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RESEARCH ARTICLE

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Frailty and prescriptions of secondary prevention medications in older people with diabetes and coronary heart disease—An observational study in Vietnam

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Abstract

Objectives: This study sought to quantify the prevalence of frailty among type 2 diabetes (T2D) patients with coronary heart disease (CHD) and examine the relationship between frailty and the prescription of secondary prevention medications.

Methods: A prospective observational study was conducted at a tertiary hospital in Vietnam from November 2022 to June 2023. Patients aged 60 years or above with T2D and CHD were included for analysis. Multivariable logistic regression was applied to examine the association between frailty and the prescription of secondary prevention medications: antiplatelets, statins, beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (ACEIs/ARBs). Frailty was measured using the Clinical Frailty Scale (CFS) version 2.0.

Results: There were 274 participants included in this analysis. Participants had a median age of 72.0 years, 28% were female and 59% were frail. The prescription rates of cardiovascular medicines for frail versus non-frail participants were as follows: antiplatelets (66% vs. 94%, $p < .001$), statins (96% vs. 92%, $p = .21$), beta-blockers (81% vs. 88%, $p = .13$), ACEIs/ARBs (75% vs. 81%, $p = .22$) and for all four types (42% vs. 64%, $p < .001$). In the multiple adjusted regression models, increased CFS score was associated with reduced prescriptions of beta-blockers, ACEIs/ARBs and all four types of medications.

Conclusions: Frailty was common among older Vietnamese patients with CHD and diabetes, and significantly affected the prescription of secondary prevention medicines. Future research should explore the link between frailty and secondary prevention medicines in a larger, more diverse population.

KEYWORDS

cardiovascular disease, frailty, prescriptions, secondary prevention, Vietnam

1 | INTRODUCTION

Coronary heart disease (CHD) is one of the main causes of death and disability in high-income countries, especially in older people.[1] In lower-income countries, there is an increasing prevalence of CHD with the increasing life span and prevalence of lifestyle risk factors in the region.[2] One of the challenges with CHD is the influence of modifiable and non-modifiable risk factors that can contribute to it. Non-modifiable risk factors include age, sex and family history. Modifiable risk factors, including high blood pressure, dyslipidaemia, diabetes and smoking, can be managed through non-pharmacological strategies like lifestyle changes or through pharmacological agents, with proven benefits.[3] Individuals with diabetes are also more likely to experience CHD than those without diabetes.[1,4] In patients with a diagnosis of CHD, secondary prevention is a key strategy to reduce the risk of cardiac events and mortality.[1] Antiplatelets, statins, beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs) are recommended as secondary prevention medications for patients with CHD.[3]

The increasing prevalence of frailty among older adults has been shown to complicate outcomes and present additional challenges.[5] Frailty-related variations in pharmacokinetics and pharmacodynamics can impact the effectiveness and safety of cardiovascular medications, potentially influencing prescribers' decisions.[6,7] To help close knowledge gaps in cardiovascular care for older adults, recommendations have been proposed for research in specific areas, such as the appropriate use of medications in older patients.[8] Furthermore, recent calls have also been made to consider frailty status when providing care for older people.[7,9]

Like its neighbouring countries in Southeast Asia, Vietnam is experiencing a growing population of older people together with a growing economy. Additionally, recent studies have also highlighted the growing prevalence of diabetes.[10] In Vietnam, there have been several studies on frailty in older people in clinical settings and in the community. The prevalence of frailty is quite high in older patients in Vietnam, particularly in those with cardiovascular disease.[11–17] The prevalence of frailty in Vietnam ranges from 11% to 22% in the community, while in hospitals estimates range from 19% to 55%.[11–19] However, there is limited evidence about frailty in older Vietnamese people with diabetes, and there have been no studies examining the association between frailty and the prescriptions of cardiovascular medicines in this population. The aim of this study was to quantify the prevalence of frailty and to examine the association between frailty and the prescription of secondary prevention medications for cardiovascular disease among patients with both diabetes and CHD in Vietnam.

Practice impact

This study showed that frailty significantly affected the prescription of secondary prevention medicines, especially beta-blockers and ACEIs/ARBs. Future longitudinal studies would be useful in exploring how frailty can be optimised to improve cardiovascular care for older persons.

2 | METHODS

This study was a secondary analysis based on a primary study investigating medication adherence in older patients with chronic CHD in Vietnam. In brief, this prospective observational study was conducted at the cardiovascular outpatient clinics of Thong Nhat Hospital, a tertiary hospital in Ho Chi Minh City from November 2022 to June 2023. A total of 643 consecutive patients aged 60 years or above with chronic CHD who visited the clinics during the study period were recruited. From the study dataset, participants with type 2 diabetes were included in this analysis.

Based on previously published studies in Vietnam,[15] we assumed that the prescription rates of each type of secondary prevention medication (antiplatelets, statins, beta-blockers and ACEIs/ARBs) in older patients with CHD would be around 60%–70% and there would be about a 20% difference between the frail and non-frail. Therefore, we estimated that a sample size of at least 186 participants (93 frail and 93 non-frail) would enable the detection of a significant difference in the prescription rates between frail and non-frail (at 80% power, 5% significance level).

2.1 | Variable definitions

Frailty was defined according to the Clinical Frailty Scale (CFS) version 2.0. The CFS score ranges from 1 to 9, with a score of 4 or above indicating the presence of frailty.[20]

Information on secondary prevention medications for cardiovascular disease was obtained from the hospital discharge summary and categorised into: antiplatelets (aspirin, clopidogrel, ticagrelor and prasugrel), statins (atorvastatin, rosuvastatin and simvastatin), beta-blockers (bisoprolol, metoprolol and nebivolol) and ACEIs/ARBs (captopril, imidapril, lisinopril, perindopril, candesartan, losartan, irbesartan, telmisartan and valsartan).

Polypharmacy was defined as the presence, on prescriptions at hospital discharge, of five or more medications.

Age and sex were as recorded in medical records. Body mass index (BMI, kg/m^2) was calculated from measured weight (kg) and height (m) and was classified into four groups: underweight (BMI < 18.5 kg/m^2), normal (BMI 18.5–22.9 kg/m^2), overweight (BMI 23–24.9 kg/m^2) and obese (BMI ≥ 25.0 kg/m^2). Smoking status was categorised based on self-report as non-smoking or smoking. Low educational status was defined as having completed only primary school or being illiterate.

Information on the history of cardiovascular conditions other than CHD (hypertension, dyslipidaemia, heart failure, atrial fibrillation, ischemic stroke, peripheral artery disease, chronic kidney disease, percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery [CABG]) was obtained from medical records.

2.2 | Statistical analysis

Continuous variables are presented as mean (standard deviation), and categorical variables as frequency and percentage. Comparisons between frail and non-frail participants were assessed using the χ^2 test or Fisher's exact test for categorical variables and Student's *t*-test or Mann–Whitney test for continuous variables. Two-tailed *p*-values <.05 were considered statistically significant.

To examine the relationship between frailty and the prescription of secondary prevention medications, odds ratios (ORs) were estimated from logistic regression models, unadjusted and adjusted for pre-specified covariates chosen based on clinical judgement, including age, sex, socioeconomic conditions (education level, living alone and having public health insurance) and total number of medications used. Frailty was treated as a continuous variable (CFS score) in the models. Models involved antiplatelets, and all four types of secondary prevention medications were also adjusted for anticoagulant use, as patients who are on oral anticoagulants usually do not receive antiplatelets. Five separate models were fitted for (1) antiplatelets, (2) statins, (3) beta-blockers, (4) angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (ACEIs/ARBs) and (5) all four types of these prevention medications. Data analysis was performed using SPSS 27.0 and R 4.4.1.

2.3 | Ethics approval

The study was approved by the Ethics Committees of the University of Medicine and Pharmacy at Ho Chi Minh City (reference number: 936/HDDD-DHYD; date: 24 November 2022). Informed consent was obtained from all participants. This study was compiled in accordance with the Declaration of Helsinki.

3 | RESULTS

A total of 274 participants with diabetes and CHD were included in this analysis. They had a median age of 72.0 years, and 28% were female. Most participants were retired (95%), had public health insurance (97%), and 11% were living alone. More than half of the participants had above normal BMI—overweight (29%) or obese (31%), 97% had a history of hypertension, 95% had dyslipidaemia, and 67% received revascularisation therapy previously (64% PCI and 3% CABG). The prevalence of polypharmacy was very high (97%).

The prevalence of frailty was 59% (161/274). The distribution of the CFS score is presented in Figure 1. Frail participants were older compared to non-frail participants (median age 75.0 vs. 68.0 years, $p < .001$) (Table 1). There was a higher percentage of low educational status (21% vs. 10%), sedentary lifestyle (85% vs. 53%) and history of PCI (79% vs. 54%) in frail participants compared to the non-frail group. The prevalence of atrial fibrillation was significantly higher in frail participants (37%) compared to the non-frail (8%), $p < .001$. The percentages of participants using oral anticoagulants for stroke prevention associated with atrial fibrillation were significantly higher in the frail group (34%) compared to the non-frail group (5%), $p < .001$.

3.1 | Prescription rates of secondary prevention medications for cardiovascular disease

Overall, 51% of the participants were prescribed all four types of secondary prevention medication, and the prescription rate was significantly lower in the frail group (42%) compared to the non-frail group (64%), $p < .001$ (Table 2). Among the four types of secondary prevention medication, there was no significant difference in the prescription rate of statins (96% in the frail group vs. 92.0% in the non-frail group, $p = .21$), beta-blockers (81% in the frail group vs. 88% in the non-frail group, $p = .13$) or ACEIs/ARBs (75% in the frail group vs. 81% in the non-frail group, $p = .22$), but the prescription of antiplatelets was lower in frail participants (66% in the frail group vs. 94% in the non-frail group, $p < .001$).

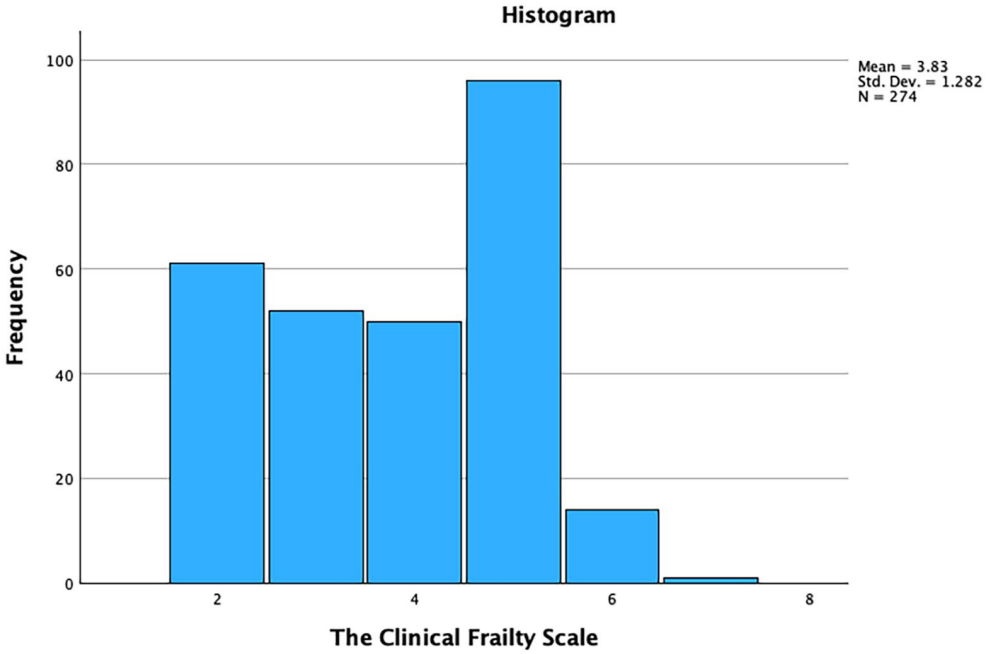

FIGURE 1 Distribution of the Clinical Frailty Scale (CFS).

3.2 | The association between the CFS score and the prescription of secondary prevention medications for cardiovascular disease

The relationship between CFS score and the prescription of secondary prevention medications is presented in Table 3. In the unadjusted models, for every 1 point increase in the CFS, we saw an OR of .54 (95% CI: .42–.71) for antiplatelets, .75 (95% CI: .58–.98) for beta-blockers, .90 (95% CI: .72–1.12) for ACEIs/ARBs, 1.14 (95% CI: .77–1.69) for statins and .74 (95% CI: .61–.90) for all 4 types of prevention medications. In the adjusted models, increased CFS score was still significantly associated with reduced prescriptions of beta-blockers, ACEIs/ARBs and all four types of medications (Table 3).

4 | DISCUSSION

In this study, more than half of older participants with diabetes and CHD had frailty (59%). Frailty reduced the likelihood of prescription of all four types of cardiovascular secondary prevention medications, and particularly of beta-blockers and ACEIs/ARBs.

The prevalence of frailty in our study is higher compared to other studies in the general population. This could be explained by differences in the study populations and the frailty definition used. The CFS has been shown to identify a higher prevalence of frailty compared to other frailty definitions.[21,22] Globally, Collard et al. reported that the overall prevalence of frailty in community-dwelling adults was 11%.[23] In a study involving 17 Asian countries (China, Hong Kong, Taiwan, India, Indonesia, Japan, Lebanon, Malaysia, Nepal, Singapore, South Korea, Sri Lanka, Thailand, Turkey, Vietnam, Saudi Arabia, Iran), the prevalence of frailty in the general population was reported to be 21%, with a range from 6% to 46%.[24] In European populations, a meta-analysis of 62 studies from 22 European countries showed that the prevalence of frailty was 18%, ranging from 12% in community-based studies to 45% in non-community-based studies.[25] A separate meta-analysis, including 31,343 adults in the United States, Switzerland, Sweden, Brazil, Taiwan, Italy, United Kingdom, Spain, France and Canada, found that frailty and pre-frailty were associated with an increased risk of any type of cardiovascular disease and higher risk of cardiovascular mortality.[26] These studies highlight the growing prevalence of frailty and its impact on cardiovascular outcomes globally. Frailty and cardiovascular disease share similar underlying pathophysiological conditions, and this may sometimes confound the association between them.[27] In another study of two prospective cohorts, the China Health and Retirement Longitudinal Study and the English Longitudinal Study of Ageing, frailty was associated with an increased risk of cardiovascular disease and all-cause mortality in patients with pre-diabetes and diabetes.[28]

Our finding of the relationship between frailty and prescription of secondary prevention medications aligns

TABLE 1 Participants characteristics by frailty status.

Characteristic	All participants ($n=274$)	Non-frail participants ($n=113$)	Frail participants ($n=161$)	p-Value (frail vs. non-frail)
Age (median and range)	72.0 (60–93)	68.0 (60–90)	75.0 (60–93)	<.001
CFS score	3.8 (1.3)	2.5 (.5)	4.8 (.6)	<.001
Sex				
Female	76 (28)	13 (12)	63 (39)	<.001
Male	198 (72)	100 (89)	98 (61)	
Working status				
Retired	261 (95)	105 (93)	156 (97)	.13
Working	13 (5)	8 (7)	5 (3)	
Carer				
None (living alone)	31 (11)	15 (13)	16 (10)	.007
Spouse	196 (72)	89 (79)	107 (67)	
Children	39 (14)	6 (5)	33 (21)	
Other	8 (3)	3 (3)	5 (3)	
Having public health insurance	267 (97)	112 (99)	155 (96)	.25
Education				
Illiterate	4 (2)	0 (.0)	4 (3)	.004
Primary school	39 (15)	11 (10)	28 (18)	
Secondary school	8 (3)	2 (2)	6 (4)	
High school	89 (34)	32 (29)	57 (37)	
Higher education	125 (47)	67 (60)	58 (38)	
Body mass index				
Underweight	6 (2)	2 (2)	4 (3)	.90
Normal	105 (38)	45 (40)	60 (37)	
Overweight	78 (29)	30 (27)	48 (30)	
Obese	85 (31.0%)	36 (32)	49 (30)	
Smoking				
Non-smoking	135 (49)	34 (30)	101 (63)	<.001
Current smoking	28 (10)	17 (15)	11 (7)	
Ex-smoking	111 (41)	62 (55)	49 (30)	
Alcohol consumption	17 (6)	6 (5)	11 (7)	.61
Sedentary lifestyle	197 (72)	60 (53)	137 (85)	<.001
Total number of medications	7.3 (1.8)	7.2 (1.6)	7.4 (1.9)	.58
Polypharmacy (using ≥5 medications)	267 (97)	112 (99)	155 (96)	.25
Cardiovascular history				
Hypertension	266 (97)	111 (98)	155 (96)	.48
Dyslipidaemia	259 (95)	110 (97)	149 (93)	.1
Peripheral artery disease	77 (28)	34 (31)	43 (27)	.50
Atrial fibrillation	68 (25)	9 (8)	59 (37)	<.001
Heart failure	52 (19)	22 (20)	30 (19)	.86
Chronic kidney disease	30 (11)	8 (7)	22 (14)	.09
Ischemic stroke	20 (7)	7 (6)	13 (8)	.56
PCI	176 (64)	89 (79)	87 (54)	<.001
CABG	8 (3)	3 (3)	5 (3)	>.99

Note: Continuous data are presented as mean (standard deviation). Categorical data are shown as *n* (%).

Abbreviations: CABG, coronary artery bypass graft surgery; CFS, Clinical Frailty Scale; PCI, percutaneous coronary intervention.

TABLE 2 Prescriptions of secondary prevention medicines by frailty status.

Medication types	All participants ($n=274$), n (%)	Non-frail ($n=113$), n (%)	Frail ($n=161$), n (%)	p
Antiplatelets	212 (77)	106 (94)	106 (66)	<.001
Statins	258 (94)	104 (92)	154 (96)	.21
Beta-blockers	229 (84)	99 (88)	130 (81)	.13
ACEIs/ARBs	213 (78)	92 (81)	121 (75)	.22
All four types (antiplatelets, statins, beta-blockers, ACEIs/ARBs)	140 (51)	72 (64)	68 (42)	<.001

Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor blockers.

TABLE 3 Relationship between the CFS score and the prescription of secondary prevention medications.

	Unadjusted model		Adjusted model 1		Adjusted model 2	
Secondary prevention medications	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Antiplatelets	.54 (.42–.71)	<.001	.57 (.43–.76)	<.001	.79 (.46–1.36)	.39
Statins	1.14 (.77–1.69)	.51	1.19 (.75–1.89)	.45	1.33 (.79–2.25)	.29
Beta-blockers	.75 (.58–.98)	.04	.72 (.53–.96)	.03	.68 (.50–.93)	.02
ACEIs/ARBs	.90 (.72–1.12)	.34	.74 (.57–.97)	.03	.71 (.55–.95)	.02
All four types	.74 (.61–.90)	.002	.68 (.54–.84)	<.001	.76 (.59–.98)	.04

Note: Model 1: adjusted for age and sex. Model 2: adjusted for age, sex, socio-economic conditions (low education, living alone and public health insurance), total number of medications used. Models involved antiplatelets and all four types of secondary prevention medications were also adjusted for anticoagulant use.

Abbreviation: ACEIs/ARBs, angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers.

with published studies worldwide. A systematic review of 16 cohort studies (145,668 participants) examining the prescribing of cardioprotective medicines post-myocardial infarction found that in most studies, the prescription rates of antiplatelets, lipid-lowering therapies, ACEIs/ARBs and beta-blockers postmyocardial infarction were lower in the frail patients compared to non-frail patients.[29] In Vietnam, increasing frailty prevalence with poorer health outcomes has been reported in patients with cardiovascular disease and diabetes.[15,16] In a study of 324 older participants with acute coronary syndrome in Vietnam, frailty was present in 48% of the study sample and was significantly associated with a higher risk of arrhythmia, in-hospital mortality, 30-day mortality and 30-day readmission.[15] In another Vietnamese study by Pham and colleagues, in older patients with acute coronary syndrome, the prevalence of frailty was found to be 33%.[30] However, there is very limited evidence about the relationship between frailty and the use of secondary prevention medications in older Vietnamese patients, particularly in those with diabetes and CHD. A novel aspect of our study is in its distinct contribution to the body of evidence regarding the prescription of secondary prevention medications in older patients with diabetes and CHD in Vietnam. Our study provides important insights into the local epidemiology and clinical practices. The high prescription rates of prevention medicines in this cohort of older patients with diabetes and CHD (including those with frailty) may reflect adherence to cardiovascular prevention guidelines among clinicians and the translation of evidence into clinical practice. However, the reduced likelihood of being prescribed all four types of preventive medication with increased CFS scores does highlight the potential impact of frailty. Clinicians may assume that frail patients have functional limitations and are less likely to benefit from intensive management of cardiovascular risk factors. Older patients with frailty may have biological changes that could amplify the side effects of medicines like beta-blockers and ACEIs/ARBs. A separate study by Zullo et al. found the use of beta-blockers was associated with increased risk of hypotension and breathlessness in frail older adults.[31] Furthermore, prescribing practices may be influenced by concerns that frail patients might struggle to adhere to complex medication regimens. To manage polypharmacy, medications that are perceived as having a better risk-to-benefit profile could be prioritised over others, especially when frailty is present. However, with growing studies on the reversibility of frailty, future research could investigate

the appropriate combination of preventive medications to improve the use of secondary prevention medications for this population.

The inclusion of frailty screening could be further investigated as a tool to help optimise care for this population. Several studies have explored the incorporation of frailty screening into cardiovascular care.[32] For settings with limited resources, how this is implemented is an opportune area for future research. Our study provides further evidence for the Vietnamese population, and the results of our analysis can be used as a reference for future studies.

This study has some limitations. Since it is a secondary epidemiological analysis, there may be some unmeasured confounding variables, such as income. The inability to control for these confounders can introduce bias and affect the validity of the findings. Information on newer cardioprotective medications, such as sodium-glucose cotransporter-2 (SGLT2) inhibitors, was not collected. In addition, the study was conducted at a single site, so the findings may not be generalisable nationally. Differences in hospital resources, patient demographics and clinical practices may influence the observed patterns of medication prescribing, thereby potentially limiting the external validity of the results. Therefore, the findings should be interpreted with caution when considering their application to different health-care systems or policy contexts.

Future multicentred studies would provide a more comprehensive understanding of the relationship between frailty and cardiovascular secondary prevention medication prescribing patterns in older patients with diabetes in Vietnam, thereby improving the generalisability of the findings. Future studies should also explore clinicians' perspectives on how frailty is perceived and influences the decision to prescribe medicines.

5 | CONCLUSIONS

This study found a high prevalence of frailty among older patients with diabetes and CHD. We found that frailty independently affected the prescription of cardiovascular secondary prevention medications in this Vietnamese population. Future research should focus on longitudinally assessing the relationship between frailty and cardiovascular medications in a more diverse and larger population of older patients with diabetes.

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CONFLICT OF INTEREST STATEMENT

Tu Nguyen is an Associate Editor of the Australasian Journal on Ageing. The remaining authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analysed in the present study are available from the corresponding author on reasonable request.

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