

Daily living activities as predictors of heart disease in elderly people: A population based case control study

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Abstract

Background:

Heart disease is a leading cause of morbidity and mortality among the older adults, often exacerbated by comorbid conditions and functional impairments. Understanding the relationship between activities of daily living (ADL) and heart disease can inform strategies for improving health outcomes in this vulnerable population. This study explores these associations among elderly individuals receiving routine geriatric care in Mashhad, Iran.

Methods:

This population-based case-control study included 7572 elderly participants, with 3786 diagnosed with heart disease (case group) and 3786 without (control group). Data were extracted from the Sina Health Information System (SINAEHR) for the period between March 1, 2017, and May 11, 2025. The Katz Index assessed ADL, focusing on six core skills. Statistical analysis involved chi-square tests for bivariate relationships and logistic regression to identify independent predictors of heart disease.

Results:

Participants in the case group had a mean age of 75.88 ± 6.98 years, with significant differences in BMI, educational attainment, and comorbidities compared to the control group. ADL impairment was significantly associated with heart disease. Compared with participants with functional independence, those with moderate impairment had higher odds of heart disease (aOR 1.49, 95% CI 1.18 – 1.88; $p < 0.001$), while severe impairment was associated with substantially higher odds (aOR 2.78, 95% CI 2.22 – 3.49; $p < 0.001$). Participants aged ≥ 80 years had higher odds of heart disease (aOR 1.43, 95% CI 1.24 – 1.65; $p < 0.001$), as did those with BMI ≥ 30 kg/m² (aOR 1.35, 95% CI 1.03 – 1.39; $p < 0.001$). Hypertension (aOR 2.64, 95% CI 2.34 – 2.99; $p < 0.001$) and cancer (aOR 2.08, 95% CI 1.58 – 2.71; $p < 0.001$) were also strongly associated with heart disease.

Conclusion:

This study evaluates ADL as a predictor of heart disease, whereas most previous studies examined ADL decline as a consequence of cardiovascular disease.

1. Introduction

Aging refers to biological changes or, more accurately, the phenomenon of aging is a biological process that results in physiological, social, and psychological transformations(1). The challenges associated with this distinct social phenomenon are continually acquiring new and broader dimension(2). Chronic

diseases and disorders such as musculoskeletal conditions, urinary and fecal incontinence, speech impairments, stroke, balance difficulties, Alzheimer's, Parkinson's, and cognitive and memory disorders are among the challenges faced by the elderly population (3–5). One of the most important diseases in old age is heart disease.

Aging is strongly associated with increased cardiovascular risk due to vascular stiffening, impaired endothelial function, and chronic inflammation. These physiological changes accelerate the development of heart disease in older adults. Likewise, higher body mass index contributes to hypertension, insulin resistance, and dyslipidemia, all of which significantly increase the likelihood of cardiovascular events.

Cardiovascular diseases are the leading cause of death in the United States and Iran and account for a significant proportion of mortality worldwide(6). Cardiovascular diseases (CVD) are the leading cause of death worldwide. An estimated 17.9 million people died from CVD in 2019, accounting for 32% of all global deaths. Of these fatalities, 85% were due to heart attacks and strokes (7, 8). Over three quarters of CVD related deaths occur in low and middle income countries. Among the 17 million premature deaths (under 70 years) caused by non-communicable diseases in 2019, 38% were attributable to CVD. Most cardiovascular diseases can be prevented by addressing behavioral and environmental risk factors such as tobacco use, unhealthy diet and obesity, physical inactivity, harmful alcohol consumption, and air pollution (8–10). Individuals with heart disease suffer from various complications such as physical activity limitations including difficulties in performing ADL(11, 12).

ADL can be defined as tasks individuals must perform daily to live independently, integrate into their usual environment, and fulfill their social roles. Dr. Sidney Katz first formulated an index of essential activities required for older adults to maintain independent living in 1963. This scale remains widely used by healthcare professionals to assess functional performance and evaluate long-term care needs in the elderly(13). Various studies have shown that the likelihood of death increases with decreasing disability and increasing ADL(14). Various studies have examined the relationship between heart disease and ADL, revealing a strong association between the severity of heart disease and reduced ADL performance(15, 16). Severe heart disease is linked to lower activity levels, though this may also be related to other factors such as diabetes, vascular insufficiency, or cerebral insufficiency (17). Epidemiological studies have demonstrated that in elderly populations, a decline in ADL performance can serve as an independent predictor of cardiovascular disease-related mortality. Individuals who lose the ability to perform basic tasks due to reduced physical activity and subsequent declines in cardiac capacity are at increased risk of cardiac complications, elevated blood pressure, and metabolic disorders(18). In an aging society, independent functional and cognitive abilities are regarded as key components of healthy life expectancy among older adults. Functional limitations are associated with aging, chronic diseases, all cause mortality, and poor prognosis in individuals with various health conditions. It has been reported that functional limitations correlate with an elevated risk of heart failure and cardiovascular diseases (19, 20).

Several studies have examined predictors of heart disease specifically among older adults, identifying age, multimorbidity, metabolic disorders, and reduced functional capacity as major determinants(21, 22). Previous studies have often evaluated ADL as an outcome of chronic diseases. However, it is still unclear whether difficulties in daily activities can predict the risk of developing heart disease. Understanding this relationship is important because early identification of functional decline may help prevent heart problems. This study was one of the first population-based case control study in Iran examining ADL in relation to heart disease among the elderly that the aim of it was investigated the association between ADL and the risk of cardiovascular diseases in the elderly individuals.

2. Methods

2.1 Participants and study design

Elderly people receiving routine geriatric care in health centers affiliated with Mashhad University of Medical Sciences were included in this population based case control study. Data were obtained from the Sina Health Information System (SINAEHR). The study covered the period from March 1, 2017 to May 11, 2025(23). The case group in this study was elderly people with age of ≥ 60 , suffering from heart disease (ICD-10 codes I20–I25). Elderly people not suffering from heart disease were considered as the control group. Controls were randomly selected and matched to cases based on age, sex, and place of residence. All variables, including ADL scores, comorbidities, demographics, and diagnoses, were extracted directly from the SINAEHR electronic health system. Data were obtained from 256 primary healthcare centers within Mashhad. Individuals who did not seek care during the study period were not included in the registry. Records with missing ADL or incomplete demographic fields were excluded. A sensitivity check was performed to assess potential bias from missing data

Inclusion criteria: age 60 years or older, registered in the SINAEHR system during the study period

Exclusion criteria: missing ADL information, missing demographic or health data, diagnoses unrelated to the study variables

2.2 Study variables:

1. Outcome variable: In this study, we looked for the relationship between daily living activities and heart disease and heart diseases in this study refer to codes (I20-I25).

2. Exposure variable: Age, BMI, Level of education, occupation, place of residence, ADL, Cancer (C91-C95, C18, C16, C33-C34), Thyroid disorders (E00-E07), Hyperlipidemia (E78), Diabetes (E10- E11), Hypertension (I10-I15), Depressive episode (F32), anxiety disorders(F40), Gender, Nationality

2.3 Measurement tool:

We used the Katz Index to measure ADL. Katz and his colleagues developed this tool in 1959. It was designed to assess basic ADL in older adults across community and healthcare settings(24). The

original Katz Index included 8 basic ADL skills, which were later refined to 6 core skills: bathing, dressing, transferring, toileting, feeding, and continence. Scoring for this tool assigns 1 point if an older adult can perform an activity independently and 0 points if they cannot. Total scores range from 6 (maximum independence) to 0 (complete dependence). A score of 6 indicates full functional independence, 4 suggests moderate impairment, and 2 or below reflects severe functional impairment(25). The Katz Index has been translated into American, Brazilian, and Turkish versions (26-28). The Persian version of the Katz Index was validated by Azad and colleagues(29). ADL assessments were recorded at the time of first registration in the health system, before the diagnosis of heart disease was documented.

Comorbidities were recorded based on clinician diagnosis in the electronic health record. Smoking and family history were not included due to incomplete availability in the system. A small city was defined as urban areas with fewer than 50,000 residents. Depressive episode and thyroid disorders were coded based on physician-diagnosed ICD-10 entries.

2.4 Sampling technique and procedure:

The number of participants in the study was 7572 elderly people, of whom 3786 were in the case group and 3786 were in the control group. The subjects in the control group were randomly selected from among the elderly who visited health centers. Because this was a population-based study a census approach was used. All eligible elderly individuals with heart disease (cases) in SINAHR were included. A 1:1 random selection of eligible individuals without heart disease was used to form the control group. (figure1)

2.5 Statistical analysis:

After data collection, the information was coded and subsequently imported into Excel. It was then transferred to Stata version 16 for analysis. Frequency, percentage, and mean were calculated to describe categorical characteristics and quantitative variables in both case and control groups. Bivariate analysis was conducted using chi-square tests to assess unadjusted relationships between each factor and heart disease. All comorbidities and demographic variables were included in the multivariable logistic regression model to control for confounding. Statistically significant variables were entered into a univariate regression model and, if they remained significant, into a multivariate regression model. The final model estimated the adjusted odds ratio (OR) and 95% confidence interval (CI), reflecting independent relationships between the variables included in the model and heart disease.

3. Results

The average age in the case group was 75.88 ± 6.98 , while the average age in the control group was 74.55 ± 7.31 . Most of the people present in the study were in the age group of 70 to 79 years, which was statistically significant. In BMI variable, most of the participants were placed in normal and overweight groups, and this difference was statistically significant So that 2257 of the participants in the case group were overweight. Most of the people in the study had functional independence in terms of activities of daily living, but in the other two categories of this variable, people with impairment were more likely to be

in the case group. The people in the study were more likely to be illiterate in terms of educational attainment, and most of these people were without income and lived in metropolitan city (< 0.001). 72% of people with cancer were in the case group, and the distribution of this variable was statistically significant. Also, the distribution of diseases such as hypertension, hyperlipidemia, thyroid disorders, diabetes, and a history of depression were statistically significant, and the frequency of these diseases was higher in the case group. (Table 1)

Based on univariate logistic regression analysis, daily living activities have a significant association with heart disease, and the association becomes stronger with increasing levels of impairment (OR = 1.46, 2.5). Also, by controlling for other factors in multivariate analysis, this relationship became stronger (OR = 1.49, 2.7). In the analysis of age and BMI as two variables, the likelihood of developing heart disease rises with higher values. The univariate analysis identified age over 80 years (OR = 1.63) and BMI exceeding 30 (OR = 1.42) as the key predictors. This relationship was statistically significant. The study findings showed that the chance of heart disease increases with increasing education level, and education beyond a bachelor's degree increases the chance of developing the disease. Also, by controlling for other factors in multivariate regression analysis, the relationship became stronger, so that having a diploma was not significant in univariate analysis, but was significant in multivariate analysis (OR = 3.07). Living in a metropolitan area, Urban Fringe, and Village increases the chance of developing heart disease, so that in univariate and multivariate analysis, living in Village and Urban Fringe has the highest chance, and this strong relationship is also statistically significant (< 0.001). The variables gender and marriage, despite a significant relationship in univariate analysis, were not significant in multivariate analysis, indicating that gender and marriage are not significantly related to heart disease in the present study. The study findings show that blood lipids, cancer, thyroid disorders, diabetes, blood pressure and a history of depression are significantly correlated, with cancer and blood pressure having a stronger correlation than other diseases (OR = 2.64, OR = 2.08). (Table 2)

Table No. 1

Comparison of frequency distribution of variables in case and control groups

Variable	Categories	control n = 3786 Freq(%)	Case n = 3786 Freq(%)	p-value
Age	60–69years	1142 (58)	820 (42)	< 0.001
	70–79years	1574 (48)	1714(52)	
	> 80	1070 (46)	1252 (54)	
BMI	< 18.5	180 (56)	142 (44)	< 0.001
	18.5–24.9	1623 (54)	1387 (46)	
	25-29.9	1294 (47)	1479 (53)	
	> 30	689 (47)	778 (53)	
ADL	functional independence	3497(52)	3255(48)	< 0.001
	moderate impairment	156(42)	213(58)	
	severe impairment	133(30)	318(70)	
Level of education	Illiterate	2095(49)	2125(51)	< 0.001
	Sub-diploma	1577(53)	1404(47)	
	Diploma	65(43)	86(57)	
	College Degree	49 (22)	171(78)	
Occupation	Unemployed (With no income)	1953(46)	2282(54)	< 0.001
	Employee	510(47)	560 (53)	
	Pensioner	1323 (58)	944(42)	
Place of residence	Small city	449(74)	159 (26)	< 0.001
	Sub-million city	594(77)	170(23)	
	Metropolitan City	1401(52)	1289(48)	
	Urban Fringe	983(38)	1575(62)	
	Village	359(38)	593(62)	
Nationality	iranian	3671 (49)	3717 (51)	< 0.001
	Foreign	115(62)	69(38)	
Gender	male	1575 (53)	1385 (47)	< 0.001
	female	2211 (48)	2401 (52)	

Variable	Categories	control n = 3786 <i>Freq(%)</i>	Case n = 3786 <i>Freq(%)</i>	p-value
Marriage	Married	2618(52)	2387(48)	< 0.001
	Single	1168(45)	1399(55)	
Cancer	Yes	88(28)	218(72)	< 0.001
	No	3698(51)	3568(49)	
Thyroid disorders	Yes	103(35)	187(65)	< 0.001
	No	3683(51)	3599(49)	
Hyperlipidemia	Yes	1559(43)	2036(56)	< 0.001
	No	2227(56)	1750(44)	
Diabetes	Yes	1165(41)	1619(59)	< 0.001
	No	2621(54)	2167(46)	
Hypertension	Yes	2457(43)	3212(57)	< 0.001
	No	1329 (70)	574(30)	
Depressive episode	Yes	497(43)	684(57)	< 0.001
	No	3289 (52)	3102(48)	

Table No. 2

Association of Activities of Daily Living with heart disease

Variables	Categories	Univariate regression analysis			Multivariate logistic regression		
		Odds Ratio	p-value	Confidence Interval	Odds Ratio	p-value	Confidence Interval
ADL	functional independence	1.46	< 0.001	1.18–1.81	1.49	< 0.001	1.18–1.88
	moderate impairment	2.5	< 0.001	2.06–3.16	2.78	< 0.001	2.22–3.49
	severe impairment						
Age	60–69years	1.51	< 0.001	1.35–1.69	1.37	< 0.001	1.2–1.55
	70–79years	1.63	< 0.001	1.44–1.84	1.43	< 0.001	1.24–1.65
	> 80						
BMI	18.5–24.9	0.91	0.4	0.72–1.16	0.94	0.6	0.73–1.22
	< 18.5	1.33	< 0.001	1.2–1.48	1.22	< 0.001	1.08–1.36
	25–29.9	1.42	< 0.001	1.16–1.49	1.35	< 0.001	1.03–1.39
	> 30						
Level of education	Illiterate	0.87	< 0.001	0.79–0.94	1.27	< 0.001	1.13–1.42
	Sub-diploma	1.37	0.1	0.94–1.8	3.07	< 0.001	2.08–4.33
	Diploma	3.44	< 0.001	2.49–4.75	5.04	< 0.001	3.55–7.17
	Degree						
Occupation	Pensioner	1.53	< 0.001	1.33–1.78	1.31	< 0.001	1.15–1.5
	Employee	1.63	< 0.001	1.47–1.81	1.29	< 0.001	1.08–1.53
	Unemployed						
Place of residence	Small city	0.8	0.09	0.63–1.03	0.77	0.57	0.59–1.007
	Sub-million city	2.5	< 0.001	2.13–3.16	2.36	< 0.001	1.91–2.91
		4.5	< 0.001	3.71–5.51	4.34	< 0.001	3.5–5.36
	Metropolitan City	4.6	< 0.001	3.73–5.83	4.4	< 0.001	3.48–5.559
	Urban Fringe		< 0.001			< 0.001	
	Village						

Variables	Categories	Univariate regression analysis			Multivariate logistic regression		
		Odds Ratio	p-value	Confidence Interval	Odds Ratio	p-value	Confidence Interval
Nationality	Foreign iranian	1.68	< 0.001	1.24–2.28	1.58	< 0.001	1.18–2.13
Gender	male female	1.23	< 0.001	1.12–1.35	1.02	0.2	0.94–1.22
Marriage	Married Single	1.31	< 0.001	1.19–1.44	1.12	0.057	0.99–1.21
Cancer	No Yes	2.56	< 0.001	1.99–3.30	2.08	< 0.001	1.58–2.71
Thyroid disorders	No Yes	1.85	< 0.001	1.45–2.37	1.52	< 0.001	1.22–2.01
Hyperlipidemia	No Yes	1.66	< 0.001	1.51–1.82	1.33	< 0.001	1.20–1.45
Diabetes	No Yes	1.68	< 0.001	1.52–1.84	1.28	< 0.001	1.15–1.48
Hypertension	No Yes	3.02	< 0.001	2.7–3.28	2.64	< 0.001	2.34–2.99
Depressive episode	No Yes	1.45	< 0.001	1.28–1.65	1.26	< 0.001	1.15–1.45

4. Discussion

The main aim of the present study is to find the relationship between daily living activities and heart disease with the control of other factors in Iranian elderly people. Important findings in this regard include: 1. there is a significant relationship between ADL and heart disease. 2. The relationship becomes stronger as this disorder increases and individuals' ability to perform ADL decreases. 3. This relationship becomes stronger when controlling for other influential factors, and decreased ability to perform ADL increases the chance of heart disease. There is growing evidence that functional limitations in ADL are associated with an increased risk of heart disease and mortality(30). A recent study from the American Heart Association found that people who performed their daily activities (such as housework, walking while shopping, or cleaning) at a moderate to vigorous intensity reduced their risk

of cardiovascular disease by 51–67% and their risk of overall death by 69%(31). In a cohort study, Tsuji et al. demonstrated that Japanese adults aged 65 and older with functional limitations in ADL had a significantly higher risk of stroke and stroke related mortality. Moreover, reduced ambulatory capacity was independently associated with an increased risk of death from heart disease(32). Similarly, a study conducted in the United States found that functional limitations were strong and independent predictors of mortality among individuals over the age of 80(33). Furthermore, a longitudinal study conducted over 15 years involving an older Dutch demographic found that functional limitations were recognized as significant. (34). According to the results of the present study and other studies in this field, ADL in the elderly can be considered as an independent factor for developing heart disease (35, 36).

The link between depression and heart disease has been confirmed in various studies. Depression can contribute to heart disease by increasing the likelihood of smoking, alcohol consumption, unhealthy eating (particularly high-fat diets), sedentary behavior, and engagement in other risky lifestyle habits. Moreover, depression is strongly associated with reduced quality of life, which in turn can lead to an increased risk of developing heart disease or experiencing disease recurrence. This relationship was also observed in the present study (37–39). Our study findings showed that heart disease is significantly associated with blood lipids, such that people with blood lipids had a 1.33 times higher chance of heart disease. After adjusting for potential confounders, diabetes remained a significant independent predictor of cardiovascular disease in our study. Individuals with type 2 diabetes face roughly a twofold higher risk of cardiovascular events including myocardial infarction than those without diabetes. Moreover, diabetic patients without prior coronary heart disease have a risk of myocardial infarction that is comparable to or even exceeds that of non-diabetic individuals with a history of myocardial infarction. Consequently, diabetes is widely regarded as a coronary heart disease risk equivalent (40–42). Our study found that hypertension was very strongly associated with cardiovascular disease: individuals with elevated blood pressure had a 2.64-fold higher likelihood of developing heart disease compared to those with normal blood pressure. The relationship between education level and risk of heart disease has been extensively studied in the recent literature. Multiple systematic reviews and meta-analyses have consistently shown that individuals with lower levels of education face a significantly higher risk of developing heart disease compared with individuals with higher levels of education. This association is believed to be mediated by a variety of factors, including socioeconomic status, lifestyle behaviors (such as diet, physical activity, and smoking), differential access to preventive and clinical health care, and variations in health literacy and awareness. These findings suggest that education level is a strong social determinant of cardiovascular health (43, 44). The results of our study show that heart disease increases with increasing education level, which is inconsistent with the results of other studies(45), but the reason for this paradox can be traced to stress caused by social and economic situations(46, 47). Age is consistently recognized as one of the strongest non-modifiable risk factors for cardiovascular disease. Epidemiological studies have shown that with each passing decade, the risk of developing heart disease increases approximately threefold, even after adjusting for other major risk factors such as hypertension, diabetes, and hyperlipidemia(48, 49). In our study, age remained a significant independent predictor of heart disease, even after adjusting for potential confounders such as diabetes, hypertension, and

dyslipidemia. It was associated with an increased risk of heart disease events. Body mass index (BMI) is recognized as an important risk factor for cardiovascular disease (CVD). Several studies have shown that increasing BMI is associated with an increased risk of heart disease. A 5-unit increase in body mass index (BMI) has been associated with a 41% higher risk of developing heart failure and a 16% increased risk of sudden cardiac death(50, 51). Longitudinal data over a 14-year follow-up period also indicate that each 1-unit increase in BMI corresponds to a 5–7% increase in the risk of heart failure in both men and women. Furthermore, individuals classified as obese (BMI ≥ 30) were found to have more than double the risk of developing heart failure compared to those with normal BMI(52). The results of the study indicated that the risk of developing heart disease increases with rising body mass index (BMI). Specifically, individuals with a BMI greater than 30 had a 35% higher likelihood of developing cardiovascular disease compared to those with a normal BMI. Place of residence can significantly influence an individual's risk of developing or managing heart disease. In certain regions, limited access to healthcare services, healthy food options, and safe environments for physical activity can hinder both prevention and treatment efforts. Additionally, environmental factors such as air pollution, chronic stress, and limited access to green spaces have been shown to negatively impact heart health. In the current study, living in a metropolitan area, Urban Fringe, and Village areas increases the chances of developing heart disease. Research has shown that people living in lower income neighborhoods, even with similar levels of education and personal income, have a higher risk of developing heart disease (53, 54). While most studies report that higher education is associated with lower cardiovascular risk, several investigations in older adults have found inconsistent or even reversed associations, possibly due to occupational stresses, lifestyle transitions after retirement, or selective survival patterns.(55)Similarly, findings on marital status vary across cultures, suggesting that social support and household structure influence heart disease differently in elderly populations(56). A systematic review conducted in 2024 found that individuals with low socioeconomic status including low income were 71% more likely to develop heart disease compared to those with high socioeconomic status(57). Additionally, another study reported that the risk of death from heart disease was 33% higher among low income groups and 18% higher in middle income groups, relative to high income individuals(57). Consistent with these findings, the results of the current study indicated that individuals with no income were at significantly greater risk of developing heart disease. Overall, low income appears to be a fundamental social determinant, contributing to the increased prevalence and mortality of cardiovascular disease through mechanisms such as limited access to healthcare resources, higher exposure to behavioral risk factors, chronic psychosocial stress, and occupational strain (58–60). Gender and marriage were not significant factors in the current study with heart disease. However, in univariate analysis, female gender and single individuals had a higher risk of developing heart disease than male gender and married individuals. Married individuals are generally more likely to engage in healthier behaviors such as reduced smoking, improved dietary habits, and more consistent use of healthcare services which collectively contribute to a lower risk of cardiovascular disease. Marriage has also been associated with lower stress levels, better medication adherence, and healthier lifestyle patterns, particularly among men(61, 62).

5. Limitations

This study has several limitations that should be considered when interpreting the findings. First, the case control design may limit the ability to establish causal relationships between ADL, comorbidities and heart disease. Longitudinal studies would provide more robust evidence of causation. Second, self-reported Data: The reliance on self-reported data for assessing activities of daily living and comorbid conditions may introduce reporting bias, as participants might underreport or over report their functional abilities and health status. Third, Potential Confounding Variables: While the study controlled for many factors, there may be unmeasured confounders (e.g., socioeconomic status, lifestyle factors) that could influence the relationship between heart disease and the variables studied. Forth, Focus on Specific ADLs: The Katz Index focuses on only six core activities, which may not encompass the full spectrum of ADL and their impact on heart disease. Additionally

“There is a possibility of reverse causality, as early undetected cardiovascular disease may influence functional capacity and ADL performance. Additionally, cultural differences in reporting dependence in daily activities, as well as variations in access to care across Iranian subpopulations, may affect the accuracy of ADL and risk factor data. These limitations suggest areas for future research and the need for caution in interpreting the findings.

6. Conclusions

Finally, the results of this study demonstrated that, even after controlling for potential confounding factors, limitations in ADL among the elderly were significantly associated with heart disease. It is recommended that ADL be considered as a potential predictive factor in future research. Moreover, assessing ADL may serve as an important criterion for informing healthcare and treatment decisions in older populations.

Declarations

Acknowledgements

Not Applicable.

Authors' contributions

AM is the principal investigator and research leader. MN and EM designed the Study and drafted the manuscript and analyzed the data. SA contributed to the conception, design, data interpretation, and revising the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki (2013 version) as adopted by the World Medical Association. Ethical approval was obtained from Mashhad University of Medical Sciences (Approval Code: IR.MUMS.FHMPM.REC.1403.218). Informed consent to participate was obtained from all participants prior to their inclusion in the study.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number: not applicable

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Figures

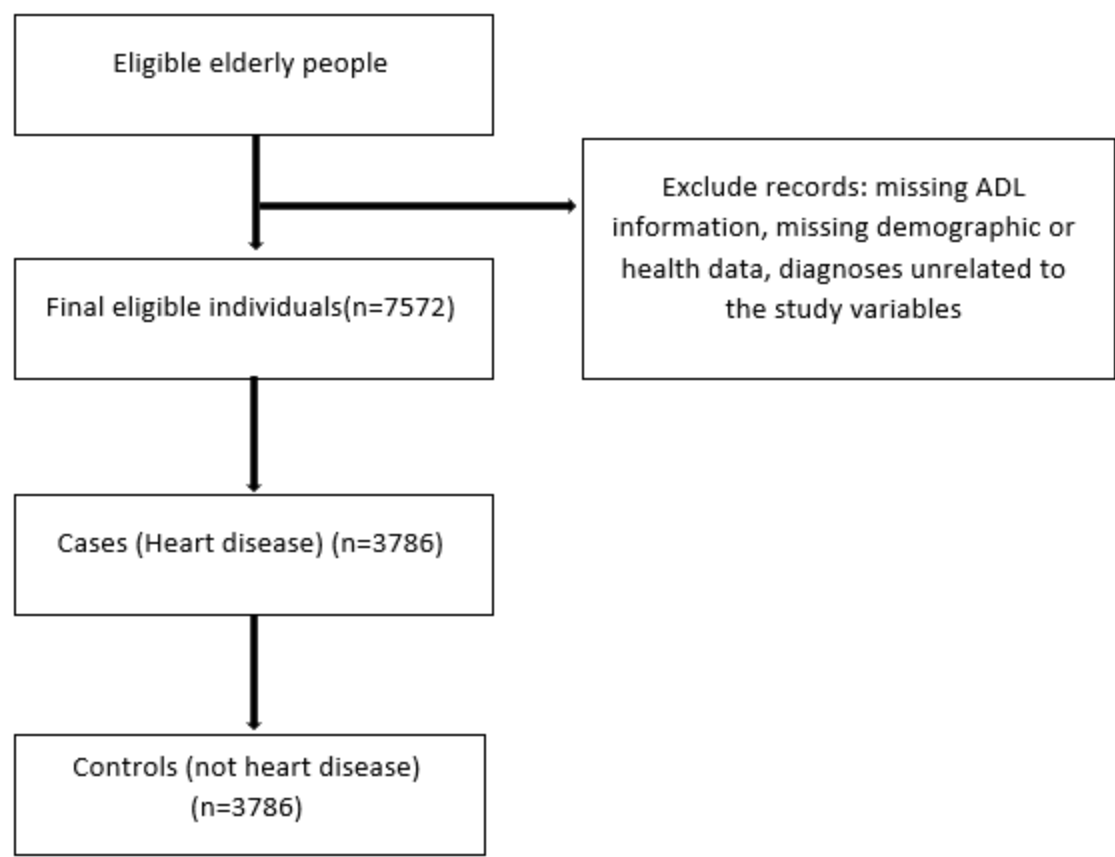


Figure 1

Flow diagram of Study