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Research Paper

Cardiometabolic diseases and risk of early-onset dementia: a population-based case-control study in Northern Italy

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ABSTRACT

Background and aims: Early-onset dementia (EOD), defined by symptom onset before 65 years, has an uncertain etiology. Cardiovascular and metabolic diseases have been suggested to increase risk for EOD, but evidence remains limited and inconsistent. We investigated the extent to which history of cardiometabolic conditions is associated with EOD, and the extent to which the associations vary by sex, age at onset, and dementia subtype.
Methods and results: We conducted a population-based case-control study in Modena, Northern Italy, including 334 EOD cases diagnosed from 1999 to 2021, and 1991 controls matched by sex, year of birth, and calendar year. Hospitalization records and drug prescriptions were retrieved from administrative databases to estimate cardiometabolic disease history before EOD onset. We estimated odds ratios (OR) and 95% confidence intervals (CI) using conditional logistic regression in the entire study population and within subgroups of age and sex. EOD cases showed higher rates of hospitalization for hypertension and diabetes. History of antidiabetic drugs (OR = 1.49, 95% CI 1.01–2.19), lipid-lowering agents (OR = 1.36, 95% CI 1.03–1.79), and antihypertensive drugs (OR = 1.47, 95% CI 0.93–2.32) was associated with higher EOD risk. Associations were stronger in males for antidiabetics (OR = 1.78, 95% CI 1.08-2.93) and antithrombotics (OR = 1.57, 95% CI 1.06-2.33), and in individuals <55 years for most antihypertensive classes. Non-Alzheimer's EOD generally showed higher associations with cardiovascular drug use than Alzheimer's type.
Conclusions: The associations we found between cardiometabolic diseases and EOD, particularly non-Alzheimer's subtypes, are consistent with a role of cardiometabolic burden or shared etiologic factors in early cognitive decline.

1. Introduction

Dementia is a neurological syndrome defined as a cognitive decline that is severe enough to interfere with daily functioning. Early-onset dementia (EOD) is the subtype of dementia whose symptom onset occurs before the age of 65 years. It represents up to 10% of all dementia cases and has a major impact on the affected individual and their family. Its causes may differ from late-onset dementia [1].

Hypertension, diabetes, and lipid metabolism disorders have all been associated with cognitive decline and dementia in older adults [2]. Among cardiovascular diseases in particular, atrial fibrillation, the most common cardiac arrhythmia, showed a positive association with EOD in previous studies [3–5]. Evidence also suggests a link of EOD with ischemic heart disease and myocardial infarction [6]. Conversely, the evidence regarding pharmacological interventions for cardiometabolic conditions in relation to the risk and prevention of cognitive decline is

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inconsistent: some drug classes (notably renin-angiotensin inhibitors) have shown inverse associations with all-cause dementia risk in some studies, while others have shown null or positive associations. Findings differ substantially by study design, population, and outcome definition [7–10], with limited literature about EOD specifically.

To address this gap, we conducted a population-based case-control study in an Italian community, aiming to assess the association between overall EOD and prior cardiometabolic conditions, identified through hospitalization records and pharmacological prescriptions. We also investigated the extent to which the association varied across dementia subtype and within subgroups of sex and age.

2. Methods

2.1. Study population

We conducted a population-based case-control study by identifying EOD cases diagnosed in Modena province, Northern Italy in the period 1999-2021. The study was approved by the Modena Ethics Committee (approval no. AOU 0027399/2021). All cases were diagnosed with EOD after being referred to the only two facilities providing care for EOD in Modena province, the Cognitive Neurology Centers of Policlinico-University Hospital and of Carpi Hospital. In this study, we enrolled patients with a diagnosis of dementia and symptoms onset before age 65. Subtypes included Alzheimer's dementia (AD), fronto-temporal dementia (FTD), vascular dementia including cerebral amyloid angiopathy, Lewy body dementia, Parkinson's disease dementia, progressive supranuclear palsy, Huntington disease and adult onset leukodystrophies [11]. We excluded individuals who had additional diagnoses of developmental disorder, major psychiatric illness, or cognitive impairment associated with other neurological conditions, such as multiple sclerosis or cerebrovascular disease with severe motor impairment [12,13]. The date of dementia diagnosis served as the index date for cases. Age and all other baseline characteristics were calculated as of this index date.

For each enrolled patient, we selected up to six matched controls from the database of National Health Service directory, in which all Italian residents are included. Cases were ineligible to be selected as controls. Controls were randomly selected among the set of residents who matched each patient by sex, year of birth, and calendar year of dementia diagnosis. Each control was assigned the same index date as their matched case.

2.2. Data collection

We retrieved data on hospitalization and pharmacological prescriptions for cases and controls from the Regional Health Service administrative directories. Conditions that required hospitalization or were detected during it were identified through ICD-9 codes, with the admission year recorded for each case. For pharmacological prescriptions, we classified the participants, both cases and controls, according to the ATC code of individually-prescribed drugs, date of the first prescription, administration duration. We used drug prescriptions as proxies for the underlying cardiometabolic conditions, because the administrative databases capture medication use more reliably than clinical diagnoses for conditions managed primarily in outpatient settings. Hospitalization records are better at capturing more severe or acute presentations and prescription data better for chronic pharmacologically managed disease. Details on the recorded hospitalizations are provided in Supplementary Table S1, while Supplementary Table S2 provides a breakdown of medications grouping process. The antihypertensive drug category (C02) includes centrally acting agents, ganglionic blockers, and adrenergic neuron blockers, as per the ATC classification. It does not include diuretics (C03), beta-blockers (C07), calcium channel blockers (C08), nor agents active on the renin-angiotensin system (C09).

2.3. Data analysis

We calculated odds ratio (OR) of EOD and the corresponding 95% confidence interval (CI), using univariable conditional logistic regression models, matching by sex, year of birth and calendar year. Participants whose first prescription was after the calendar year were classified as not exposed for that drug. We conducted stratified analysis by sex (males/females) and age at diagnosis (<55 and ≥ 55 years). We also carried out separate analyses according to category of EOD diagnosis, i.e. separately for Alzheimer's dementia (AD) and non-AD forms. We also performed sensitivity analysis excluding Huntington's disease cases, and their matched controls, due to influence of genetic susceptibility.

We performed all analyses using the Stata-19.0 package (Stata Corp., College Station, TX, USA, 2025).

3. Results

A total of 2325 participants were included in the study, comprising 334 individuals with EOD and 1991 controls, having median (interquartile range) age at index date of 60 (57-64) years (Table 1). Alzheimer's dementia was the most frequent diagnosis, followed by frontotemporal dementia. Supplementary Table S3 provides a detailed breakdown of EOD diagnosis and subtypes.

History of hospitalization for cardiometabolic disease was more frequent among EOD cases than among controls for hypertension, diabetes and lipid metabolism disorders, while chronic ischemic disease, myocardial infarction, and atrial fibrillation were similarly distributed between the two study groups (Table 1).

Table 2 shows that history of cardiometabolic disease as assessed through drug prescriptions was generally associated with modestly increased odds of EOD. The most notable elevations were observed for antidiabetic (OR = 1.49, 95% CI 1.01–2.19), antihypertensive (OR = 1.47, 95% CI 0.93–2.32), and lipid-lowering drugs (OR = 1.36, 95% CI 1.03–1.79), while other cardiovascular treatments displayed weaker or more uncertain associations. Among these cardiac glycosides had the lowest association (OR = 0.46, 95% CI 0.11–1.96).

Table 3 displays how these associations vary by sex and age. Among males, diabetes medications (OR = 1.78, 95% CI 1.08–2.93) and antithrombotics (OR = 1.57, 95% CI 1.06–2.33) showed the highest odds ratios, whereas in females, antihypertensive (OR = 1.92, 95% CI 0.96–3.85) and lipid modifying agents (OR = 1.40, 95% CI 0.95–2.08) had the largest ORs. Across age groups, the younger group (<55 years) showed stronger associations for antihypertensive drugs such as diuretics (OR = 2.78, 95% CI 1.07–7.22), beta-blockers (OR 2.43, 95% CI 1.07–5.50), and renin–angiotensin agents (OR = 2.28, 95% CI 1.08–4.81), while among those ≥55 years, diabetes medications (OR = 1.53, 95% CI 1.03–2.29) and antiarrhythmics (OR = 1.56, 95% CI 0.67–3.63) displayed the highest estimates.

In Supplementary Table S4, we report the analysis using combined exposure variable for six antihypertensive classes (C02, C03, C04, C07, C08, C09) for overall EOD and subgroups, showing a positive association in males (OR = 1.46, 95% CI 1.02–2.09) and younger participants (OR = 2.26, 95% CI 1.18–4.35).

Table 4 shows that hospitalization for metabolic and vascular conditions was most strongly associated with EOD. Diabetes (OR = 2.22, 95% CI 1.33–3.69) and hypertension (OR 1.85, 95% CI 1.32–2.61) showed the highest overall odds ratio regardless of age, with stronger association for diabetes seen in males (OR 2.89, 95% CI 1.57-5.32, vs 1.26, 95% CI 0.47-3.37). Chronic ischemic disease showed the opposite pattern, being higher in females and inversely associated in males (OR 1.61, 95% CI 0.45-5.79 vs 0.77, 95% CI 0.35-1.74). Myocardial infarction was positively associated with EOD in individuals younger than 55 years, whereas the association among older individuals was modestly negative (OR 2.00, 95% CI 0.21-19.23 vs 0.80, 95% CI 0.34-1.90).

Supplementary Table S5 shows analyses by dementia pathologic subtype and highlights distinct patterns between AD and non-AD EOD.

Table 1
Demographic and clinical characteristics of the study population in Modena (Italy) 1999-2021, divided by early-onset dementia (EOD) cases and controls.

	EOD cases N = 334	Controls N = 1991
	N (%)	N (%)
Sex		
Male	157 (47.01)	937 (47.06)
Female	177 (52.99)	1054 (52.94)
Age		
Median (interquartile range)	60 (57-64)	60 (57-64)
<55 years	52 (15.57)	310 (15.57)
≥55 years	282 (84.43)	1681 (84.43)
Hospitalizations		
Atrial Fibrillation	5 (1.50)	29 (1.46)
Chronic Ischemic Disease	10 (2.99)	64 (3.21)
Diabetes	22 (6.59)	63 (3.16)
Hypertension	50 (14.97)	174 (8.74)
Lipid Metabolism Disorders	19 (5.69)	83 (5.17)
Myocardial Infarction	7 (2.10)	47 (2.36)
Prescriptions (all-time)		
A10 – Diabetes medications	39 (11.68)	173 (8.69)
B01 – Antithrombotics	79 (23.65)	400 (20.09)
C01A – Glycosides	2 (0.60)	26 (1.31)
C01B – Antiarrhythmics	8 (2.40)	33 (1.66)
C02 – Antihypertensives	28 (8.38)	112 (5.63)
C03 – Diuretics	59 (17.66)	327 (16.42)
C04 – Vasodilators	0 (0.00)	1 (0.05)
C07 – Beta-blockers	84 (25.15)	452 (22.70)
C08 – Calcium antagonist	55 (16.47)	313 (15.72)
C09 – Renin-angiotensin	128 (38.32)	732 (36.77)
C10 – Lipid modifying agents	94 (28.14)	469 (23.56)
Prescriptions (at least one year prior)		
A10 – Diabetes medications	36 (10.78)	151 (7.58)
B01 – Antithrombotics	71 (21.26)	346 (17.38)
C01A – Glycosides	2 (0.60)	25 (1.26)
C01B – Antiarrhythmics	7 (2.10)	29 (1.46)
C02 – Antihypertensives	25 (7.49)	104 (5.22)
C03 – Diuretics	54 (16.17)	289 (14.52)
C04 – Vasodilators	0 (0.00)	1 (0.05)
C07 – Beta-blockers	78 (23.35)	415 (20.84)
C08 – Calcium antagonist	54 (16.17)	289 (14.52)
C09 – Renin-angiotensin	124 (37.13)	665 (33.40)
C10 – Lipid modifying agents	87 (26.05)	416 (20.89)
EOD diagnosis		
Alzheimer's dementia (AD)	154 (46.11)	
Frontotemporal dementia (FTD)	88 (26.35)	
Amyotrophic lateral sclerosis with FTD	32 (9.58)	
Lewy body dementia	10 (2.99)	
Leukodystrophy	7 (2.10)	
Alcohol related dementia	6 (1.80)	
Progressive supranuclear palsy	6 (1.80)	
Corticobasal syndrome	5 (1.50)	
Parkinson's disease dementia	5 (1.50)	
Cerebral amyloid angiopathy	3 (0.90)	
Huntington's disease	3 (0.90)	
Vascular dementia	3 (0.90)	
Other	12 (3.59)	

Non-AD cases showed a clear associations with drugs acting on metabolic and cardiovascular systems, particularly antiarrhythmics (OR = 2.50, 95% CI 0.94–6.64), diabetes medications (OR = 2.24, 95% CI 1.40–3.60) and calcium antagonists (OR = 1.51, 95% CI 1.01–2.25). In contrast, AD cases displayed generally weaker or modest associations, with no class showing markedly elevated odds, with the exception of lipid-modifying agents (OR = 1.40, 95% CI 0.92–2.14) and antihypertensives (OR = 1.31, 95% CI 0.61–2.78). Contrary to what was observed for non-AD, for the AD form both antiarrhythmics, diabetes medications and calcium antagonists showed a negative association. Renin–angiotensin inhibitors and beta-blockers showed comparable associations across dementia subtypes. When the analysis was restricted to FTD only (Supplementary Table S6), the associations observed for non-AD EOD were generally attenuated, with weaker effect estimates, particularly for calcium antagonists and lipid-modifying agents.

Table 2
Odds ratio (OR) with 95% confidence interval (CI) of early-onset dementia (EOD) according to drug consumption history before EOD diagnosis in the study population, Modena (Italy) 1999-2021. ORs were calculated using univariable conditional logistic regression model matched by sex, age and calendar year.

Prescription	Cases (y/n)	Controls (y/n)	OR	(95% CI)
A10 – Diabetes medications	36/298	151/1840	1.49	1.01 – 2.19
B01 – Antithrombotics	71/263	346/1645	1.30	0.97 – 1.75
C01A – Glycosides	2/332	25/1966	0.46	0.11 – 1.96
C01B – Antiarrhythmics	7/327	29/1962	1.45	0.63 – 3.35
C02 – Antihypertensives	25/309	104/1887	1.47	0.93 – 2.32
C03 – Diuretics	54/280	289/1702	1.14	0.83 – 1.58
C04 – Vasodilators	0/334	1/1990	–	–
C07 – Beta-blockers	78/256	415/1576	1.16	0.88 – 1.53
C08 – Calcium antagonist	54/280	289/1702	1.14	0.83 – 1.57
C09 – Renin-angiotensin	124/210	665/1326	1.19	0.93 – 1.52
C10 – Lipid modifying agents	87/247	416/1575	1.36	1.03 – 1.79

After excluding the three participants with Huntington's disease and their matched controls, we obtained results nearly identical to the primary analysis across all drug classes and hospitalization categories (Supplementary Table S7); none of the three cases had been exposed to any of the investigated drugs or hospitalized for any of the cardiometabolic conditions under study.

4. Discussion

In the present study, we found that hospitalization for hypertension, diabetes, or lipid metabolism disorder, or greater use of medications targeting these conditions, was associated with an increased risk for EOD. These findings are consistent with the hypothesis that these diseases increase EOD risk or that EOD shares one or more etiologic factors with these conditions [14,15]. The hypothesis that EOD is an adverse effect of drugs used to treat these conditions is less plausible, given the consistency of the associations for the different classes of medications used for the same disease.

Use of antidiabetic drugs was associated with higher EOD risk, particularly among males, individuals ≥55 years, particularly for the non-AD subtypes [16]. This result is consistent with previous indications that type 2 diabetes is associated with overall dementia risk [17–19]. However, we did not find an increased risk among diabetic females as other studies did [20], and the stronger association in males could reflect a higher burden of comorbidities and poorer glycemic control [21,22], as indicated by greater overall hospitalization rates and a threefold higher rate of diabetes-related hospitalizations in males. This pattern supports the strong contribution of metabolic dysfunction, compounded by vascular injury, to the development of 'early' neurodegeneration [23].

The positive association between antithrombotic drug use and EOD, particularly in males and in older individuals, is also of interest given the association between atrial fibrillation and early cognitive decline [3]. This association could be due to cortical microinfarcts, hypoperfusion, and vascular inflammation [3,24–26], and the higher association we observed in males could reflect a higher frequency of vascular alterations [27–29]. This evidence, however, remains debated, as findings from a large cohort indicate elevated risk in both sexes [30]. The pattern

Table 3
Odds ratio (OR) with 95% confidence interval (CI) of early-onset dementia (EOD) according to drug consumption history before EOD diagnosis in the study population, Modena (Italy) 1999-2021, by sex, and by age (<55 and ≥ 55 years). ORs were calculated using univariable conditional logistic regression model matched by sex, age and calendar year.

	Males				Females			
Prescription	Cases (y/n)	Controls (y/n)	OR	(95% CI)	Cases (y/n)	Controls (y/n)	OR	(95% CI)
A10 – Diabetes medications	23/134	83/854	1.78	1.08 – 2.93	13/164	68/986	1.16	0.62 – 2.15
B01 – Antithrombotics	44/113	189/748	1.57	1.06 – 2.33	27/150	157/897	1.03	0.65 – 1.62
C01A – Glycosides	2/155	13/924	0.91	0.20 – 4.09	0/177	12/1042	–	–
C01B – Antiarrhythmics	6/151	16/921	2.31	0.88 – 6.06	1/176	13/1041	0.46	0.06 – 3.53
C02 – Antihypertensives	14/143	69/868	1.23	0.67 – 2.24	11/166	35/1019	1.92	0.96 – 3.85
C03 – Diuretics	23/134	118/819	1.20	0.74 – 1.96	31/146	171/883	1.10	0.72 – 1.69
C04 – Vasodilators	0/157	0/937	–	–	0/177	1/1053	–	–
C07 – Beta-blockers	39/118	195/742	1.27	0.85 – 1.90	39/138	220/834	1.07	0.73 – 1.58
C08 – Calcium antagonist	29/128	151/786	1.17	0.76 – 1.82	25/152	138/916	1.10	0.69 – 1.75
C09 – Renin-angiotensin	72/85	350/587	1.45	1.02 – 2.06	52/125	315/739	0.97	0.68 – 1.39
C10 – Lipid modifying agents	45/112	221/716	1.32	0.89 – 1.93	42/135	195/859	1.40	0.95 – 2.08
	< 55 years				**≥ 55 years**			
A10 – Diabetes medications	2/50	12/298	1.00	0.22 – 4.64	34/248	139/1542	1.53	1.03 – 2.29
B01 – Antithrombotics	3/49	15/295	1.21	0.34 – 4.37	68/214	331/1350	1.31	0.97 – 1.77
C01A – Glycosides	0/52	0/310	–	–	2/280	25/1656	0.46	0.11 – 1.96
C01B – Antiarrhythmics	0/52	2/308	–	–	7/275	27/1654	1.56	0.67 – 3.63
C02 – Antihypertensives	1/51	9/301	0.66	0.08 – 5.33	24/258	95/1586	1.55	0.97 – 2.48
C03 – Diuretics	7/45	17/293	2.78	1.07 – 7.22	47/235	272/1409	1.04	0.74 – 1.47
C04 – Vasodilators	0/52	0/310	–	–	0/282	1/1680	–	–
C07 – Beta-blockers	9/43	24/286	2.43	1.07 – 5.50	69/213	391/1290	1.07	0.79 – 1.44
C08 – Calcium antagonist	7/45	28/282	1.60	0.65 – 3.98	47/235	261/1420	1.09	0.77 – 1.53
C09 – Renin-angiotensin	13/39	42/268	2.28	1.08 – 4.81	111/171	623/1058	1.10	0.85 – 1.43
C10 – Lipid modifying agents	3/49	17/293	1.06	0.31 – 3.61	84/198	399/1282	1.38	1.04 – 1.83

for antiarrhythmic agents, mainly in males and in non-AD EOD, further confirms the findings for antithrombotic drugs [31,32]. The wide confidence intervals for antiarrhythmics reflect sparse data, and estimates in subgroups should be interpreted tentatively due to that statistical imprecision. The inverse association for glycosides is difficult to interpret given the rarity of the exposure (only 2 EOD cases, in males ≥55 years with non-AD EOD)

All classes of antihypertensive agents were positively associated with overall EOD, particularly in individuals <55 years and with reference to the non-AD form, suggesting an etiologic role of high blood pressure in early cognitive decline. Hypertension documented during hospitalization was related to high dementia risk, consistently with a detrimental role of poorly controlled blood pressure on brain health. Importantly, all antihypertensive subclasses showed stronger associations with onset of non-AD than AD, consistent with a vascular pathway linking hypertension to early cognitive impairment [33]. The present results more plausibly reflect the impact of chronic cardiometabolic disease on EOD risk (or of shared genetic [34] and non-genetic [35] etiologic factors) rather than the effect of drugs used to treat those conditions, as all antihypertensive classes showed consistent associations rather than the class-specific variation expected if drug mechanisms were responsible. Additionally, effective control of hypertension is generally achieved in only a minority of patients [36]. Among drug subclasses, the stronger associations in individuals <55 years may indicate that younger users represent patients with severe or early-onset hypertension, in whom either vascular injury or the underlying risk factors may trigger cognitive decline at relatively young age [37–39].

Our findings suggest differential age-related associations with EOD subtypes, with younger users possibly representing individuals with more severe or early-onset hypertension, and with a stronger association with non-AD EOD compared with AD EOD. Though calcium antagonists showed weak positive associations overall, more evident in younger individuals and in relation with non-AD dementia, results are consistent with midlife vascular injury as a potential precursor of dementia, and with beneficial effects of such anti-hypertensive treatment [40–42]. Agents acting on the renin-angiotensin system showed a modest positive association overall, more evident in males and in younger individuals, consistent with sex-specific differences in vascular risk profiles and responsiveness to treatment [43,44].

Lipid-modifying agents were positively associated with overall EOD, particularly among individuals ≥55 years, with no notable sex- or subtype-specific differences [45]. Dysregulated lipid metabolism may contribute to both vascular injury and neurodegenerative processes, consistent with its role in EOD pathogenesis. Although statins have been associated with better cognitive outcomes in some observational studies, other studies have reported null or even potentially adverse associations [46], and randomized trials have not confirmed a robust protective effect [47,48].

Regarding dementia subtype, associations with antecedent cardiometabolic drug prescription were stronger with the non-AD than with the AD EOD form, particularly for diabetes medications and antiarrhythmics, suggesting a stronger role of cardiometabolic conditions in favoring the first 'broad' category of EOD compared with the second type. In contrast, lipid-modifying agents showed similar positive associations across all dementia subtypes. The associations in non-AD EOD were attenuated when we limited our analysis to the FTD subgroup, and therefore the stronger associations observed in the non-AD subtype were driven by other forms of dementia [49].

This study has important limitations. One is the lack of an individual detailed pathological profile for each case; using medication as a proxy for the underlying disease introduces misclassification. Another limitation is the lack of information on variables such as genetic and lifestyle factors, socioeconomic status, and education for study participants. Environmental and behavioral factors such as unhealthy diet, physical inactivity, and prolonged exposure to air pollution, heavy metals, or pesticides are associated with both cardiometabolic conditions and EOD [50–53]. Residual confounding from these factors, which were not available in the administrative databases, cannot be excluded. Furthermore, there is exposure misclassification stemming from the reliance on drug prescriptions without information on actual adherence to therapy. Finally, the stratification by ATC class is at times overly broad, grouping together drugs with widely different mechanisms or different disease-specific indications. Despite these sources of uncertainty, the pattern of associations seen in these data indicate a possibly fruitful line of inquiry to improve our understanding of EOD.

Table 4
Odds ratio (OR) with 95% confidence interval (CI) of early-onset dementia (EOD) according to hospitalization history in the study population, Modena (Italy) 1999-2021. ORs were calculated using univariable conditional logistic regression model matched by sex, age and calendar year.

Hospitalization	Cases (y/n)	Controls (y/n)	OR	(95% CI)
All subjects				
Atrial Fibrillation	5/329	29/1962	1.03	0.39 – 2.70
Chronic Ischemic Disease	10/324	64/1967	0.92	0.47 – 1.83
Diabetes	22/312	63/1928	2.22	1.33 – 3.69
Hypertension	50/284	174/1817	1.85	1.32 – 2.61
Lipid Metabolism Disorders	19/315	83/1908	1.74	0.83 – 2.36
Myocardial Infarction	7/327	47/1944	0.88	0.39 – 1.96
Males				
Atrial Fibrillation	5/152	21/916	1.44	0.55 – 3.91
Chronic Ischemic Disease	7/150	53/884	0.77	0.35 – 1.74
Diabetes	17/104	39/898	2.89	1.57 – 5.32
Hypertension	30/127	108/829	1.80	1.16 – 2.81
Lipid Metabolism Disorders	12/145	51/886	1.44	0.74 – 2.80
Myocardial Infarction	5/152	37/900	0.80	0.31 – 2.04
Females				
Atrial Fibrillation	0/177	8/1046	–	–
Chronic Ischemic Disease	3/174	11/1043	1.61	0.45 – 5.79
Diabetes	5/172	24/1030	1.26	0.47 – 3.37
Hypertension	20/157	66/988	1.93	1.13 – 3.29
Lipid Metabolism Disorders	7/170	32/1022	1.33	0.57 – 3.12
Myocardial Infarction	2/175	10/1044	1.18	0.26 – 5.39
< 55 years				
Atrial Fibrillation	0/52	2/308	–	–
Chronic Ischemic Disease	0/52	1/309	–	–
Diabetes	3/49	2/308	15.00	1.52 – 147.62
Hypertension	7/45	7/303	5.92	2.08 – 16.89
Lipid Metabolism Disorders	1/51	5/305	1.20	0.14 – 10.27
Myocardial Infarction	1/51	3/307	2.00	0.21 – 19.23
≥ 55 years				
Atrial Fibrillation	5/277	27/1654	1.11	0.42 – 2.92
Chronic Ischemic Disease	10/272	63/1618	0.94	0.47 – 1.86
Diabetes	19/263	61/1620	1.96	1.14 – 3.35
Hypertension	43/239	167/1514	1.64	1.14 – 2.36
Lipid Metabolism Disorders	18/264	78/1603	1.41	0.82 – 2.42
Myocardial Infarction	6/276	44/1637	0.80	0.34 – 1.90

Author contributions

Conceptualization: AC, TF, MVin, RM and TF; Data curation: AC, TF, GC, GDG, MVit and RM; Formal analysis: TF and RM; Funding acquisition: TF; Investigation: TF, MV and RM; Methodology: AC, TF, GB, GC, KJR, MVin and MVit; Resources: AC, GC, GDG and MT; Project administration: TF and MVin; Supervision: TF, GB, KJR and MVin; Writing – original draft: KJR, TF, MVin and RM; Writing – review & editing: All authors.

Data statement

The data that has been used are confidential and are not publicly available due to restrictions in their containing information that could compromise the privacy of research participants.

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Declaration of competing interest

Authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2026.104760.

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