

Ticagrelor Versus Clopidogrel in Elderly Patients With Acute Coronary Syndromes

A Substudy From the Prospective Randomized PLATelet Inhibition and Patient Outcomes (PLATO) Trial

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Background—Elderly patients with acute coronary syndrome are at high risk of recurrent ischemic events and death, and for both antithrombotic therapy and catheter-based complications. This prespecified analysis investigates the effect and treatment-related complications of ticagrelor versus clopidogrel in elderly patients (≥ 75 years of age) with acute coronary syndrome compared with those < 75 years of age.

Methods and Results—The association between age and the primary composite outcome, as well as major bleeding were evaluated in the PLATelet inhibition and patient Outcomes (PLATO) trial using Cox proportional hazards. Similar models were used to evaluate the interaction of age with treatment effects. Hazard ratios were adjusted for baseline characteristics. The clinical benefit of ticagrelor over clopidogrel was not significantly different between patients aged ≥ 75 years of age ($n=2878$) and those < 75 years of age ($n=15\,744$) with respect to the composite of cardiovascular death, myocardial infarction, or stroke (interaction $P=0.56$), myocardial infarction ($P=0.33$), cardiovascular death ($P=0.47$), definite stent thrombosis ($P=0.81$), or all-cause mortality ($P=0.76$). No increase in PLATO-defined overall major bleeding with ticagrelor versus clopidogrel was observed in patients aged ≥ 75 years (hazard ratio, 1.02; 95% confidence interval, 0.82–1.27) or patients aged < 75 years (hazard ratio, 1.04; 95% confidence interval, 0.94–1.15). Dyspnea and ventricular pauses were more common during ticagrelor than clopidogrel treatment, with no evidence of an age-by-treatment interaction.

Conclusions—The significant clinical benefit and overall safety of ticagrelor compared with clopidogrel in acute coronary syndrome patients in the PLATO cohort were not found to depend on age.

Clinical Trial Registration—URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT00391872.

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Key Words: acute coronary syndrome ■ age factors ■ platelets ■ P2Y₁₂ receptor ■ thrombosis ■ bleeding

Age is a strong predictor of adverse outcomes after acute coronary syndrome (ACS).¹⁻³ As a result of higher prevalence of cardiac risk factors and impaired healing processes,⁴⁻⁶ elderly patients with ACS are at higher risk of recurrent ischemic events and death, as well as treatment-related complications compared with younger patients. It has been reported that patients > 75 years of age comprise one third of overall ACS episodes and that this age group accounts for around 60% of the overall mortality from ACS.^{7,8} Further, after allowance for confounding factors, the odds for in-hospital death from acute events increases by 70% for each 10-year increase in age (odds ratio, 1.70; 95% confidence interval [CI], 1.52–1.82).³

Atypical symptoms are more common in elderly patients presenting with ACS,⁹ dyspnea, and confusion are relatively common, whereas ischemic pain is less likely to be present or is present in an atypical location.^{7,9}

Age features as a risk factor in many bleeding risk stratification models.¹⁰⁻¹² Indeed, bleeding risk is greater in elderly versus younger patients; in a recent meta-analysis of stroke prevention in elderly patients with atrial fibrillation, the risk of serious bleeding increased for each decade increase of age (hazard ratio (HR), 1.61; 95% CI, 1.47–1.77¹³). Furthermore, the use of several antiplatelet and anticoagulant therapies is associated with increased bleeding risk in the elderly with a

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WHAT IS KNOWN

- Elderly patients with acute coronary syndrome have a high prevalence of cardiovascular risk factors and are at high risk of recurrent ischemic events and death.
- Elderly patients have a high risk of complications during antithrombotic therapy and revascularization.
- The increased risk of bleeding in elderly as compared with younger patients using some antiplatelet and anticoagulant therapies reduces the net clinical benefit of these therapies.

WHAT THE STUDY ADDS

- The clinical benefit of ticagrelor over clopidogrel in patients with acute coronary syndrome with respect to the composite of cardiovascular death, myocardial infarction and stroke; myocardial infarction; cardiovascular death; stent thrombosis or all-cause mortality, was not significantly different between patients aged ≥ 75 and those aged < 75 years.
- No increased risk of major bleeding complications with ticagrelor versus clopidogrel was observed in patients aged ≥ 75 years or patients aged < 75 years.
- Side-effects dyspnea and ventricular pauses were more common during treatment with ticagrelor than clopidogrel, with no evidence of an age-by-treatment interaction.

resulting reduction in net clinical benefit. For example, age is a predictor of intracranial hemorrhage in patients receiving antiplatelet or anticoagulant therapy.^{14,15} In the Assessment of the Safety and Efficacy of a New Thrombolytic Regimen (ASSENT)-III PLUS trial, enoxaparin as a conjunctive therapy to tenecteplase in patients with ST-segment elevation myocardial infarction was associated with an unacceptable risk of intracranial hemorrhage in the elderly population, warranting a dose reduction in patients aged > 75 years.¹⁶ Similarly, the oral antiplatelet agent prasugrel is generally not recommended in patients ≥ 75 years of age because of the increased risk of fatal and intracranial bleeding and uncertain benefit, except in high-risk situations where its effect appears to be greater.^{17,18}

The clinical picture of ACS in the elderly is often further complicated by comorbid conditions, including atrial fibrillation, diabetes mellitus, renal impairment, heart failure, and cerebrovascular disease.^{19,20} With lengthening life expectancy and the expansion of the older population,²¹ these individuals will account for an increasing proportion of patients with ACS in the future.^{7,8}

Given the increased risk of recurrent ischemic events, bleeding, and death in elderly patients with ACS, and the problems associated with the use of existing antithrombotic therapies in this population, the clinical use of ticagrelor in elderly patients was evaluated, as prespecified in the protocol of the Phase III PLATelet inhibition and patient Outcomes (PLATO) trial. Herein, we present the results of a secondary analysis of the PLATO cohort assessing clinical outcomes in elderly (≥ 75 years of age) versus younger (< 75 years of age) patients treated with ticagrelor or clopidogrel.

Methods

PLATO was an international, multicenter, randomized trial. Previous publications have detailed the methodology of the PLATO trial, including study design, inclusion, and exclusion criteria, patients, and outcome variables.^{22,23} Briefly, 18 624 patients with ST-segment elevation or non-ST-segment elevation ACS were randomized to treatment with ticagrelor or clopidogrel, administered in double-blind, double-dummy fashion as soon as possible after admission and within 24 hours of the acute event. Ticagrelor was administered as a 180-mg loading dose and then 90 mg twice daily. Clopidogrel treatment comprised a maintenance dose of 75 mg/d; in patients who had not received an open-label loading dose and had not been receiving clopidogrel for at least 5 days before randomization, a loading dose of 300 mg was used. An additional 300-mg clopidogrel dose was allowed before percutaneous coronary intervention procedures at the discretion of the investigator. The allocated study treatment was continued for at least 6 months, and a maximum of 12 months. Patients also received acetylsalicylic acid (aspirin) 75 to 100 mg/d, unless they were aspirin-intolerant; a daily aspirin dose up to 325 mg was allowed after stent placement.

The primary efficacy variable was the composite of time to first occurrence of myocardial infarction (MI), stroke, or death from vascular causes. Secondary efficacy variables included the following: the composite of all-cause mortality, MI, or stroke; the composite of death from vascular causes, MI, stroke, severe recurrent cardiac ischemia, recurrent cardiac ischemia, transient ischemic attack, or other arterial thrombotic event; individual components of the primary end point; and all-cause mortality.

The primary safety end point was time to PLATO-defined and adjudicated first major bleeding event.²² Data for PLATO-defined minor bleeding, TIMI (Thrombolysis in Myocardial Infarction), and GUSTO (Global Utilization of Streptokinase and Tissue plasminogen activator for Occluded coronary arteries)-defined bleeding, other clinical adverse events including dyspnea and ventricular pauses, as well as laboratory safety tests, were also included in safety analyses.

Statistical Analyses

Patient characteristics were compared according to age ≥ 75 years or < 75 years using χ^2 and Wilcoxon rank-sum tests. Cox proportional hazards models were used to analyze the association between age subgroup and the primary composite outcome, secondary outcomes, based on intent-to-treat analyses; bleeding end points were analyzed using the same models but only included events that occurred during, and until 7 days after, treatment with study drug. Adjustment variables were selected from baseline characteristics (Table 1), as well as height, waist circumference, race, final diagnosis, randomized treatment, and treatment approach. Region and aspirin dose at randomization were also included as candidate adjustment variables when the treatment effect was assessed. In addition, the relationship between age as a continuous variable and selected outcomes was analyzed using Cox proportional-hazards models including age as continuous variable, treatment, and an age-by-treatment interaction. Baseline-adjusted event rates at 12 months were derived and represent the expected rate of event in a population with the same characteristics as PLATO.

All analyses were based on the intent-to-treat approach, and were performed using SAS, version 9.2. Comparisons for exploratory analyses used a 2-sided significance level of 0.05 without correction for multiple comparisons.

Results

Comparison of Patient Characteristics, Procedures, and Clinical Outcomes in Elderly and Young Patients

Of the 18 622 subjects from the total PLATO population with age data available, 15.5% were aged ≥ 75 years ($n=2878$). Most baseline characteristics differed significantly between the elderly (≥ 75 years of age) and younger (< 75 years of age)

Table 1. Patient Baseline Characteristics, Final Diagnosis, and Planned Management

Characteristic	≥75 Years (n=2878)	<75 Years (n=15 744)	P
Women, %	43.5	25.6	<0.0001
Median body weight, kg (25th–75th percentile)	73 (65–82)	80 (70–90)	<0.0001
Body weight <60 kg, %	12.0	6.2	<0.0001
Median BMI, kg/m ² (25th–75th percentile)	26.2 (23.9–29.1)	27.6 (24.9–30.7)	<0.0001
CV risk factors and history, %			
Diabetes mellitus	28.1	24.5	<0.0001
Habitual smoker	10.0	40.6	<0.0001
Hypertension	75.2	63.7	<0.0001
Dyslipidemia including hypercholesterolemia	46.1	46.8	0.4731
Angina pectoris	53.2	43.4	<0.0001
MI	26.5	19.4	<0.0001
Congestive heart failure	10.5	4.8	<0.0001
PCI	14.6	13.2	0.04
CABG	8.9	5.4	<0.0001
Transient ischemic attack	4.8	2.3	<0.0001
Nonhemorrhagic stroke	5.8	3.5	<0.0001
Peripheral arterial disease	7.9	5.8	<0.0001
Chronic renal disease	9.8	3.2	<0.0001
Baseline laboratory values, median (25th–75th percentile)			
Glucose (mmol/L)	6.9 (5.8–8.8)	6.8 (5.7–8.8)	0.4146
HbA1c (%)	6.1 (5.7–6.6)	6.0 (5.6–6.6)	0.0001
EGFR (mL/min/1.73 m ²)	64 (52–84)	85 (70–102)	<0.0001
Final diagnosis, %			
STEMI	25.9	40.0	
NSTEMI	52.6	41.0	
Unstable angina	19.1	16.3	<0.0001
Other	2.4	2.7	
Planned invasive management, %*	61.5	73.9	<0.0001
PCI during study	73.2	78.8	<0.0001
Coronary angiography during study	96.6	97.8	0.0036
CABG during study	10.0	10.0	0.9946
Planned noninvasive management, %*	38.5	26.1	<0.0001
PCI during study	23.2	30.6	<0.0001
Coronary angiography during study	44.0	58.6	<0.0001
CABG during study	8.1	11.4	0.0017
Region, %			
Asia and Australia	6.6	9.7	
Central and South America	5.8	6.8	
Europe, Middle East, and Africa	78.4	73.7	<0.0001
North America	9.2	9.8	
Aspirin on randomization day, %†			
None	6.6	6.4	
<100 mg	19.3	13.5	
100–299 mg	40.6	39.7	<0.0001
≥300 mg	33.5	40.4	

BMI indicates body mass index; CV, cardiovascular; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; HbA1c, glycosylated hemoglobin; EGFR, estimated glomerular filtration rate; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction.

*Subgroup based on prerandomization management strategy.

†Aspirin dose taken during the trial does not correlate with aspirin dose at randomization, but does correlate with geographic region. Nevertheless, a landmark analysis using aspirin dose on trial day 2 yields results comparable with those obtained using aspirin dose at randomization.

patient populations (Table 1). Compared with younger patients, the elderly subgroup had a higher proportion of women, lower body weight and body mass index, a higher proportion of subjects with body weight <60 kg, a higher proportion of subjects with history of cardiovascular (CV) morbidity, and lower estimated glomerular filtration rate.

Elderly patients had a higher rate of final diagnosis of non-ST-segment elevation MI or unstable angina, and a lower rate of ST-segment elevation myocardial infarction diagnosis than younger patients. Invasive or noninvasive management was a stated prerandomization strategy. At admission, invasive treatment was planned in a lower proportion and noninvasive treatment in a higher proportion of elderly versus younger patients. Percutaneous coronary intervention or coronary angiography was performed in a lower percentage of elderly than younger patients (Table 1). There was a significant regional difference in the recruitment of elderly versus younger patients (Table 1). With regards to aspirin dose at randomization, a higher proportion of elderly patients were receiving <100 mg, whereas a higher proportion of younger patients were on ≥300-mg aspirin (Table 1). No age-by-region interaction was found (data not shown).

After adjustment for differences in baseline characteristics, and irrespective of treatment received, the older age subgroup had consistently poorer outcomes compared with patients aged <75 years, in the primary composite end point and its individual components, as well as in all-cause mortality and

stent thrombosis (Figure 1). Among safety end points, patients aged ≥75 years were at higher risk of PLATO-defined non-coronary artery bypass grafting (non-CABG)-related major bleeding and fatal bleeding compared with the younger subgroup, but at lower risk of CABG-related major bleeding (Figure 1). Similar results were found for these end points using the TIMI bleeding definitions (data not shown).

Efficacy in Elderly and Younger Patients

Ticagrelor was more effective than clopidogrel in reducing the primary outcome in the younger patients, as assessed by Cox proportional-hazards analysis (HR, 0.84; 95% CI, 0.75–0.93; Figure 2). In the elderly patients, the primary outcome occurred in 17.2% of patients receiving ticagrelor and 18.3% of patients receiving clopidogrel (HR, 0.89; 95% CI, 0.74–1.08; Figure 2). The clinical benefit of ticagrelor over clopidogrel did not differ between patients aged ≥75 years and those <75 years with respect to the primary composite outcome of CV death, MI, or stroke (interaction $P=0.56$). Analysis of 12-month composite event rates using age as a continuous variable showed that ticagrelor was more effective than clopidogrel throughout the age range evaluated (interaction $P=0.82$; Figure 3A); examination of age at 5-year intervals confirmed that ticagrelor was more effective than clopidogrel for all age categories (Figure 3B).

Similarly, the clinical benefit of ticagrelor over clopidogrel did not differ between patients aged ≥75 years and those <75 years

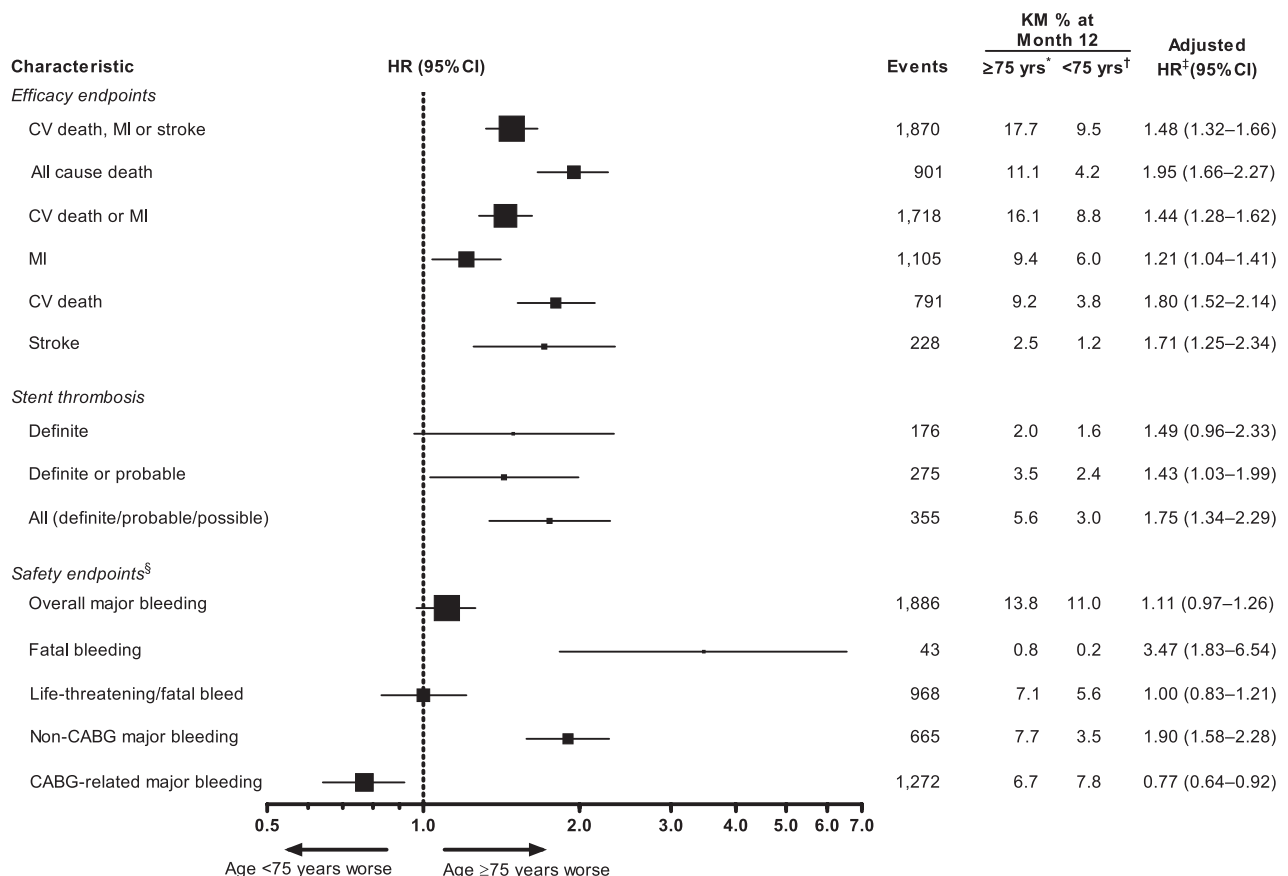


Figure 1. Association of age (<75 vs ≥75 years) with clinical outcome. * $n=2878$; $n=15\,744$; [†]See methods for adjustment variables; [§]PLATElet inhibition and patient Outcomes (PLATO)-defined.²² CABG indicates coronary artery bypass graft; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; KM, Kaplan-Meier estimate; and MI, myocardial infarction.

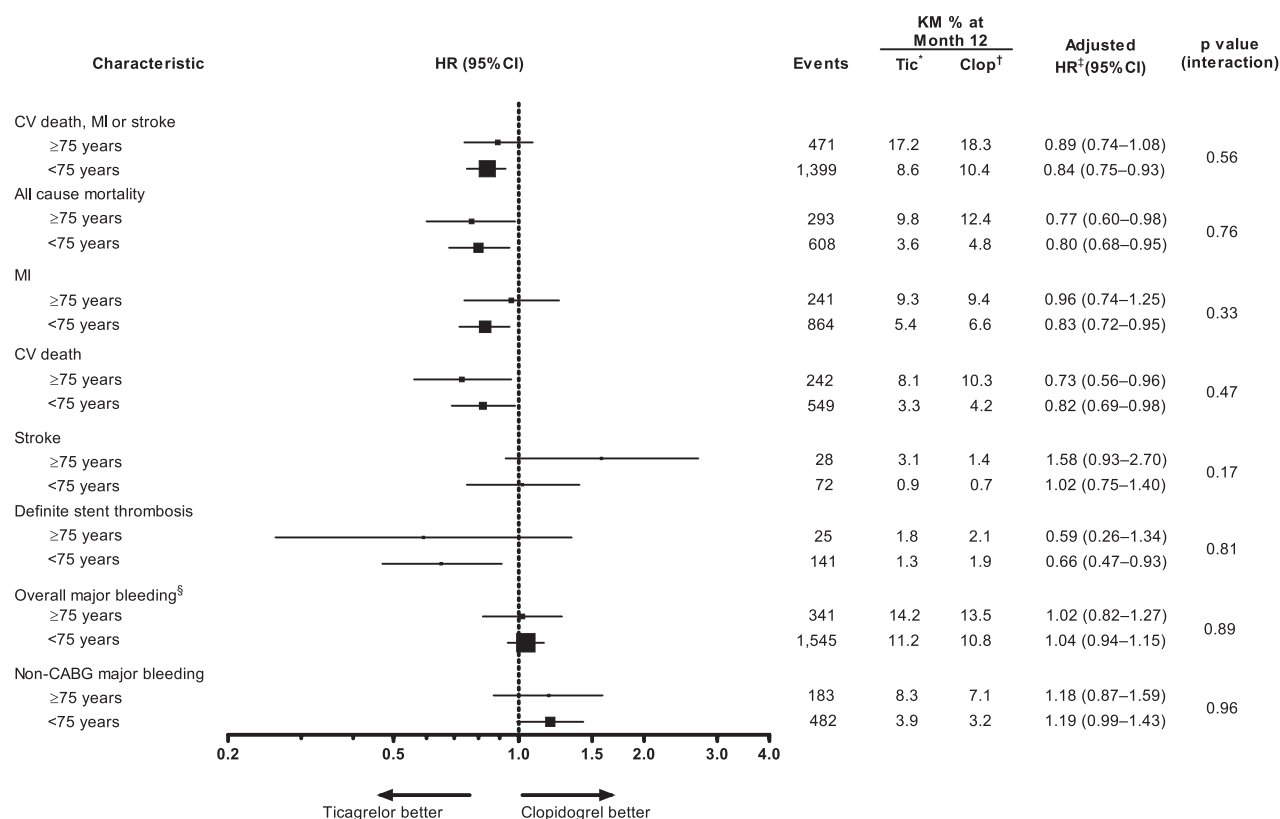


Figure 2. Association of age (<75 vs ≥75 years) and treatment with outcome. Tic = ticagrelor (n=9333); Clop = clopidogrel (n=9291); [†]See methods for adjustment variables; [§]PLATElet inhibition and patient Outcomes (PLATO)-defined;²² CABG indicates coronary artery bypass graft; CV, cardiovascular; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; and MI, myocardial infarction.

with respect to the secondary end points of MI (interaction $P=0.33$), CV death (interaction $P=0.47$), stroke (interaction $P=0.17$), definite stent thrombosis (interaction $P=0.81$), or all-cause mortality (interaction $P=0.76$; Figure 2). Ticagrelor was more effective than clopidogrel in reducing all-cause mortality over the full age range of the study (interaction $P=0.99$; Figure 4A); similarly, ticagrelor was nominally more effective than clopidogrel in reducing all-cause mortality for all age categories calculated using 5-year categorical age ranges (Figure 4B). Although the incidence of stroke events was numerically greater with ticagrelor than with clopidogrel, neither elderly nor younger patients achieved nominally statistically significant treatment effects separately (Figure 2), and no treatment-by-age-group interaction was found ($P=0.17$).

Safety in Elderly and Younger Patients

The risk of PLATO-defined overall major bleeding was similar in ticagrelor- and clopidogrel-treated patients, and was not significantly different between age subgroups (interaction $P=0.89$; Figure 2). The rate of overall PLATO-defined major bleeding was similar between ticagrelor and clopidogrel treatments throughout the age range evaluated in the trial (interaction $P=0.95$; Figure 5A) and examination of age at 5-year intervals confirmed that PLATO-defined overall major bleeding was similar in ticagrelor- and clopidogrel-treated patients for all age categories (Figure 5B); however, after the age of 65, the rise in the rate of major bleeding rates occurred less quickly with ticagrelor than with clopidogrel, as seen by the

monotonically decreasing HRs in Figure 5B. The risk of non-CABG-related bleeding was lower in younger patients treated with clopidogrel versus ticagrelor (Figure 2), but was not significantly higher in elderly patients treated with ticagrelor, versus clopidogrel (Figure 2). There was no significant difference between age subgroups (interaction $P=0.96$). The rate of non-CABG-related bleeding was slightly lower with clopidogrel compared with ticagrelor treatment throughout the evaluated age range (interaction $P=0.98$; Figure 6A), and this observation was confirmed by examination of age at 5-year intervals (Figure 6B).

The rates of TIMI-defined major bleeding and of TIMI-defined “major plus minor” bleeding, and the risk of GUSTO-defined severe and moderate bleeding, were similar in ticagrelor- and clopidogrel-treated patients in each age subgroup (≥75 years and <75 years; data not shown). The rate of TIMI non-CABG-related major bleeding was lower for patients aged <75 years treated with clopidogrel versus ticagrelor (2.0%/year versus 2.4%/year; $P=0.02$), as was the rate of GUSTO mild bleeding (9.3%/year versus 10.4%/year; $P=0.02$); no treatment difference in rates for either bleeding scale occurred for patients ≥75 years of age.

With regards to dyspnea, rates were higher in elderly versus younger patients in both treatment groups: the risk of dyspnea was higher with ticagrelor compared with clopidogrel, with no evidence of an age-treatment interaction (interaction $P=0.21$; Table 2). In addition, during the first week after randomization, ventricular pauses on Holter monitoring were more

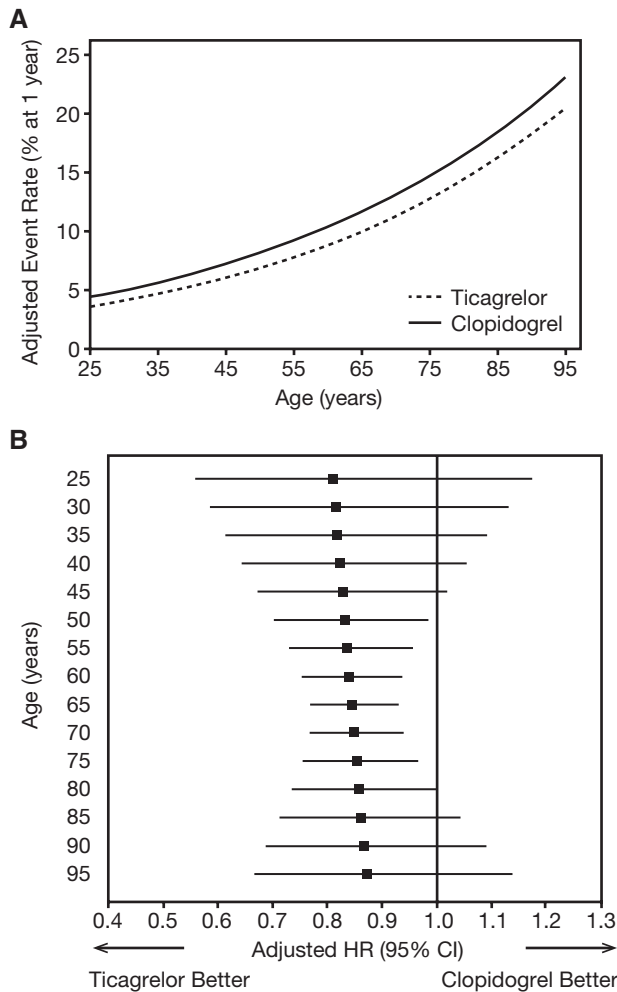


Figure 3. Primary composite outcome—cardiovascular death/MI/stroke according to age. **A**, Estimated event rate at 12 months, ticagrelor vs clopidogrel. **B**, treatment effect by patient age. HR indicates hazard ratio; CI, confidence interval.

common with ticagrelor than clopidogrel, with no evidence of an age-treatment interaction (Table 2). The difference in ventricular pauses was not evident after 30 days (Table 2), and there was no need for pacemaker implantation.

Discussion

The clinical benefit of ticagrelor over clopidogrel was not significantly different between patients aged ≥ 75 years and those aged < 75 years with respect to the composite of CV death, MI, or stroke. Our findings in elderly subjects are consistent with those for the main PLATO cohort,²³ and indicate that the antithrombotic benefits of ticagrelor apply throughout the age range evaluated. Furthermore, the absolute reduction in all-cause mortality was numerically greater (2.6%) in elderly (≥ 75 years of age) than younger (< 75 years of age) patients (1.2%). Corresponding absolute reductions in the primary outcome were 1.1% in the elderly and 1.8% in younger patients. The relative increase in risks of PLATO-defined overall major bleeding, non-CABG-related major bleeding, dyspnea, and ventricular bradycardia with ticagrelor compared with clopidogrel were also not significantly different between age categories, although the absolute increase in non-CABG-related

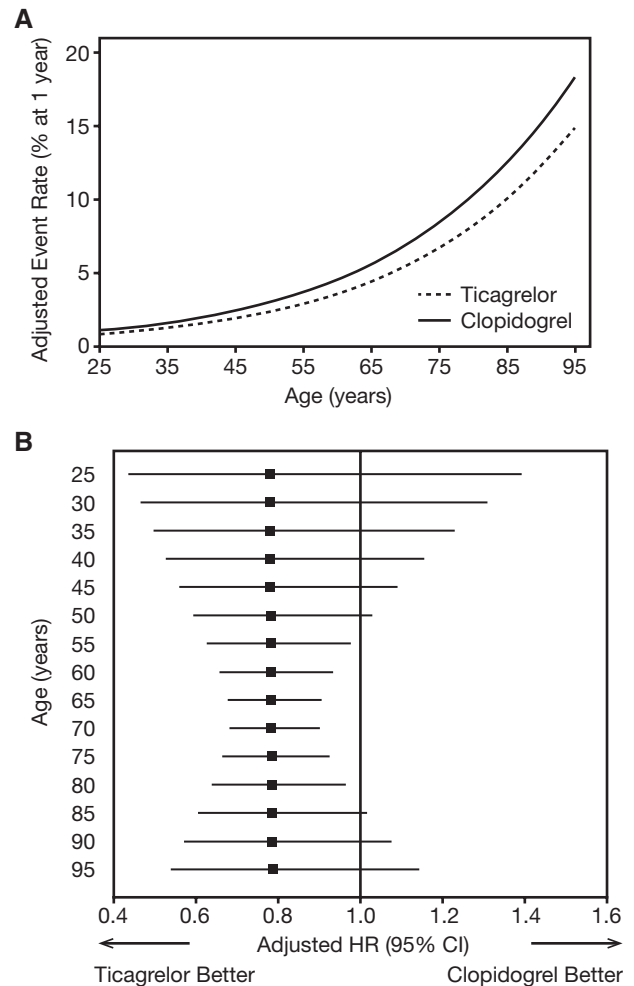


Figure 4. All-cause mortality according to age. **A**, Estimated event rate at 12 months, ticagrelor vs clopidogrel. **B**, treatment effect by patient age. HR indicates hazard ratio; CI, confidence interval.

major bleeding with ticagrelor versus clopidogrel was numerically greater in elderly (1.2%) versus younger (0.7%) patients (HR, 1.18 and 1.19, respectively).

This subanalysis of the PLATO study also demonstrated the generally higher-risk profile of elderly versus younger ACS patients. Among other risk factors, patients aged ≥ 75 years had significantly lower body weight and estimated glomerular filtration rate, along with higher rates of renal disease, pre-existing CV diseases, and prior intervention. Age was also associated with mortality, ischemic, and bleeding outcomes, irrespective of treatment received and independently of baseline characteristics. As would be expected, the incidence of the primary composite outcome (CV death/MI/stroke), its individual components, as well as stent thrombosis, and all-cause mortality were significantly higher in the older subgroup.

Outcomes in age-based subgroups have been evaluated in other phase III studies of oral antiplatelet agents. The Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel—Thrombolysis in Myocardial Infarction 38 (TRITON-TIMI 38) trial compared prasugrel (60-mg loading dose followed by 10 mg/d) with clopidogrel (300-mg loading dose followed by 75 mg/d) in 13 608

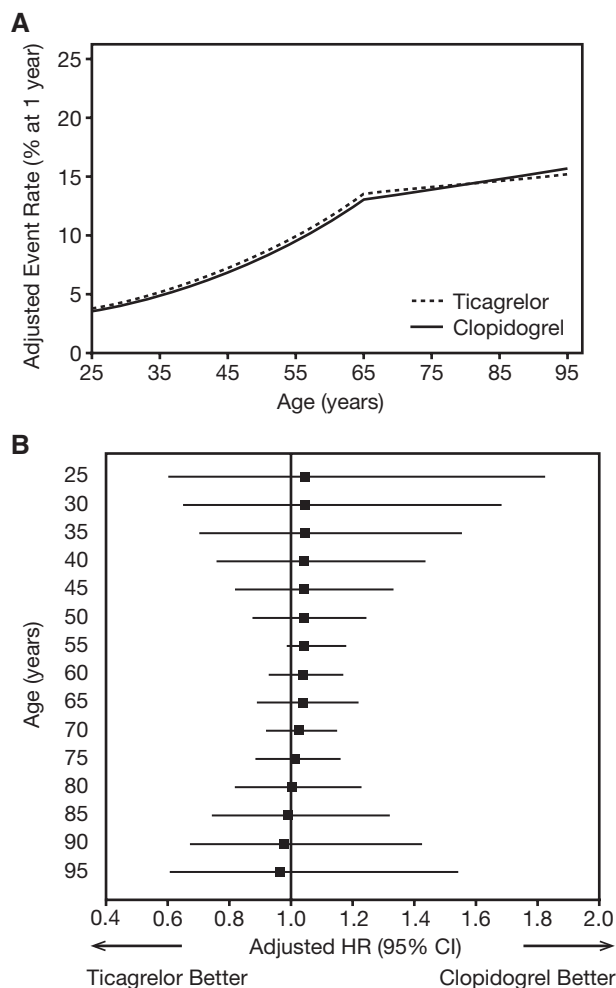


Figure 5. Overall major bleeding (PLATElet inhibition and patient Outcomes (PLATO)-defined)²² according to age*. **A**, Estimated event rate at 12 months, ticagrelor vs clopidogrel. **B**, treatment effect by patient age. *As the relationship between age and major bleeding was not linear, age was considered as 2 linear splines. HR indicates hazard ratio; CI, confidence interval.

patients with moderate- to high-risk ACS and planned percutaneous coronary intervention.²⁴ Elderly patients had substantially higher event rates and a diminished benefit of prasugrel (17.2% prasugrel versus 18.3% clopidogrel) compared with primary efficacy events for prasugrel versus clopidogrel in the overall cohort (9.9% versus 12.1%; HR, 0.81; $P < 0.001$). In addition, prasugrel was associated with higher absolute non-CABG-related TIMI major bleeding rates (4.3% versus 3.3%) and an excess of spontaneous fatal hemorrhage in elderly patients, eliminating the net benefit in this subpopulation. Indeed, regulatory authorities in the United States and Europe have discouraged the use of prasugrel in elderly (≥ 75 years of age) patients.^{25,26} In the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial, clopidogrel plus aspirin resulted in a 20% relative reduction in the first primary composite outcome of death from cardiovascular causes, non-fatal MI, or stroke, at 12 months versus aspirin alone.²⁷ When compared with younger patients (< 65 years of age), patients ≥ 65 years of age had a smaller relative risk reduction (13.1% versus 28.9%), but a similar, significant absolute risk reduction (2.0% versus 2.2%) with clopidogrel plus aspirin, versus

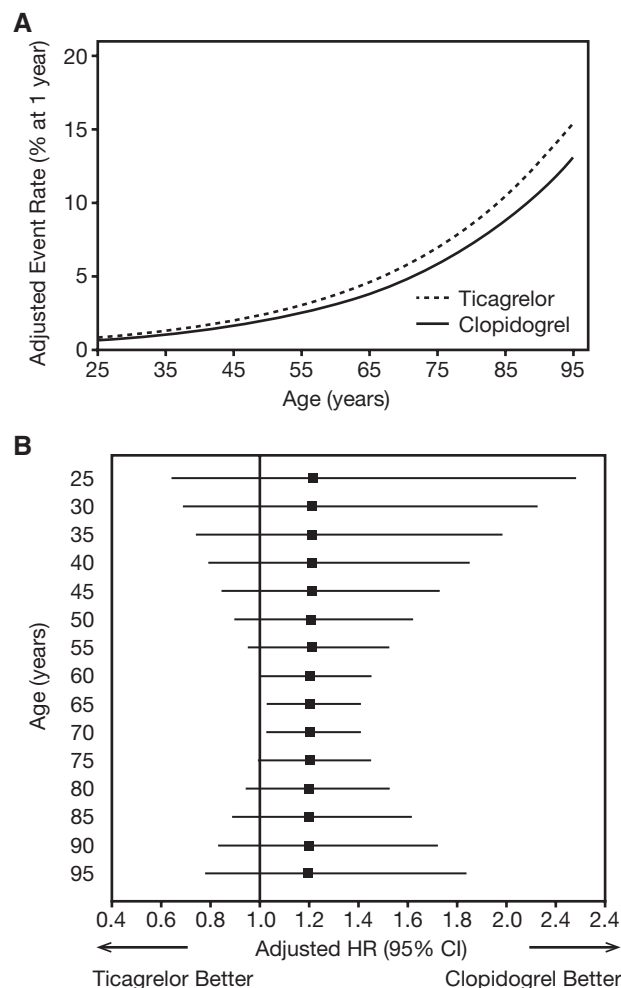


Figure 6. Overall non-coronary artery bypass graft-related bleeding (PLATElet inhibition and patient Outcomes (PLATO)-defined)²² according to age. **A**, Estimated event rate at 12 months, ticagrelor vs clopidogrel. **B**, treatment effect by patient age. HR indicates hazard ratio; CI, confidence interval.

aspirin alone.^{19,27} Similarly, the substudy of CURE evaluating patients undergoing percutaneous coronary intervention (PCI CURE) reported a relative risk for CV death/MI at 12 months for clopidogrel versus placebo of 0.79 (95% CI, 0.57–1.08) in the subgroup ≥ 65 years of age versus 0.59 (95% CI, 0.41–0.84) in younger patients.²⁸ The corresponding reductions in absolute risk were 3.5% and 3.9%, respectively.²⁸

One limitation of the present analysis is that, although the analyses based on age groups were prespecified, the subgroup of patients aged ≥ 75 years was relatively small ($n = 2878$), which would have affected the power to reach statistical significance in comparisons between the treatment groups. Although these exploratory analyses performed comparisons not corrected for multiplicity, the treatment-by-interaction significance levels for all tested outcomes suggested no treatment-by-age effect. Randomization in PLATO was not stratified by age group, but baseline characteristics were adequately matched between the treatment groups in each age category (data not shown). A similar pattern of results for the main end points of the PLATO trial was obtained when a cut-off of 65 years was used to define age categories: the effects of

Table 2. Side Effects: Dyspnea and Holter Monitoring

	Ticagrelor (n=9333)	Clopidogrel (n=9291)	HR (95% CI)	Interaction P
	KM %	KM %		
Dyspnea				
≥75 y	18.8	12.2	1.63 (1.33–1.90)	0.21
<75 y	14.2	7.8	1.89 (1.70–2.09)	
Ventricular pauses				
First week	% (n=1461)	% (n=1432)	OR (95% CI)	
≥3 s				
≥75 y	7.2	6.9	1.06 (0.54–2.08)	0.14
<75 y	5.5	2.9	1.92 (1.26–2.93)	
≥5 s				
≥75 y	2.8	2.7	1.05 (0.36–3.05)	0.28
<75 y	1.8	0.9	2.14 (1.01–4.55)	
At 30 days	% (n=992)	% (n=1012)	OR (95% CI)	
≥3 s				
≥75 y	2.4	3.4	0.70 (0.20–2.54)	0.29
<75 y	2.1	1.3	1.57 (0.73–3.38)	
≥5 s				
≥75 y	0.0	1.1	—	—
<75 y	1.0	0.5	2.03 (0.61–6.77)	

KM indicates Kaplan–Meier estimate; HR, hazard ratio; and CI, confidence interval; OR, odds ratio.

ticagrelor compared with clopidogrel were independent of age (<65 versus ≥65 years of age) for the primary composite outcome (interaction $P=0.86$) and the primary safety outcome of major bleeding (interaction $P=0.42$).²³

Conclusions

In elderly subjects, ACS carries an increased risk of recurrent ischemic events and death that can be reduced by antiplatelet therapy. This predefined subanalysis assessed clinical outcomes in elderly (≥75 years of age) versus younger (<75 years of age) patients in the PLATO trial and showed that ticagrelor compared with clopidogrel reduced ischemic outcomes and mortality without increasing overall major bleeding rates; these advantages were not found to depend on age category. The present findings are consistent with the overall results of the PLATO trial, and suggest that the antithrombotic benefits of ticagrelor also apply to the age group >75 years.

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