Olfaction and cardiovascular risk: a connection yet to be explored

Original Article

Authors

Carlota Sousa
Unidade Local de Saúde Lisboa Ocidental, Lisboa, Portugal

Joana Guincho
Unidade Local de Saúde Lisboa Ocidental, Lisboa, Portugal

Luís Baptista
Unidade Local de Saúde Lisboa Ocidental, Lisboa, Portugal

Filipe Correia
Unidade Local de Saúde Lisboa Ocidental, Lisboa, Portugal

Mariana Donato
Unidade Local de Saúde Lisboa Ocidental, Lisboa, Portugal

Pedro Escada
Unidade Local de Saúde Lisboa Ocidental, Lisboa, Portugal

Correspondence:
Carlota Sousa
sousadecarlota@gmail.com

Article received on May 4, 2025.
Accepted for publication on July 3, 2025.

Abstract

Introduction: Cardiovascular disease (CVD) is highly prevalent in the general population, especially in older age groups. Published studies associate loss of smell with comorbidities such as dyslipidemia, stroke, and heart failure. However, results are inconsistent, and the relationship between CVD and olfactory dysfunction remains unclear.

Objective: To evaluate the correlation between loss of smell, cardiovascular risk factors (CVRFs), and overall cardiovascular risk (CVR).

Material and methods: A retrospective study design, recruiting patients aged 40 years and older, observed on our Olfaction Clinic at a tertiary hospital between 2016 and 2024. CVRFs (sex, age, systolic blood pressure, total and HDL cholesterol, weight, height, smoking habits, and the presence of diabetes mellitus (DM)) were assessed. The degree of loss of smell was quantified using the Burghart Sniffin' Sticks Identification Test (0-16). CVR was calculated using the SCORE2, SCORE2-OP (patients >70 years), and SCORE2-DM (diabetic patients). A case-control study and correlation analysis between the identification score and the other variables were performed. The control group included age- and sex-matched individuals with no subjective loss of smell. Statistical analysis was performed using SPSS® 30.0 for MacOs.

Results: 119 patients were included (81 with changed sense of smell and 38 in the control group). The mean age was 61 ± 11 years, 79 were female; 16.8% had diabetes. The study group had a mean olfactory identification score of 8.4 ± 4 and a mean CVR of 7.7% ± 6%.Our results showed that our patients with olfactory dysfunction have significantly higher total cholesterol levels and a greater tendency to DM (p = 0.054), although this was not statistically significant. When subgroup analysis was applied and patients with smell loss due to sinonasal pathology were excluded, a statistically significant relationship was found between smell identification results and CVR (p = 0.031), as well as with total cholesterol (p = 0.044). No other statistically significant associations were found in the other variables evaluated.

Conclusion: This is the first study to explore the relationship between CVR and smell disorders in the Brazilian population. This study suggests an

association between smell loss, elevated serum cholesterol, and increased CVR.
Keywords: Smell, cardiovascular disease

Introduction

Cardiovascular diseases (CVD) are the leading cause of morbidity and mortality in adults and predominantly affect older age groups. There is a potential association between olfactory dysfunction and cardiovascular diseases such as stroke, heart failure, and dyslipidemia[1-4] . Furthermore, some authors shave suggested that olfactory dysfunction may be an early marker of underlying vascular disorders[1]. However, the available data are limited and inconclusive, and the relationship between CVD and olfactory dysfunction remains unclear. Thus, this study aimed to explore the relationship between olfactory loss and established cardiovascular risk (CVR) factors, along with the estimated global CVR.

Materials and Methods

A retrospective study as well as a case-control study were conducted to understand the connection between CVR and olfactory loss.

The study included patients followed up for 8 years in the olfaction and taste subspecialty clinic of a tertiary hospital from 2016 to 2024. The inclusion criteria were patients with olfactory loss of any etiology over the age of 40 years. The control group included individuals with a subjective perception of normal olfactory function, who had no nasal pathology, and were being followed up in general otorhinolaryngology (ORL) visits. These participants were selected based on age and sex to ensure comparability with the study population. Thus, the total population consisted of patients included in the study group and individuals in the control group. Clinical and laboratory data, including age, sex, systolic blood pressure (SBP), total cholesterol, high-density lipoprotein (HDL) cholesterol, weight, height (for body mass index [BMI] calculation), smoking habits, and presence of diabetes mellitus (DM) were analyzed. Patients for whom data on these parameters were unavailable were excluded from the study.

The olfactory function was assessed with the Burghart Sniffin' Sticks identification test, commonly used for screening asymptomatic patients. Test results range from 0–16 points. The etiology of olfactory loss was recorded in the study group. The global CVR was estimated using the European Society of Cardiology[5] Systematic COronary Risk Evaluation 2 (SCORE2) for participants between 40 and 69 years of age, the SCORE2-OP for older patients (> 70 years), and SCORE2-DM for patients with DM. Concomitant with the case-control study, a retrospective analysis of the entire population was conducted to assess the correlation between olfactory function (measured by the identification scores), each CVR factor, and the global CVR. Subsequently, the same correlation analysis was performed after excluding patients with olfactory loss due to nasal sinus causes.

Statistical analysis was performed using SPSS® software v30.0 (MacOS). The Mann-Whitney test and Student's t-test were used for group comparisons, while Spearman correlation was used to evaluate associations. Statistical significance was defined as $p < 0.05$.

Results

Population characteristics

A total of 119 individuals were included in the study: 81 with olfactory dysfunction and 38 in the control group. The average age was 61.7 ± 11.5 years, with 66.4% of the participants being women. Among them, 16.8% had DM (Table 1). The study group had an average age of 62 ± 11.5 years. Of the 81 patients, 27 were men and 13 had DM. This group had an average identification score of 8.4 ± 4 and average CVR of 7.7% ± 6% (CVR was low in 32 patients, intermediate in 29, and high in 20). The average total cholesterol and HDL levels in this group were 196.9 ± 40.1 mg/dL and 56.7 ± 13.7 mg/dL, respectively. The average BMI was 27.5 ± 5.4 (Table 1). The primary etiology of olfactory loss was nasal sinus pathology, followed by post-infectious causes.

Table 1
General population characteristics

	Total population	Study population	Control population
Number of patients	119	81	36
Men: Women	40 : 79	27 : 54	13 : 25
Average age	61,7 ± 11,5	62 ± 11,5	61 ± 11,8
Diabetic: Non-diabetic	20 : 99	13 : 68	7 : 31
Smoker: Non-smoker	19 : 100	11 : 70	8 : 30
Average CVR	7,24% ± 6,3	7,8% ± 6	8,3% ± 7,2
Average total cholesterol	191,7 ± 39,4	197 ± 40,1	181 ± 36,2
Average HDL	56,1 ± 14,8	56,7 ± 13,7	54,9 ± 16,7
Average BMI	27 ± 5	27,2 ± 5,4	26,3 ± 3,8
Average identification score	9,71 ± 4,1	8,4 ± 4,2	12,5 ± 2,6

CVR, cardiovascular risk; HDL, high-density lipoprotein; BMI, body mass index

The control group comprised 38 participants, including 13 men. The average age was 61 ± 11.8 years, with an average olfactory identification score of 12.5 ± 2.6 and average CVR of 8.3% ± 7.2%. The average total cholesterol and HDL levels in this group were 181.1 ± 36.2 mg/dL and 54.9 ± 16.7 mg/dL, respectively (Table 1).

Case-control study

Statistical analysis was conducted using the Student's t-test for variables with a normal distribution: age, total cholesterol, and HDL cholesterol. The Mann–Whitney test was used for SBP, global CVR, BMI, and identification scores. Among all variables, only total cholesterol showed a statistically significant difference (Table 2), being higher in the group with olfactory loss ($p = 0.042$). No statistically significant differences were observed for the remaining variables, particularly for global CVR (Tables 2 and 3).

Retrospective study

Spearman's correlation test was used to evaluate the relationship between the total population's identification score and other variables, which revealed a statistically significant correlation only with age (Tables 4, 5, and 6). This correlation was negative, with the identification score decreasing as the age increased. The Mann–Whitney test showed a trend toward a higher prevalence of DM in patients with lower scores ($p = 0.054$) (Table 5). When the same analysis was conducted after excluding patients with olfactory loss due to nasal sinus pathology, olfactory function (identification score) demonstrated a statistically significant negative correlation with CVR ($\rho = -0.245$, $p = 0.031$), total cholesterol ($\rho = -0.229$; $p = 0.044$), and age (Table 7). This indicates that a higher CVR, elevated cholesterol levels, and older age are associated with lower identification scores. The other analyzed variables showed no significant associations (Table 7).

Discussion

In this study, we evaluated 119 patients and found that individuals with olfactory loss have higher serum cholesterol levels. Furthermore, an association between non-nasal olfactory loss, CVR and elevated total cholesterol levels was identified. Finally, a trend indicating a higher prevalence of DM in patients with olfactory dysfunction was observed.

In addition to the case-control study, a retrospective analysis was conducted to investigate discrepancies between subjective reports and objective findings: some patients who reported olfactory loss showed no dysfunction on psychophysical testing, while some control participants who reported

Table 2
Case-control study results, Student's t-test for the variables age, total cholesterol, and HDL cholesterol

Independent samples test					
		t-test for comparison of means			
		Significance			
		One-tailed p	Two-tailed p	Mean difference	Standard error of difference
Age	Assumed equal variances	,312	,624	-1,118	2,276
	Assumed unequal variances	,314	,628	-1,118	2,297
Total cholesterol	Assumed equal variances	,021	,042	-15,757	7,657
	Assumed unequal variances	,018	,036	-15,757	7,373
HDL	Assumed equal variances	,264	,528	-1,851	2,924
	Assumed unequal variances	,279	,559	-1,851	3,150

Group statistics				
Group: Study =1; Control= 0		N	Mean	Standard deviation
Age	Control	38	60,89	11.777
	Population with olfactory loss	81	62,01	11,484
Total cholesterol	Control	38	181,13	36,189
	Population with olfactory loss	81	196,89	40,151
HDL	Control	37	54,86	16,762
	Population with olfactory loss	81	56,72	13,731

Table 3
Case-control study results, Mann–Whitney test for the variables SBP, BMI, SCORE, and identification score

Mann–Whitney test				
	Group: Study =1; Control= 0	N	Mean	Sum of classifications
SBP	Control	38	64,20	2439,50
	Population with olfactory loss	81	58,03	4700,50
	Total	119		
RCV Score	Control	38	60,09	2283,50
	Population with olfactory loss	81	59,96	4856,50
	Total	119		
BMI	Control	38	58,37	2218,00
	Population with olfactory loss	81	60,77	4922,00
	Total	119		
Identification	Control	38	83,34	3167,00
	Population with olfactory loss	81	49,05	3973,00
	Total	119		

Test statistics (Grouping variable: Group: Study =1; Control= 0)				
	SBP	RCV Score	BMI	Identification
Mann–Whitney U	1379,500	1535,500	1477,000	652,000
Wilcoxon W	4700,500	4856,500	2218,000	3973,000
Z	-,910	-,020	-,353	-5,074
Significance (2 ends)	,363	,984	,724	<,001

SBP, systolic blood pressure; BMI, body mass index; SCORE2, European Society of Cardiology[5] Systematic COronary Risk Evaluation 2

Table 4
Retrospective study results for the total population using Spearman's correlation analysis

			Identification
Spearman	Age	Correlation coefficient	-,202*
		Sig. (2 ends)	,028
		N	119
	SBP	Correlation coefficient	-,045
		Sig. (2 ends)	,624
		N	119
	Total cholesterol	Correlation coefficient	-,158
		Sig. (2 ends)	,086
		N	119
	HDL	Correlation coefficient	,051
		Sig. (2 ends)	,582
		N	118
	RCV Score	Correlation coefficient	-,174
		Sig. (2 ends)	,058
		N	119
	BMI	Correlation coefficient	-,043
		Sig. (2 ends)	,644
		N	119

SBP, systolic blood pressure; BMI, body mass index; HDL, high-density lipoprotein; SCORE2, European Society of Cardiology[5] Systematic COronary Risk Evaluation 2

Table 5
Retrospective study results for the association between DM and identification scores in the total population

Diabetes	
	Identificação
Mann–Whitney U	720,000
Wilcoxon W	5670,000
Z	-1,926
Significance (2 ends)	,054

Table 6
Retrospective study results for the association between smoking and identification in the total population

Smoking	
	Identification
Mann–Whitney U	812,500
Wilcoxon W	5372,500
Z	-,687
Significance (2 ends)	,492

Table 7
Retrospective study results for the total population after excluding patients with olfactory loss due to nasal sinus pathology (Spearman correlation)

			Identificação
Spearman	Age	Correlation coefficient	-0,309
		Sig. (2 ends)	0,006
		N	
	SBP	Correlation coefficient	-0,034
		Sig. (2 ends)	0,796
		N	
	Total cholesterol	Correlation coefficient	-0,229
		Sig. (2 ends)	0,044
		N	
	HDL	Correlation coefficient	-0,030
		Sig. (2 ends)	0,796
		N	
	RCV Score	Correlation coefficient	-0,245
		Sig. (2 ends)	0,031
		N	
	BMI	Correlation coefficient	-0,093
		Sig. (2 ends)	0,427
		N	

SBP, systolic blood pressure; BMI, body mass index; HDL, high-density lipoprotein; SCORE2, European Society of Cardiology[5] Systematic COronary Risk Evaluation 2

normal olfaction had scores outside the normal range. Thus, the relationship between identification scores and CVR factors appears to more accurately reflect the relationship between CVR and olfaction.

This is the first study to explore the relationship between olfactory dysfunction and global CVR in a Portuguese population using widely validated CVR stratification algorithms[5]. The use of standardized methods for assessing olfactory function, specifically the Burghart Sniffin' Sticks identification test, increases the reliability of the olfactory dysfunction measurements.

Subgroup analyses after excluding patients with nasal sinus disease enabled the isolation of the neurosensory component of olfactory dysfunction. The identified association between olfactory loss, total cholesterol levels, and SCORE2 results may not be solely due to local factors, such as nasal inflammation, but may instead reflect a systemic (endothelial injury) or neurovascular mechanism[1,7,8] .

This study has several limitations. First, the relatively small sample size, although adequate for preliminary analysis, limits the generalizability of the findings and may reduce the statistical power to detect subtle associations.

Second, the selection of the control group from patients followed up in the general ORL clinic may have introduced selection bias, as this population may not fully represent the general population. Third, although the control group did not report subjective olfactory complaints, some participants demonstrated a below-average performance on objective identification tests, which may have attenuated the observed differences between the groups. Fourth, the study assessed only olfactory

identification scores, without evaluating other domains such as detection and discrimination, potentially limiting a comprehensive of the global olfactory function. Fifth, the group with olfactory dysfunction included patients with heterogeneous etiologies. Although a sub-analysis was performed after excluding patients with nasal and sinus causes, some residual heterogeneity may persist.

Finally, as this was an observational study, a causal relationship between olfactory dysfunction and increased global CVR could not be established.

Conclusion

This study examined the relationship between CVR and olfactory dysfunction in the Portuguese population, and found an association between olfactory loss, elevated serum cholesterol levels, and increased CVR. Future prospective studies with larger sample sizes and more comprehensive olfactory assessments are warranted to validate and expand upon these findings.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols used at their working center regarding patient data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and the 2013 Helsinki Declaration of The World Medical Association.

Funding Sources

This work did not receive any contribution, funding, or scholarship.

Availability of scientific data

There are no datasets available, or publicity related to this work.

References

1. Roh D, Lee DH, Kim SW, Kim SW, Kim BG, Kim DH. et al. The association between olfactory dysfunction and cardiovascular disease and its risk factors in middle-aged and older adults. Sci Rep. 2021 Jan 13;11(1):1248. doi: 10.1038/s41598-020-80943-5.
2. Wehling E, Naess H, Wollschlaeger D, Hofstad H, Bramerson A, Bende M. et al. Olfactory dysfunction in chronic stroke patients. BMC Neurol. 2015 Oct 12:15:199. doi: 10.1186/s12883-015-0463-5.
3. Chamberlin KW, Yuan Y, Li C, Luo Z, Reeves M, Kucharska-Newton A. et al. Olfactory impairment and the risk of major adverse cardiovascular outcomes in older adults. J Am Heart Assoc. 2024 Jun 18;13(12):e033320. doi: 10.1161/JAHA.123.033320.
4. Liu G, Zong G, Doty RL, Sun Q. Prevalence and risk factors of taste and smell impairment in a nationwide representative sample of the US population: a cross-sectional study. BMJ Open. 2016 Nov 9;6(11):e013246. doi: 10.1136/bmjopen-2016-013246.
5. Task Force Members, Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C. et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts): Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur J Prev Cardiol. 2016 Jul;23(11):NP1-NP96. doi: 10.1177/2047487316653709
6. Desiato VM, Levy DA, Byun YJ, Nguyen SA, Soler ZM, Schlosser RJ. The prevalence of olfactory dysfunction in the general population: a systematic review and meta-analysis. Am J Rhinol Allergy. 2021 Mar;35(2):195-205. doi: 10.1177/1945892420946254.
7. Frasnelli J, Lundström JN, Boyle JA, Djordjevic J, Zatorre RJ, Jones-Gotman M. Neuroanatomical correlates of olfactory performance. Exp Brain Res. 2010 Feb;201(1):1-11. doi: 10.1007/s00221-009-1999-7.
8. Cardella A, Ferrulli A, Vujosevic S, Preti A, Ambrogi F, Terruzzi I. et al. Olfactory dysfunction in patients with type 2 diabetes mellitus. Rhinology. 2024 Oct 1;62(5):537-547. doi: 10.4193/Rhin23.451.