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ORIGINAL RESEARCH

Antithrombotic Therapy Strategies and Clinical Outcomes in Chinese Patients Aged 65 and Older with High Ischemic Risk Coronary Artery Disease

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Background: Elderly patients with coronary artery disease (CAD) are at heightened risk for ischemic and bleeding complications. This study evaluates antithrombotic therapy use and its clinical outcomes in Chinese patients aged ≥65 years with CAD and elevated ischemic risk.

Methods: This prospective cohort study enrolled patients aged ≥65 years with diagnosed CAD and ≥ 1 high ischemic risk factor from two centers. We recorded major adverse cardiovascular events (MACE)—death, nonfatal myocardial infarction, nonfatal ischemic stroke—and bleeding events over a 2-year follow-up.

Results: Of 1005 patients (mean age 76.3 ± 7.2 years; 25.3% female), 49.0% were aged 65–75 and 51.0% were >75. Antithrombotic regimens included no therapy (1.8%), single antiplatelet therapy (SAPT, 23.0%), dual antiplatelet therapy (DAPT, 64.3%), and anticoagulation (10.9%), with 60.9% of the latter combining antiplatelet therapy. Older patients (>75 years) experienced higher MACE rates (11.5% vs 6.3%; RR: 1.825; 95% CI: 1.203–2.769; p = 0.004) and a trend towards increased bleeding (8.4% vs 6.5%; p = 0.257). Notably, all-cause and cardiovascular mortality were significantly higher in this group. Anticoagulation therapy was linked to a higher, yet non-significant, MACE rate and significantly increased bleeding risk compared to SAPT and DAPT. Multivariate analysis identified age >75, LVEF <50%, and eGFR <50 mL/min/1.73 m^2 as predictors of mortality and MACE, with anticoagulation therapy increasing bleeding risk.

Conclusion: In elderly CAD patients, those aged >75 years exhibit higher mortality and MACE rates, with anticoagulation therapy associated with increased bleeding. Age, reduced LVEF, and renal function emerge as critical predictors of adverse outcomes.

Keywords: coronary artery disease, antithrombotic therapy, high ischemic risk, elderly patients, clinical outcomes

Introduction

Coronary artery disease (CAD) is a leading cause of mortality globally.[1,2] The risks of morbidity and mortality associated with CAD escalate with advancing age.[3] According to the seventh national census conducted by the China National Bureau of Statistics in 2021, mainland China is home to over 190 million individuals aged 65 years or older.[4] This demographic shift presents a substantial challenge and public health concern, particularly as cardiovascular disease, including CAD, is the primary cause of death in the region, and its incidence is on an upward trend.[5] Prophylactic measures against CAD can markedly reduce mortality among the elderly. Antithrombotic therapy serves as a cornerstone in CAD management; however, it carries an increased risk of bleeding, especially in older individuals. Both ischemic and bleeding risks are correlated with age. Elderly patients with CAD are particularly susceptible to ischemic and bleeding complications. Existing data on the utilization of antithrombotic strategies in Chinese elderly CAD patients at high ischemic risk are limited. In this study, we aim to explore the antithrombotic therapy and clinical outcomes in Chinese individuals aged 65 years or older with CAD who are at elevated ischemic risk.

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Methods

Study Design and Participants

This prospective, observational study enrolled participants from the Peking University First Hospital and the General Hospital of Northern Theater Command in China between May 2018 and January 2020. Inclusion criteria encompassed patients with diagnosed CAD who were aged 65 years or older and exhibited at least one of the following high ischemic risk conditions: female sex, diabetes mellitus treated with medications (oral hypoglycemic therapy or subcutaneous insulin), chronic kidney disease (defined as an estimated glomerular filtration rate< 60 mL/min per 1.73 m^2), diagnosed atrial fibrillation (AF), acute coronary syndrome (ACS), prior myocardial infarction (MI), previous ischemic stroke, or diagnosed peripheral artery disease (PAD). Considering the contraindications and bleeding risk of antithrombotic treatment, exclusion criteria included: (1) active bleeding or recent major surgery, (2) contraindications to antithrombotic agents, (3) diagnosed severe hepatic dysfunction or hematologic diseases.

For each participant, data were collected on concomitant diseases, including MI, percutaneous coronary intervention (PCI), AF, PAD, stroke, and cardiovascular risk factors such as hypertension, diabetes mellitus, chronic kidney disease, family history of CAD, and smoking. Additional information on body weight index, serum creatinine level, left ventricular ejection fraction (LVEF), and medications was obtained from each hospital's electronic records. Clinical follow-up was systematically scheduled at intervals of 3, 6, 9, 12, 18, and 24 months, with monitoring through telephonic calls, clinical visits, or hospitalizations.

The trial was registered in the Chinese Clinical Trial Registry (registration no.: ChiCTR1800015545) and conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of each participating center, and written informed consent was obtained from all participants prior to recruitment.

Outcomes

Data on clinical events, such as death, MI, stroke, or bleeding, were systematically gathered through telephonic calls, clinical visits, or hospitalization records. The primary composite endpoint encompassed all-cause mortality, nonfatal MI, and nonfatal stroke. Bleeding events were classified according to the Bleeding Academic Research Consortium (BARC) criteria, specifically types 2, 3, or 5,[6] with major bleeding defined as BARC type 3 or 5.

Statistical Analyses

Continuous variables were represented as mean ± standard deviation (SD) and analyzed using Student's *t*-test in the event of normal distribution, or the Mann–Whitney *U*-test if the distribution was non-normal. Categorical variables were depicted as counts and percentages and assessed using the χ^2-test or Fisher's exact test, where appropriate. Adjusted risk ratios (RRs) and 95% confidence intervals (CIs) for endpoints such as all-cause mortality, composite outcomes, and bleeding incidents were derived using multivariate logistic regression analysis. This adjustment was performed concurrently for variables including sex, age, ACS, hypertension, diabetes mellitus, stroke, PAD, previous PCI, family history of CAD, current smoking status, LVEF, renal functionality, dual antiplatelet therapy (DAPT), and anticoagulation status at discharge. A p-value of < 0.05 was considered to indicate statistical significance. All statistical evaluations were carried out using SPSS version 20.0 software (IBM Corp, Armonk, NY, USA). The cumulative incidence curves were generated with R version 4.3.3 software (2024 The R Foundation for Statistical Computing Platform).

Results

Baseline Characteristics of the Study Population

A total of 1109 participants were initially recruited for this study. Of these, 79 declined to consent, 13 were excluded due to fragility and diminished self-care capabilities, 2 because of hepatic cirrhosis, 4 were undergoing dialysis, and 6 presented with active gastrointestinal bleeding. This resulted in 1005 participants being enrolled. Their mean age was 76.27 ± 7.22 years (range: 65–96), with 74.7% being male. Of these, 492 (49.0%) were aged 65–75 years, and 513 (51.0%) were over 75 years. All patients had diagnosed as atherosclerotic CAD: 52.8% with ACS and 47.2% with stable CAD. Patients over 75 years reported higher incidences of prior MI, previous PCI, hypertension, diabetes, PAD, previous

Table 1 The Basic Clinical Characteristics of the Study Participants

Variables	All Participants (n = 1005)	Participants Aged 65–75 Years (n = 492)	Participants Aged > 75 Years (n = 513)	*p*
Age, y	76.27 ± 7.22	70.11 ± 2.97	82.17 ± 4.72	< 0.001*
Male, n (%)	751 (74.7%)	356 (72.4%)	395 (77.0%)	0.091
BMI, kg/m^2	24.24 ± 3.19	24.43 ± 3.11	24.05 ± 3.25	0.099
ACS, n (%)	531 (52.8%)	327 (66.5%)	204 (39.8%)	< 0.001*
SCAD, n (%)	474 (47.2%)	165 (33.5%)	309 (60.2%)	< 0.001*
Prior MI, n (%)	151 (15.0%)	63 (12.8%)	88 (17.2%)	0.054
Previous PCI, n (%)	373 (37.1%)	133 (27.0%)	240 (46.8%)	< 0.001*
Hypertension, n (%)	793 (78.9%)	360 (73.2%)	433 (84.4%)	< 0.001*
Diabetes mellitus, n (%)	353 (35.1%)	152 (30.9%)	201 (39.2%)	0.006*
PAD, n (%)	137 (13.6%)	24 (4.9%)	113 (22.0%)	< 0.001*
Previous Ischemic Stroke, n (%)	192 (19.1%)	58 (11.8%)	134 (26.1%)	< 0.001*
AF, n (%)	129 (12.8%)	36 (7.3%)	93 (18.1%)	< 0.001*
Family history of CAD, n (%)	244 (24.3%)	114 (23.2%)	130 (25.3%)	0.422
Current smoking, n (%)	185 (18.4%)	128 (26.0%)	57 (11.1%)	< 0.001*
LVEF, %	58.85 ± 8.09	59.59 ± 8.61	58.12 ± 7.49	< 0.001*
eGFR†, mL/min/1.73 m^2	71.43 ± 21.09	79.34 ± 20.14	63.86 ± 19.13	< 0.001*

Notes: †eGFR, estimated using the Chronic Kidney Disease Epidemiology Collaboration equation. *$p < 0.05$ vs participants aged 65–75 years.
Abbreviations: BMI, body mass index; ACS, acute coronary syndrome; SCAD, stable coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; PAD, peripheral artery disease; AF, atrial fibrillation; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate.

ischemic stroke, AF, as well as lower LVEF and estimated glomerular filtration rate (eGFR) values. Conversely, they had fewer incidences of ACS compared to the 65–75 age bracket. Clinical characteristics of the participants are detailed in Table 1.

Antiplatelet Therapy Status

Among the elderly patients with diagnosed CAD, 18 (1.8%) were not administered any form of antithrombotic therapy. At discharge, 944 (93.9%) patients received a prescription for at least one antiplatelet agent: 89.7% were prescribed aspirin, 66.3% clopidogrel, and 2.7% the newer P2Y12 inhibitor, ticagrelor. Patients aged 65–75 years showed higher utilization of aspirin and clopidogrel than those over 75 years (95.1% vs 84.4% for aspirin, and 79.1% vs 54.0% for clopidogrel, all $p < 0.001$, Table 2).

During the 2-year follow-up, there was an observed increase in single antiplatelet therapy (SAPT) with aspirin alone: 19.0% at discharge to 29.1% at 1-year, and 49.2% at 2-year follow-up. SAPT utilization with the P2Y12 inhibitor

Table 2 Antithrombotic Medications at Discharge in Elderly Patients with Coronary Artery Disease

Variables	All Participants (n = 1005)	Participants Aged 65–75 Years (n = 492)	Participants Aged > 75 Years (n = 513)	*p*
Antiplatelet agents	944 (93.9%)	480 (97.6%)	464 (90.4%)	< 0.001*
Aspirin, n (%)	901 (89.7%)	468 (95.1%)	433 (84.4%)	< 0.001*
Clopidogrel, n (%)	666 (66.3%)	389 (79.1%)	277 (54.0%)	< 0.001*
Ticagrelor, n (%)	27 (2.7%)	15 (3.0%)	12 (2.3%)	0.506
Anticoagulation agents	110 (10.9%)	20 (4.1%)	90 (17.5%)	< 0.001*
Warfarin, n (%)	27 (2.7%)	7 (1.4%)	20 (3.9%)	0.015*
Dabigatran, n (%)	61 (6.1%)	8 (1.6%)	53 (10.3%)	< 0.001*
Rivaroxaban, n (%)	22 (2.2%)	5 (1.0%)	17 (3.3%)	0.013*

Notes: Categorical variables are presented as n (%). *$p < 0.05$ vs participants aged 65–75 years.

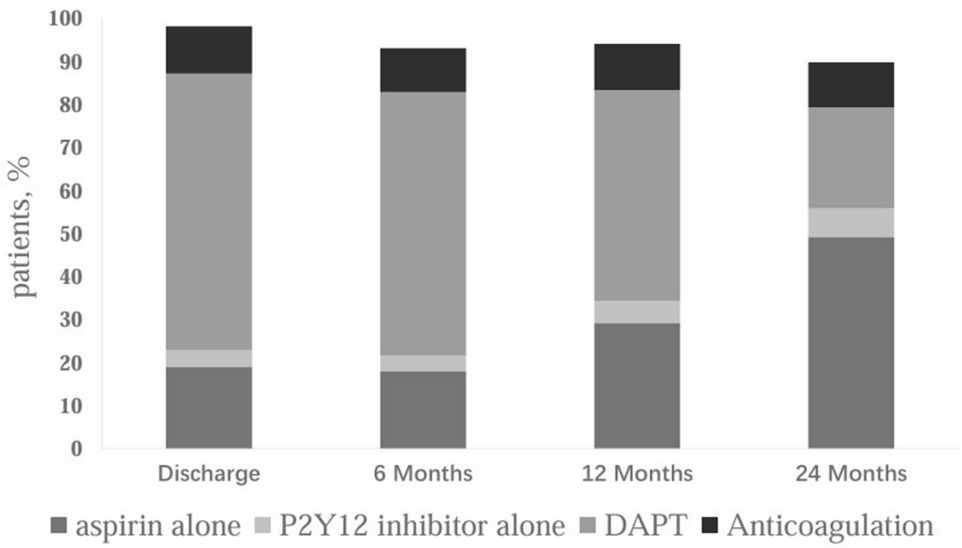

Figure 1 Antithrombotic therapy in elderly patients with coronary artery disease during the 2-year follow-up.

clopidogrel (excluding ticagrelor) also increased from 4.0% at discharge to 5.3% at 1-year and 6.7% at 2-year follow-up. In contrast, DAPT usage, comprising aspirin in conjunction with either clopidogrel (95.8%) or ticagrelor (4.2%), decreased from 64.3% at discharge to 49.1% at 1-year, and 23.5% at 2-year follow-up. Aspirin remains the cornerstone antiplatelet agent for elderly CAD patients, while clopidogrel continues as the most frequently prescribed component within the DAPT regimen. Alterations in antithrombotic therapy across the 2-year follow-up period are delineated in Figure 1.

Anticoagulation Therapy Status

Of the elderly patients diagnosed with CAD, 110 (10.9%) were administered anticoagulation therapy. This includes 2.7% on warfarin, 6.1% on dabigatran, and 2.2% on rivaroxaban. Among these, 70 (63.6%) presented with AF, while 40 (36.4%) had either confirmed or suspected pulmonary embolism (PE) or deep vein thrombosis (DVT). The anticoagulation usage remained stable at 10.6% during the 1-year follow-up and 10.3% at the 2-year mark (Figure 1). Patients aged over 75 years demonstrated a higher rate of anticoagulation than those aged between 65–75 years (17.5% vs 4.1%, $p < 0.001$, Table 2).

At discharge, 43 (39.1%) patients were solely on anticoagulation therapy, whereas 67 (60.9%) were on a combination of anticoagulation and antiplatelet therapy—of these, 54.6% were prescribed aspirin, 2.7% clopidogrel, and 3.6% DAPT. The trend in anticoagulation therapy remained largely consistent throughout the 2-year follow-up, as outlined in Table 3. Notably, a significant proportion (over 50%) of those on anticoagulation were also administered aspirin. Triple therapy, encompassing anticoagulation and DAPT, was infrequently prescribed for elderly CAD patients.

Antithrombotic Therapy in Elderly CAD Patients with AF

Of the elderly patients with confirmed CAD, 129 (12.8%) were concurrently diagnosed with AF. Upon discharge, 56 (43.4%) were prescribed antiplatelet therapy without anticoagulation, including 10.1% on aspirin alone, 6.2% on a sole P2Y12 inhibitor, and 27.1% on DAPT. Meanwhile, 70 (54.3%) patients were administered anticoagulation therapy.

Among the AF patients receiving anticoagulation therapy at discharge, 26 (37.1%) were solely on anticoagulation, and 44 (62.9%) were on combined anticoagulation and antiplatelet therapy. Within this subgroup, 39 (55.7%) were prescribed aspirin, and a minority received either a P2Y12 inhibitor (2.9%) or DAPT therapy (4.3%). Over the course of the 2-year follow-up, the trend in anticoagulation remained generally stable; the utilization of DAPT diminished to 10.7%, while SAPT with only aspirin increased to 23.3% (Table 4).

Table 3 Anticoagulation Therapy in Elderly Patients with Coronary Artery Disease During the 2-year Follow-up

Anticoagulation Plus	Discharge (n = 110)	6 Months (n = 96)	12 Months (n = 97)	24 Months (n = 92)
Aspirin, n (%)	60 (54.6%)	51 (53.1%)	48 (49.5%)	48 (52.2%)
Clopidogrel, n (%)	3 (2.7%)	2 (2.1%)	5 (5.2%)	4 (4.3%)
DAPT, n (%)	4 (3.6%)	7 (7.3%)	6 (6.2%)	1 (1.1%)
Anticoagulation alone, n (%)	43 (39.1%)	36 (37.5%)	38 (39.1%)	39 (42.4%)

Abbreviation: DAPT, dual antiplatelet therapy.

Mortality, Composite Endpoint, and Bleeding Events Post Discharge

During the study period, 64 (6.4%) patients were lost to follow-up and remained event-free at their last contact. 90 (9.0%) patients incurred a composite endpoint consisting of all-cause death, nonfatal myocardial infarction (MI), and nonfatal ischemic stroke, with 53 (5.3%) resulting in death, of which 35 (3.5%) were cardiovascular-related. Furthermore, 43 (4.3%) patients experienced nonfatal MI and nonfatal ischemic stroke. Those patients aged over 75 years manifested more composite endpoints as compared to those aged 65–75 years (Table 5). Although a significant difference in all-cause or cardiovascular death between the two age groups was observed, no notable difference emerged in nonfatal MI or ischemic stroke or bleeding events. The cumulative incidence curves of composite endpoint and bleeding events were showed between patients aged 65–75 years and over 75 years in Figure 2. When evaluating patients under different antithrombotic strategies, those treated with anticoagulation therapy showed a non-significant higher trend in composite endpoints (anticoagulation 10.9% vs DAPT 8.9% vs SAPT 6.5%, p = 0.339) (Table 6).

Of the patients, 75 (7.5%) encountered bleeding events; the majority (66, 6.6%) were classified as minor according to BARC-2 criteria, while major bleeding, as per BARC-3 criteria, was least reported (9, 0.9%). Compared to patients aged 65–75 years, those over 75 years exhibited a non-significant elevated bleeding trend (8.4% vs 6.5%, p = 0.257). Additionally, patients treated with anticoagulation therapy were found to have a higher bleeding risk (13.6%) than those treated with either SAPT (5.2%, p = 0.007) or DAPT (7.3%, p = 0.025) (Table 6). And patients with atrial fibrillation had a higher bleeding risk (12.4%) than those without atrial fibrillation (6.7%) (Table 7), probably due to higher anticoagulation treatment in patients with atrial fibrillation. The cumulative incidence curves of composite endpoint and bleeding events were showed between patients with and without atrial fibrillation in Figure 3.

We conducted a distinct multivariate logistic regression analysis to delineate the risk factors associated with the composite endpoint, all-cause mortality, and bleeding incidents in elderly patients with diagnosed CAD (Table 8). After comprehensive adjustment for confounding variables, an age greater than 75 years emerged as a significant predictor of both all-cause mortality (RR: 2.994, 95% CI: 1.446–6.201, p = 0.003) and the composite endpoint (RR: 1.906, 95% CI: 1.134–3.206, p = 0.015). The analysis further demonstrated that a LVEF below 50% (RR: 3.371, 95% CI: 1.687–6.736, p = 0.001) and an eGFR less than 50 mL/min/1.73 m^2 (RR: 2.830, 95% CI: 1.479–5.415, p = 0.002) were associated with an elevated risk of all-cause death. Additional factors, such as current smoking (RR: 2.029, 95% CI: 1.132–3.637, p =

Table 4 Antithrombotic Therapy in Elderly Coronary Artery Disease Patients with AF During the 2-year Follow-up

Antithrombotic Therapy	Discharge (n = 129)	6 Months (n = 110)	12 Months (n = 109)	24 Months (n = 103)
Non, n (%)	3 (2.3%)	7 (6.4%)	5 (4.6%)	7 (6.8%)
Aspirin alone, n (%)	13 (10.1%)	7 (6.4%)	13 (11.9%)	24 (23.3%)
P2Y12 inhibitor alone, n (%)	8 (6.2%)	4 (3.6%)	6 (5.5%)	8 (7.8%)
DAPT, n (%)	35 (27.1%)	35 (31.8%)	28 (25.7%)	11 (10.7%)
Anticoagulation plus	70 (54.3%)	57 (51.8%)	57 (52.3%)	53 (51.5%)
Aspirin, n (%)	39 (30.2%)	33 (30.0%)	29 (26.6%)	28 (27.2%)
P2Y12 inhibitor, n (%)	2 (1.6%)	1 (0.9%)	3 (2.8%)	3 (2.9%)
DAPT, n (%)	3 (2.3%)	4 (3.6%)	3 (2.8%)	1 (1.0%)
Anticoagulation alone, n (%)	26 (20.2%)	19 (17.3%)	22 (20.2%)	21 (20.4%)

Abbreviation: DAPT, dual antiplatelet therapy.

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Table 5 Composite Endpoint and Bleeding Events Compared Between Elderly Patients with Coronary Artery Disease Aged 65–75 years and > 75 years

Variables	All Participants (n = 1005)	Participants Aged 65–75 Years (n = 492)	Participants Aged > 75 Years (n = 513)	RR	95% CI	*p*
Composite endpoint	90 (9.0%)	31 (6.3%)	59 (11.5%)	1.825	1.203–2.769	0.004*
All-cause death	53 (5.3%)	12 (2.4%)	41 (8.0%)	3.277	1.743–6.160	< 0.001*
Cardiovascular death	35 (3.5%)	5 (1.0%)	30 (5.8%)	5.754	2.251–14.711	< 0.001*
Nonfatal MI	13 (1.3%)	5 (1.0%)	8 (1.6%)	1.535	0.505–4.658	0.446
Nonfatal ischemic stroke	30 (3.0%)	18 (3.7%)	12 (2.3%)	0.639	0.311–1.313	0.219
Bleeding events	75 (7.5%)	32 (6.5%)	43 (8.4%)	1.289	0.830–2.002	0.257
BARC-2	66 (6.6%)	28 (5.7%)	38 (7.4%)			
BARC-3	9 (0.9%)	4 (0.8%)	5 (1.0%)			

Note: *$p < 0.05$ vs participants aged 65–75 years.
Abbreviations: RR, risk ratio; CI, confidence interval; MI, myocardial infarction; BARC, Bleeding Academic Research Consortium.

0.018) and the aforementioned LVEF below 50% (RR: 2.325, 95% CI: 1.291–4.186, $p = 0.005$) and eGFR less than 50 mL/min/1.73 m^2 (RR: 1.907, 95% CI: 1.091–3.333, $p = 0.023$) thresholds, were linked to an increased risk of the composite endpoint. Lastly, the analysis identified anticoagulation at discharge (RR: 2.838, 95% CI: 1.275–6.320, p = 0.011), prior PCI (RR: 1.905, 95% CI: 1.134–3.200, p = 0.015), and a history of stroke (RR: 1.944, 95% CI: 1.111–3.403, p = 0.020) as risk factors for bleeding.

Discussion

The present study illustrates that in elderly Chinese CAD patients with elevated ischemic risk, aspirin remains the primary antiplatelet agent. Clopidogrel is frequently prescribed as part of the DAPT regimen, while the newer P2Y12 inhibitor, ticagrelor, is less commonly administered.

As the inaugural antiplatelet medication, aspirin continues to be the most widely prescribed single antiplatelet therapy (SAPT) agent across the globe. Since the 1980s, aspirin's beneficial effects in treating Acute Coronary Syndrome (ACS) have been firmly established.[7] A seminal Antithrombotic Trialists' Collaboration meta-analysis, comprising 287 clinical trials and 135,000 individuals, underscored its efficacy in cardiovascular secondary prevention.[8] Hence, owing to its proven efficacy and affordability, aspirin monotherapy is consistently recommended in international guidelines for cardiovascular secondary prevention, although increased bleeding risks, particularly gastrointestinal bleeding, warrant

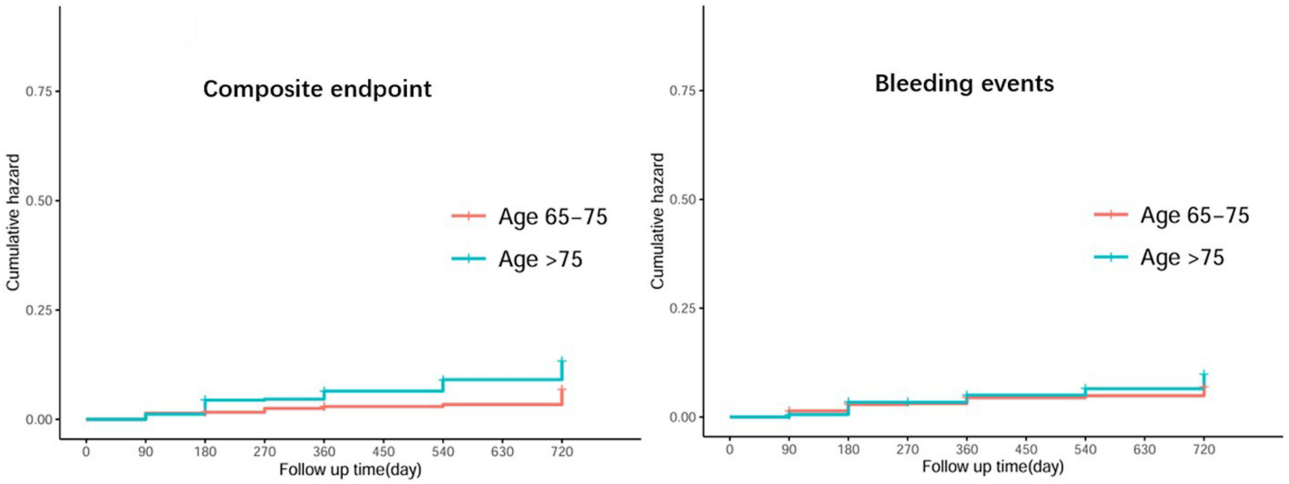

Figure 2 The cumulative incidence curves of composite endpoint and bleeding events between patients aged 65–75 years and over 75 years.

Table 6 Composite Endpoint and Bleeding Events in Different Antithrombotic Therapies at Discharge

Variables	SAPT (n = 231)	DAPT (n = 646)	Anticoagulation (n = 110)	*p*
Composite endpoint	15 (6.5%)	58 (8.9%)	12 (10.9%)	0.339
All-cause death	11 (4.8%)	33 (5.1%)	6 (5.5%)	0.960
Nonfatal MI	1 (0.4%)	9 (1.4%)	3 (2.7%)	0.200
Nonfatal ischemic stroke	3 (1.3%)	22 (3.4%)	3 (2.7%)	0.256
Bleeding events	12 (5.2%)	47 (7.3%)	15 (13.6%)*	0.020

Note: *$p < 0.05$ vs SAPT or DAPT.
Abbreviations: SAPT, single antiplatelet therapy; DAPT, dual antiplatelet therapy; MI, myocardial infarction.

Table 7 Composite Endpoint and Bleeding Events in Patients with or without AF

Variables	Patients with AF (n = 129)	Patients without AF (n = 876)	RR	95% CI	*p*
Composite endpoint	17 (13.2%)	73 (8.3%)	1.670	0.950–2.934	0.072
All-cause death	11 (8.5%)	42 (4.8%)	1.851	0.927–3.695	0.077
Nonfatal MI	2 (1.6%)	11 (1.3%)	1.238	0.980–1.026	0.782
Nonfatal ischemic stroke	5 (3.9%)	25 (2.9%)	1.373	0.516–3.652	0.524
Bleeding events	16 (12.4%)	59 (6.7%)	1.961	1.091–3.524	0.022*

Note: *$p < 0.05$ vs patients without AF.
Abbreviations: AF, atrial fibrillation; MI, myocardial infarction.

caution.[9,10] The emergence of novel antiplatelet agents has spurred aspirin-free strategies, such as P2Y12 inhibitor monotherapy for cardiovascular secondary prevention. A significant clinical trial in 1996, contrasting clopidogrel monotherapy with aspirin monotherapy in 19,185 patients, revealed minor differences in primary endpoints but less frequent gastrointestinal bleeding with clopidogrel (0.49% vs 0.71%, p = 0.05).[11] Subsequent trials and meta-analyses have corroborated these findings, with no significant disparities in major cardiovascular or bleeding events.[12–14] At present, no definitive evidence establishes the superiority of P2Y12 inhibitor monotherapy over aspirin monotherapy, thereby reinforcing the continued recommendation of long-term aspirin monotherapy.[9] In this study, real-world clinical observations align with these guidelines, highlighting the mainstay status of aspirin monotherapy, secondary utilization of clopidogrel, and absence of ticagrelor monotherapy.

In Chinese populations, the higher morbidity of CYP2C19 loss-of-function alleles may contribute to a preference for aspirin monotherapy over clopidogrel in elderly CAD patients with elevated ischemic risk.[15,16] For those with high

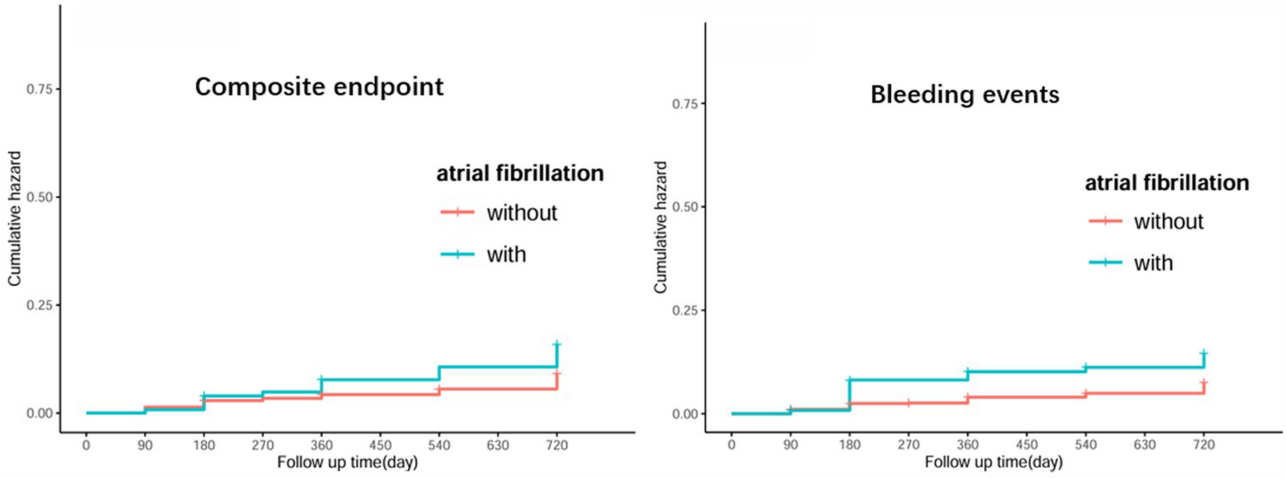

Figure 3 The cumulative incidence curves of composite endpoint and bleeding events between patients with and without atrial fibrillation.

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Table 8 Multivariate Logistic Regression Analysis for the Baseline Risk Factors Predictive of the Clinical Endpoints at the 2-year Follow-up

Variables	All-Cause Deaths		Composite Endpoints		Bleeding Events	
	RR (95% CI)	*p*	RR (95% CI)	*p*	RR (95% CI)	*p*
Male	0.872 (0.432, 1.759)	0.702	0.817 (0.480, 1.390)	0.456	1.503 (0.798, 2.829)	0.207
Age >75	2.994 (1.446, 6.201)	0.003*	1.906 (1.134, 3.206)	0.015*	1.005 (0.576, 1.753)	0.987
ACS	0.691 (0.326, 1.466)	0.336	1.277 (0.719, 2.270)	0.404	1.064 (0.598, 1.893)	0.833
Hypertension	0.862 (0.398, 1.867)	0.706	1.109 (0.611, 2.012)	0.734	1.399 (0.702, 2.787)	0.339
Diabetes	1.007 (0.542, 1.872)	0.982	1.075 (0.665, 1.739)	0.767	0.579 (0.330, 1.014)	0.056
Previous Ischemic Stroke	1.203 (0.601, 2.411)	0.602	1.467 (0.852, 2.525)	0.167	1.944 (1.111, 3.403)	0.020*
PAD	1.358 (0.628, 2.938)	0.437	1.142 (0.586, 2.226)	0.697	1.002 (0.479, 2.097)	0.995
Prior PCI	0.731 (0.381, 1.401)	0.345	0.898 (0.544, 1.482)	0.674	1.905 (1.134, 3.200)	0.015*
Family history of CAD	0.842 (0.403, 1.759)	0.647	0.767 (0.427, 1.380)	0.377	0.698 (0.381, 1.277)	0.243
Current smoking	1.351 (0.575, 3.172)	0.490	2.029 (1.132, 3.637)	0.018*	0.726 (0.350, 1.507)	0.390
LVEF < 50%	3.371 (1.687, 6.736)	0.001*	2.325 (1.291, 4.186)	0.005*	0.468 (0.164, 1.335)	0.156
eGFR < 50 mL/min/1.73 m^2	2.830 (1.479, 5.415)	0.002*	1.907 (1.091, 3.333)	0.023*	0.803 (0.382, 1.687)	0.563
DAPT at discharge	1.173 (0.541, 2.545)	0.686	0.995 (0.527, 1.878)	0.988	1.594 (0.792, 3.206)	0.191
Anticoagulation at discharge	0.690 (0.249, 1.915)	0.476	1.174 (0.539, 2.557)	0.686	2.838 (1.275, 6.320)	0.011*

Note: *$p < 0.05$.

Abbreviations: ACS, acute coronary syndrome; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; CAD, coronary artery disease; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; DAPT, dual antiplatelet therapy.

bleeding risk, aspirin allergy, or major gastrointestinal concerns, clopidogrel remains an alternative. Ticagrelor's limited use may be attributed to factors such as higher costs, increased bleeding risk, non-bleeding adverse effects, and Medicare reimbursement policies.

The current standard treatment after ACS or PCI remains DAPT with aspirin in conjunction with a P2Y12 inhibitor.[17,18] The newer P2Y12 inhibitors, ticagrelor and prasugrel, are generally favored over clopidogrel, yet prasugrel is limited due to increased fatal bleeding risk in certain patient demographics and unavailability in mainland China.[19,20] Recent trials and real-world studies have raised questions regarding ticagrelor's efficacy over clopidogrel, especially concerning major bleeding risk.[19–23] The particular concern over bleeding risk in the elderly necessitates caution, as it may lead to treatment cessation and subsequent recurrent ischemic events or mortality. Clopidogrel thus remains the most frequently prescribed P2Y12 inhibitor for DAPT, especially in elderly patients.[24,25]

The current study also indicates that 10.9% of elderly CAD patients received anticoagulation therapy due to concomitant AF or PE or DVT, with 75.5% opting for new oral anticoagulants (NOACs) over vitamin K antagonists (VKAs).[26,27] The selection of NOACs over VKAs may reflect their convenience, efficacy, and safety, particularly for elderly patients. This study also shows that there was a higher bleeding risk in those patients treated with anticoagulation, probably due to higher proportion (60.9%) combined with antiplatelet therapy.

Furthermore, this study revealed the unique challenges faced by elderly patients, who often have more complex clinical conditions. Comparatively higher incidences of various conditions were observed in patients aged over 75, accompanied by a poorer prognosis.[25,28] There is higher AF incidence in older patients who need to take anticoagulation therapy for prevention of ischemic stroke, but older patients always have lower eGFR and LVEF leading to the increased bleeding risk. Balancing ischemic benefit and bleeding risk remains a formidable clinical challenge in older patients. An observable trend of prescribing less effective drugs to older or more vulnerable patients further complicates treatment strategies.

Although insightful, this study's limitations include its relatively small sample size and its focus on only two well-equipped university hospitals and cardiac centers in Northern China. The findings may not reflect the broader national scenario, necessitating further large-scale research to thoroughly evaluate antithrombotic management for secondary prevention of CAD in elderly Chinese patients.

Conclusions

In elderly Chinese patients with CAD and high ischemic risk, aspirin is the preferred antiplatelet agent, with clopidogrel mainly used within dual antiplatelet therapy (DAPT) regimens. The adoption of the novel P2Y12 inhibitor ticagrelor is notably lower in this population. NOACs are favored over VKAs for required anticoagulation. Patients aged above 75 years demonstrate significantly higher all-cause and cardiovascular mortality compared to those aged 65–75 years, with a trend towards increased bleeding that warrants further investigation. Risk factors including age above 75, LVEF below 50%, and eGFR under 50 mL/min/1.73 m² are linked to increased mortality and adverse composite outcomes. Moreover, anticoagulation therapy elevates bleeding risk, probably due to higher proportion combined with antiplatelet therapy. The complexity of antithrombotic therapy management in this demographic underscores the challenge of optimizing ischemic protection while minimizing bleeding hazards. For the elderly CAD patients with high bleeding risk, it should be recommended to shorten DAPT durations and P2Y12 inhibitor clopidogrel monotherapy post-PCI to reduce the bleeding risk. For the elderly CAD patients with the long-term indication for anticoagulation therapy, considering the high bleeding risk, it should shorten the durations of combination of anticoagulation and antiplatelet treatment, and anticoagulation alone should be preferable.

Data Sharing Statement

Data used and/or analyzed for the current study are available from the corresponding author upon reasonable request.

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Disclosure

The authors report no conflicts of interest in this work.

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