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Detection of Frank's sign in the dental setting: A population-based cohort study

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Abstract

Background: In 1973, Saunders T. Frank described the diagonal earlobe crease (DELC) as a potential marker of cardiovascular disease. However, this anatomical finding is not routinely examined. The aim of this study was to assess the presence of this crease in the general population attending a dental setting and describe its anatomical variations to be able to categorize it as a physical sign.

Methodology: A study group of 1050 white adults were selected, as participants in the framework of the "A Estrada Study of Glycation and Inflammation" (AEGIS), a cross-sectional, population-based descriptive study of a representative sample of the general adult population of the municipality of A Estrada (Pontevedra, Spain). Each participant's age, sex, and preferred head position when sleeping were recorded. Both earlobes were visually inspected and the anatomical variables of the crease were recorded (unilateral or bilateral, length, depth, and presence of secondary creases). The relationship between the study variables was analyzed using the chi-squared test, Student's *t*-test, the analysis of variance (ANOVA), and the nonparametric tests of Mann–Whitney and Kruskal–Wallis.

Results: The DELC was observed in 65.2% of the participants. In 71.5% of the cases, the sign was complete (occupying the space from the tragus to the posterior edge of the earlobe); in 56.9% of the cases, the sign was bilateral; in 45.1% of the cases it was deep; and in the 43.6% of the cases, accessory creases were identified. Neither sex nor the habitual head position when sleeping were related to the prevalence or characteristics of the DELC. The prevalence, extent and depth of Frank's sign increased significantly with age ($p < .001$).

Conclusion: The prevalence of the DELC increases significantly with age, and its morphological characteristics are accentuated. This finding, therefore, gains special relevance as a marker of potential cardiovascular disease when observed in young adults.

KEYWORDS
cardiovascular risk, earlobe, ear anomalies, physical examination, skin manifestations

1 | INTRODUCTION

The signs and symptoms recorded when performing the case history and physical examination are the first signals that allow healthcare providers to start the diagnostic process. It has been suggested that the ear examination (including the pinna as part of the external ear) should be implemented in the standardized physical examination, particularly by medical professionals such as otolaryngologists, primary care physicians, pediatricians, emergency room physicians, and paramedics.[1] Although dentists routinely examine anatomical areas very close to the ear such as the parotid gland and temporomandibular joint, the earlobe is a structure that is often unintentionally overlooked despite its direct visual accessibility.

The diagonal earlobe crease (DELC) has been described as an oblique linear fold, clearly visible to the naked eye, which extends from the tragus to the posterior edge of the pinna, with no solution of continuity.[2–4] In a letter to the editor published in the prestigious *New England Journal of Medicine* in 1973, the American pulmonologist Saunders T. Frank reported the DELC in some of his patients between the ages of 20 and 60 years, whose medical history included a case of chest angina, electrocardiographic ischemic changes, and angiographically confirmed coronary artery disease.[2] Accordingly, this author was attributed the initial description of an association between this physical sign (which was named after him as "Frank's sign") and coronary artery disease, representing the first recognized marker of extracardiac risk of coronary disease.

Frank's proposal was immediately replicated in a clinical study published in 1974, which showed a statistically significant and independent association between the presence of the DELC and the presence of coronary artery disease.[5] Since then, numerous articles have been published that have affirmed that DELC is an independent predictor of the onset of atherosclerotic disease and is closely associated with an increase in its prevalence, extent, and severity.[6–8] However, numerous researchers do not agree with this statement and argue that the association between the DELC and atherosclerotic disease is not independent and is due to the fact that the two entities share particular atherogenic risk factors,[9] the primary of which is age.[10–12]

Due to the disparity of results, the utility of Frank's sign still generates controversy even after more than 45 years. The discrepancies observed between the published studies are due to various reasons, including a lack of uniformity among the criteria for identifying and categorizing the presence of DELCs.

The aim of this study was to study the presence of the DELC in the general population attending a dental setting, describing its anatomical variations, to be able to categorize it as a physical sign.

2 | METHODS

The participants in this study were selected within the framework of the "A Estrada Study of Glycation and Inflammation" (AEGIS), a cross-sectional descriptive population-based study of a representative sample of the general adult population. All of the participants were white adults of Spanish nationality who attended a consultation at the Health Center of A Estrada (Pontevedra, Spain) between 2016 and 2019. On the date recruitment was started, the municipality had a population older than 18 years of 18 744 inhabitants. The randomized sample of participants was taken from the healthcare card registry of the Spanish health system, which covers more than 95% of the population. The sample selection was stratified by the following age groups (in years): 18–29, 30–39, 40–49, 50–59, 60–69, 70–79, and older than 79. Ultimately, the DELC study included 1050 participants (Figure 1).

Each participant's age, sex, and preferred head position when sleeping (right side, left side, alternating sides, or face up) were recorded. Both earlobes were visually inspected while the participants lay in a dental chair in supine decubitus, under dental chair light, after removing all types of earrings, bands or other ornaments.

The absence/presence of DELCs was recorded and the length of each crease was categorized, considering as "full length" the oblique line that extends from the tragus to the posterior edge of the pinna. Three categories were established: (1) extending < 1/3 the full length; (2) extending 1/3–2/3 the full length; (3) extending > 2/3 the full length. Based on these scores, the variable "total length" was calculated as the result of summing the values corresponding to the categories of the crease length for both ears. Thus, the total length achieved a score within the range of 1–6.

The depth of the DELC was also recorded according to its skin penetration, attributing it the scores corresponding

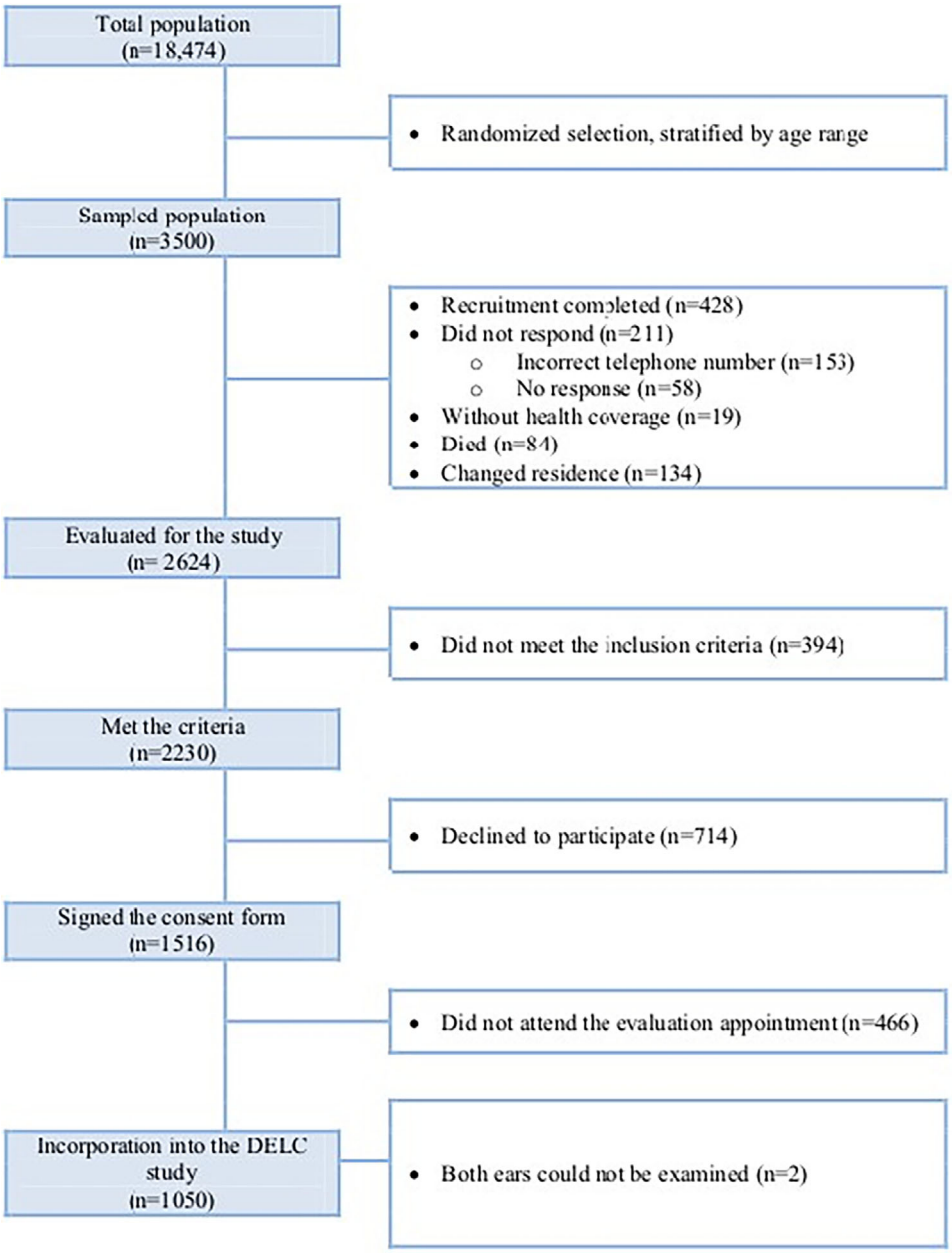

FIGURE 1 Flow diagram for the selection of study group participants.

to two categories: (1) superficial crease and (2) deep crease (Figures 2 and 3). The variable "total depth" was calculated as the result of summing the values corresponding to the categories of crease depth for both ears, which resulted in a score between 1 and 4.

Lastly, the absence/presence of secondary or accessory creases in each lobe was analyzed, considering this variable to be any additional crease to the main crease.

These variables were measured and calibrated by two trained examiners. To check the reproducibility of the results, we repeated the measurements of 10 randomly selected cases 1 month after the first measurements, obtaining for all evaluated variables an intraclass correlation coefficient that varied between .89 and 1.

The qualitative variables are expressed as frequencies and percentages. The relationship between two qualitative variables was evaluated using the chi-squared test. To study the influence of a qualitative variable (for example, the presence/absence of DELC) with regard to the quantitative variable age, Student's *t*-test and the analysis of variance (ANOVA) or the nonparametric tests of Mann–Whitney and Kruskal–Wallis were employed in the case of non-normal distributions. *p*-Values $< .05$ were considered statistically significant.

FIGURE 2 Full length superficial diagonal earlobe crease.

FIGURE 3 The prevalence of the diagonal earlobe crease (DELC) increases significantly with age, and its morphological characteristics are accentuated.

3 | RESULTS

3.1 | Presence, length, and depth of the diagonal earlobe crease and presence of secondary creases

Of the 1050 individuals who participated in the study, 1048 completed the examination of both ears. Two patients could not have both ears analyzed (absence of lobe due to a traffic accident and anatomical lobe abnormality due to laceration, respectively). The total number of ears examined was 2098. The DELC was bilateral in 56.9% of the participants, unilateral in 8.3% and not detected in 34.9% of the cases. No predilection for any particular ear was observed; 59.2% of the sample presented a right ear crease and 59.3% presented a left ear crease (Table 1).

According to the three established length categories, similar values for the two ears were observed. In the patients in whom the crease was present, the most common characteristic was that its length occupied at least 2/3 of the full length (33.6% of the examined right ears and 33.4% of the left) (Table 1).

When analyzing the distribution of the participants with DELCs according to the total crease length, 71.5% had one or two creases that occupied at least 2/3 of the full length. Additionally, the creases of both ears achieved the maximum score in 45.7% of the individuals (bilateral category 3 extension) (Table 1).

The crease depth was examined in 1050 right ears and 1048 left ears. The percentage distribution of deep and superficial creases was 32.4% and 26.1% for the right ears versus 31.3% and 27.6% for the left ears, respectively.

When analyzing the distribution of the participants according to the total DELC depth, 45.1% of the cases achieved the maximum score, which implies the bilateral presence of deep creases. In contrast, the most uncommon situation (9.1% of the cases) was the coexistence in the same individual of a superficial crease and a deep crease (Table 1).

Regarding the presence of secondary creases among the patients with DELCs, the predominant situation was the presence of this type of crease, which was detected in 68.0% and 65.4% of the right and left ears, respectively. Also, when the DELC was bilateral, the rate of secondary creases in both ears was 62.5%.

TABLE 1 Distribution of participants according to the total length and total depth of the diagonal earlobe crease.

		Right and left ears						
		1	**2**	**3**	**4**	**5**	**6**	***n***
Length of the crease	**Frequency**	49	83	62	101	75	312	682
	%	7.2	12.2	9.1	14.8	11	45.7	100
Depth of the crease	**Frequency**	77	224	60	297	–	–	658
	%	11.7	34.0	9.1	45.1	–	–	100

Note: LENGTH (1, 2, 3, 4, 5, and 6) was calculated as sum of the values of the length of the crease for both ears; values for each crease: (1) extending < 1/3 the total length, (2) extending 1/3–2/3 the full length, (3) extending > 2/3 extension the total length); n = individuals with at least a unilateral crease.
DEPTH (1, 2, 3, and 4) was calculated as sum of the values of the depth of the crease for both ears; values for each crease: (1) superficial crease, (2) deep crease; n = individuals with at least a unilateral sulcus.

3.2 | Relationship with sex and age

The prevalence of DELCs was similar among the men (63.1%) and women (67.6%) ($p = .167$). There were also no statistically significant differences between the two sexes, in the score of the total length of the creases obtained for each individual ($p = .380$), in the total depth of the crease ($p = .735$), or in the presence of secondary creases ($p = .675$).

The onset of unilateral or bilateral creases increased significantly with the individual's age ($p < .001$). Their presence in only one ear increased up to the age range of 50–59 years and then began to decrease, in large part, at the expense of an increase in the frequency of bilateral DELCs. The presence of bilateral creases increased from 10.6% in the 18–29-year age range to 91.7% in the ≤80-year age range. In these age groups, the rate of absent creases reduced from 84.4% to 4.6% (Table 2).

The total length increased progressively as the age stratum increased, with the exception of the DELCs that extended more than 2/3 the full length in those older than 79 years (Table 2). The total DELC depth values increased significantly with age ($p < .001$) (Table 2).

The rate of secondary creases increased significantly with age ($p < .001$). In the extreme case of secondary creases in both ears, its prevalence went from 0.7% in the 18–29-year age group to 73.4% in the ≥80-year age group (Table 2).

3.3 | Relationship with the preferential head position when sleeping

The distribution of the participants according to the habitual head position when sleeping was as follows: right side ($n = 340$), left side ($n = 237$), alternating sides ($n = 260$), and face up ($n = 30$). The preferred head position when sleeping did not affect the presence of DELCs ($p = .527$), their length ($p = .703$), or depth ($p = .322$).

4 | DISCUSSION

Even assuming that the classical definition of DELC is widely applied,[3–5] there are few references in the literature on its characteristics and regarding the criteria for identifying and categorizing the condition, which represents a considerable challenge when comparing the results of various studies.

Various identification criteria have been applied based mainly on its length. Numerous authors have considered that the DELC was present when it occupied at least 2/3 of the distance between the tragus and the edge of the pinna.[13–15] Other authors acknowledge its presence when its length reaches at least half this distance,[16,17] and other authors, as in the present study, are satisfied with creases that occupy 1/3 of this distance.[18–20] Furthermore, a number of authors consider that the ear crease was present when it appears on at least one ear,[4,13,21] while others only acknowledge the bilateral presentation.[3,18,22] Coinciding with our study, only a minority of authors also conduct an analysis of the DELC taking into account whether it is unilateral or bilateral.[19,23,24]

In this study, a representative sample of the general adult population was randomly selected, without known severe disease (such as cerebrovascular disease, cancer, and terminal processes), which prevents the bias of hospitalized patients, who typically present a larger number of and/or more severe comorbidities. DELC prevalence values were found greater than those obtained in other series with these characteristics,[4,25,26] a finding that could be due to the different identification criteria and/or to the fact that our study covered a very wide age range, including patients older than 80 years, who are typically excluded from series that investigate the relationship between DELC and atherosclerotic disease.

A number of authors have suggested that DELCs are more common among men.[25,26] However, most published studies, including ours, have not detected significant differences in terms of the prevalence of DELCs among men and women.[15,19,27] The participants' sex was also not

TABLE 2 Distribution of the presence/absence of the diagonal earlobe crease, the total length, the total depth, and the presence/absence of secondary creases by age group.

		Age group (years)							
		18–29	**30–39**	**40–49**	**50–59**	**60–69**	**70–79**	**≥80**	**Total**
PRESENCE Frequency (%)	**0**	119 (84.4)	122 (63.5)	74 (41.6)	26 (17.6)	13 (8.8)	7 (5.3)	5 (4.6)	366 (34.8)
	1	7 (5)	21 (10.9)	21 (11.8)	19 (12.8)	8 (5.4)	7 (5.3)	4 (3.7)	87 (8.3)
	2	15 (10.6)	49 (25.6)	83 (46.6)	103 (69.6)	126 (85.7)	119 (89.5)	100 (91.7)	595 (56.9)
	n	141 (100)	192 (100)	178 (100)	148 (100)	147 (100)	133 (100)	109 (100)	1048 (100)
LENGTH Frequency (%)	**1**	3 (25)	20 (29.4)	12 (11.3)	8 (6.3)	3 (2.2)	2 (1.6)	1 (1)	49 (7.3)
	2	4 (33.3)	15 (22.1)	22 (20.8)	21 (16.5)	9 (6.6)	8 (6.3)	4 (3.8)	83 (12.1)
	3	1 (8.3)	15 (22.1)	14 (13.2)	13 (10.2)	8 (5.9)	6 (4.7)	5 (4.7)	62 (9.1)
	4	3 (25)	8 (11.8)	18 (17)	25 (19.7)	24 (17.6)	10 (7.9)	13 (12.3)	101 (14.8)
	5	0 (0)	4 (5.9)	9 (8.5)	11 (8.7)	20 (14.7)	13 (10.2)	18 (17)	75 (11.2)
	6	1 (8.3)	6 (8.7)	31 (29.2)	49 (38.6)	72 (53)	88 (69.3)	65 (61.2)	312 (45.6)
	n	12 (100)	68 (100)	106 (100)	127 (100)	136 (100)	127 (100)	106 (100)	682 (100)
DEPTH Frequency (%)	**1**	6 (46.1)	25 (33.8)	15 (13.5)	15 (12.8)	6 (5.4)	5 (4.0)	5 (4.7)	77 (11.7)
	2	6 (46.1)	35 (47.3)	58 (52.2)	44 (37.6)	29 (26.1)	34 (27.0)	18 (17.0)	224 (34.0)
	3	0 (0)	5 (6.8)	12 (10.8)	7 (6.0)	14 (12.6)	8 (6.3)	14 (13.2)	60 (9.1)
	4	1 (7.7)	9 (12.2)	26 (23.4)	51 (43.6)	62 (55.9)	79 (62.7)	69 (65.1)	297 (45.1)
	n	13 (100)	74 (100)	111 (100)	117 (100)	111 (100)	126 (100)	106 (100)	658 (100)
SECONDARY Frequency (%)	**0**	140 (99.3)	169 (88,9)	129 (72.1)	73 (49)	41 (27.9)	25 (18.8)	14 (12.8)	591 (56.4)
	1	0 (0)	5 (2.6)	16 (8.9)	13 (8.7)	23 (15.6)	13 (9.8)	15 (13.8)	85 (8.1)
	2	1 (0.7)	16 (8.4)	34 (19)	63 (42.3)	83 (56.5)	95 (71.4)	80 (73.4)	372 (35.5)
	n	141 (100)	190 (100)	179 (100)	149 (100)	147 (100)	133 (100)	109 (100)	1048 (100)

Note: PRESENCE is denoted by (0) absent crease, (1) unilateral crease, (2) bilateral crease, (*n*) individuals in whom the presence of creases was examined.

LENGTH (1, 2, 3, 4, 5, and 6) was calculated as sum of the values of the length of the crease for both ears; values for each crease: (1) extending < 1/3 the total length, (2) extending 1/3–2/3 the full length, (3) extending > 2/3 extension the total length; n = individuals with at least a unilateral crease.

DEPTH (1, 2, 3, and 4) was calculated as sum of the values of the depth of the crease for both ears; values for each crease: (1) superficial crease, (2) deep crease; n = individuals with at least a unilateral sulcus.

SECONDARY CREASES are denoted by (0) missing secondary creases, (1) secondary creases present in one ear, (2) secondary creases present in both ears; n = individuals in whom the presence of secondary creases was examined.

relevant when analyzing the characteristics of DELCs such as the total length, the total depth, and the presence of secondary creases. In the literature, we found no other references in which these variables were analyzed.

Various authors have indicated that the prevalence of DELC increases with age, presumably starting at 30 years of age.[16,28] The present study, which included participants older than 18 years, found a positive correlation between age and DELC in terms of the presence and bilaterality, confirming the results of the majority of previous studies.[14,19,26] This study confirmed that the prevalence of full-length creases, of deep creases, and of accessory creases also increased significantly with age, findings that have not been reported simultaneously in previously published articles.

Although the mechanism of DELC formation is unknown, articles in the literature assume that it does not involve a congenital trait but rather an acquired characteristic.[5,29] Among the various theories that have been postulated about its etiopathogenesis, a number of authors have suggested that it could be consequence of pressure exerted on the earlobe when sleeping in certain positions.[29] In the present study, we observed no statistically significant differences between the typical positions during sleep and the presence, length, or depth of the DELC.

Since the initial description of the DELC, various published studies have sought to verify the association between the crease as a marker of coronary risk and other atherosclerotic diseases, including peripheral arterial disease and cerebrovascular disorders.[5,30] Although the pathophysiological mechanism underlying the onset of DELC has not yet been established, we recently suggested that this physical sign could be a marker of an individual's biological age and an early indicator of peripheral microangiopathy.[31] Accordingly, it is important to identify the physical signs that lead to the suspicion and perform an initial atherosclerosis screening.

Despite the anatomical proximity between the mouth and the otorhinolaryngological structures, the likelihood that the dentist is the one to detect lesions of the ear, nose, and throat has been suggested only anecdotally.[32] The examination of Frank's sign is simple and entails no additional costs and should therefore be implemented routinely within the dental setting as a predictor or early sign of potential coronary artery disease.

5 | CONCLUSIONS

The DELC is observed in more than half of the adult population of both sexes. It is generally full length (covering the space between the tragus and the posterior edge of the earlobe), bilateral, deep, and has accessory creases. Its prevalence increases significantly with age, and its morphological characteristics become accentuated. This finding in young adults could, therefore, constitute an indication for establishing an initial atherosclerosis screening in the dental setting.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest regarding the research, authorship, or publication of this study. This research project was supported by a grant from Spain's Carlos III Institute of Health (Instituto de Salud CarlosIII/ISCIII) (PI11/02219).

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