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The Relationship Between Frank Sign and Coronary Artery Disease: A Literature Review

Frank İşareti ve Koroner Arter Hastalığı Arasındaki İlişki: Literatür Taraması

Furkan Bostancı **Yusuf Yürümez**

Sakarya University, Department of Emergency Medicine, Sakarya, Türkiye

ABSTRACT

Objective: *Coronary artery disease (CAD) is a leading cause of death and a significant public health concern. The identification of individuals at risk for CAD has been a subject of research for many years. The Frank sign is one such approach.*

Material and Methods: *This study was conducted by searching the MEDLINE database through PubMed.*

Results: *The majority of studies were conducted in China, with sample sizes ranging from 125 to 1377. Male gender was significantly predominant, and the studies focused on older age groups, with a mean age of at least 51.9 years. The results of the studies indicated that the coexistence of both conditions, namely the Frank sign and CAD, exhibited a wide range of prevalence.*

Conclusions: *The Frank sign is an independent risk factor for CAD and can be utilized in diagnostic processes, particularly in the early identification of individuals at risk. However, further studies and larger series are necessary to confirm this conclusion.*

ÖZET

Amaç: *Koroner arter hastalığı (KAH) önde gelen bir ölüm nedenidir ve önemli bir halk sağlığı sorunudur. KAH için risk altında olan bireylerin belirlenmesi uzun yıllardır araştırma konusu olmuştur. Frank işareti bu yaklaşımlardan biridir.*

Gereç ve Yöntem: *Bu çalışma PubMed aracılığıyla MEDLINE veri tabanı taranarak gerçekleştirilmiştir.*

Bulgular: *Çalışmaların çoğunluğu Çin'de gerçekleştirilmiş olup örneklem büyüklükleri 125 ila 1377 arasında değişmektedir. Erkek cinsiyet önemli ölçüde baskındır ve çalışmalar ortalama yaşı en az 51,9 olan ileri yaş gruplarına odaklanmıştır. Çalışmaların sonuçları, her iki durumun, yani Frank işareti ve KAH'ın bir arada bulunmasının geniş bir yaygınlık aralığı sergilediğini göstermiştir.*

Sonuç: *Frank işareti KAH için bağımsız bir risk faktörüdür ve tanı süreçlerinde, özellikle de risk altındaki bireylerin erken belirlenmesinde kullanılabilir. Ancak bu sonucun doğrulanması için daha fazla çalışmaya ve daha geniş serilere ihtiyaç vardır.*

Keywords:
Frank Sign
Coronary Artery Disease
Diagnosis
Emergency

Anahtar Kelimeler:
Frank İşareti
Koroner Arter Hastalığı
Tanı
Acil

INTRODUCTION

Coronary artery disease (CAD) is a leading cause of death worldwide and represents a preventable public health issue (1). Consequently, clinicians have been investigating simple and reliable risk factors in conjunction with non-invasive biomarkers for the early detection of individuals at risk of CAD, with this research ongoing (2,3). As a consequence of these studies, the Diagonal Earlobe Crease (DELC), also known as Frank sign, was first described by Sonder T. Frank in 1973, suggesting its association with vascular atherosclerosis and CAD (4).

Frank sign is a crease that extends diagonally from the tragus towards the border of the earlobe (Figure 1) (5,6). The formation of this crease in the earlobe, nourished by end arteries without collateral circulation, has been suggested to contribute to pathological conditions affecting the microvascular system, such as CAD, diabetes, and hypertension. Indeed, widespread elastin and elastic fibre loss, a pathognomonic feature of CAD reflecting

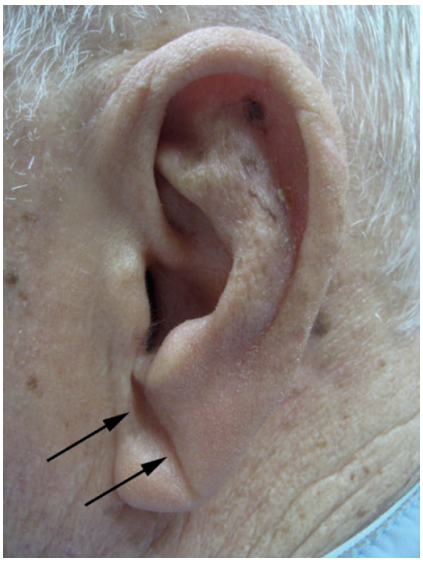

Figure 1: Frank sign in the left ear (6).

Correspondence: Furkan Bostancı, Sakarya Üniversitesi, Acil Tıp Kliniği, Sakarya, Türkiye.
E-mail: drfurkanbostanci@hotmail.com
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the morphology of the coronary vasculature, has been demonstrated in biopsy samples taken from earlobe creases (3). Nevertheless, despite the existence of significant positive associations between Frank sign and CAD in some studies conducted since its initial description, others have yet to establish such a relationship. Consequently, Frank sign has been considered a contentious physical indicator for predicting CAD formation over the years (3,7).

This text aims to conduct a literature review on the Frank sign and provide recommendations to clinicians regarding its utility in clinical practice based on the findings of existing studies.

MATERIAL AND METHODS

This study was conducted by searching the MEDLINE database through PubMed using combinations of the keywords "Frank's sign", "Frank sign", "Franks sign", "earlobe crease", "ear lobe crease", "ear-lobe crease", "ear crease", "ear creases", "ear lobe creases" and "earlobes crease" on 18 December 2023. Following the initial search, 98 articles were identified in the second search, combined with "AND (Coronary Artery Disease)". The inclusion criteria were defined as being written in English, prospective in nature, including patients aged 18 and above, having undergone angiography, and having full-text accessibility. Upon reevaluation based on these criteria, it was found that only eight studies met all the requirements (Figure 2). The included studies were presented in tabular form, including the author, country of origin, year of study, number of cases, mean age, gender distribution, presence of the Frank sign, and presence of coronary artery disease according to angiography results (Table 1).

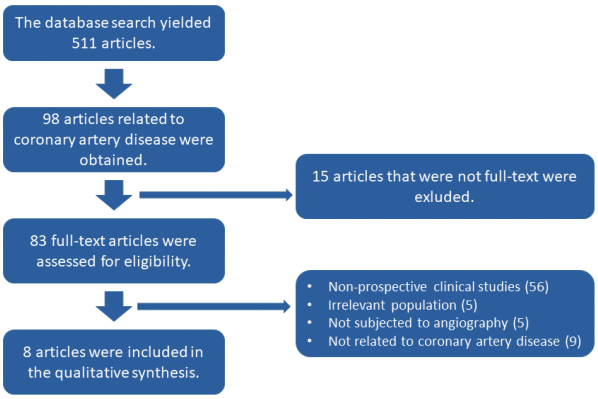

Figure 2: Flow diagram of study selection.

RESULTS

The data about the studies included in the research are presented in Table 1. The majority of studies were conducted in China, with sample sizes ranging from 125 to 1377. Male gender was significantly predominant, and the studies focused on older age groups, with a mean age of at least 51.9 years. The results of the studies indicated that the coexistence of both conditions, namely the Frank sign and CAD, exhibited a wide range of prevalence. The coexistence of both conditions being positive (Frank sign and CAD positive) was observed to vary between 35.46% and 68.42%, while the coexistence of both conditions being negative (Frank sign and CAD negative) was observed to vary between 7% and 32%. Upon examination of the relationship between the Frank sign and CAD, the majority of studies yielded a positive answer to the question of whether there is a significant relationship between the two.

DISCUSSION

The Frank sign is purported to be a straightforward physical examination finding that is harmless to the patient, easily applicable, cost-free, and purportedly associated with CAD (4). Indeed, our literature review yielded seven out of the eight studies included in our analysis mentioning the existence of this relationship, which supports this claim.

In a study conducted by Gakovic B. and colleagues related to the topic, it was claimed that the Frank sign has an acceptable level of accuracy in predicting CAD. However, in comparison with traditional cardiovascular risk factors, the Frank sign, despite providing supplementary information regarding the presence of CAD, is not a reliable indicator. Consequently, the authors recommended that diagnostic approaches should remain unchanged in patients presenting with chest pain (8). It is crucial to highlight that this recommendation was made about the evaluation of patients presenting with chest pain.

Several studies have offered differing recommendations for patients without chest pain within routine diagnostic processes. For instance, risk factors should be considered in the diagnostic methods of CAD. Accordingly, our reviewed studies also assess this aspect. In a survey by Kamal R. et al. examining the relationship between risk factors and the Frank sign, it was reported that the frequency of the Frank sign was correlated with hypertension and diabetes but not with smoking (3). Sasaki O. and colleagues investigated

Table 1: Characteristics of Included Studies.

References	Year	Country	n	Male (%)	The Average Age	Frank (+) CAD (+) (%)	Frank (+) CAD (-) (%)	Frank (-) CAD (+) (%)	Frank (-) CAD (-) (%)	Meaningful Relationship
Wang Y	2016	Chinese	558	402 (72.04)	63.63	345 (61.83)	44 (7.89)	100 (17.92)	69 (12.36)	Yes
Xing-li Wu	2014	Chinese	449	278 (61.91)	63.29 ± 11.95	188 (41.87)	92 (20.48)	62 (13.80)	107 (23.83)	Yes
Kamal R	2017	Pakistan	200	126 (63)	Unspecified	76 (38)	36 (18)	24 (12)	64 (32)	Yes
Hou X	2015	Chinese	956	546 (57.11)	53.35 ± 8.1	339 (35.46)	345 (36.09)	107 (11.19)	165 (17.26)	Yes
Sasaki O	2023	Japan	1086	826 (76.06)	66.1 ± 11.4	743 (68.42)	98 (9.02)	169 (15.56)	76 (7)	Yes
Gakovic B	2023	Serbia	1377	876 (63.62)	65 ± 10	483 (35.08)	236 (17.14)	395 (28.69)	263 (19.10)	Yes
Evrengül H	2004	Turkey	415	301 (72.53)	58.9 ± 10.3	152 (36.63)	18 (4.34)	144 (34.70)	101 (24.33)	Yes
DJ Kenny	1989	Ireland	125	112 (89.6)	51.9	56 (44.8)	9 (7.2)	45 (36)	15 (12)	No

the relationship between age and the Frank sign, suggesting that the Frank sign could serve as a valuable marker for risk stratification of patients before coronary angiography, regardless of age (7). Hou X. and colleagues emphasised the importance of combining the Frank sign and CAD risk factors, stating that the Frank sign is more reliable in individuals with multiple risk factors for CAD (4). In a study by Evrengül H. et al., it was reported that the prevalence of the Frank sign significantly increased in CAD independently of other risk factors, suggesting that the Frank sign could be an independent variable for CAD (9). Similarly, Xing-li Wu et al. also mentioned that the Frank sign could assist in the early identification of individuals at risk and in adopting active primary or secondary prevention for atherosclerosis (2). Moreover, the significant association of the Frank sign with major coronary risk factors is another important finding (9), which is consistent with the study conducted by Sasaki O. et al., where the Frank sign was independently associated with CAD, multi-vessel disease, and severe CAD (7).

Despite the aforementioned findings, it is observed that recommendations to be considered are included in the conclusion sections of the studies. For instance, DJ Kenny and colleagues stated that the Frank sign is not a marker for CAD, and both CAD and the Frank sign are associated with age. Kamal R. and colleagues proposed that further prospective studies are required to confirm this relationship. In contrast, Wang Y. and colleagues emphasized the necessity for further studies to elucidate the underlying mechanism (1, 3, 10).

LIMITATION

This study demonstrates the limitations of relying on a single search engine. However, the fact that the search engine used is one of the most widely followed sources helps to mitigate this limitation to a reasonable extent.

CONCLUSION

The Frank sign is an independent risk factor for CAD. Although it is not recommended as a criterion for evaluation in patients presenting with chest pain, it can be used in diagnostic processes, particularly in the early identification of individuals at risk. However, given the number of publications and the number of patients, further studies and larger series are required to support this conclusion.

Conflict of Interest: No conflict of interest was declared by the authors.
Ethics: The study does not require ethics committee approval. There is no such thing as any blood, saliva, violation of the rights of the patient, etc.
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Approval of final manuscript: All authors.

REFERENCES

1. Wang Y, Mao LH, Jia EZ, Li ZY, Ding XQ, Ge PC, et al. Relationship between diagonal earlobe creases and coronary artery disease as determined via angiography. BMJ Open. 2016;6(2):e008558. doi: 10.1136/bmjopen-2015-008558.
2. Wu XL, Yang DY, Zhao YS, Chai WH, Jin ML. Diagonal earlobe crease and coronary artery disease in a Chinese population. BMC Cardiovasc Disord. 2014;14:43. doi: 10.1186/1471-2261-14-43.
3. Kamal R, Kausar K, Qavi AH, Minto MH, Ilyas F, Assad S, et al. Diagonal Earlobe Crease as a Significant Marker for Coronary Artery Disease: A Case-control Study. Cureus. 2017;9(2):e1013. doi: 10.7759/cureus.1013.
4. Hou X, Jiang Y, Wang N, Shen Y, Wang X, Zhong Y, et al. The Combined Effect of Ear Lobe Crease and Conventional Risk Factor in the Diagnosis of Angiographically Diagnosed Coronary Artery Disease and the Short-Term Prognosis in Patients Who Underwent Coronary Stents. Medicine (Baltimore). 2015;94(26):e815. doi: 10.1097/MD.0000000000000815.
5. Więckowski K, Gallina T, Surdacki A, Chyrchel B. Diagonal Earlobe Crease (Frank's Sign) for Diagnosis of Coronary Artery Disease: A Systematic Review of Diagnostic Test Accuracy Studies. J Clin Med. 2021;10(13):2799. doi: 10.3390/jcm10132799.
6. Friedlander AH, Scully C. Diagonal ear lobe crease and atherosclerosis: a review of the medical literature and oral and maxillofacial implications. J Oral Maxillofac Surg. 2010;68(12):3043-50. doi: 10.1016/j.joms.2010.07.009.
7. Sasaki O, Nishioka T, Sasaki H. Earlobe Creases as a Marker of the Risk for Coronary Atherosclerosis Before Angiography in Elderly and Non-elderly Patients. Cureus. 2023;15(3):e36609. doi: 10.7759/cureus.36609.
8. Gakovic B, Neskovic SA, Vranic I, Grujicic K, Mijatovic S, Ljubojevic A, et al. The relationship of diagonal earlobe crease (Frank's sign) and obstructive coronary artery disease in patients undergoing coronary angiography. Wien Klin Wochenschr. 2023;135(23-24):667-673. doi: 10.1007/s00508-023-02297-y.
9. Evrengül H, Dursunoğlu D, Kaftan A, Zoghi M, Tanriverdi H, Zungur M, et al. Bilateral diagonal earlobe crease and coronary artery disease: a significant association. Dermatology. 2004;209(4):271-5. doi: 10.1159/000080847.
10. Kenny DJ, Gilligan D. Ear lobe crease and coronary artery disease in patients undergoing coronary arteriography. Cardiology. 1989;76(4):293-8. doi: 10.1159/000174506.