



# Relationship between Diagonal Earlobes Crease and Ischemic Stroke Risk

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## Abstract

**BACKGROUND:** Diagonal earlobe crease has been shown as the association between atherosclerotic diseases.

**AIM:** The aim of the study was to examine the relationship between diagonal earlobes crease (DELIC) and ischemic stroke.

**METHODS:** This prospective study recruited 175 consecutive acute ischemic stroke patients admitted to the Stroke Unit of Srinagarind Hospital, Faculty of Medicine, Khon Kaen University between May 2021 and August 2021. Clinical data included age, gender, underlying disease, clinical presentation, vital signs, brain computed tomography (CT), and DELIC assessed for both ears. The study was approved by the Human Ethics Research Committee of Khon Kaen University, Thailand.

**RESULTS:** All patients were assessed on clinical presentation and brain CT findings. There were 31 patients with transient ischemic attacks (17.7% of the patients) and 144 patients with cerebral infarction (82.3%). In all participants were male 58.9% and 72 were female (41.1%). The top three clinical presentations were hemiparesis (29.6%), dysarthria (27.0%), and facial palsy (17.5%). One hundred and thirty-one patients (74.9%) had underlying diseases; hypertension (24.2%), diabetic mellitus (14.4%), atrial fibrillation (4.9%), chronic kidney disease (2.0%), dyslipidemia (8.0%), valvular heart disease (2.3%), coronary heart disease (2.6%), previous stroke (8.1%), and other diseases (8.4%). Only 44 patients (25.1%) had no underlying disease. Frank's sign (DELIC) was present in only 13 patients (7.4%). There were similar proportions of major underlying conditions, hypertension, and diabetic mellitus for both groups and no differences apparent for gender or old age. On CT scans both DELIC and non-DELIC patients showed lacunar infarction as the major source of ischemic stroke.

**CONCLUSIONS:** Due to our very small sample of DELIC patients, we could draw no conclusions about the relationship between DELIC and ischemic stroke and its predictive utility as a biomarker for ischemic stroke. Given the much higher proportions of DELIC patients reported in the international literature, we raise the possibility of physiological, genetic, or ethnic differences in Thai, or Asian samples, for the future research.

## Introduction

According to the World Health Organization (1970) definition, "stroke is rapidly developing clinical signs of focal or global disturbance of cerebral function, with symptoms lasting 24 h, or longer, or leading to death, with no apparent cause other than of vascular origin." Ischemic stroke is one of the most prevalent cerebrovascular occurrences worldwide, and it is a one of the leading causes of death and long-term disability in Thailand. As a result, stroke is a major public health issue with substantial economic and social ramifications.

Some stroke risk factors, such as gender, age, and family history, are uncontrollable [1]. However, many stroke risk factors are lifestyle related, and stroke risk can be lowered by changing one's lifestyle. High

blood pressure, cigarette smoking, diabetes, high blood cholesterol levels, heavy drinking, a diet high in fat (especially saturated) and salt, poor in fiber, fruit and vegetables, lack of regular exercise, and obesity are all lifestyle-related variables that raise their risk of stroke [2].

The diagonal earlobes crease (DELIC), also known as Frank's sign, was initially identified in 1973 in the New England Journal of Medicine by an American physician (T. Frank) in a case series of patients with coronary artery disease. It is a diagonal crease in the earlobe which starts from the tragus to the edge of the auricle at an angle of 45° in varying depths as shown in Figures 1 and 2 [3]. Stoyanov *et al.* [4] described DELIC earlobes in a cardiac patient sample in an autopsy investigation published in 2020. DELIC-positive earlobes had myoelastofibrosis in the arterial vessel



Figure 1: Complete ear lobes crease

at the base of the earlobe, fibrosis, and Wallerian-like degeneration with eosinophilic inclusions in the peripheral nerves, according to the histopathology examination. According to the authors, this area is a line of merging of preexisting prenatal structures, making it vulnerable to atherosclerosis-related chronic hypoxia-reoxygenation harm.



Figure 2: Mild, moderate, and severe degree of diagonal earlobe crease

These patients' medical information and biomarker levels for atherosclerosis were also obtained. Male ratio, prevalence of hypertension, diabetes mellitus, Malondialdehyde-Low density lipoprotein, high sensitivity C-reactive protein (hs-CRP), and Pentraxin 3 (PTX3) levels were all shown to be greater in the DELC group as compared to the non-DELC group in this study. A multiple logistic regression analysis showed that PTX3 levels, rather than hs-CRP, constituted the strongest predictive factor for the appearance of DELC. The presence of DELC has also been linked to vascular inflammation and oxidative stress [5], [6].

In 376 postmortem examinations, Patel *et al.* [7] highlighted at the relationship between the grade of earlobe wrinkles and the degree of atheromatous disease. Each earlobe wrinkle was given a score of 0–3. Men with Grade 3 creases in both earlobes had an almost doubled risk of atherosclerosis, whereas women with bilateral high-grade creases had a nearly tripled risk. The risk of death from myocardial infarction was 2.50 in males and 3.70 in women with high-grade wrinkles. They came to the conclusion that DELC is a

significant marker of atheromatous illnesses and that includes it in a patient's clinical examination could be beneficial.

As DELC has been recommended as a marker for generalized atherosclerosis, researchers have looked at whether people with DELC have a shorter telomere, which is linked to faster cell turnover and early aging, which can lead to atherosclerosis [8]. DELC has also been proposed as a valuable dermatological indicator of accelerated aging, as seen by excessive telomere loss, as well as an indirect marker of high-risk metabolic syndrome patients [9].

Coronary heart disease and DELC as a risk indicator have also been reported to have a higher correlation than coronary heart disease and risk variables including arterial hypertension, cigarette smoking, or diabetes mellitus [10], [11]. Our research aimed to learn more about the association between DELC and ischemic stroke, as well as if DELC may be used as a simple, non-invasive predictor of the future ischemic stroke. If it does, physicians and healthy people may be able to undertake early-warning monitoring of earlobe alterations for prospective ischemic stroke events.

## Methods

### **Study design and patient recruitment**

This was a descriptive prospective study of 175 consecutive ischemic stroke patients admitted to Srinagarind Hospital, Faculty of Medicine, Khon Kaen University for standard investigation and treatment. Data were collected between May and August 2021.

Based on the previous typical 3–5 ischemic stroke hospital admissions per day, we had anticipated enrolling over 300 patients. However, the COVID-19

pandemic changed admission ward practices, patient capacity, and hospital resource allocations and referral practices. Thus, we could only enroll 175 consecutive patients.

**Data collection**

The DELC starts from the tragus to the edge of the auricle at an angle of 45° in varying depths. DELC grading was defined by three depth levels; mild, moderate, and severe using Patel et al.'s (1992) scale for reference (Figure 2) [5], [12]. Figures 1 and 2 present a range of DELC classifications, Figure 3 presents normal DELC, and Figure 4 shows traumatic earlobe creases from ear piercing. All patients went through the three-step data collection process below;



Figure 3: Normal earlobe

1. I first explained the research purpose and obtained patient consent
2. Then, personal and standard ischemic stroke physical examination data were recorded
3. I graded the DELC and photographed DELC patient's earlobes for reference comparison (Figures 1 and 2).

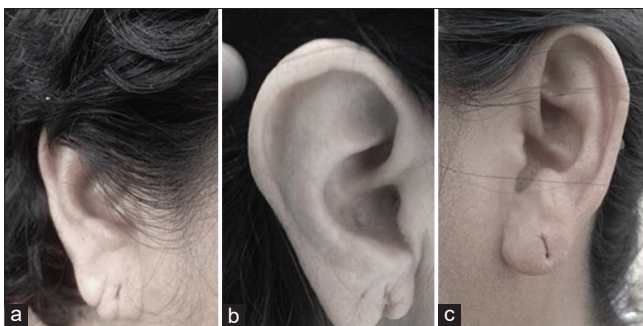


Figure 4: (a-c) Traumatic earlobe creases from ear piercing (exclusion list)

**Data analysis**

Descriptive data were calculated by frequency and percentage. However, the DELC group sample size was too small for meaningful statistical comparison with

**Table 1: Demographic data of ischemic stroke patients**

Clinical Characteristics	Total	Percentage	DELC (%)	No DELC (%)
<b>Age (years) (n = 175)</b>				
18–30	3	1.7	0	3 (1.8)
31–40	2	1.2	0	2 (1.2)
41–50	15	8.6	0	15 (9.3)
51–60	37	21.1	3 (23.1)	34 (21.0)
61–70	64	36.5	6 (46.1)	58 (35.8)
71–80	35	20.0	3 (23.1)	32 (19.8)
81–90	19	10.9	1 (7.7)	18 (11.1)
<b>Gender (n = 175)</b>				
Male	103	58.9	9 (69.2)	94 (58.0)
Female	72	41.1	4 (30.8)	68 (42.0)
<b>Systolic blood pressure (mmHg) (n = 174)</b>				
91–100	2	1.1	0	2
101–110	2	1.1	1	1
111–120	13	7.5	0	13
121–130	22	12.6	0	22
131–140	20	11.5	3	17
141–150	29	16.7	0	29
151–160	25	14.4	2	23
161–170	17	9.8	1	16
171–180	14	8.0	1	13
181–190	11	6.3	4	7
191–200	11	6.3	1	10
201–210	8	4.7	0	8
<b>Underlying diseases (n = 304)</b>				
Hypertension	84	24.2	8	76
Diabetic mellitus	50	14.4	4	46
Atrial fibrillation	17	4.9	0	17
Chronic kidney disease	7	2.0	0	7
Dyslipidemia	28	8.0	1	27
Valvular heart disease	8	2.3	1	7
Coronary heart disease	9	2.6	0	9
Previous stroke	28	8.1	2	26
Others	29	8.4	2	27
No underlying disease	44	25.1	3	41
<b>Primary presenting symptoms (n = 412)</b>				
Hemiparesis	122	29.6	8	114
Hemiparesthesia	56	13.6	7	49
Alteration of consciousness	10	2.4	0	10
Facial palsy	72	17.5	4	68
Dysarthria	111	27.0	8	103
Hemianopia	5	1.2	0	5
Dizziness	21	5.1	0	21
Aphasia	15	3.6	3	12
<b>NIHSS (n = 175)</b>				
TIA (0)	30	17.2	1 (7.7)	29 (18.0)
Mild stroke (1–3)	45	25.7	3 (23.0)	42 (26.0)
Moderate stroke (4–7)	44	25.1	4 (30.8)	40 (25.0)
Moderate to severe (8–15)	39	22.3	1 (7.7)	38 (23.0)
Severe stroke (>16)	17	9.7	4 (30.8)	13 (8.0)

DELC: Diagonal earlobes crease, NIHSS: National institute of health stroke scale, TIA: Transient ischemic attack.

the non-DELC group. All calculations were performed on SPSS (version19).

**Ethical considerations**

This research was reviewed and approved by the Human Ethics Research Committee of Khon Kaen University before any data were collected (HE641017). There were no conflicts of interest or funding sources, to declare.

**Results**

**Demographic data and clinical presentation**

The majority of the 175 patients were male 58.9% with 41.1% female. The largest group of ischemic stroke patients was in the 61–70 years age group (64 patients, 36.5%). For most cases, systolic



blood pressure (SBP) at diagnosis was high, over 140 mmHg (66.2%). We used the 2020 International Society of Hypertension Global Hypertension Guideline classification defining Stage 1 hypertension as 130–139, and Stage 2 as more than 140. In total of our patients, 66.2% had Stage 2 of hypertension. The top three presenting ischemic stroke symptoms were hemiparesis 29.6%, dysarthria 27.0%, and facial palsy 17.5%.

The top three underlying diseases were hypertension 24.2%, diabetic mellitus 14.4%, dyslipidemia 8.0%, and plus previous stroke history 8.1%. Other comorbidities were shown in Table 1. On assessment, 13 patients (7.4%) were classified with DELC and 162 without DELC (92.6%). Using National Institutes of Health Stroke Scale (NIHSS), 69.3% of DELC patients had moderate or severe strokes compared to 56.0% for non-DELC patients. However, given the small DELC sample size, this can only be a descriptive observation.

Of the 13 DELC patients (nine male and four female), 3 male patients presented without underlying disease. Most (eight patients) had underlying disease such as hypertension and diabetes mellitus. Almost all (12 patients) had high SBP on admission. CT brain findings were mostly lacunar infarction, two had normal findings, and three had large vessel occlusion. Table 2 presents the clinical case data for the 13 DELC patients.

## Discussion

This study set out to investigate the relationship between DELC and ischemic stroke, and, if DELC was potentially a simple, non-invasive marker for the future ischemic stroke. Unfortunately, due to the very small sample of DELC patients recruited here, no conclusion could be drawn about its predictive utility.

The previous international research has

shown relationships between DELC and ischemic stroke, suggesting its possible role as a non-invasive predictor for ischemic stroke. In addition, DELC has been linked with atherosclerosis processes associated with metabolic syndromes such as hypertension, diabetic mellitus, dyslipidemia, and obesity. Kamal *et al.* [12] found a high frequency of DELC in patients suffering from hypertension and diabetic mellitus at risk of atherosclerotic cerebrovascular and cardiovascular events. Nazzal *et al.* in a prospective series of 241 ischemic stroke patients found 190 had Frank's sign. Frank's sign (DELC) was found in patients with hypertension and diabetic mellitus and there was a significant correlation with old age, but no gender differences [6].

In contrast to the research above, our study found only a very small proportion, 13 (7.04%), of 175 ischemic stroke patients with DELC. There were similar proportions of underlying hypertension and diabetic mellitus for both groups. There were no differences between DELC and non-DELC patients for gender or old age. On CT brain scan, both DELC and non-DELC patients showed lacunar infarction as the major source of ischemic stroke.

In contrast to the international studies, we found only a very small proportion of DELC patients in our sample, thus we were not able to draw meaningful conclusions about the relationship between DELC and ischemic stroke. However, given that difference, the possibility of physiological, genetic, or ethnic differences between Thai, or Asian patients, and North American and European patients in the international literature could also be considered in further research. If further research supports an association between DELC and ischemic stroke risk, there could be useful artificial intelligence applications using standardized earlobe comparison pictures that physicians and community members could use for simple, non-invasive prediction, and prevention of ischemic stroke risk.

**Table 2: Clinical data of patients with diagonal earlobes crease**

Gender	Age	DELC grading	Underlying disease	NIHSS	SBP	CT brain	Diagnosis
Female	57	Bilateral mild	HTN, T2DM, and previous stroke	11	181	Lacunar infarction	Ischemic stroke
Male	69	Bilateral moderate	HTN	23	162	LVO	Ischemic stroke
Female	58	Bilateral moderate	-	3	175	Normal	Ischemic stroke
Male	85	Bilateral severe	HTN, DLD, and ICH	25	133	LVO	Ischemic stroke
Male	72	Bilateral moderate	-	0	152	Normal	TIA
				ABCD <sub>2</sub> = 4			
Male	60	Unilateral moderate	HTN	7	186	LVO	Ischemic stroke
Male	66	Bilateral mild	-	21	135	LVO	Ischemic stroke
Male	73	Bilateral severe	-	4	196	Lacunar infarction	Ischemic stroke
Female	64	Bilateral severe	HTN and T2DM	1	187	Lacunar infarction	Ischemic stroke
Female	78	Bilateral moderate	HTN and VHD	3	186	Lacunar infarction	Ischemic stroke
Male	64	Bilateral severe	HTN and T2DM	17	139	Lacunar infarction	Ischemic stroke
Male	66	Bilateral moderate	HTN and T2DM	4	152	Lacunar infarction	Ischemic stroke
Male	66	Unilateral moderate	BPH and Gout previous stroke	5	102	Lacunar infarction	Ischemic stroke

\*DELC\* Diagonal earlobes crease, NIHSS: National institute of health stroke scale, SBP: Systolic blood pressure, CT: Computed tomography, HTN: Hypertension, T2DM: Type 2 of diabetic mellitus, LVO: Large vessel occlusion, TIA: Transient ischemic attack, VHD: Valvular heart disease, BPH: Benign prostate hyperplasia.

## Conclusions

Our study demonstrated no conclusions about the relationship between DELC and ischemic stroke and its predictive utility as a biomarker for ischemic stroke.

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