Contemporary antiplatelet therapy in acute coronary syndromes: are there differences in outcomes and discontinuation between clopidogrel and ticagrelor?

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Key words
acute coronary syndromes, antiplatelet therapy, clinical outcome.

Abstract

Background/Aim: We studied clinical outcomes and discontinuation rates in a ‘real-world’ population presenting with myocardial infarction treated with ticagrelor or clopidogrel.

Methods: Between January 2012 and May 2015, 992 patients with acute myocardial infarction undergoing invasive management and adequately pre-treated with dual anti-platelet therapy were prospectively enrolled. Platelet aggregation was measured using the Multiplate analyser. Baseline characteristics, in-hospital outcomes and 1-year outcomes were collected.

Results: Patients treated with ticagrelor were younger and less likely to be diabetic, have a previous myocardial infarction or present with a ST-elevation myocardial infarction (all \( P < 0.05 \)). Those treated with ticagrelor also had lower CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines; 20/19 vs 23/10.1, \( P < 0.0001 \)) and GRACE (119/28 vs 126/32, \( P = 0.002 \)) scores. High platelet reactivity was greatly reduced with ticagrelor compared to clopidogrel (16.1% vs 37.0%, respectively; \( P < 0.0001 \)). Non-coronary artery bypass grafting-related thrombolysis in myocardial infarction major and minor bleeding occurred at similar rates in those treated with ticagrelor and clopidogrel. Rates of drug discontinuation in those treated with ticagrelor and clopidogrel were similar in hospital (20.2% vs 16.2%, \( P = 0.18 \)) and between discharge and 1 year (29.9% vs 27.9%, \( P = 0.63 \)). However, discontinuation due to dyspnoea, (3.3% vs 0%, \( P < 0.0001 \)) and discontinuation due to any possible drug-related adverse event (9.3% vs 2.2%, \( P = 0.0001 \)) was more common in those treated with ticagrelor compared to clopidogrel.

Conclusion: Ticagrelor is paradoxically being used in lower-risk patients rather than those most likely to benefit. Ticagrelor was associated with similar rates of bleeding but higher discontinuation rates due to adverse effects compared to clopidogrel.

Introduction

Dual antiplatelet therapy (DAPT) with aspirin and a P2Y\(_{12}\) receptor antagonist is a cornerstone of therapy for acute coronary syndromes (ACS).\(^1\) Clopidogrel, a thienopyridine, has been the standard P2Y\(_{12}\) receptor antagonist prescribed for ACS but has a number of limitations, the most important of which is significant inter-patient variability in the levels of the active metabolite and effect of the drug.\(^2\)\(^3\) Ticagrelor, a drug in a new chemical class, is a direct-acting, reversible P2Y\(_{12}\) receptor antagonist, which does not require metabolism for activity, unlike the thienopyridines.\(^4\)\(^5\)

In the landmark Platelet Inhibition and Patient Outcomes (PLATO) trial, therapy with ticagrelor demonstrated superior efficacy in cardiovascular outcomes compared to clopidogrel in patients with ACS, regardless of whether invasive or non-invasive management was planned.\(^6\)\(^7\) On the basis of this trial, ticagrelor is now recommended as first-line therapy for patients with ACS in international guidelines.\(^8\)\(^9\)\(^10\)

Although ticagrelor represents advancement in antiplatelet therapy, several adverse effects have been
informed consent was obtained from all patients. The study was approved by the Upper South A Regional Ethics Committee (URA/11/05/016), and written informed consent was obtained from all patients who were recruited 1064 patients between January 2012 and May 2015. Patients with acute myocardial infarction undergoing invasive management, who were adequately pre-treated with dual antiplatelet therapy, were eligible for enrolment. Patients were excluded if they had a platelet count less than 100 × 10⁹/L, known platelet function disorder, administration of a fibrinolytic agent within 24 h of enrolment or administration of a glycoprotein IIb/IIIa receptor antagonist within a week prior to enrolment. From this cohort, we excluded 56 patients who were subsequently reclassified as having an alternative diagnosis (myocarditis, pericarditis, takotsubo cardiomyopathy, other diagnosis). Eight patients (0.8%) were lost to follow up and were excluded from analysis, leaving 992 patients in the final analysis of this study. All patient management and treatment decisions were at the discretion of the attending physician. A regional guideline was introduced in 2013 stating that ticagrelor was the drug of choice in moderate- to high-risk ACS without high bleeding risk. The study was approved by the Upper South A Regional Ethics Committee (URA/11/05/016), and written informed consent was obtained from all patients.

**Methods**

**Study design and population**

In this prospective, single-centre, cohort study, we recruited 1064 patients between January 2012 and May 2015. Patients with acute myocardial infarction undergoing invasive management, who were adequately pre-treated with dual antiplatelet therapy, were eligible for enrolment. Patients were excluded if they had a platelet count less than 100 × 10⁹/L, known platelet function disorder, administration of a fibrinolytic agent within 24 h of enrolment or administration of a glycoprotein IIb/IIIa receptor antagonist within a week prior to enrolment. From this cohort, we excluded 56 patients who were subsequently reclassified as having an alternative diagnosis (myocarditis, pericarditis, takotsubo cardiomyopathy, other diagnosis). Eight patients (0.8%) were lost to follow up and were excluded from analysis, leaving 992 patients in the final analysis of this study. All patient management and treatment decisions were at the discretion of the attending physician. A regional guideline was introduced in 2013 stating that ticagrelor was the drug of choice in moderate- to high-risk ACS without high bleeding risk. The study was approved by the Upper South A Regional Ethics Committee (URA/11/05/016), and written informed consent was obtained from all patients.

**Data collection**

Patient demographics, clinical characteristics, medications, clinical management and procedural variables were collected prospectively from a review of the medical records and the cardiac catheterisation database. Follow-up data were collected from the National Admissions Database and with telephone calls at 30 days and 1 year. Additional data related to dyspnoea were collected from a subset of 581 consecutive patients by administering a standardised questionnaire at 1 year. Where necessary, a review of case notes was performed, and the appropriate general practitioner was contacted to classify further clinical outcomes.

**Definitions**

Adequate pre-treatment with antiplatelet medications was defined as chronic therapy with aspirin (≥75 mg daily); ticagrelor (90 mg twice daily); clopidogrel (≥75 mg daily) or loading with aspirin ≥300 mg at least 2 h before, ticagrelor 180 mg at least 2 h before or clopidogrel ≥300 mg at least 6 h before enrolment. Myocardial infarction was defined according to the third universal definition of myocardial infarction. Stent thrombosis was defined according to the Academic Research Consortium criteria of definite stent thrombosis. Major adverse cardiovascular events (MACE) was defined as a composite of all-cause death, non-fatal myocardial infarction, stent thrombosis or stroke. Bleeding was defined using the thrombolysis in myocardial infarction (TIMI) major and minor bleeding criteria.

**Platelet function testing**

Blood for platelet function testing was collected using a 21-gauge needle from a peripheral vein prior to angiography or, alternatively, in the cardiac catheterisation laboratory from the arterial sheath immediately after insertion and before heparin administration. All samples were collected in tubes anticoagulated with hirudin (25 µg/mL) and tested 30 ± 15 min post-collection. Platelet aggregation was measured in whole blood by multiple electrode impedance aggregometry with the Multiplate analyser as previously described. High on-treatment platelet reactivity (HPR) was defined as >46 AU.

**Statistical analysis**

Categorical variables are expressed as frequencies and percentages. Continuous variables are expressed as mean ± standard deviation or median and interquartile range for non-parametric variables. Statistical analyses were performed with Chi squared tests for categorical data and independent t-tests or the Mann–Whitney U test for continuous data. As the assignment of antiplatelet therapy was at the discretion of the treating physician, the increased bleeding risk, distinctive adverse effects of this novel chemical entity, including dyspnoea and ventricular pauses, have also been reported. Clinical trial populations are often highly selective and tend to exclude those who are likely to be non-compliant or at high risk of drug-related adverse events. It is therefore possible that the safety profile and discontinuation rates of ticagrelor may differ in a ‘real-world’ population. We therefore conducted a prospective registry to evaluate prescription patterns and rates of adverse events, including bleeding, dyspnoea and bradyarrhythmias, as well as discontinuation rates in patients presenting with myocardial infarction treated with ticagrelor and clopidogrel in routine clinical practice.
physicians, there was significant discontinuation, and switching of the primary approach to analysis was an ‘on-treatment’ analysis. For this, events that occurred >1 week after discontinuation were censored. A secondary ‘intention-to-treat’ analysis was also performed. For all statistical analyses, a P-value <0.05 was considered significant. All statistical analyses were conducted using SPSS v.22 (IBM; New York, NY, USA).

Results

Of the 992 patients in the study cohort, 243 (24.5%) were treated with ticagrelor and 749 (75.5%) with clopidogrel at the time of enrolment. During the study, the frequency with which ticagrelor was prescribed slowly increased, with ticagrelor being prescribed in 52.9% of patients during the last 6 months of the study period (Fig. 1). Patient demographics and clinical characteristics are shown in Table 1. Patients treated with ticagrelor were younger (61.5 ± 9.6 years vs 64 ± 11 years, P = 0.002) and were less likely to be diabetic (13.6% vs 21.4%, P = 0.008), have a past history of myocardial infarction (16.4% vs 26.6%, P = 0.001), have a history of atrial fibrillation (3.7% vs 7.3%, P = 0.45) or present with a ST-elevation myocardial infarction (14% vs 20.8%, P = 0.019). Those treated with ticagrelor had lower CRUSADE (Can Rapid risk stratiﬁcation of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines) (20 ± 9.4 vs 23 ± 10.1, P < 0.0001) and GRACE (119 ± 28 vs 126 ± 32, P = 0.002) scores. They were also more likely to undergo revascularisation.

Platelet function testing

Patients administered ticagrelor demonstrated significantly lower platelet reactivity when stimulated with adenosine diphosphate than patients administered clopidogrel (26 AU (18–39) vs 37 AU (34–56), P < 0.0001) (Fig. 2). The proportion of patients with HPR was also greatly reduced in the ticagrelor group (16.1% vs 37.0%, respectively; P < 0.0001).

Drug efficacy

MACE at 1 year was numerically reduced in those treated with ticagrelor (7.1% vs 11%, P = 0.07), but this did not reach statistical significance (Table 2). Rates of each of the components of the composite endpoint and stent thrombosis were all numerically lower in those treated with ticagrelor compared to clopidogrel, but none of these differences was statistically significant (Table 2). An intention-to-treat analysis yielded similar results, with MACE at 1 year being numerically lower but not statistically different in those treated with ticagrelor (9.1% vs 12.8%, P = 0.11).

Bleeding

On-treatment analysis demonstrated that TIMI major bleeding was infrequent, occurring in none of the ticagrelor treated group and in 1.1% of the clopidogrel treated group (P = 0.09, Table 2). TIMI minor bleeding at 1 year was more common and occurred at similar rates in the ticagrelor-treated patients compared to the clopidogrel-treated patients (11.9% vs 11.2%, P = 0.73).

Figure 1 Change in prescription rates of ticagrelor and clopidogrel over time. (–), Clopidogrel; (––), ticagrelor.
An intention-to-treat analysis yielded very similar results, with TIMI major or minor bleeding occurring in 14% of those treated with ticagrelor and 13.2% of those treated with clopidogrel ($P = 0.76$).

**Dyspnoea**

A subgroup of 581 consecutive patients was asked about dyspnoea at 1 year. Dyspnoea was commonly reported in the year following hospital discharge and occurred at similar rates in patients treated with ticagrelor and clopidogrel (37.4% vs 34.8%, $P = 0.82$). When asked whether this dyspnoea was new or worsened compared to that experienced prior to their myocardial infarction, similar numbers treated with ticagrelor and clopidogrel (27.8% vs 23%, $P = 0.44$) reported that it was. Discontinuation of therapy due to dyspnoea was infrequent but occurred more commonly in those treated with ticagrelor compared with clopidogrel (3.3% vs 0%, $P < 0.0001$).

**Table 1** Demographics, clinical characteristics and management strategies

<table>
<thead>
<tr>
<th></th>
<th>All MI, $n = 992$</th>
<th>Ticagrelor, $n = 243$</th>
<th>Clopidogrel, $n = 749$</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63.4 ± 10.7</td>
<td>61.5 ± 9.6</td>
<td>64 ± 11</td>
<td>0.002</td>
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<tr>
<td>Male gender</td>
<td>717 (72.3)</td>
<td>184 (75.7)</td>
<td>533 (71.2)</td>
<td>0.168</td>
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<td>BMI (kg/m²)</td>
<td>29.3 ± 5.6</td>
<td>29.2 ± 5.2</td>
<td>29.3 ± 5.7</td>
<td>0.922</td>
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<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>849 (85.6)</td>
<td>211 (86.8)</td>
<td>638 (85.2)</td>
<td>0.784</td>
</tr>
<tr>
<td>Maori and PP</td>
<td>110 (11.1)</td>
<td>24 (9.9)</td>
<td>86 (11.5)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>33 (3.3)</td>
<td>8 (3.3)</td>
<td>25 (3.3)</td>
<td></td>
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<tr>
<td>Diabetes</td>
<td>193 (19.5)</td>
<td>33 (13.6)</td>
<td>160 (21.4)</td>
<td>0.008</td>
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<td>Hypertension</td>
<td>606 (61.2)</td>
<td>141 (58)</td>
<td>465 (62.1)</td>
<td>0.260</td>
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<tr>
<td>Dyslipidaemia</td>
<td>688 (69.4)</td>
<td>159 (65.4)</td>
<td>529 (70.6)</td>
<td>0.127</td>
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<tr>
<td>Current smoker</td>
<td>224 (22.6)</td>
<td>55 (22.6)</td>
<td>169 (22.6)</td>
<td>0.345</td>
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<tr>
<td>Family history of premature CAD</td>
<td>363 (36.6)</td>
<td>90 (37)</td>
<td>273 (36.4)</td>
<td>0.869</td>
</tr>
<tr>
<td>Prior MI</td>
<td>238 (23.4)</td>
<td>39 (16.4)</td>
<td>199 (26.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>68 (6.9)</td>
<td>10 (4.1)</td>
<td>58 (7.7)</td>
<td>0.052</td>
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<tr>
<td>Heart failure</td>
<td>17 (1.7)</td>
<td>1 (0.4)</td>
<td>16 (2.1)</td>
<td>0.072</td>
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<tr>
<td>Renal dysfunction</td>
<td>53 (5.3)</td>
<td>9 (3.7)</td>
<td>44 (5.9)</td>
<td>0.191</td>
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<tr>
<td>Atrial fibrillation</td>
<td>64 (6.5)</td>
<td>9 (3.7)</td>
<td>55 (7.3)</td>
<td>0.045</td>
</tr>
<tr>
<td>STEMI</td>
<td>190 (19.2)</td>
<td>34 (14)</td>
<td>156 (20.8)</td>
<td>0.019</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>802 (80.8)</td>
<td>209 (86)</td>
<td>593 (79.2)</td>
<td></td>
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<tr>
<td>CRUSADE</td>
<td>22 ± 10</td>
<td>20 ± 9.4</td>
<td>23 ± 10.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>GRACE</td>
<td>125 ± 31</td>
<td>119 ± 28</td>
<td>126 ± 32</td>
<td>0.002</td>
</tr>
<tr>
<td>Management strategy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>250 (25.2)</td>
<td>44 (18.1)</td>
<td>206 (27.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>PCI</td>
<td>599 (60.4)</td>
<td>156 (64.2)</td>
<td>443 (59.1)</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>143 (14.4)</td>
<td>43 (17.7)</td>
<td>100 (13.4)</td>
<td></td>
</tr>
</tbody>
</table>

BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CRUSADE, Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines; GRACE, Global Registry of Acute Coronary Events; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; PP, Pacific peoples; STEMI, ST-elevation myocardial infarction.

An intention-to-treat analysis yielded very similar results, with TIMI major or minor bleeding occurring in 14% of those treated with ticagrelor and 13.2% of those treated with clopidogrel ($P = 0.76$).

**Figure 2** (A) Platelet reactivity of patients treated with ticagrelor ($n = 237$) and clopidogrel ($n = 746$) analysed by Mann–Whitney U-test ($P < 0.0001$). The red dotted line represents the 47 AU high on-treatment platelet reactivity (HPR) threshold. The median and interquartile range are represented in blue. (B) The rate of HPR in patients treated with ticagrelor and clopidogrel analysed by Chi-squared test ($P < 0.0001$).
Bradycardia

Presentations with presyncope, syncope or bradyarrhythmias requiring admission were rare, occurring in two patients (0.8%) treated with ticagrelor and 6 (0.8%) patients treated with clopidogrel. Two patients required pacemakers, both of whom were treated with clopidogrel.

Drug discontinuation and switching

Similar rates of drug discontinuation were seen in those treated with ticagrelor and clopidogrel in hospital (20.2% vs 16.2%, \( P = 0.18 \)), between discharge and 30 days (4.2% vs 4.5%, \( P = 0.99 \)) and between discharge and 1 year (29.9% vs 27.9%, \( P = 0.63 \)). The most common reasons for drug discontinuation were prior to cardiac bypass surgery (ticagrelor 18.1%, clopidogrel 13.4%) and prescription for less than 1 year (ticagrelor 12.6%, clopidogrel 17.2%) (Figs 3, 4). Patients who were medically managed were much more likely to have DAPT prescribed for less than 12 months compared to those treated with percutaneous coronary intervention (PCI; 52.7% vs 4%, \( P < 0.0001 \)). Discontinuation due to a possible drug-related adverse event was more common in those treated with ticagrelor compared to clopidogrel (9.3% vs 2.2%, \( P = 0.0001 \)). Following discontinuation, switching from ticagrelor to clopidogrel occurred in 9.9% and was more frequent than switching from clopidogrel to ticagrelor (3.3%, \( P < 0.0001 \)).

<table>
<thead>
<tr>
<th>Clinical outcomes – on-treatment analysis</th>
<th>30-day outcomes</th>
<th>1-year outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ticagrelor, ( n = 263 )</td>
<td>Clopidogrel, ( n = 763 )</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
<td>8 (1.0)</td>
</tr>
<tr>
<td>Spontaneous MI</td>
<td>0 (0)</td>
<td>6 (0.8)</td>
</tr>
<tr>
<td>Peri-procedural MI</td>
<td>9 (3.4)</td>
<td>29 (3.8)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2 (0.4)</td>
<td>3 (0.3)</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>0</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>All MACE</td>
<td>11 (4.2)</td>
<td>43 (5.6)</td>
</tr>
</tbody>
</table>

MACE, major adverse cardiovascular events; MI, myocardial infarction; TIMI, thrombolysis in myocardial infarction.

**Table 2**

**In-Hospital discontinuation**

![In-Hospital discontinuation](image1)

**Discontinuation from discharge to 1 year**

![Discontinuation from discharge to 1 year](image2)

**Figure 3** Reasons for in-hospital discontinuation of antplatelet medication in patients treated with either ticagrelor or clopidogrel. □, Ticagrelor; □, clopidogrel. CABG, coronary artery bypass grafting.

**Figure 4** Reasons for antiplatelet medication discontinuation between discharge and 1 year in patients treated with either ticagrelor or clopidogrel. □, Ticagrelor; □, clopidogrel; ACS, acute coronary syndromes; CABG, coronary artery bypass grafting.
Discussion

The major finding of this study is that ticagrelor treatment in this real-world cohort of ACS patients was well tolerated, with low rates of bleeding and discontinuation due to dyspnoea and bradycardia. This study also demonstrated that, paradoxically, those treated with ticagrelor were at lower ischaemic risk, being younger with fewer risk factors and a lower mean GRACE score. Discontinuation of both ticagrelor and clopidogrel before 1 year was common and occurred at a similar rate, with the most frequent reasons being discontinuation prior to CABG and prescription for a shorter duration.

Our study demonstrated that there was a selection bias when allocating antplatelet therapy. Paradoxically, those treated with ticagrelor had a lower overall ischaemic risk, being younger with a lower prevalence of diabetes, prior myocardial infarction and a lower GRACE score. This finding is not unique to our cohort. In both the SWEDHEART and TRANSLATE registries, patients prescribed ticagrelor or prasugrel had lower ischaemic risk than those prescribed clopidogrel.20,21 These findings suggest that, as physicians, we may be more focused on avoiding harm than ischaemic benefit. An important implication of this study is that if we reallocate use of ticagrelor to include those at higher ischaemic risk, then we might be able to derive a larger therapeutic benefit in clinical practice.

Consistent with previous studies, we found ticagrelor to have more potent platelet inhibition and a greatly reduced frequency of HPR.4,11 As such, one may expect that ticagrelor treatment would be associated with greater bleeding. Consistent with this, the PLATO study found that ticagrelor was associated with a small but significant increase in non-CABG-related major bleeding according to the PLATO-defined criteria (4.5% vs 3.8%, \( P = 0.03 \)) and the TIMI criteria (2.8% vs 2.2%, \( P = 0.03 \)). However, in this study, at 1 year, there was no non-CABG-related TIMI major bleeding in those treated with ticagrelor, and rates of non-CABG-related TIMI minor bleeding were similar with ticagrelor and clopidogrel treatment. It is possible that this finding may be related to the differences in baseline characteristics between the two treatment groups. The ticagrelor group did have a statistically lower CRUSADE risk score, but the numerical difference was small, with both means being within the low-risk range. An analysis from the SWEDHEART registry, the largest real-world study comparing ticagrelor with clopidogrel, found that ticagrelor was associated with a small increase in re-admission, with bleeding with ticagrelor versus clopidogrel occurring in 5.5% versus 5.2% (adjusted hazard ratio 1.20 (1.04–1.40)).20

In our study, dyspnoea was commonly reported in the year following myocardial infarction, occurring at similar rates in patients treated with ticagrelor and clopidogrel (37% vs 34.8%, \( P = 0.82 \)). Dyspnoea is a well documented, dose-dependent adverse effect of ticagrelor and a potential cause for the premature discontinuation of the drug.4,11 However, dyspnoea following myocardial infarction may occur for a number of other reasons, including heart failure, recurrent ischaemia, respiratory infections, anaemia, adverse reactions to beta-blockers and pre-existing respiratory disorders. In the Prospective Registry Evaluating Myocardial Infarction: Events and Recovery (PREMIER) of 1835 patients who survived acute myocardial infarction, 47% of patients, none of whom was treated with ticagrelor, reported dyspnoea at 1 month.22

The rates of discontinuation of ticagrelor due to dyspnoea have varied considerably in previous studies, ranging from 0.9% in the PLATO trial to 14.3% in a retrospective cohort study.2,7–20 Discontinuation of ticagrelor due to dyspnoea at 1 year in our study was infrequent but occurred more commonly when compared to those treated with clopidogrel (3.3% vs 0%, \( P < 0.0001 \)). The reason for the variation in the reported rates of dyspnoea-related discontinuation is likely to be multifactorial. However, it is likely that patient and physician education plays an important role.

Discontinuation of both ticagrelor and clopidogrel in the year following enrolment was common and occurred at similar rates. The most common reason for discontinuation in hospital was CABG, while in the year following discharge, the most common reason for discontinuation was prescription for less than 12 months. Prescription duration of less than a year was more common in those managed without revascularisation compared with those managed with PCI. Subgroup analysis from the CURE, PLATO and TRITON-TIMI 38 studies have all consistently shown benefit for DAPT following ACS patients whether patients are treated medically, with CABG or PCI.5,7,27–30 As a result, current guidelines recommend treatment with DAPT for 12 months in all of these groups. However, it appears that some physicians and surgeons are either not aware or convinced by the data supporting post-CABG DAPT or the need for treatment with DAPT for 12 months following a myocardial infarction in patients who do not undergo revascularisation.

A limitation of our study is the observational design, which meant that treatment assignment was at the discretion of treating physicians. Selection bias resulted in significant baseline differences between those treated with ticagrelor and clopidogrel, which in itself is an important finding of this study. The study was not powered to find differences in ischaemic outcomes, but our findings are consistent with the greater reduction of
recurrent ischaemic events in those treated with ticagrelor in the PLATO study. We did not find a difference in TIMI major or minor bleeding between the treatment groups. One possible explanation for this is that baseline differences between the groups meant that the ticagrelor group had a lower bleeding risk. Whilst there was a statistically significant difference in the CRUSADE scores between the groups, the absolute difference of 3 points is small and would not be expected to have a major clinical impact. We did not attempt to adjust for these baseline differences given the lower number of bleeding events.

**Conclusion**

Our study demonstrated that, in clinical practice, ticagrelor is preferentially being used in lower-risk patients rather than those most likely to benefit. Ticagrelor was well tolerated in this real-world cohort, with discontinuation due to bleeding, dyspnoea or bradyarrhythmia being relatively uncommon. However, discontinuation following CABG and prescription for a period of less than 12 months was common, particularly in those treated without revascularisation. These findings suggest that further education of physicians and surgeons is warranted.

**References**


