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Association Between Coronary Artery Atherosclerosis and Diagonal Earlobe Crease (Frank's Sign): A Prospective Autopsy Study in Sri Lanka

Lowe W.M.T.[1], Hulathduwa S.R.[2], Ekanayake E.M.K.B.[3]

[1]Registrar in Forensic Medicine, Faculty of Medical Sciences, University of Sri Jayewardenepura,
Sri Lanka

[2]Professor in Forensic Medicine, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka

[3]Registrar in Forensic Medicine, Faculty of Medicine, University of Peradeniya, Sri Lanka

Corresponding Author:

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Abstract

Frank's sign (FS) or the diagonal earlobe crease (DELC) was first described in 1973, with histopathological findings showing myoelastofibrosis, diffuse fibrosis and Wallerian-like degeneration in the underlying arterial vessels at the base of the crease. Recent studies have suggested a potential association between the presence of DELC and an increased risk of coronary artery atherosclerosis (CAA). This study was aimed to investigate the association between the presence of FS with age, CAA and cause of death and explore associations with comorbidities like ischemic heart disease (IHD), hypertension, dyslipidemia (DL) and diabetes mellitus (DM). The severity of Frank's sign was assessed and correlated with macroscopic narrowing of the coronary arteries, cause of death and the presence of major cardiovascular risk factors (IHD, hypertension, dyslipidemia and diabetes) in 224 autopsy samples at Colombo South Teaching Hospital, Kalubowila, Sri Lanka, conducted during 2024-2025. The study included 224 cases (152 males, 72 females) above the age of 30 years, with a mean age of 64 years and a mean left-ventricular thickness of 15 mm. There was a statistically significant association between FS and the age ($p = 0.001$), with individuals with prominent FS being older on average. Cardiac-related deaths were significantly commoner among those with Frank's sign compared to non-cardiac causes ($p=0.002$). The severity of Frank's sign showed a moderate, positive and statistically significant correlation with major coronary artery narrowing and occlusion ($p<0.001$). Significant associations were also observed between higher severity/degree of Frank's sign and a history of hypertension ($p=0.010$), IHD ($p=0.002$) and dyslipidemia ($p=0.005$). However, the association with DM was not statistically significant ($p=0.053$). These findings support the use of Frank's sign as a potential external indicator for the risk and severity of CAA.

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Keywords: Frank sign, Coronary Artery Atherosclerosis, Hypertension, Dyslipidemia

Introduction

The Frank sign, also known as the diagonal earlobe crease (DELC) is one of those fascinating clinical features that, by a quick look of a physician from the outside appearance, might disclose the possibility of internal pathology pertaining to cardio-vascular system. Dr. Sandra T. Frank first described the DELC as a deep diagonal groove that runs from the tragus across the lobule to the rear edge of the earlobe1. The histopathological changes associated with the DELC include myoelastofibrosis in arterial walls, diffuse fibrosis and Wallerian-like degeneration with eosinophilic inclusion in the peripheral nerves2, 19.

This sign had been traced back to the 2nd century A.D where the statues of the Roman emperor Hadrian (76–138 A.D) clearly depict this crease. According to the ancient legends, his death was often interpreted as being caused by exacerbated heart failure3. Modern studies suggest that Frank's sign is associated with endothelial dysfunction representing an early stage of systemic atherosclerosis. For decades, researchers have investigated the link between the crease and atherosclerosis. The earlobe and the heart share similar pathways of microvascular supply.

Frank sign

The histopathological changes associated with the DELC include myoelastofibrosis in arterial walls and Wallerian-like degeneration with eosinophilic inclusion in the peripheral nerves2. There was diffuse fibrosis at the base of the crease. These changes suggest progression of the crease changes with advancement of age4. Sometimes, a corkscrew-like twisted arterial vessel with myoelastofibrosis was seen at the base of the crease. The unbalanced collagen-elastin ratio in the ear lobe vasculature is also seen in coronary artery beds. From an embryological point, the diagonal ear lobe crease connecting the tragus to the tip of the earlobe is a tissue weak point, which may cause the crease4. The nature of the changes in the ear lobe seems to be based on the physiological law of oxygen level of the ear lobe due to development4. The ear lobe is embryologically formed by the fusion of the first and the sixth hillocks of His, on the first and second pharyngeal arches. This site represents decreased vasculature compared to other sites4. These changes make it more susceptible to chronic hypoxia and re-oxygenation injury before it is displayed in any other surface structure such as cyanosis in acute events and epidermal degeneration in chronic events4.

A patient with heart failure shows chronic hypoxia and re-oxygenation-related changes especially after physical stress or exertion even without an anginal attack. This affects the auricular blood vessels with segmental myeloelastofibrosis, Wallerian-like degeneration and nerve damage; ultimately leading to the formation of a crease on top of the changed tissue. The Wallerian degeneration has been described in the cardiac muscles after both myocardial infarction and heart failure4. These changes are also seen in the tip of the helix of the ear but due to the rigid cartilaginous support, it will take a longer period for the changes to be grossly

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visible. Genetics, environmental and behavioural factors such as smoking and medications can play a role as a causative factor in the development of this crease. This sign is associated with HLA-B27, C3-F Arteriosclerosis gene and chromosome5. For the study purposes, this diagonal ear lobe crease was divided into four categories. Grade 01 is the wrinkling of the skin at the earlobe, grade 2a is the superficial crease that runs diagonally at the earlobe 50%, grade 2b is the crease more than 50% across the earlobe and grade 03 is a deep cleft across the whole earlobe.

Justification

Frank's sign, the diagonal ear lobe crease (DELC) was described in 1973 by an American Pulmonologist, Sandras T Frank1. It was described as a diagonal skin fold between the tragus and outer edge of the ear lobe extending 450 backward from the tragus1. Recent observational studies have suggested a potential link between the presence of DELC and an increased risk of coronary artery atherosclerosis. The histopathological changes associated with the DELC include myoelastofibrosis in an arterial vessel, diffuse fibrosis and Wallerian-like degeneration with eosinophilic inclusion in the peripheral nerves. These changes suggest the progression of the crease with age. Corresponding studies are based on clinical and angiographic findings while only a few are related to autopsy findings with histopathology.

The studies suggest that DELC is associated with endothelial dysfunction, which is known to represent an early stage of systemic atherosclerosis2. This proposal outlines a comprehensive research study aimed at investigating and understanding the association between DELC and the gross morphology of coronary artery atherosclerosis with demographic data and history of cardiac disease in the Sri Lankan population. This is a pioneer study designed for Sri Lanka. The study population already includes all males and females above 30 years (with the below-mentioned exclusion criteria) subjected to a medico legal autopsy. They may or may not have a history of IHD and further, their cardiac atherosclerotic findings would be different. Thereby, the researchers would be able to find out whether the earlobe sign carries any significance for Sri Lankan populations as an indicator of premature cardiovascular risk and if so, to what extent is this predictive value reliable for the aforesaid population.

Material and Methods

This is a cohort study with prospective analysis of the postmortem samples. The entire adult population (bodies) over 30 years, referred to postmortem examinations at the Colombo South Teaching Hospital, Kalubowila, Sri Lanka from 2024/04/01 onwards were included in this study. Bodies with damaged and/or deformed ear lobes (congenital malformations, acquired injuries during life and traumatic deaths to head and neck area etc.), age less than 30 years, decomposed/putrefied bodies, anasarca (extensive generalized oedema), any alteration which alters the appearance of the ear lobes (extended piercing etc.) and where the consent had not been granted by the claimants of the body were excluded from the study. These criteria were applied to maintain the reliability of the research. Epidemiological data and clinical data were collected from the deceased's clinic books, previous medical records, medical investigations and

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bed head tickets. The appearance of the ear lobe (photographic evidence), macroscopic appearance of the heart and the degree of coronary artery narrowing were collected by the authors by themselves during the autopsy. The deceased were grouped according to the age, earlobe appearance and coronary artery narrowing. Photographs of both ear lobes were taken and used to categorize the ear lobe appearance as following: Grade 1 (Wrinkling), Grade 2a (Superficial crease), Grade 2b (Crease more than 50% across the ear lobe) and Grade 3 (Deep cleft across whole ear lobe). Macroscopic examination of the coronary arteries was done. Narrowing of the coronary artery lumen was noted down in major coronary arteries, left common trunk, left anterior descending artery, circumflex artery and the right coronary artery. All forms of coronary artery narrowing (eccentric and concentric) and presence of thrombosis were taken into consideration to categorize the coronary artery narrowing as follows: CAD RADS 01 (1% - 24%), CAD RADS 02 (25% - 49%), CAD RADS 03 (50% - 69%), CAD RADS 04 (70% - 99%) and CAD RADS 05 (100%).

Data of the findings were entered and statistically analyzed using the latest version of Statistical Package for Social Sciences (SPSS version 26). A value of <0.05 was considered as statistically significant. Data are described using percentages, mean and median according to their relevance to cover the study objectives. Chi-square test was used where necessary. The median age, sex, and associated factors were analyzed and presented through tables, graphs and charts. The association of the Frank's sign vs age was analyzed by the Mann-Whitney U test. The association of the Frank's sign vs cause of death (Cardiac/non cardiac) was analyzed by Chi square test. The association of the Frank's sign vs coronary artery atherosclerosis was analyzed by Spearman's correlation.



Fig 1. Grade 1 (wrinkling)

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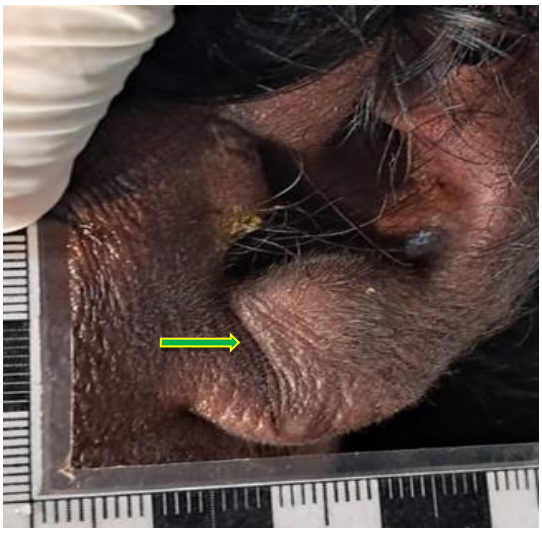


Fig 2. Grade 2a (superficial crease)



Fig 3. Grade 2b (crease more than 50% across the ear lobe)

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Fig 4. Grade 3 (deep cleft across the whole ear lobe)

Results

A total of 224 autopsies which were conducted at Colombo South Teaching Hospital, Kalubowila, Sri Lanka since 1st of April 2024 were included in the analysis. Among them, 67.9% (n=152) were male and 32.1% (n=72) were female.

Table 01: Percentage of males and females in the study

Male	Percentage	Female	Percentage
152	67.9%	72	32.1%

Table 02: Frank's sign positive percentage among males and females

Frank's sign was positive in 204 cases and it was not evident in 20 cases.

Male (Frank's sign positive)	Positive percentage from total positive cases	Female (Frank's sign positive)	Positive percentage from total positive cases
145	71%	59	29%

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The mean age was 62.76 years for this data series. The minimum age obtained for the study was 30 years and the oldest deceased found in the study was 94 years of age. According to the analysis, individuals with Frank's sign were older on average than those without (According to the Mann-Whitney U test, P = 0.001). According to the Kruskal-Wallis test, the data showed a clear trend that the older ages are more associated with a higher severity of Frank's sign (older the individual is, higher the grading of the sign tend to be).

Table 03: The categories/grading of Frank's sign with the number of cases for each

Ear lobe appearance	cases
None	16
Wrinkling	40
More than 50% crease	54
100% crease	56
Deep cleft	58
Total	224

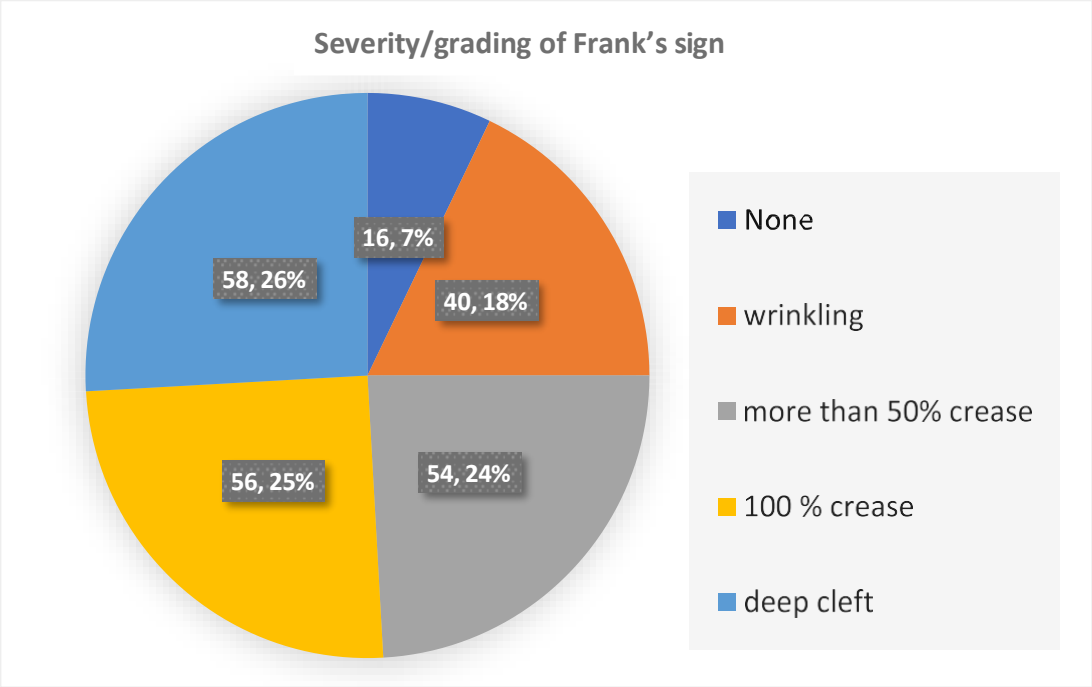


Fig 5. Severity/grading of Frank's sign

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Mean ranks increase consistently with the severity of Frank's sign: None = 57.91, Wrinkling = 89.39, more than 50% crease = 110.68, 100% crease = 111.59 and Deep cleft = 138.86. This shows a clear trend that older ages are associated with more severe degree of earlobe creasing.

Frank's sign (present/absent) vs COD (cardiac/non-cardiac)

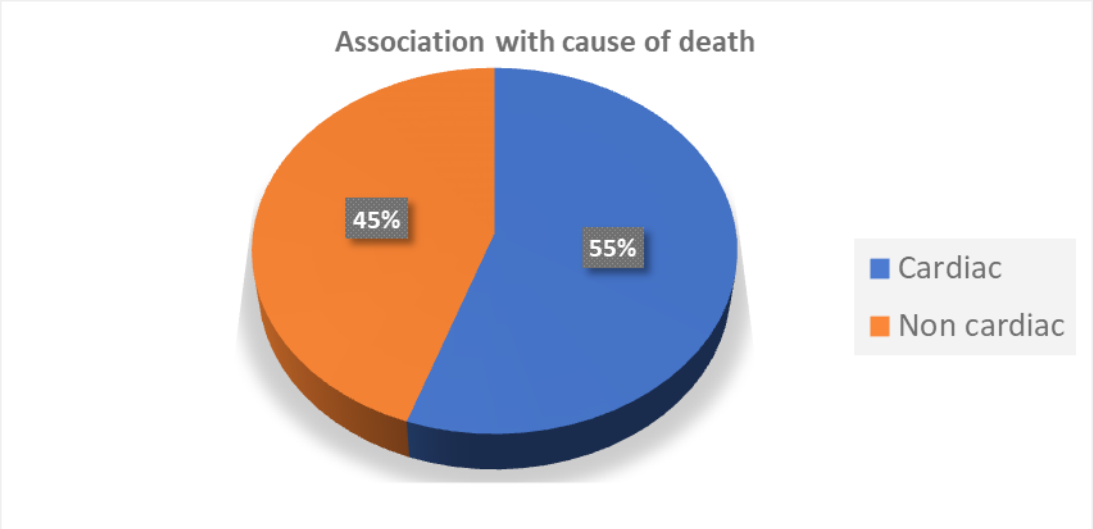


Fig 6. Frank's sign positive cases with cause of death

In the absence of Frank's sign, non-cardiac deaths were 13/16 (81.3%) and cardiac deaths were 3/16 (18.8%). In the presence of Frank's sign, non-cardiac deaths were 87/208 (41.8%) and cardiac deaths 121/208 (58.2%). There is a high tendency that, according to the chi-square test, individuals with Frank's sign are more likely to have died from cardiac causes

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Frank's sign (5 categories) vs Coronary Artery (CA) narrowing

Table 04: Frank's sign positive percentage with the degree of narrowing of the Left anterior descending artery

Left anterior descending artery		
Degree of narrowing	Frequency (number)	Percentage
Category **01** (1-24%)	21	9.4
Category **02** (25-49%)	38	17.0
Category **03** (50-69%)	40	17.9
Category **04** (70-99%)	95	42.4
Category **05** (100%)	30	13.4
Total	224	100.0

Table 05: Frank's sign positive percentage with the degree of narrowing of the Right coronary artery

Right coronary artery		
Degree of narrowing	Frequency (number)	Percentage
Category **01** (1-24%)	36	16.1
Category **02** (25-49%)	32	14.3
Category **03** (50-69%)	62	27.7
Category **04** (70-99%)	76	33.9
Category **05** (100%)	18	8.0
Total	224	100.0

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Table 06: Frank's sign positive percentage with the degree of narrowing of the Left circumflex artery

Left circumflex artery		
Degree of narrowing	Frequency (number)	Percentage
Category **01** (1-24%)	38	17.0
Category **02** (25-49%)	42	18.8
Category **03** (50-69%)	54	24.1
Category **04** (70-99%)	74	33.0
Category **05** (100%)	16	7.1
Total	224	100.0

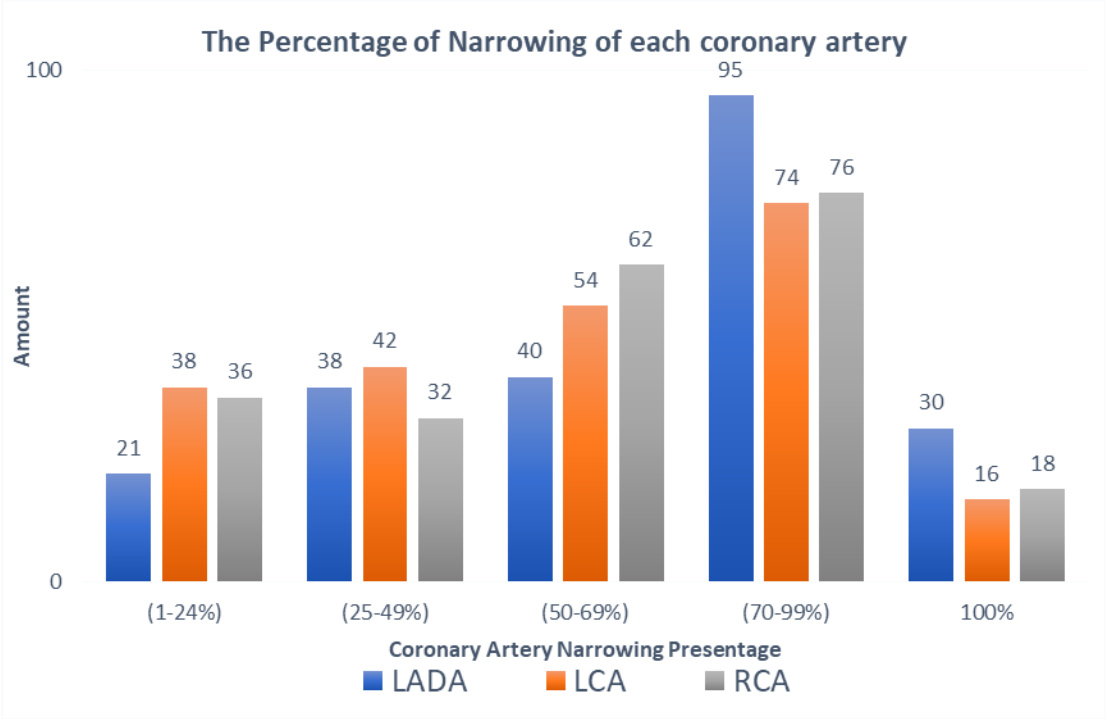


Fig 7. The percentage of narrowing of each coronary artery

Table 07: Left anterior descending artery narrowing crosstab

Left anterior descending artery narrowing

			1-24%	25-49%	49-69%	70-99%	100%	Total
Ear lobe	None	Count	8	2	3	2	1	16
		% within Ear lobe	50.0%	12.5%	18.8%	12.5%	6.3%	100.0%
	Wrinkling	Count	10	14	6	6	4	40
		% within Ear lobe	25.0%	35.0%	15.0%	15.0%	10.0%	100.0%
	50% crease	Count	3	10	17	19	5	54
		% within Ear lobe	5.6%	18.5%	31.5%	35.2%	9.3%	100.0%
	100% crease	Count	0	7	8	33	8	56
		% within Ear lobe	0.0%	12.5%	14.3%	58.9%	14.3%	100.0%
	Deep cleft	Count	0	5	6	35	12	58
		% within Ear lobe	0.0%	8.6%	10.3%	60.3%	20.7%	100.0%
Total		Count	21	38	40	95	30	224
		% within Ear lobe	9.4%	17.0%	17.9%	42.4%	13.4%	100.0%

There was a significant association between the degree of Frank's sign and left anterior descending artery narrowing. In those with no crease, 50% had only 1–24% narrowing and only 6.3% had total occlusion. In contrast, in those with deep cleft, 60.3% had 70–99% stenosis and 20.7% had 100% occlusion. The association is highly significant (Chi-square, $p<0.001$) with the linear-by-linear association confirms a graded trend ($\chi^2=55.7$, $p<0.001$). The strength of this association was moderate, as indicated by Cramer's V of 0.32.

Table 08: Left circumflex artery narrowing crosstab

Left circumflex artery narrowing

			LCx Narrowing					Total
			1-24%	25-49%	49-69%	70-99%	100%	
Ear lobe	None	Count	8	2	5	1	0	16
		% within Ear lobe	50.0%	12.5%	31.3%	6.3%	0.0%	100.0%
	Wrinkling	Count	18	10	5	7	0	40
		% within Ear lobe	45.0%	25.0%	12.5%	17.5%	0.0%	100.0%
	50% crease	Count	10	16	13	12	3	54
		% within Ear lobe	18.5%	29.6%	24.1%	22.2%	5.6%	100.0%
	100% crease	Count	2	8	17	27	2	56
		% within Ear lobe	3.6%	14.3%	30.4%	48.2%	3.6%	100.0%
	Deep cleft	Count	0	6	14	27	11	58
		% within Ear lobe	0.0%	10.3%	24.1%	46.6%	19.0%	100.0%
Total		Count	38	42	54	74	16	224
		% within Ear lobe	17.0%	18.8%	24.1%	33.0%	7.1%	100.0%

There was a significant association between degree of Frank's sign and left circumflex artery narrowing. In those with no crease, 50% had 1–24% narrowing but there was no 100% occlusion. In contrast in those with deep cleft, almost half (46.6%) had 70–99% stenosis and 19% had total occlusion. The association was statistically significant on Chi-square analysis ($P< 0.001$) and the trend test also demonstrated a significant increase in the severity of stenosis with the presence of deep clefts ($\chi^2=65.1$, $p<0.001$). The strength of this association was moderate, as indicated by Cramer's V of 0.31.

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Right Coronary artery narrowing

Table 09: Right coronary artery narrowing crosstab

			RCA Narrowing					Total
			1-24%	25-49%	49-69%	70-99%	100%	
Ear lobe	None	Count	7	2	4	2	1	16
		% within Ear lobe	43.8%	12.5%	25.0%	12.5%	6.3%	100.0%
	Wrinkling	Count	20	7	5	8	0	40
		% within Ear lobe	50.0%	17.5%	12.5%	20.0%	0.0%	100.0%
	50% crease	Count	9	11	20	12	2	54
		% within Ear lobe	16.7%	20.4%	37.0%	22.2%	3.7%	100.0%
	100% crease	Count	0	7	19	27	3	56
		% within Ear lobe	0.0%	12.5%	33.9%	48.2%	5.4%	100.0%
	Deep cleft	Count	0	5	14	27	12	58
		% within Ear lobe	0.0%	8.6%	24.1%	46.6%	20.7%	100.0%
Total		Count	36	32	62	76	18	224
		% within Ear lobe	16.1%	14.3%	27.7%	33.9%	8.0%	100.0%

There was a significant association between degree of Frank's sign and right coronary artery narrowing. In those with no crease, 43.8% had 1–24% narrowing and 6.3% had 100% occlusion. In contrast in those with deep cleft, almost half (46.6%) had 70–99% stenosis and 20.7% had total occlusion. The association was statistically significant on Chi-square analysis ($P< 0.001$) and the trend test also demonstrated a significant increase in the severity of stenosis with the presence of deep clefts ($\chi^2=62.4$, $p<0.001$). The strength of this association was moderate, as indicated by Cramer's V of 0.32.

Table 10: Spearman's correlation of coronary artery narrowing and earlobe (Frank's) sign

Frank's sign (ear lobe category) vs coronary narrowing

Spearman's correlation

Correlations

			Ear lobe	LAD Narrowing	LCx Narrowing	RCA Narrowing
Spearman's rho	Ear lobe	Correlation Coefficient	1.000	.471**	.533**	.515**
		Sig. (2-tailed)	.	.000	.000	.000
		N	224	224	224	224
	LAD Narrowing	Correlation Coefficient	.471**	1.000	.748**	.744**
		Sig. (2-tailed)	.000	.	.000	.000
		N	224	224	224	224
	LCx Narrowing	Correlation Coefficient	.533**	.748**	1.000	.778**
		Sig. (2-tailed)	.000	.000	.	.000
		N	224	224	224	224
	RCA Narrowing	Correlation Coefficient	.515**	.744**	.778**	1.000
		Sig. (2-tailed)	.000	.000	.000	.
		N	224	224	224	224

**. Correlation is significant at the 0.01 level (2-tailed).

All are moderate, positive and statistically significant correlations with the DATA analysis (LAD: $\rho = 0.471$, $p < 0.001$, LCx: $\rho = 0.533$, $p < 0.001$ and RCA: $\rho = 0.515$, $p < 0.001$). Based on the above results of the Spearman's rho correlation table, the Spearman correlation measures the strength and direction of the association between two ranked variables, which is the relationship between Frank's sign and the degree of narrowing in the three major coronary arteries. The Coefficient Range value always falls between -1.00 and +1.00. The "+" Sign: A positive rho (ρ) number (0.471 /0.515/0 .533) means that as one variable increases, the other tends to increase as well. So, these two variables have positive correlation coefficients. The higher the number of earlobe creases, are associated with higher the score in the arterial narrowing. Statistical Significance: The p-value (labelled as Sig. 2-tailed) is .000 for all three. This is less than 0.05 (and even 0.01).

This means the more severe the ear lobe crease, the greater the degree of coronary artery narrowing across all three coronary arteries.

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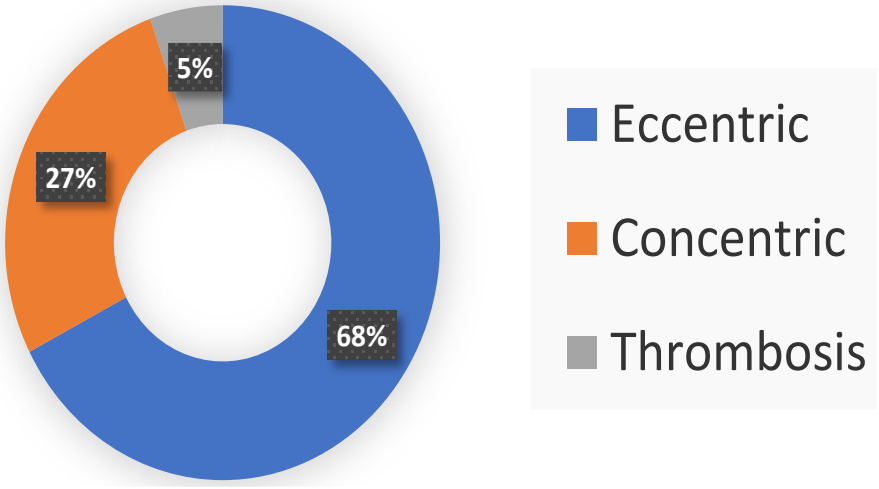


Fig 8. Coronary artery narrowing methods

Table 11: Categories of the Frank's sign with percentage of existing co-morbidities

Frank's sign vs co-morbidities

Category of the crease	Co-morbidities %
none	23.1
Grade 01 – Wrinkling	47.1
Grade 2a - Superficial crease	68.1
Grade 2b - Crease more than 50% across the earlobe	84.9
Grade 03 - Deep cleft across the whole earlobe	68.4

According to the chi-square test, an individual with a higher degree of Frank's sign is more likely to have cardiovascular co-morbidity.

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Table 12: Each Frank's categories with the percentage of existing hypertension

Frank's sign vs hypertension

			Hypertension	
			No	Yes
Ear lobe	None	Cases	11	3
		percentages	78.6%	21.4%
	Wrinkling	Cases	19	16
		percentages	54.3%	45.7%
	50% crease	Cases	22	25
		percentages	46.8%	53.2%
	100% crease	Cases	17	36
		percentages	32.1%	67.9%
	Deep cleft	Cases	20	37
		percentages	35.1%	64.9%
Total		Cases	89	117
		percentages	43.2%	56.8%

The individuals with Hypertension tend to have higher Frank's sign severity than individuals without hypertension (Statistically significant).

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Table 13: Each Frank's categories with the percentage of existing Dyslipidemia

Frank's sign vs dyslipidemia

			Dyslipidemia	
			No	Yes
Ear lobe	None	Cases	13	1
		percentages	92.9%	7.1%
	Wrinkling	Cases	29	6
		percentages	82.9%	17.1%
	50% crease	Cases	34	11
		percentages	75.6%	24.4%
	100% crease	Cases	36	14
		percentages	72.0%	28.0%
	Deep cleft	Cases	34	21
		percentages	61.8%	38.2%
Total		Cases	146	53
		percentages	73.4%	26.6%

The individuals with Dyslipidemia tend to have higher Frank's sign severity than individuals without dyslipidemia (statistically significant).

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Table 14: Each Frank's categories with the percentage of existing ischemic heart disease

Frank's sign vs ischemic heart disease

			IHD	
			No	Yes
Ear lobe	None	Cases	13	1
		percentages	92.9%	7.1%
	Wrinkling	Cases	30	5
		percentages	85.7%	14.3%
	50% crease	Cases	37	8
		percentages	82.2%	17.8%
	100% crease	Cases	34	18
		percentages	65.4%	34.6%
	Deep cleft	Cases	36	19
		percentages	65.5%	34.5%
Total		cases	150	51
		percentages	74.6%	25.4%

The individuals who had higher Frank's sign severity were more likely to have ischemic heart disease.

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Table 15: Each Frank's categories with the percentage of Diabetes Mellitus

Frank's sign vs Diabetes mellitus

			DM	
			No	Yes
Ear lobe	None	Cases	11	0
		percentages	100.0%	0.0%
	Wrinkling	Cases	19	1
		percentages	95.0%	5.0%
	50% crease	Cases	29	5
		percentages	85.3%	14.7%
	100% crease	Cases	30	5
		percentages	85.7%	14.3%
	Deep cleft	Cases	33	8
		percentages	80.5%	19.5%
Total		Cases	122	19
		percentages	86.5%	13.5%

Individuals who had diabetes tend to have slightly higher Frank's sign severity, and it is not statistically significant.

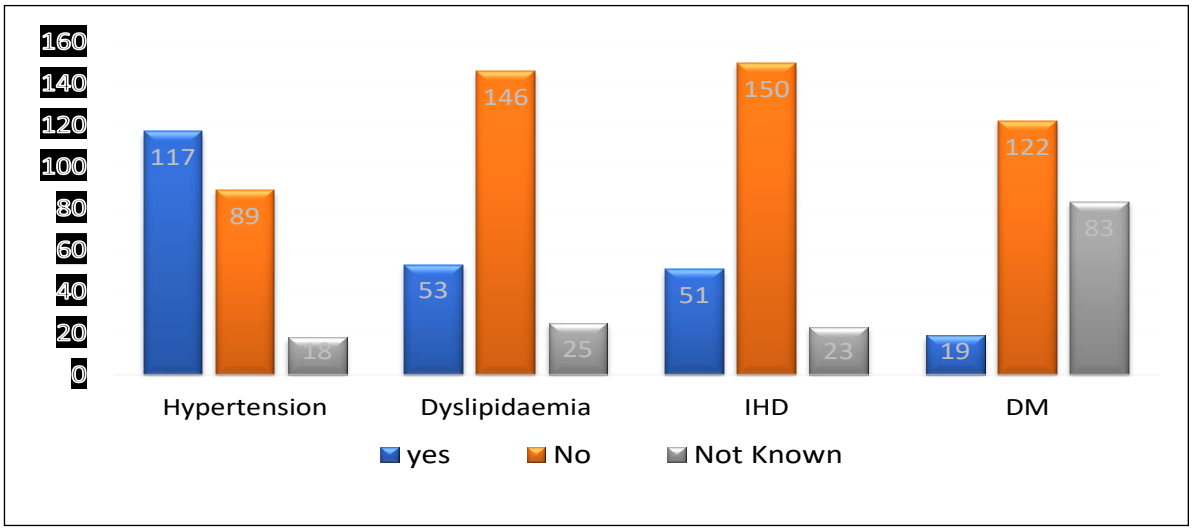


Fig 9. The number of cases positive and negative of each co-morbidities

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Discussion

The study included 224 cases (152 males, 72 females) above the age of 30 years, with a mean age of 62.7 (SD=14.4) years and a mean left ventricular thickness of 1.61 cm (SD=0.36). Among the total sample, 60.3% reported comorbidities and 55.4% experienced a cardiac death. There were 92.9% of the sample with a positive Frank's sign. There was a statistically significant association between Frank's sign (FS) and age (p=0.001) in individuals with FS, being older on average. Cardiac-related deaths were significantly more common among those with FS compared to non-cardiac causes (p=0.002). The severity of FS showed a moderate, positive and statistically significant correlation with major coronary artery narrowing and occlusion (p<0.001). Significant associations were also observed between higher severity of FS and a history of hypertension (p=0.010), IHD (p=0.002) and dyslipidemia (p=0.005). However, the association with DM was not statistically significant (p=0.053).

This study used a cohort design with prospective components, which allowed systematic data collection over a defined period and reduced recall bias. Although the population consisted only of post-mortem cases from a single tertiary care hospital, it was a major center where dead bodies from different areas of the country with multiethnic variability were autopsied, giving a well representative sample. Assessment of ear lobe appearance was based on photographic documentation and visual grading. Although this allows permanent records and review, it is still subject to observer variation. However, data collection only by the principal investigator himself has ensured less inter-observer bias and misclassification bias.

Coronary artery narrowing was assessed macroscopically rather than by histopathology or advanced imaging. While macroscopic examination of coronary artery narrowing was practical in a mortuary setting, it could be subjective and may underestimate subtle atherosclerotic changes, leading to possible misclassification of disease severity. Clinical and epidemiological data were collected from existing records such as BHTs, clinic books and angiogram reports. These secondary data sources may contain missing or inaccurately recorded information, introducing information bias. The six-month study period may not capture seasonal or long-term variations in disease patterns. A longer duration with a greater study population could have improved the validity of the results.

There were 92.9% of the sample with a positive FS in the current study. The prevalence of FS was 27% in a study done among younger individuals with median age of 35 years9. However in a similar study with a mean age of 61 years (SD=19.01) has only 7.3% who do not have the visible FS compared to current study with 7.1% who do not have the FS10. FS is not congenital. Age-related changes occur in the ear- lobe. There was a statistically significant association between Frank Sign (FS) and age (p=0.001), in individuals with FS being older on average in the current study. The findings are consistent with the previous studies which revealed the mean age of participants diagnosed with FS was higher than those without FS and was statistically significant in both younger age groups11 and older age groups10.

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Cardiac-related deaths were significantly more common among those with FS compared to non-cardiac causes (p=0.002). The severity of FS showed a moderate, positive and statistically significant correlation with major coronary artery narrowing and occlusion (p <0.001). Similarly, in other studies, among cases involving a fatal cardiac event, most (78%) had FS (high-grade DELC). DELC grade showed a significant positive correlation with the severity of coronary artery disease (rs=0.474, p<0.001) and with overall atherosclerotic burden (rs=0.606, p<0.001), indicating moderate and strong effect sizes respectively2. Several other study results showed significant association of FS with CAD4, 5, 6. Moreover, FS was significantly associated with sudden cardiac death of men (p<0.04) as revealed by a study of 520 autopsy cases15.

Significant associations were also observed between higher severity of FS and a history of hypertension (p=0.010), IHD (p=0.002) and dyslipidemia (p=0.005). However, the association with DM was not statistically significant (p=0.053). A case control study which investigated 118 cases with CAD and 50 no-CAD controls, revealed a significant association of FS with hypertension in addition to male gender and advanced age16. The association of dyslipidemia, diabetes mellitus with FS were statistically significant in other studies which explored the association of cardiovascular risk factors and FS9. According to this study, patients with Frank's sign most commonly had type 2 diabetes mellitus (55%, p=0.003), dyslipidemia (53%, p=0.026) and a history of smoking (68%, p=0.002). Multivariate analysis showed that severe coronary artery disease was independently associated with the presence of Frank's sign (OR 3.26; 95% CI 1.98–5.38; $p \leq 0.001$), male sex (OR 2.28; 95% CI 1.20–4.35; p=0.012), and dyslipidemia (OR 1.81; 95% CI 1.11–2.97; p=0.017)18.

Conclusion and Recommendations

The findings suggest that ear lobe crease/Frank's sign may serve as a simple, low-cost external marker for underlying coronary artery disease, especially in settings with limited access to advanced investigations. If validated further, routine inspection of ear lobes during clinical examination could help identify individuals who may benefit from early cardiovascular risk assessment and closer monitoring. These results can inform future prospective studies in the living populations and support the development of screening strategies that combine clinical examination with traditional risk factors for ischemic heart disease.

Strengths, Limitations and Conflict of interest

The study examined both clinical risk factors and a visible physical sign (Frank's sign), allowing practical bedside relevance. Inclusion of established cardiovascular risk factors such as diabetes, dyslipidemia and hypertension improved clinical validity.

Objective assessment of coronary artery disease severity increased reliability of outcome measurement. However, the study showed several limitations. Retrospective or record-based data collection (regarding co-morbidities etc.) could introduce missing or inaccurate data, which is common in autopsy studies. Potential confounding factors that may have influenced the

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associations were not excluded in the analysis through a multivariate regression model. The authors claim no conflict of interest.

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