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Frank's Sign And Its Relationship With The Lobular Vascular Arcade And Cardiovascular Risk

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Abstract
Introduction: *Heart disease (HD) remains the leading cause of mortality globally and in Brazil, with projections indicating a 90% increase in the incidence of cardiovascular diseases by 2050. Given this scenario, the search for early and non-invasive physical indicators becomes crucial. Frank's sign—a diagonal fold in the earlobe described in 1973—has been studied as a potential external marker of atherosclerosis and coronary artery disease (CAD).*
Objective: *To review the literature on the association between Frank's sign, the vascular anatomy of the earlobe, and cardiovascular risks, analyzing its viability as a preventive diagnostic tool.*
Development: *Anatomically, the earlobe has an abundant blood supply through anastomoses between the superficial temporal artery and the posterior auricular artery. Histopathological and autopsy studies have revealed that the presence of the fold is correlated with significant morphological changes in the myocardium, such as increased cardiac weight and ventricular thickness. At the base of the fold, arterial myoelastofibrosis and Wallerian degeneration were identified, suggesting that the region is vulnerable to chronic hypoxia-reoxygenation damage resulting from atherosclerosis. Clinical analyses indicate that the sign has high specificity (above 85%) and sensitivity greater than 75% for identifying critical coronary occlusion.*
Conclusion: *The literature establishes a relevant connection between Frank's Sign and an increased risk of cardiovascular mortality, especially when present bilaterally. Although it should not be used as an isolated diagnosis, the sign serves as a valuable clinical indicator that, combined with medical history and physical examination, helps in the early identification of patients with a higher probability of acute coronary events.*
Keywords: *Frank's sign; Cardiovascular diseases; Atherosclerosis; Ear lobe; Preventive diagnosis.*

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I. Introduction

Heart disease (HD) is the leading cause of death globally, accounting for approximately 17.9 million deaths annually. Ischemic heart disease alone accounts for about 16% of all fatalities, highlighting its importance in global mortality patterns.[1]

In 2025, heart disease will still be the leading cause of death in Brazil, with estimates from the Brazilian Society of Cardiology (SBC) indicating approximately 400,000 deaths by the end of the year. By mid-September 2025, the cardiometer had recorded more than 260,000 deaths, revealing an average of 46 deaths per hour or one every minute and a half.[2]

Based on historical data on mortality and disability-adjusted life years (DALYs) from the 2019 Global Burden of Disease (GBD) study, which covers the period between 1990 and 2019, a Poisson regression was applied to analyze the mortality rate and DALYs related to cardiovascular diseases (CVD) and their risk factors from 2025 to 2050. Subgroup assessment was based on the super-regions defined by the GBD. Between 2025 and 2050, a 90.0% increase in the incidence of cardiovascular diseases, a 73.4% increase in overall mortality rates, and a 54.7% increase in overall DALYs are expected, with a forecast of 35.6 million deaths from cardiovascular diseases by 2050 (compared to 20.5 million in 2025). However, the age-adjusted prevalence of cardiovascular disease is expected to remain almost unchanged (-3.6%), while age-adjusted mortality is expected to decrease by 30.5%, and age-adjusted DALYs are expected to fall by 29.6%. In 2050, ischemic heart disease will continue to be the leading cause of cardiovascular deaths (20 million deaths), while systolic hypertension will be the predominant cardiovascular risk factor driving mortality (18.9 million deaths). The Central Europe, Eastern Europe and Central Asia superregion is expected to have the highest age-adjusted cardiovascular mortality rate in 2050 (305 deaths per 100,000 inhabitants).[3]

Frank's sign, a slanted fold in the earlobe first identified in 1973, has been studied as a potential external indicator of atherosclerotic cardiovascular disease. This sign is defined by a noticeable line, depression, or deep cleft with a darkened base. Suggested causes involve microvascular changes and an accelerated aging process..[4,5]

The potential connection between earlobe crease (OLC) and coronary artery disease (CAD) was first mentioned by Frank in a letter to the editor of the New England Journal of Medicine in 1973. The author noted that 19 out of 20 patients with OLC had one or more risk factors related to CAD and indicated that this connection should be investigated.[4,5,6]

This study aims to conduct a literature review that associates Frank's sign with the anatomy of the lobular artery and cardiovascular risks, understanding the etiology of cardiovascular diseases and the possibilities of preventive diagnosis.

II. Literature Review

The Ear

The visible part of the auditory system is the outer ear. It consists of the auricle, also called the pinna, and the external auditory canal, which includes the lateral surface of the tympanic membrane. Together with the tympanic membrane and the middle ear, the auricle functions to amplify sound intensity. The auricle acts like a funnel, directing sound towards the external auditory meatus, while the external auditory canal focuses the sound onto the tympanic membrane for transmission.[7,8]

Anatomically, there is no single structure specifically named the "lobular artery of the ear." The blood supply to the earlobe (the lower, fleshy part) comes from a complex vascular network formed by branches of larger arteries from the head and neck. Unlike the rest of the external ear, the earlobe does not contain cartilage, being composed of connective and adipose tissue, which gives it an abundant blood supply and a dense capillary network.[9]

The arterial vascular pattern of the auricle is based on vascular interconnections between branches of the superficial temporal artery (STA), which supply the anterior (i.e., lateral) surface of the auricle, and branches of the posterior auricular artery (PAA), which supply the posterior (i.e., medial) surface and contribute more prominently to auricle irrigation. Recent research has demonstrated that the PAA has multiple perforating branches that traverse the auricular cartilage and emerge on the anterior surface of the auricle, anastomosing with branches of the STA. These multiple vascular anastomoses.[9,10] Figure 1,2

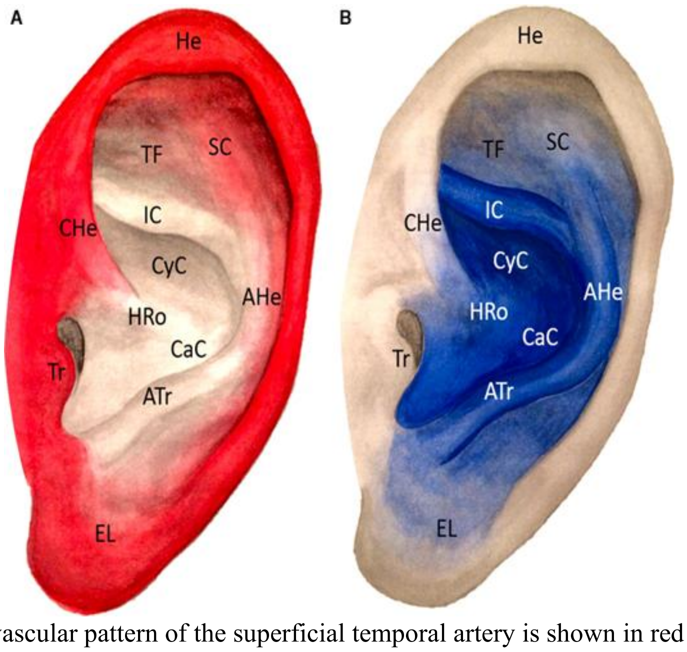

Figure 1. The arterial vascular pattern of the superficial temporal artery is shown in red (Image A) and that of the posterior auricular artery in blue (Image B). AHe, Antihelix; Atr, Antitragus; CaC, Cavum conchae; CyC, Cymba conchae; EL, Ear lobe; HRo, Root of the helix; He, Helix; HeC, Crus of the helix; IC, Inferior crus of the antihelix; SC, Superior crus of the antihelix; TF, Triangular fossa; Tr, Tragus.[9]

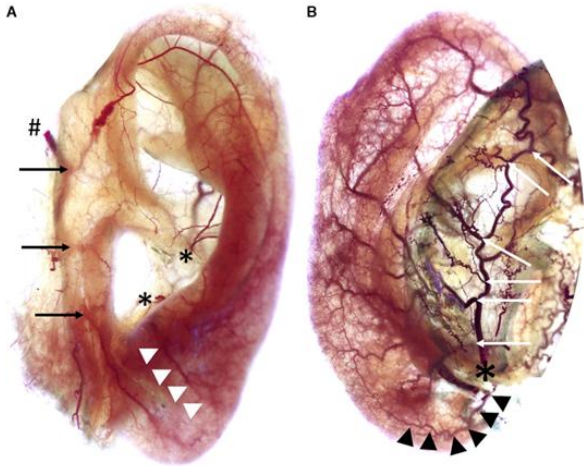

Figure 2: The images show the anterior (A) and posterior (B) views of the left auricles stained using the Spalteholz method. Image A: # Superficial temporal artery; black arrows indicate the superior, middle, and inferior anterior auricular arteries; *Helical root and antitragal perforator; white arrowheads indicate the branch of the antitragal perforator that irrigates the earlobe. Image B: *Posterior auricular artery; white arrows indicate the perforating and non-perforating branches; black arrowheads indicate the inferior anterior auricular artery that goes to the earlobe.[9]

The earlobe

The earlobe has attracted increasing attention, since the arterial network that irrigates it connects with the Zilinsky-Cotofana arcade. Anatomical study demonstrates that the vascularization of the earlobe is supplied by anastomotic connections through the superficial temporal artery (STA) and the posterior auricular artery (PAA), specifically the inferior anterior auricular artery originating from the STA and the antitragal perforating vessel originating from the PAA.[9,10],11Figure 3.

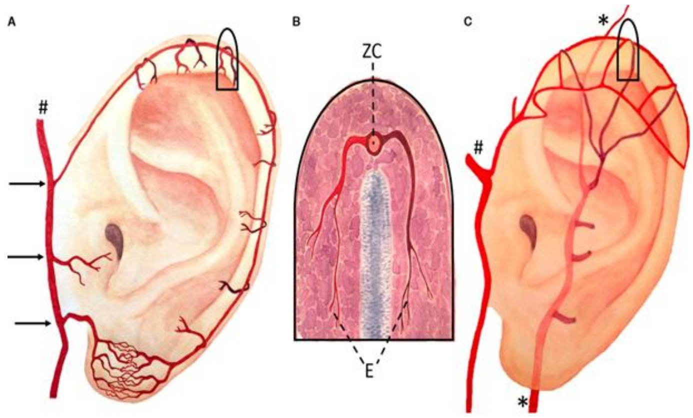

Figure 3. Image A: Artistic drawing of the helical arcade (Zilinsky-Cotofana arcade) and its position on the helix edge; # Superficial temporal artery, the black arrows indicate the superior/middle/inferior anterior auricular arteries. Image B shows a schematic drawing of a cross-section of the helix edge in the upper third. The posterior branch is shown in dark red and the anterior branch in light red. Both branches form the transverse helical arcade (E, Erdmann's arcade). The anterior and posterior branches connect to the longitudinal helical arcade (ZC, Zilinsky-Cotofana arcade). Image C: Artistic drawing of the helical arcade (Erdmann's arcade) and its position on the helix edge in the upper third; # Superficial temporal artery, *Posterior auricular artery. Note the lobular arcade.[9]

Frank's sign

Frank's sign (Figure 4) appears as a diagonal fold in the earlobe, closely linked to heart disease and strongly associated with atherosclerosis in the coronary arteries. A detailed study was conducted with 45 adult patients who underwent autopsies over a period of one and a half years. Samples were collected from both earlobes for histopathological analysis, in addition to cardiac samples from the four chambers of the heart. Upon comparison, there was no statistically significant difference in age between patients with and without Frank's sign ($p = 0.0575$). However, a statistically significant increase was observed in heart weight ($p = 0.0005$), left ventricular wall thickness ($p = 0.0002$), and right ventricular wall thickness ($p = 0.0043$). Histopathological analysis of the earlobes identified myoelastofibrosis in an arterial vessel at the base of the fold, as well as diffuse fibrosis and Wallerian degeneration, with eosinophilic inclusions in the peripheral nerves. These findings indicate a temporal evolution of the changes associated with the folds. The findings indicated a significant connection between morphological changes in the myocardium and the presence of folds in the earlobe, with the observed arterial myoelastofibrosis, Wallerian degeneration in the peripheral nerves, and deep fibrosis found at the base of the fold. Histopathological analysis of the ears of people up to 65 years old showed the presence of myoelastofibrosis in an arterial vessel in the lower part of the fold, while older individuals presented diffuse fibrosis in the same region. With greater magnification, in both groups analyzed, the peripheral nerves showed signs of Wallerian degeneration, accompanied by eosinophilic inclusions. These modifications indicate a temporal evolution of changes related to the fold.[6,12,13] Figures 5 (A, B and C).

Figure 4. Frank's Sign – Bilateral – Source: the author.

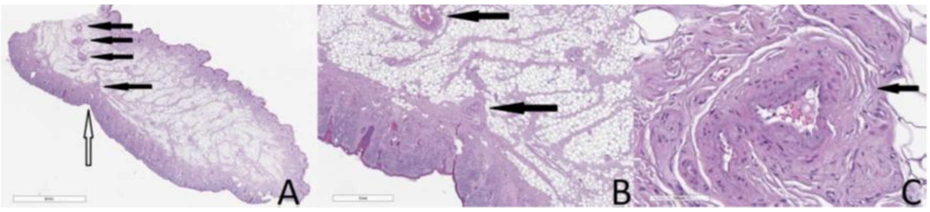

Fig. 5 (A, B, and C). Histopathology extracted from the same patient illustrated in Frank image (dashed arrow) demonstrating the absence of fibrosis in the interstitial space and a corkscrew-shaped twisted blood vessel exhibiting myoelastofibrosis (black arrows) located at the base of the fold (a), large-scale view of the histological slide; the vessel (black arrows), the fold, and adjacent tissues (b), with original magnification of 100x; the blood vessels revealing myoelastofibrotic changes (c), original magnification of 200x. Images b and c are enlarged sections of a, stained with hematoxylin and eosin.[12]

In 2020, Stoyanov and colleagues published a study that examined earlobes along with heart samples during a post-mortem analysis. Histopathological analysis of earlobes positive for DELC revealed the presence of myoelastofibrosis in the arterial vessels at the base of the lobe, as well as fibrosis and Wallerian degeneration, with eosinophilic inclusions in the peripheral nerves. The researchers indicated that this area serves as a connection to structures already formed in the prenatal period, and therefore may be vulnerable to chronic damage caused by hypoxia-reoxygenation due to atherosclerosis. Furthermore, they observed an increase in heart weight and thickness of the left and right ventricles in individuals with DELC, with no age variations between the groups. This study provides evidence for the idea that DELC is not a random phenomenon, but rather is closely related to atherosclerosis. Previous investigations into the pathophysiology of DELC have suggested other factors that may contribute to its development, such as skin aging, collagen degeneration, or telomere shortening.[14,15,16,17]

An autopsy study of 102 cases (51 deaths from cardiovascular causes and 51 deaths from non-cardiovascular causes matched), with a mean age of 46.5 years, identified a strong association between Frank's sign and deaths from cardiovascular causes, with a significantly higher prevalence in deaths with critical coronary occlusion. Frank's sign was validated as an independent predictor of coronary occlusion, with an adjusted odds ratio of 7.77 and moderate discriminative capacity.[5]

The most common coronary occlusions in clinical practice manifest both acutely, usually due to thrombosis over atherosclerotic plaque resulting in acute myocardial infarction (AMI), and as chronic total occlusions (CTO) in cases of advanced coronary artery disease (CAD). In the acute setting, the distribution of culprit arteries follows a consistent pattern led by the left anterior descending artery (LAD), responsible for 40-50% of cases, followed by the right coronary artery (RCA) with 25-40% and the left circumflex artery (LCX) with 15-25%, occurring predominantly in the proximal thirds and at bifurcations due to shear stress. As for CTOs, present in 15-30% of patients with symptomatic CAD, they maintain a similar prevalence hierarchy among the same vessels, consolidating the LAD and RCA as the most frequent occlusion sites in clinical cardiology.[18,19,20,21] Figure 6.

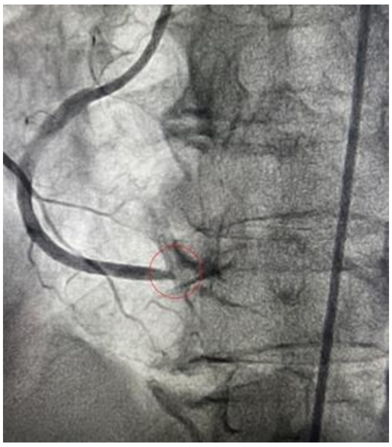

Figure 6. Example of occlusion of the distal third of the right coronary artery (red circle), before the origin of the posterior descending branch. Image kindly provided by Professor Dr. Gustavo Eugênio Martins Marinho.

Cardiovascular risk assessment involves a series of mathematical functions that define the probability of an individual experiencing a cardiovascular event, especially an acute coronary event or stroke, within a specific period. The most commonly used cardiovascular risk prediction indices are the Framingham-Anderson equation, the Systematic Assessment of Coronary Risk (SCORE) equation, and the Atherosclerotic Cardiovascular Disease Risk Score (ASCVD). While the ideal scenario would be the ability to estimate cardiovascular risk in all adults, it is important to identify the most common physical signs related to atherosclerosis and cardiovascular disease, such as xanthelasma, acanthosis nigricans, and Frank's sign.[22]

An analysis of 1048 individuals associated a diagonal fold in the earlobe (Frank's sign), present bilaterally in 56.9% of cases, with a significantly higher risk of cardiovascular mortality, with prevalence and severity increasing with age. The presence of the fold, especially bilaterally, raised the cardiovascular risk classification from low to moderate or high in the Framingham, SCORE, and ASCVD indices. For more information, consult the medical literature on dermatological signs of cardiovascular risk.[22]

A three-week retrospective study at the Tygerberg morgue in South Africa analyzed 100 unnatural deaths, finding a prevalence of 27% for Frank's sign and 28% for coronary artery disease (CAD). Frank's sign showed high specificity (86.1%) and negative predictive value (84.9%) for fatal CAD, but with moderate sensitivity (60.7%) and limited diagnostic efficacy, indicating moderate discriminatory power for identifying fatal cases.[23]

Several studies have validated that the diagonal ear fold is an independent sign of heart disease and is strongly related to increased heart rate and severity. Most published studies revealed that the sensitivity of the diagonal ear fold as a diagnostic method for atherosclerosis exceeded 75%, while its specificity was above 85%. Only a small number of researchers have stated that the link between the diagonal ear fold and atherosclerosis can be attributed to common risk factors related to atherogenesis, such as high blood pressure, smoking, overweight, diabetes, and high cholesterol levels. However, histomorphological analysis of the diagonal ear fold revealed a change in the arrangement of connective tissue and a low number of blood vessels, suggesting that it may be an early sign of peripheral microangiopathy.[1,3,4,6,12,14,18,22,23,24]

III. Conclusion

Literature points to a significant relationship between morphological changes in the myocardium and the presence of folds in the earlobe. The suggested hypoxia/reoxygenation model in heart failure, along with reduced oxygen saturation in the earlobe and the embryonic development process, are considered responsible for the observed alterations. This is the first model that helps to understand the development of Frank's sign and its link to clinically observable cardiovascular changes. The absence of Frank's sign can be useful in ruling out mortality related to coronary artery disease (CAD); however, its presence still raises many discussions in the literature, being considered an unreliable indicator for isolated diagnoses of the disease. We emphasize the relevance of physical examination, collection of clinical history, clinical perception, and patient anamnesis, as well as the importance of acting in the prevention of intrinsic and extrinsic factors that can facilitate the onset of cardiovascular diseases.

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