the thickness of intima-media tunica of the common carotid artery in 15 subjects with type 2 diabetes mellitus and 15 subjects with hypertension in India, resulted a positive correlation between HbA1C levels and CIMT of the common carotid arteries ($r = 0.44$; $p = 0.009$). A study with the same method by Perumal, et al., (2015) on 35 subjects with type 2 diabetes mellitus and 20 healthy subjects also described similar results. In a study at the Faculty of Pharmacy, Brawijaya University Malang with 54 children: 27 came from parents with ischemic stroke as a case group and 27 came from healthy parents as a control group, resulted a genetic variation in the osteopontin promoter T-443C and G- 156GG that increases the thickness of the carotid intima-media [5].

At the Saiful Anwar Hospital, Malang, Indonesia there were recorded as 9,567 patients with diabetes mellitus, which was the second most frequent outpatient visit in 2014. The study aimed to determine the relationship of HbA1C levels, LDL levels, blood pressure, and BMI with the CIMT score in patients with type 2 diabetes mellitus in Saiful Anwar Hospital, Malang, Indonesia which has never been done before.

METHOD
Population and Sample
The study population was type 2 diabetes mellitus patient in the endocrine clinic in Saiful Anwar hospital, Malang, Indonesia from September 2018 to December 2019. The inclusion criteria were patients with third or more visit to endocrine clinic with Type 2 DM with glycated hemoglobin (HbA1c) levels which is greater than or equal to 6.5%, age ranging from 30-75 and were agreed to participate in the study. Meanwhile, the exclusion criteria were non-cooperative patients or had involuntary movement disorders so that carotid ultrasound examination was difficult to be performed. Based on Indonesian basic health research, the prevalence of diabetes mellitus in Indonesia was estimated 8.5% of total population in 2018 (Riskesdas, 2018). Based on these data, it is possible to calculate the number of research samples using the Cochran's formula ($n = (Z^2 * P * (P-1) / D^2)$) where Z is a standard normal deviation set of 95% confidence level P is a prevalence rate, and D is confidence interval. Then we got the calculation become $n = (1.96^2 * 0.085 * (1-0.085) / 0.1^{2-}) = 0.298 / 0.01 = 30$ participants.

Method
This study was an observational analytic design with a cross-sectional approach, to determine the relationship between glycated Hb levels, LDL levels, blood pressure, and BMI to CIMT score in type 2 DM patients. This study was conducted in the USG room, Radiology Unit, Saiful Anwar Hospital, Malang, Indonesia. This study used a primary data. The first primary data was the ultrasound results of four ultrasound machines, two Philips Epiq 5 machines and two GE Logiq S8 using a linear probe

(5-12 MHz). IMT (Intimal-Media Thickness) sampling was carried out according to the Manneheim protocol on the proximal segment of the right-left common carotid artery manually or automatically using IMT auto measurement software. The data obtained from the measurements of the right and left carotid arteries were sampled and then calculated on its average [6]. Around 3 cc of peripheral blood was drawn from patient to obtain the HbA1C and LDL levels. Body height and weight and blood pressure also measured from every patient.

Statistical Analysis

Descriptive data were analyzed using descriptive statistics and presented in distribution frequency tables. After the data were grouped, statistical analysis was carried out using SPSS version 20 with Kolmogorov-smirnov test and Pearson correlation test. If a significant correlation is obtained, then followed by the analysis to determine which risk factor has the biggest role in increasing the thickness of carotid intimal media, a linear regression analysis regression was also obtained. CI 95%.

RESULTS

Subject characteristics

The study sample was limited to the first 30 people who were collected in this study, the sample consisted of 13 men and 17 women, along with the characteristics of samples (Table 1).

Table 1. Subject clinical characteristics

Variable	Means and Standard Deviation	Score Range
HbA1C levels	9,827 ± 2,629	6,6-16,0 %
Systolic blood pressure	144,33 ± 21,121	100 – 180 mmHg
Diastolic blood pressure	80,67 ± 11,121	60 – 110 mmHg
LDL levels	147,167 ± 44,693	48 – 225 mg dL
BMI	26,83 ± 6,482	16,61 – 47,91 kg/cm^2
CIMT	0,729 ± 0,212	0,455 – 1,200 mm
Age	57,27 ± 11,453	33 – 75 years

Table 2. Age and sex characteristics based on CIMT score

Variable	CIMT < 0,9	CIMT > 0,9	p-value
Age (means and standard deviation)	57.78 ± 10.929	55.57 ± 13.843	0.663
Sex			
Male	11 (36.7%)	2 (6.7%)	0.368
Female	12 (40%)	5 (16.7%)	

The age and gender characteristics of samples in this study were grouped based CIMT score category with a cut off score of 0.9 mm. In the group with CIMT score below 0.9 mm was with a mean age of 57.78. In the different test for the age variable using the Independent T-Test, it was obtained a value of 0.663, which indicates that there was no significant difference in the age variable in the CIMT score group below 0.9 mm or scores above 0.9 mm. Meanwhile, sex variable showed that both men and women were more likely to have a CIMT score below 0.9 mm. Whereas the chi square test showed no significant difference in CIMT scores based on sex variables (p value = 0.368) and the odds ratio score showed that female sex had a risk of 2.292 times higher than male sex to have a CIMT score of more than 0.9 mm.

CIMT characteristics

The results after measuring the common carotid artery wall, from the CIMT characteristic chart below, we obtained the highest CIMT reaches 1.1 mm in men and 1.2 mm in women. Meanwhile, the lowest CIMT was at 0.5 mm for men and 0.45 mm for women. It can be concluded that the thickness of carotid vessel walls on type 2 diabetes patients varies widely. Thickening indicates that the patient has subclinical atherosclerosis if CIMT score > 0.9 mm.
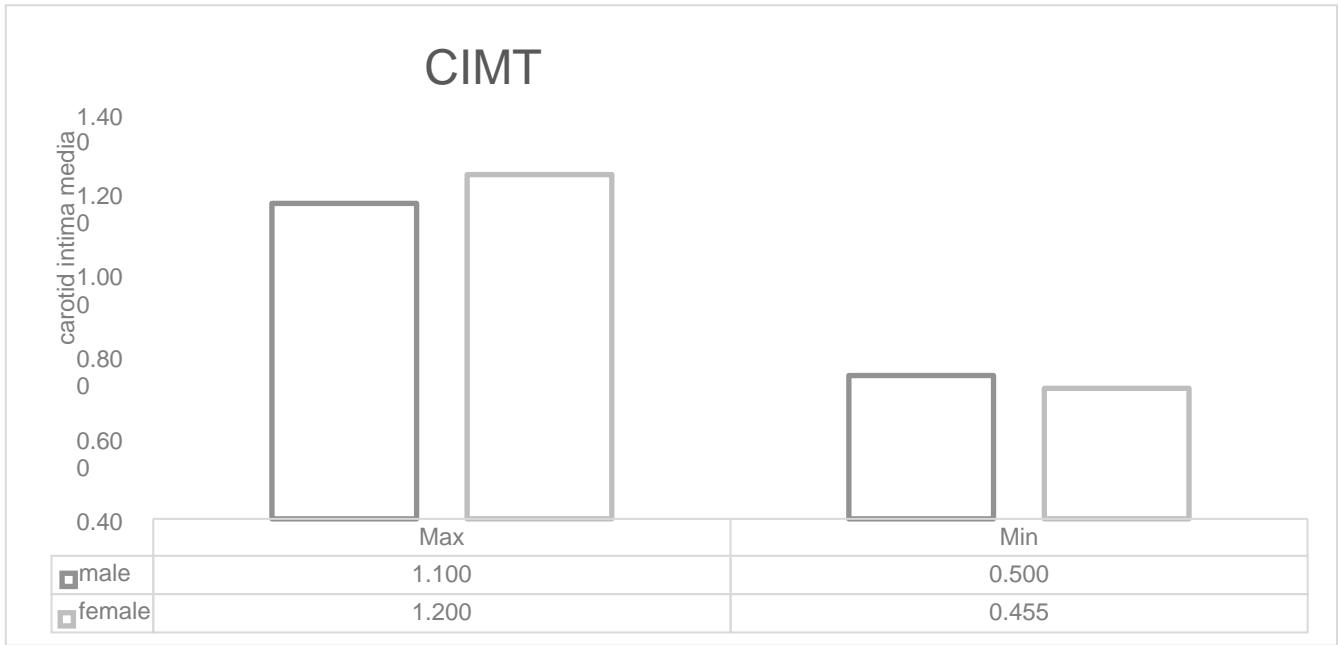
Figure 1. Diagram of CIMT characteristic based on sex

Deviation that occurs in the boxplot also shows the condition than most patients do not experience atherosclerosis, especially in men. Meanwhile in women there is a tendency to experience atherosclerosis even though the proportion of atherosclerosis from the collected is low.
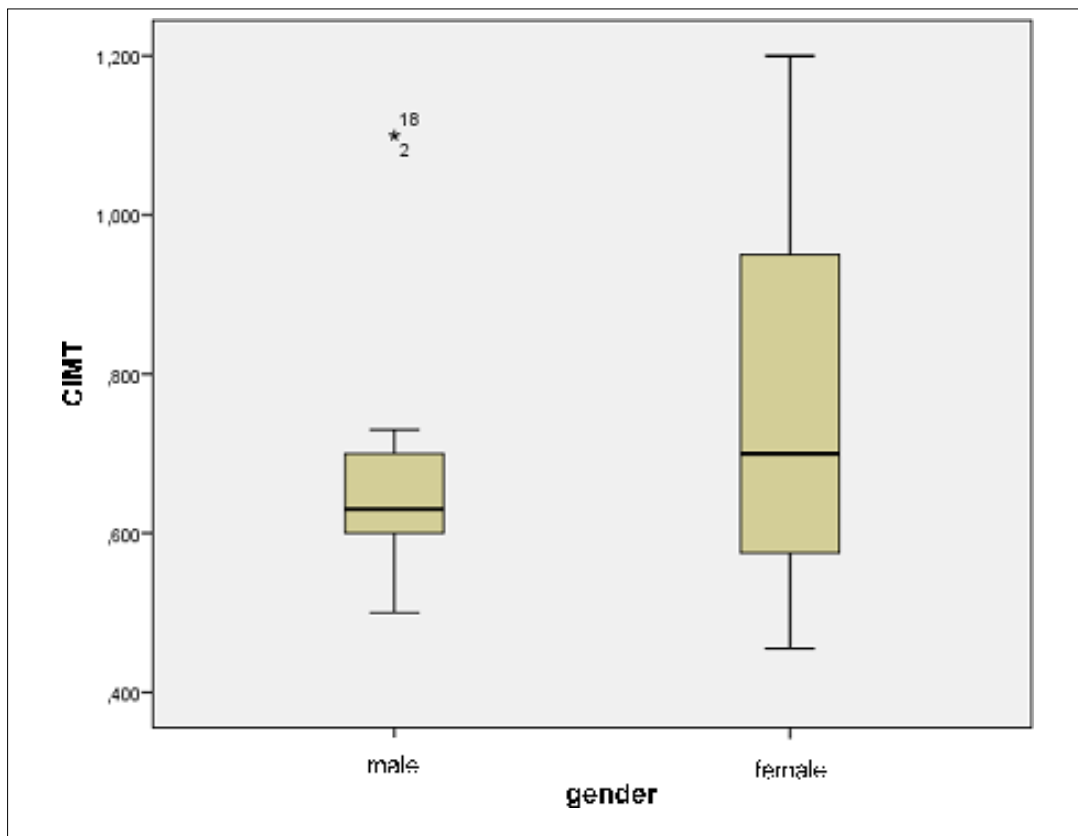

Figure 2. Boxplot of carotid characteristics based on sex

Correlation between Carotid Artery Intima-Media Thickness with Glycated Hb Levels, LDL Levels, Blood Pressure, and BMI

Table 3. The Correlation between Carotid Artery Intima-Media Thickness and Glycated Hb Levels, LDL Levels, Blood Pressure, and BMI

Correlation CIMT and Glycated Hb Levels	
p-value	0.015
Coefficient correlation	-0.441
Correlation CIMT and LDL Levels	
p-value	0.696
Coefficient correlation	+0.074
Correlation CIMT and Systolic Blood Pressure	
p-value	0.350
Coefficient correlation	+0.177
Correlation CIMT and BMI	
p-value	0.831
Coefficient correlation	+0.041

Table 3 shows there was a significant relationship between the Glycated Hb Level and the Carotid Artery Intima-Media Tunica Thickness with the calculation of the correlation coefficient of -0.441 which indicates that the relationship that occurs has the opposite direction, namely the higher the Hb content, the lower the thickness of the arterial wall carotid. In addition, it also shows that there was no significant relationship between the variables of LDL levels, blood pressure, and BMI with the carotid artery intima-media thickness.

Multivariate Analysis
To determine the form of the relationship that occurs in each predictor variable in this study, a linear regression test was carried out with the prerequisite that a linearity test was carried out to determine whether the variable has a linear relationship so that a regression test can be carried out.

Table 4. Data Linearity Analysis

Independent Variable	Dependent Variable	Df	F Score	F Table*	Note
BMI	CIMT	1:28	102,417	249	Linear
LDL		1:28	3,080	249	Linear
HbA1C		6:23	1,486	3,87	Linear
Systolic Blood Pressure		21:8	0,859	2,42	Linear
*. F Table at the 0,05 level					

It can be interpreted from table 4 that all independent variables have a linear relationship to the dependent variable, so that these variables can be continued in the next regression test. After that, linear regression tests were carried out at a significance level of 0.05 as follows:

Table 5. Data Linearity Analysis

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	R Square Change
		B	Std. Error	Beta			
1	(Constant)	1,516	,316		4,796	,000	0,183
	HbA1C	-,805	,321	-,428	-2,506	,018	

The form of the relationship obtained on the variable this time is:
$Y = a + bX$
$Y = 1,52 - 0,81 X$

Table 5 shows the R Square between variable HbA1C and CIMT is 0.183 and it can be interpreted that the effectiveness of the relationship between HbA1C and CIMT is 18.3%. In all predictor variables (HbA1C, LDL, BMI, and systolic blood pressure) the effectiveness was 18.3% contributed by the HbA1C predictor variable.

DISCUSSION

In this study, there was a significant correlation between the glycated Hb levels and CIMT with negative weak relationship. It is different from the previous researches where the higher of HbA1C levels will be followed by an increase in the thickening of the intima-media tunica wall of the carotid artery. These antithetical results may occur due to a different duration of increased HbA1C levels in the study subjects. Carotid intima media wall thickening takes a long time and high HbA1C levels are one of its risk factors. Some of study subjects that had lower HbA1C levels but had higher CIMT scores, could had been experienced type 2 diabetes for a long time and had received treatment already, so that when data was obtained the subjects had a lower HbA1C levels than before. The opposite results can also occurred in subjects with higher HbA1C levels and lower CIMT scores, could be due to recent increase of HbA1C levels. Singh et al. (2013) revealed that this type of cross-sectional study could not determine the relationship between HbA1C levels and the occurrence of ischemic stroke, without knowing the duration of the increase in HbA1C [7]. The importance of including the duration of DM disease was supported by the study of Kota et al. (2013) showed that the prevalence of CIMT in DM patients with a duration of more than 10 years was higher than DM patients with a duration of less than 10 years [8]. The limitation of this research is this is done in cross sectional not cohort study so the length of HBA1C increase cannot be evaluated. Patient also do not have previous HBA1C result.

Metabolic factors, such as hyperglycemia, obesity, insulin resistance, hypertension, hyperlipidemia, and increased inflammatory states have all been shown to contribute to the development of CIMT in diabetics. Variable LDL levels that indicate hyperlipidemia in DM patients, this study showed results ranging from 48-225 mg / dL with a mean value of 147.167 mg / dL and a normal threshold value of 100 mg / dL. There was no correlation between LDL levels and CIMT score in this study (p = 0.696). This finding were in contrary to previous research by Bulut (2019) which stated that there was a relationship between LDL levels and CIMT (p = 0.001). LDL plays an important role in the pathogenesis of atherosclerosis and the evolution of atherosclerotic plaque in studies worldwide [13]. The development of atherogenesis is associated with an abnormally high accumulation of low density lipoproteins in the intima. LDL is responsible for the transport of cholesterol from the liver to all tissues of the human body. Due to its role as a precursor to atherosclerosis the problem of transporting LDL molecules in the arterial walls [14]. Another factor is that VEGF can mediate the transport of LDL across the endothelial barrier via specific signaling pathways that have recently been demonstrated. Studies show that LDL, by binding to LDLR, induces

the auto phosphorylation of VEGFR1 and internalizes it together with LDL and LDLR, thus providing an additional mechanical route for LDL transport and leading to increased CIMT [9].

There was no significant relationship between blood pressure and CIMT in this study. This can be influenced by a wide range of blood pressure level obtained in this study. Previous study by Kota (2013) found higher CIMT score in diabetes patients with hypertension in compare to those without hypertension [8]. In addition, the study of Kong et al. (2000) stated there was no association between CIMT and fasting glucose level in normotensive individuals with type 2 diabetes mellitus[15].

In another study, measurement of the right carotid artery intima-media tunica in 394 healthy individuals, 327 uncontrolled hypertension, and 528 uncontrolled hypertension showed that the thickness in both patient groups, who are not taking any treatment, was higher than in the healthy group. In another study in 6975 people aged 19-90 years resulted the mean progression of the CIMT was significantly higher, especially having a significant association with arterial risk factors such as age, sex, hypertension, diabetes, and smoking habits [16].

The BMI data for the sample of this study resulted with a range from 16.61 to 47.91 and a mean value of 26.83. This study showed there was no significant relationship between BMI and CIMT (p = 0.831).

Several recent studies also found an activation of the cytokine resistin that secreted by adipocytes has been associated with obesity, insulin resistance, and atherosclerosis and has been specifically shown to increase endothelial permeability and thickness[19]. Body mass index and visceral fat accumulation in Human subjects are associated, inter alia, with elevated serum VEGF levels that exacerbate the thickness of the tunica in the carotid arteries [20]. However according to Jin et al. (2018), to examine the risk of obesity against CIMT, it is also necessary to measure the total fat mass or body fat distribution, because a high BMI value does not always indicate a person's high fat content, which refers to dyslipidemia conditions [12].

Besides that, several other factors that can affect a person's CIMT condition are drugs consumption, albumin levels, smoking habits, alcohol consumption habits, physical activity levels, and diet. A meta-analysis study by Ji et al. (2019) revealed that several cohort studies examining types of drugs such as antihypertensives, lowering fat levels drugs, and antidiabetics showed protective characteristics against CIMT process [21]. Research by Bots et al. (2009) and Herder et al. (2013) showed that the long-term use of lipid-lowering drugs was more effective in preventing CIMT than short-term use [22,23]. Therefore, in this study were not in line with other similar studies, it could be due to the consumption of drugs by the research subjects that can affect the condition of CIMT.

Smoking habits can increase macrophage infiltration and plaque thrombogenicity that lead to the risk of atherosclerosis [24]. Longitudinal study by Ji et al. (2017) stated that smoking habits can be associated with extracranial carotid atherosclerosis but not intracranial arteries [25]. Alcohol consumption habits can increase LDL oxidation and oxidative stress to increase the risk of atherosclerosis in men who consume alcohol more than 40 g / day [21]. Revealed by Gao et al. (2017) patients with type 2 diabetes have a higher risk factor for experiencing CIMT if they have a habit of consuming alcohol [26].

Physical activity and diet also play an important role on the CIMT score. Study by Park et al. (2017) who provided aerobic exercise intervention and endurance for 24 weeks resulted in a significant reduction in CIMT and an increase in the ratio of carotid flow velocity wall shear in a sample of overweight and obese elderly women [27]. Blekkenhorst et al. al. (2018) stated that the intervention of a Mediterranean diet which is rich in vegetables and fish show an oxidative stress inhibition and has a long-term prevention of the development of carotid atherosclerosis in patients newly diagnosed with type 2 diabetes[28].

CONCLUSION

There was a negative relationship between HbA1C level and CIMT in type 2 diabetes mellitus patients and no relationship of LDL levels, systolic blood pressure, BMI towards CIMT in type 2 diabetes mellitus patients

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A DESCRIPTIVE STUDY ON CHARACTERISTICS OF PATIENTS WITH MYOCARDIAL INFARCTION AND THEIR OUTCOMES: A RURAL PRIMARY HEALTHCARE SETTING IN LUBOK ANTU DISTRICT, SARAWAK

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ABSTRACT

**Introduction*:* Myocardial infarction (MI) is the leading cause of death worldwide. More studies are needed to provide insight of rural MI care in Malaysia.
Objective: This study aims to explore patient and non-patient factors in MI and mortality outcomes.
**Methods*:* We conducted an observational study involving secondary data collection through medical records review of whom presented to rural primary healthcare facilities before being referred to regional secondary and/or tertiary centres. We explored their inpatient and 30-day cardiac-related mortality outcomes. All MI patients from the locality were included, excluding those whose final diagnosis were not MI.
Results: Nine patients were included. Eight (88.9%) experienced STEMI. Eight (88.9%) were male. Median age was 53 (Q1:40.5–Q3:64.5) years. Median duration from symptoms onset to presentation was 2 (1.125 – 35.250) hours. Median time from presentation to aspirin delivery was 45 (12.5 – 86.0) minutes. The median door-to-needle time was 190 (163.0 – 212.5) minutes. Five (55.6%) received medical thrombolysis in secondary hospital prior to elective percutaneous coronary intervention (PCI). Inpatient mortality was 11.1% corresponding to 30-day mortality.
Conclusions: Logistic challenges and local healthcare limitations pose difficulties for rural MI care. Better equipped healthcare facilities is essential for prompt diagnosis and interventions for MI patients.

KEYWORDS: Myocardial infarction, rural, primary healthcare, Malaysia

INTRODUCTION

Myocardial infarction (MI) is the leading cause of death worldwide [1]. 17.9 million people died of cardiovascular disease each year, with an estimation of 32% of all deaths worldwide [2]. More than 75% of cardiovascular deaths occurs in low-income and middle-income countries [3]. Acute occlusion of coronary artery causing ST segment elevated myocardial infarction (STEMI) commonly leads to early mortality and myocardial damage [4]. In the UK, between the year of 2013-2014, there were 187,421 hospital visits due to MI.

This is translated into the fact that there was a patient being diagnosed with MI every 3 minutes on average [5]. According to National Cardiovascular Disease, Acute Coronary Syndrome (NCVD-ACS) Registry in Malaysia, there were a total of 17,771 patients diagnosed with acute coronary syndrome (ACS) throughout the country from 2014-2015, with 46.1% being STEMI, 25.2% being NSTEMI, 28.7% being unstable angina [6]. This translates into 0.03% of Malaysian population being diagnosed with ACS per year, considering a population of 32.7 million [7].

According to a study done in a rural hospital in Bangladesh, the in-hospital mortality rate of STEMI is high despite adherence to published guidelines and thrombolysis, highlighting the multifactorial contribution to cardiac mortality, including prolonged pain-to-door time, poor coverage of ambulance service, low community awareness of acute coronary syndrome, and lack of emergency medical services in rural settings [8]. Another study undertaken in north of Scotland looking at the discrepancy between the treatment of STEMI in remote compared to central locations, had identified the potential challenges to this discrepancy to include staffing availability and training, public awareness and inter-hospital communication [9].

Malaysia is a middle-income country with limited resources, especially in rural settings [10]. In rural areas of Malaysia, most patients with STEMI have limited or delayed access to thrombolysis or primary cutaneous intervention. Cardiac catheterisation laboratories are not readily available in rural hospitals. Moreover, long distances to the nearest hospitals limiting accessibility to thrombolysis, causes a delay in treatment. Great efforts are needed to overcome these challenges in rural settings in order to provide better care and outcome for patients with MI. There remain significant opportunities to improve STEMI care in rural setting of Malaysia.

Limited studies are available to provide insight of cardiovascular disease and MI care in rural settings in Malaysia. This study aims to explore patient and non-patient related factors among myocardial infarction patient population and their in-hospital and 30-day cardiac mortalities.

METHODS
Study type and design
This is a descriptive study involving retrospective data collection. We included patients who presented to primary healthcare facilities in a rural setting and subsequently referred to secondary or tertiary healthcare centers for further investigation and management.

Through a review of medical records from 7 primary healthcare facilities in Lubok Antu District, all consecutive study subjects who were diagnosed with myocardial infarction from 1 January to 30 June 2021 were included, subsequently being followed up on their status of in-patient cardiac mortality and 30-day cardiac mortality. Data collected from primary healthcare centers included patients' demographics, risk factors for cardiovascular disease, prior history of ischaemic heart disease, vital signs upon presentation, duration of symptoms prior to presentation, distance from place of onset to nearest clinics, treatment received in primary healthcare centers, and transportation journey from primary healthcare centers to secondary or tertiary healthcare facilities. Data on the level of cardiac enzymes and duration of hospital stay were obtained from secondary hospital, namely Sri Aman Hospital. Subsequently, in-hospital cardiac mortality and 30-day cardiac mortality post-MI were recorded for each patient through review of their inpatient records and medical records during their follow-ups in primary healthcare clinics after discharge. Patients who failed to present to primary healthcare clinics after discharge were contacted via phone calls to assess their post-discharge mortality status. No subject was lost to follow-up.

Study population, inclusion, and exclusion criteria
All consecutive patients diagnosed with myocardial infarction from 1 January 2021 till 30 June 2021 in primary healthcare clinics within Lubok Antu District, Sri Aman Division, were included; namely Lubok Antu Health Clinic, Engkelili Health Clinic, Batang Ai Health Clinic, Merindun Health Clinic, Nanga Kesit Health

Clinic, Nanga Stamang Health Clinic, Nanga Delok Health Clinic, and Nanga Patoh Health Clinic, were included. Patients who did not have a final diagnosis of a myocardial infarction were excluded.

Primary and secondary outcomes

The primary outcome of this study was in-hospital cardiac mortality. The secondary outcome was 30-day post MI cardiac mortality.

Ethics consent

This study was approved by Medical Review and Ethics Committee (MREC), Ministry of Health Malaysia (MOH) in 2021 (Approval Code: NMRR-21-285-58514). MREC waived informed consent for this study.

Statistical analysis

The data analysis was done using the SPSS version 22. Continuous variables were expressed as median with inter-quartile range as these data were skewed. Categorical variables were described as frequency and percentages.

RESULTS

Table 1: Characteristics of Patients with Myocardial Infarction and Their Outcomes

Characteristic	Total (n=9)	(Q1 ; Q3)	(min ; max)
Median age (IQR) – yr	53 (24)	(40.5;64.5)	37;79
Age < 55 yrs - no. (%)	5(55.6)		
Age > 55 yrs - no. (%)	4(44.4)		
Sex – no. (%)			
Male	8(88.9)		
Female	1(11.1)		
Race or ethnic groups - no. (%)			
Iban	8(88.9)		
Chinese	1(11.1)		
Types of MI – no. (%)			
STEMI	8 (88.9)		
NSTEMI	1 (11.1)		
Risk factors – no. (%)			
Hypertension	6(66.7)		
Diabetes mellitus	2(22.2)		
Dyslipidaemia	5(55.6)		
Family history of premature CVD	4(44.4)		
Smoking	6(66.7)		
Ex-smoker	1(11.1)		
Alcoholic	5(55.6)		
Ex-alcoholic	1(11.1)		
Past history of coronary revascularization	0		
Anti-platelet usage	2(22.2)		
Other variables – median (IQR)		Q1 : Q3	Min ; Max
Onset of symptoms to presentation – hour	2(34.13)	1.125;35.25	0.75;144
Duration from place of onset to primary healthcare facility – minutes	10(12.5)	5.0;17.5	2;20
Time from presentation to aspirin given – minutes	45(73.5)	12.5;86.0	10;102

Time from departure to arrival – minutes	80 (25)	75.0;100	70;105
Systolic BP – mmHg	114(39)	101;140	85;144
Diastolic BP – mmHg	78(15.5)	70.5;86	64;94
Heart rate – bpm	95(71.5)	83;154.5	74;240
SpO2 - %	97(9)	89.5;98.5	80;100
Respiratory rate – breath per minute	20 (4)	18;22	18;28
Random capillary blood sugar – mmol/L	10.4(4.27)	7.3;11.58	6.5;11.6
TIMI score	4 (4)	3;7	1;13
Treatment – no. (%)			
Medical thrombolysis	5(55.6)		
PCI	7(77.8)		
Hospitalization duration (days) - median (IQR)	4(3)	4;7.25	3;8
Door to needle time (min) - median (IQR)	190(49.5)	163;212.5	146;225
Total ischaemic time (min) - median (IQR)	270(92)	243;335	231;340
Outcomes (in-hospital) – no. (%)			
Alive	8(88.9)		
Death	1(11.1)		

IQR = Interquartile range
Q1= Lower quartile or First quartile
Q3= Upper quartile or Third quartile

Nine adult patients were included (refer Table 1). Eight (88.9%) patients experienced STEMI. Eight (88.9%) were male, and 8 (88.9%) were Iban. Median age was 53 (Q1: 40.5 – Q3: 64.5) years, the youngest being 37 years old. Median duration from onset of symptoms to presentation was 2 (1.125 – 35.250) hours. Median time from presentation to aspirin delivery was 45 (12.5 – 86.0) minutes. Median duration of the journey from place of onset to primary healthcare facilities was 10 (5.0 – 17.5) minutes. Median duration of the journey from primary healthcare to secondary hospital was 80 (75 – 100) minutes, the longest being 6 days. Median door-to-needle time was 190 (163.0 – 212.5) minutes. Median total ischaemic time was 270 (243 – 335) minutes. Five (55.6%) received medical thrombolysis in secondary hospital prior to elective percutaneous coronary intervention (PCI). In-patient mortality was 11.1% while 30-day mortality was correspondingly 11.1% as well.

DISCUSSION
Lubok Antu District in Sarawak consists of a population of 27,984 people, with the majority being Iban (indigenous group)/Malay (90.4%). Chinese occupied 5.8% of the population while Indian and others occupied 0.4% [11]. Hence, 88.9% of our study population consisted of Iban. National statistics show 1.4% incidence of ACS among Iban [6]. It is however, unable to conclude that Iban has higher prevalence of myocardial infarction from this study as the cohort population comes from an Iban predominant area.

Majority of the patients who experienced MI in this setting were relatively young compared to national data (median age groups of this study and national data were 53 and 58.6 years respectively). They were male predominant which was consistent with the national data from NCVD-ACS Registry (79.3% male) [6]. Eight (88.9%) of the study patients experienced STEMI. The alarming proportion of study population with STEMI is an area of concern, which deserves further exploration as to factors which might be

associated with the higher incidence of STEMI compared to 46.1% from national data [6]. However, there is also the possibility of under-reporting of NSTEMI due to non-presentation to healthcare facility, or death at home due to MI; which render further exploration in future study. Logistic challenge is also an issue in most rural settings in Malaysia which might affect the true reflection of incidence and prevalence of MI in rural.

Study shows that patient delay accounts for the time taken from onset of symptoms to first medical contact (FMC). FMC is defined as the time of first assessment by a healthcare professional who has the knowledge of obtaining and interpreting a 12-lead electrocardiogram (ECG) and administer initial treatment [12]. The longest duration from symptom onset to FMC in our study population was 144 hours which shows much room of improvement for early presentation. Early presentation and early initiation of treatment are the central goal in AMI management which have influence on the outcome of AMI [13]. Although exact factors which causes late presentation have yet to be established, patients who stayed in impoverished area are more likely to present late after symptoms onset [14]. Hence, further study is needed to investigate the factors which contribute to late presentation which might include patient's awareness, education level and socioeconomic background for subsequent measure to be taken to address the issue.

Another point that worth highlighting is the median time from presentation to aspirin delivery, which took 45 minutes, with the longest received aspirin only after more than 1 hour of presentation. The reason of delay in delivery of initial treatment needs to be explored in future study, which might include prompt recognition of the diagnosis by healthcare workers. This is important as it could potentially influence the cardiac-related outcome of MI patients and quality of MI care in rural settings.

Among the 8 (88.9%) patients presented with STEMI, only 5 (55.6%) received fibrinolytic therapy, as compared to national data of 69.2%. None of the patients in the study received primary PCI. The median door-to-needle time of 190 minutes in the study was longer compared to 45 minutes in the national data [6]. Late presentation

had resulted in patients missing the thrombolysis window. Logistic challenges, particularly long distance and journey time to the nearest hospitals, had also resulted in long door-to-needle time in our setting. There was no Cardiac catherisation laboratories available in the vicinity hospital for primary PCI even if patients presented within the appropriate thrombolysis window.

The overall in-patient and 30-day mortality rates from our study were 11.1% and 11.1% respectively. National data from NCVD-ACS Registry shows figures of 7.4% and 9.2% for in-patient and 30-day mortality respectively [6]. However, direct comparison of the statistics of our study's primary and secondary outcomes might not be valid due to the low power of study which is the main limitation of this study. The single mortality of this study was a gentleman of Chinese ethnicity with multiple cardiovascular risk factors of hypertension, dyslipidaemia and active smoker while taking aspirin for the past 7 days. Although he presented within 2 hours from symptoms onset and initial treatment was given within 15 minutes of FMC, he eventually succumbed with the diagnosis of STEMI. He had symptoms of severe angina which is defined as more than 2 angina episodes within 24 hours prior to presentation. Further study on the association between ethnicity or severe angina, and mortality outcome need to be carried out to ascertain the relationship between the factors and outcomes. Due to the low number of recruits of study population, analysis on association between different factors and the in-patient and 30-day mortality outcomes cannot be performed. However, it can be postulated that the mortality outcomes among patients in rural setting may be multifactorial, including long journey time from primary to secondary healthcare settings, delay in the delivery of antiplatelet therapy, non-availability of primary PCI, and lower thrombolysis rate. Measures should be undertaken to address logistic challenges and rural primary healthcare limitations in order to improve the standard of care for MI patients. Short duration of study is another limitation of this study. If a longer duration study is conducted, a larger sample size can be recruited to increase the power of the study and to explore the mortality outcome at longer interval.

More studies are needed to explore the regional epidemiology as the demography of the local population might be different from the national data for focus effort to be instituted to overcome local healthcare limitations. Larger power study will be useful to investigate factors which are associated with cardiac-related outcome.

CONCLUSION

The standard of MI care in rural setting still below the par of national standard due to logistic challenges and local healthcare limitations. These imply that more resources eg. laboratory cardiac enzyme markers need to be more readily available and widely accessible for prompt diagnosis of MI while enabling early intervention. Infrastructure in rural areas needs to be improved in order the overcome the logistic challenges faced by the remote community to present to healthcare to seek medical attention in the event of potentially life-threatening diagnosis. Furthermore, the high mortality rate of MI among young patients translates into a worrying fact that we are losing these productive individuals who could otherwise significantly contribute to the economy and growth of our country. It is a healthcare issue that should not be overlooked or undermined as it carries a significant impact to the community and the country. Therefore, concerted efforts are needed in raising awareness among the community on importance of early presentation to healthcare centres once developing symptoms suggestive of MI. In addition, facilities to bridge the gap in logistic challenges can be life-saving for the community, especially those from more remote area. More local secondary hospitals and cardiac catherisation laboratoreis are needed to support the large population in rural settings. If patients in rural settings were able to get to the nearest, adequately-equipped hospitals in a timelier manner with prompt and accurate diagnosis of acute MI was made, this potentially enables their outcomes to be comparable to those in urban and suburban settings in Malaysia. With the improvement of MI care in rural setting, the benefit will translate into greater quality of life among the community, potentially longer life-span and undeniably a considerable growth of the country's economy from the contribution of the productive group of individuals who enjoy better health while reducing the healthcare burden of dealing with morbidities and mortalities in long run.

CONFLICTS OF INTEREST

All authors of the study have no conflicts of interest to declare.

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THE IVY SIGN IN ADULT MOYAMOYA DISEASE

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A 30 years old gentleman with no known medical illness presented with headache and vomiting associated with right hemiparesis. Neurological examination revealed reduced power of both lower limbs (4/5). The patient's condition deteriorated, and he subsequently passed away.

"Ivy sign" was first described in 1995, so called because of its resemblance to 'ivy creeping on stone' (1) noted in post contrast MR images of approximately 70% of Moyamoya patients (2). It appears as continuous or discontinuous linear leptomeningeal enhancement due to accumulation of gadolinium in engorged pial vascular network formation that causes leptomeningeal collateral development (1, 2).

It can also be depicted on FLAIR image since fluid signal is effectively suppressed in this sequence; appears as high signal intensities along the cortical sulci and subarachnoid spaces (3). Recognizing Ivy sign as part of Moyamoya disease will avoid misdiagnosis, confusion with other differential diagnosis and eliminate potential unnecessary investigations.
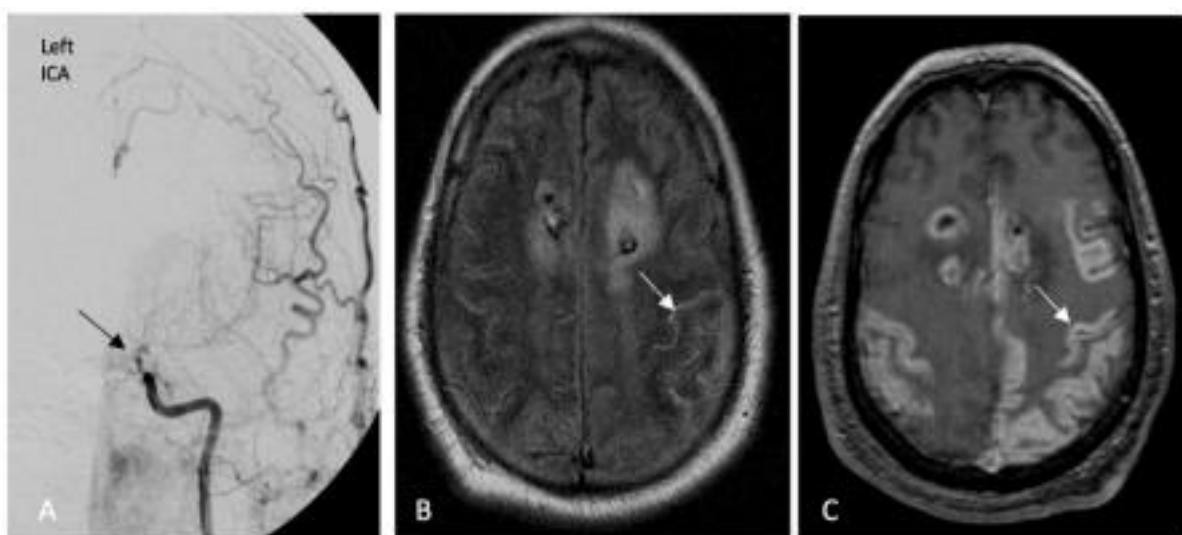

Figure 1: (A) Selective left ICA DSA shows steno-occlusion of distal left ICA, A1 segment of left ACA and M1 segment of left MCA with associated collateral vessels that gives the appearance of

puff of smoke (black arrow) in a Moyamoya disease. (B) Axial T2 FLAIR shows hyperintensity in bilateral cerebral sulci and (C) axial post gadolinium T1 weighted demonstrates marked leptomeningeal enhancement suggestive of Ivy sign (white arrows) in a Moyamoya disease.
Abbreviation: DSA - digital subtraction angiography

CONFLICTS OF INTEREST
I have no potential conflicts of interest to report with regard to this presentation

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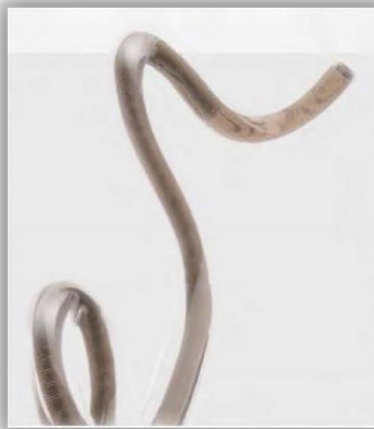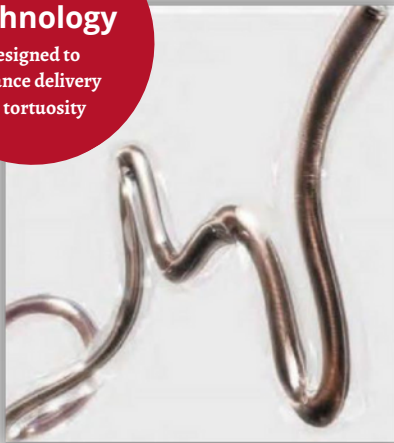
Penumbra

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REPERFUSION CATHETERS

62

68

72

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Designed to enhance delivery in tortuosity

62
.062" ID
1.93mm (0.76") OD
138cm Length

68
.068" ID
2.13mm (0.84") OD
132cm Length

72
.072" ID
2.16mm (0.85") OD
132cm Length