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Authors

Ozaki, Aya F
Jackevicius, Cynthia A
Chong, Alice
et al.

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ORIGINAL RESEARCH

Hospital-Level Variation in Ticagrelor Use in Patients With Acute Coronary Syndrome

Aya F. Ozaki (ID), BSPharm, PharmD; Cynthia A. Jackevicius (ID), BScPhm, PharmD, MSc; Alice Chong, BS; Maneesh Sud, MD; Jiming Fang, PhD; Peter C. Austin (ID), PhD; Dennis T. Ko (ID), MD, MSc

BACKGROUND: Despite improved outcomes associated with ticagrelor compared with clopidogrel in acute coronary syndrome (ACS), many studies have demonstrated slow adoption of ticagrelor in the United States because of its increased cost. Less is known about how ticagrelor is adopted when there is no added cost consideration. Our objectives were to determine patterns of use of ticagrelor, hospital-level adoption of ticagrelor use, and factors associated with its use after ACS in a publicly funded health care system.

METHODS AND RESULTS: We conducted a population-based cohort study including patients (≥65 years) hospitalized with their first ACS from April 2014 to March 2018 in Ontario, Canada. We determined temporal trends in ticagrelor use and hospital-level adoption of its use post-ACS discharge. Using hierarchical regression models, we identified significant predictors of ticagrelor use. There were 23 962 patients with ACS (mean age 76.3 years, 59.7% men) hospitalized in 156 hospitals. Overall ticagrelor use increased from 32.6% in 2014/2015 to 51.8% in 2017/2018. There was substantial variation in ticagrelor use post-ACS across hospitals, with hospital-specific prescribing rates ranging from 0% to 83.6%. Lower odds of ticagrelor use was associated with advanced age and the presence of comorbidities. Besides patient factors, being admitted to a rurally located hospital more than halved the odds of being prescribed ticagrelor (odds ratio [OR], 0.49; 95% CI, 0.32–0.77). Being managed by a cardiologist during the index ACS hospitalization was associated with higher odds of having a ticagrelor prescription after ACS (OR, 2.80; 95% CI, 2.36–3.33).

CONCLUSIONS: Ticagrelor use rates varied substantially across hospitals and were strongly associated with physician and hospital factors independent of patient characteristics.

Key Words: acute coronary syndrome ■ antiplatelet agents ■ hospital variation ■ outcomes research ■ quality of care ■ ticagrelor

Ticagrelor has been shown to significantly reduce cardiovascular death, myocardial infarction and stroke in patients hospitalized with an acute coronary syndrome (ACS), without significantly increasing major bleeding compared with clopidogrel.[1] Based on data from randomized clinical trials, practice guidelines from the United States, Europe, and Canada strongly endorse the use of ticagrelor over clopidogrel in patients with ACS.[2,3] Despite the increasing focus on implementing guideline-recommended therapy to clinical practice, adoption of ticagrelor in ACS appears to be relatively slow.[4–6] The National Cardiovascular Data Registry evaluated the practice of 801 hospitals in the United States to reveal that only 33.7% of patients were prescribed ticagrelor in 2017.[4] Even among patients with ST-segment–elevation myocardial infarction, rates of ticagrelor use were only 44%.[5] One of the major impediments to ticagrelor prescription in the United States is the added cost.[6,7] According to the National Average Drug Acquisition Cost, ticagrelor, which is a brand name drug, costs $7.88/day of use as opposed to only $0.11 for clopidogrel, a generic medication.[8] Few studies have evaluated ticagrelor adoption in countries where drug coverage is provided to

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CLINICAL PERSPECTIVE

What Is New?
- In this population-based study of older patients with acute coronary syndrome (aged ≥65 years) in a publicly funded health care system in Ontario, Canada, we found only half of patients with acute coronary syndrome were prescribed ticagrelor at hospital discharge in 2018.
- Ticagrelor use rates varied substantially across hospitals with its rates ranging from 0% to 83.6%.
- Ticagrelor use is strongly associated with physician and hospital factors beyond consideration of patient factors.

What Are the Clinical Implications?
- Future studies should identify hospital-level barriers of ticagrelor use and provide a standardized approach to prescribe medications.

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patients at no additional patient cost than clopidogrel. Given that Ontario provides prescriptions of ticagrelor or clopidogrel for all patients aged ≥65 years at minimal cost, if we find that adoption of ticagrelor was much higher in Canada than in the United States, then a solution could be supplementation of the added drug cost. Accordingly, the main objective of our study was to evaluate: (1) temporal trends in ticagrelor use after ACS, (2) ticagrelor adoption according to hospital of ACS admission, and (3) factors associated with its use.

METHODS

Study Design and Data Sources

We conducted an observational study using population-based health data in Ontario, Canada that included the following databases: (1) Ontario Drug Benefit database, which includes detailed information on outpatient prescription drug use for patients aged ≥65 years; (2) Canadian Institute for Health Information Discharge Abstract Database for patient comorbidities and hospital admissions; (3) Ontario Registered Persons Database, a registry of all Ontario residents with health insurance coverage providing information on vital status; and (4) Statistics Canada database to capture the median neighborhood income of patients. These data sets were linked using unique encoded identifiers and analyzed at ICES. Our group has extensive experience in linking together databases for cardiac research and additional detail can be found elsewhere.[9,10] The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board for the purpose of analysis or compiling statistical information with respect to the management of, evaluation or monitoring of, the allocation of resources to or planning for all or part of the health system. The data set from this study is held securely in coded form at ICES. While legal data sharing agreements between ICES and data providers (eg, healthcare organizations and government) prohibit ICES from making the data set publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at www.ices.on.ca/DAS (email: das@ices.on.ca).

Study Population

Patients aged ≥65 years who were hospitalized with an ACS from April 1, 2014 to March 31, 2018 in Ontario were included in the initial study sample. We chose 2014 as the start date of our cohort because ticagrelor was included on the provincial drug formulary on April 30, 2013. ACS hospitalization included myocardial infarction and unstable angina and were identified using *International Classification of Diseases, Tenth Revision* (*ICD-10*) codes I20, I21, and I22 in the Canadian Institute for Health Information Discharge Abstract Database. For each patient, only the first ACS hospitalization during the study period was included, and this served as the index hospitalization. Patients who filled a prescription for ticagrelor or clopidogrel within 7 days of discharge were included in the study cohort. Patients who had coronary artery bypass grafting or major bleeding during index hospitalization were excluded because they were unlikely to receive ticagrelor. We also excluded individuals who were prescribed warfarin or direct oral anticoagulants 90 days before index admission and after hospital discharge because they were also less likely to receive ticagrelor.

Definition of P2Y12 Inhibitor Use

A patient with ACS was considered to have been prescribed ticagrelor or clopidogrel if a prescription claim was identified in the Ontario Drug Benefit database within 7 days of hospital discharge. Additionally, we measured the proportions of patients who filled the common cardiovascular medications, including angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, beta blockers, and statins within 90 days post discharge.

Statistical Analysis

We first assessed temporal trends of ticagrelor use after ACS by determining the annual prescription rate of all patients during the study period. We then calculated the proportion of patients with ACS at each hospital that were dispensed a prescription for ticagrelor within 7 days of index ACS discharge to examine hospital variations.

We categorized hospitals into quartiles based on ticagrelor prescription rates and created strata of low, low-medium, medium, and high ticagrelor-use hospitals. Descriptive statistics were used to describe the baseline clinical characteristics between hospital groups. X^2 tests were used to compare categorical variables, and Kruskal–Wallis tests were used for the comparison of continuous variables.

Hierarchical multivariable logistic regression models were used to determine predictors of ticagrelor use among patients with ACS in the overall cohort. The following covariates were included in the model based on clinical judgment and prior studies: (1) patient characteristics, including age, sex, median neighborhood income, rural or urban residency, comorbidities, prior cardiac invasive procedures, and cardiovascular medication use within 90 days prior index admission, (2) physician characteristics, including specialty, of the most responsible physician during the index hospitalization, and (3) hospital characteristics, including teaching status, the volume of ACS, having a cardiac catheterization laboratory, and location. The regression model incorporated physician-specific and hospital-specific random effects to account for the clustering of patients within physicians and hospitals. To determine the incremental impact of patient, physician, and hospital characteristics on ticagrelor use, we evaluated sequence of multivariable logistic regression models. We quantified the between-hospital variability of ticagrelor use using the median odds ratios (OR), which is a measure obtained by comparing the odds of receiving ticagrelor at the higher-use hospital compared with the lower-use hospital.[11] Higher median OR indicates higher use of ticagrelor at the hospital level adjusting for other factors. All analyses were conducted using SAS statistical software, version 9.3 (SAS Institute, Cary, NC) and a 2-sided *P* value of <0.05 was used to determine statistical significance.

RESULTS

Study Population

We initially identified 92 657 patients who were hospitalized with an ACS from April 1, 2014 to March 31, 2018 in Ontario, Canada (Figure 1). Of those, we included patients who were between 65 to 105 years of age and filled a prescription for ticagrelor or clopidogrel within 7 days post index discharge. We excluded 11 050 patients who had coronary artery bypass grafting, major bleeding or died during the index hospitalization, and 7912 patients who received warfarin or direct oral anticoagulant 90 days before admission until 30 days post index discharge. After applying the inclusion and exclusion criteria, the final cohort consisted of 23 962 patients from 156 hospitals. Among these,

10 185 (42.5%) were prescribed ticagrelor ≤7 days post-hospital discharge and 13 777 (57.5%) were prescribed clopidogrel.

Rates of Ticagrelor Use

In the overall cohort, ticagrelor use increased from 32.6% in 2014/2015, 39.8% in 2015/2016, 46.4% in 2016/2017, and 51.8% in 2017/2018.

Figure 2 shows ticagrelor use after ACS at the hospital level and superimposed on the number of patients with ACS included at each of the 156 hospitals included in our study. Between hospitals, there was substantial variation in ticagrelor use from 0% to 83.6%. No clear relationship was seen with hospital volume qualitatively, as some high-volume hospitals had low use of ticagrelor.

Patient, Physician, and Hospital Characteristics by Ticagrelor-Use Hospital Category

Table 1 shows the patient, physician, and hospital characteristics according to quartiles of hospital ticagrelor use. The median hospital-specific ticagrelor prescription use for patients discharged post-ACS admission was 1.6%, 13.7%, 27.4%, and 50.0% in low, low-medium, medium and high ticagrelor-use hospitals. Patients hospitalized at the high ticagrelor-use hospitals appeared to differ more in that they were younger and had generally fewer comorbidities (*P*<0.001). For example, the median age was 74 years in the high ticagrelor-use hospitals and 76 years in the remaining hospitals. Rates of prior myocardial infarction were 8.7%, 8.2%, 8.2% in the lower 3 quartile hospitals and 6.4% in the high ticagrelor-use hospital. Patients differed substantially in their location of residence and the location of admitting hospitals. Patients were more likely to reside in rural areas (52.3%, 16.1%, 5.0%, and 11%) among hospitalized to low, low-medium, medium, high ticagrelor-use hospitals (*P*<0.001). Similarly, having a cardiologist as the most responsible physician for the index ACS admission differed greatly across hospital groups with 0%, 26.1%, 43.4%, and 67.9% among low, low-medium, medium, and high ticagrelor-use hospitals (*P*<0.001) (Table 1).

Evidenced-Based Therapy Use According to Ticagrelor-Use Hospitals

Significantly lower utilization of evidence-based therapy was seen in patients discharged post-ACS from lower ticagrelor-use hospitals. The use of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers was 73.3% in low, 76.5% in low-medium, 78.5% in medium and 83.3% in high ticagrelor use hospitals (*P*<0.001). Further, 1-year adherence rates of both ticagrelor and
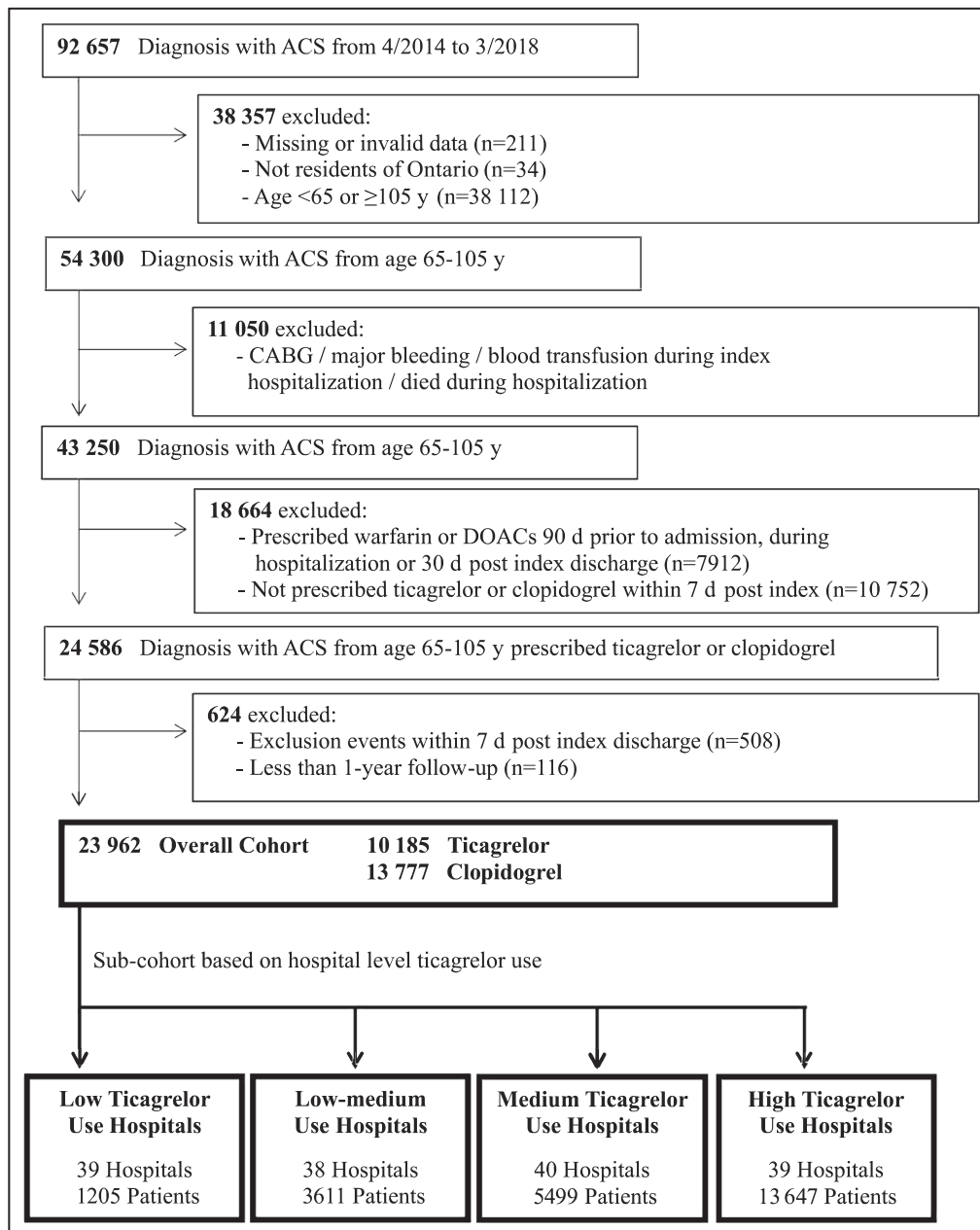
Figure 1. Flowchart of cohort creation.
ACS indicates acute coronary syndrome; CABG, coronary artery bypass grafting; and DOACs, direct oral anticoagulants.

clopidogrel were significantly higher at high ticagrelor use hospitals compared with low use hospitals (mean proportion of days covered 80.9% versus 76.7% for ticagrelor, 85.9% versus 82.5% for clopidogrel, both *P*<0.001, high versus low ticagrelor use hospitals, respectively) (Table 2).

Factors Associated With Ticagrelor Use at the Patient Level

Advanced age was significantly associated with lower odds of receiving ticagrelor after an ACS (Table 3). Compared with patients aged 65 to 74 years, the odds

of receiving ticagrelor was 0.23 (95% CI, 0.21–0.26) for patients ≥85 years, and 0.64 (95% CI, 0.66–0.69) for patients 75 to 84 years. While many clinical factors were statistically significantly associated with increased or reduced ticagrelor use, odds ratios revealed that their influence was modest. Out of these clinical factors, having prior percutaneous coronary or coronary artery bypass grafting was associated with the highest increased odds ratio (odds ratio [OR], 1.35; 95% CI, 1.15–1.58), while a history of anemia or blood disease had the lowest odds (OR, 0.75; 95% CI, 0.66–0.86, *P*<0.001) of ticagrelor use.
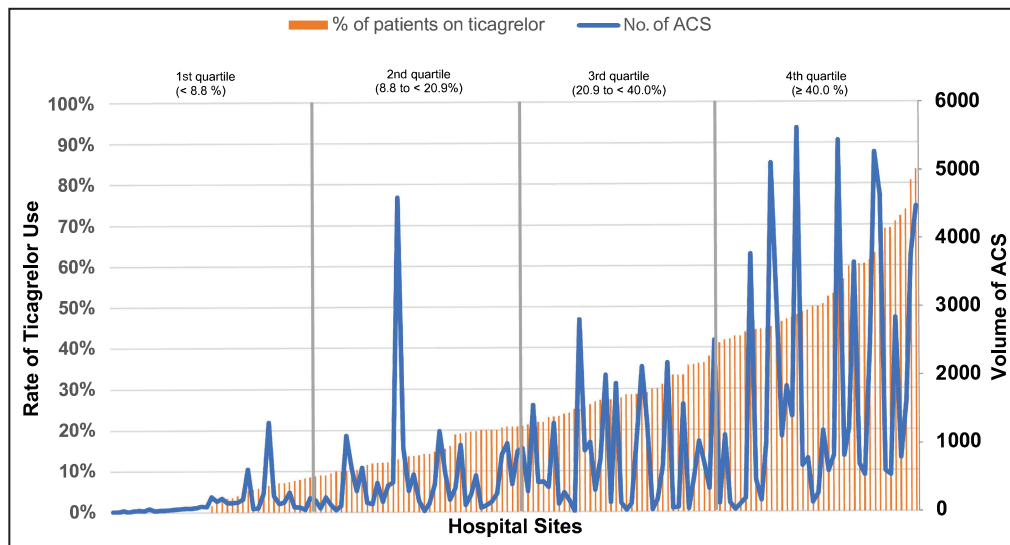
Figure 2. Ticagrelor use and acute coronary syndrome volume by hospital site.
There is a substantial hospital-level variation in ticagrelor use in patients with acute coronary syndrome without clear relationship with the volume of patients with acute coronary syndrome each hospital. ACS indicates acute coronary syndrome.

Several physician and hospital factors were strongly associated with ticagrelor prescription immediately after hospital discharge (Table 2). Being managed by a cardiologist had almost a 3-fold increase in the odds of having a ticagrelor prescription (OR, 2.80; 95% CI, 2.36–3.33). In contrast, being admitted to a rurally-located hospital reduced the odds by 51% (OR, 0.49; 95% CI, 0.32–0.77; P=0.002). Teaching hospital status and procedural volume of ACS were not significantly associated with ticagrelor use.

After adjusting for patient-, prescriber- and hospital-level characteristics, and accounting for clustering of hospitals, substantial variation remained between hospitals in the likelihood of patients receiving ticagrelor at discharge (median OR, 2.54), while the median OR without adjustment was 2.87 (Table S1).

DISCUSSION

Our study examining ticagrelor use since its first being added to provincial drug formulary afforded several new insights. First, we found slow adoption of ticagrelor treatment despite the fact that it is provided at no additional cost to patients in Ontario, Canada. Even though randomized trial data emerged in 2009 that showed ticagrelor was associated with an incremental benefit compared with clopidogrel, we found only half of all patients with ACS over 65 years were prescribed ticagrelor at hospital discharge. We observed that older patients or patients who had more medical comorbidities were less likely to be treated with ticagrelor. Yet, nonclinical factors such as physician and

hospital factors appeared to be even more influential in the decision for ticagrelor prescription.

Our study adds to the literature showing that ticagrelor adoption is relatively slow globally. Turgeon et al evaluated patients with ACS undergoing percutaneous coronary intervention from 2012 to 2016 in Alberta, Canada and found that 36.4% of patients used ticagrelor.[12] Data from South Korea found ticagrelor use was 32% in 2016.[13] In patients with ST-segment myocardial infarction, Schucker found ticagrelor use to be at ≈60% for patients aged >75 years in Germany while Szummer and colleagues found 39.8% use among patients aged >80 years in Sweden.[14,15] Even without the cost burdens for the patient populations in our study, we demonstrated suboptimal use of ticagrelor, highlighting that needs to overcome noncost related barriers as well to improve medication use.

Although rates of major bleeding were not statistically different between ticagrelor and clopidogrel in the Study of Platelet Inhibition and Patient Outcomes (PLATO) trial, the rates of other bleeding types, such as non-CABG-related major bleeding, were significantly higher in ticagrelor, and observational studies have consistently demonstrated that ticagrelor use is associated with more bleeding among patients with ACS.[1,9,15,16] Not surprisingly, we found that advanced age, history of bleeding, and other comorbidities reduced odds of ticagrelor prescriptions, which was also consistent with other data.[4,5] Adverse event concerns have been demonstrated to be strongly associated with evidence-based treatments even more than its potential incremental benefit, which could have in part explained our observation that higher risk patients were less likely to receive ticagrelor.[17]

Table 1. Patients, Physicians, and Hospitals Characteristics by Quartile of Ticagrelor Use

Characteristics	Quartiles			
	Q1 Low	Q2 Low-medium	Q3 Medium	Q4 High
Hospital ticagrelor use, %	<8.8	8.8 to <20.9	20.9 to <40.0	≥40.0
Hospital ticagrelor use, %, median (IQR)	1.6 (0.0–6.5)	13.7 (10.5–19.1)	27.4 (23.7–31.6)	50.0 (44.7–61.3)
No. of hospitals	39	38	40	39
No. of patients	1205	3611	5499	13 647
Patient characteristics, %				
Age categories, y				
65–74	43.4	45.8	44.5	50.3
75–84	34.0	33.0	33.4	33.1
≥85	22.6	21.2	22.1	16.7
Men	56.3	58.3	57.7	61.1
Income quintiles				
Highest	15.4	14.6	17.8	17.9
Rural	53.9	32.0	14.4	8.9
Cardiovascular comorbidities				
Prior myocardial infarction	8.7	8.2	8.2	6.4
Chronic ischemic heart disease	18.6	18.8	20.3	17.2
Angina*	6.6	5.9	6.0	5.5
Atrial fibrillation/flutter	3.6	3.8	3.6	2.2
Diabetes	41.5	37.5	39.3	36.8
Heart failure	7.4	7.4	7.4	5.0
Hypertension	80.2	79.7	79.8	76.9
Dyslipidemia	42.6	41.1	48.4	47.6
Peripheral vascular disease	2.7	2.7	2.8	2.0
Cerebrovascular disease	3.0	4.2	3.7	2.6
Ischemic/hemorrhagic stroke/TIA	3.0	3.2	2.8	2.1
Shock*	1.2	1.3	1.3	1.1
Medical comorbidities				
Renal disease	3.7	4.8	4.4	3.3
Cancer	6.2	7.5	7.1	5.6
Chronic obstructive pulmonary disease	9.5	8.4	6.6	4.4
Peptic ulcer disease	2.7	2.0	1.7	1.4
Anemia/blood disease	10.3	9.0	8.6	6.6
Charlson's Score, mean±SD	1.14±1.68	1.10±1.77	1.07±1.73	0.83±1.50
Prior cardiac invasive procedures				
Percutaneous coronary intervention	5.6	5.7	7.7	7.8
Coronary artery bypass grafting*	1.5	1.7	1.9	1.4
Coronary catheterization*	13.4	14.2	15.5	14.9
Medication use within 90 d prior index episode admission				
Ticagrelor*	(≤ 5 patients)	0.3	0.5	0.4
Clopidogrel	11.5	9.3	9.9	8.2
ACEi/ARB	47.9	48.5	49.5	46.5
Beta blocker	32.3	30.9	31.5	28.0
Statins*	42.6	42.2	46.4	42.8
Physician characteristics, %				
Specialty of most responsible physician during index hospitalization				
Cardiology	0.0	26.1	43.4	67.9

(Continued)

Table 1.   (Continued)

Characteristics	Quartiles			
	Q1 Low	Q2 Low-medium	Q3 Medium	Q4 High
Internal medicine	29.3	34.8	29.1	25.3
Other	70.7	39.0	27.5	6.8
Hospital characteristics, %				
Teaching status	0.8	28.8	32.0	33.9
Volume of MI/UA, mean±SD	483.1 (482.3)	1476.0 (1614.9)	1490.4 (813.4)	3598.0 (1722.8)
Having catheterization laboratory	0.0	27.7	35.4	76.9
Rural	52.3	16.1	5.0	1.1

ACEi indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; IQR, interquartile range; MI, myocardial infarction; TIA, transient ischemic attack; and UA, unstable angina.

*Not statistically significant.

We observed strong hospital variation in ticagrelor use with use ranging from 0% to 83.6% by hospital regardless of the volume of ACS at each site, and nearly 10% of acute care hospitals in Ontario did not prescribe ticagrelor at all. Examination of the low ticagrelor-use hospitals demonstrated that these hospitals had a higher proportion of rurally located hospitals, limited number of cardiologists, and limited capacity to perform cardiac procedures. We also examined the use of evidence-based medication as a potential surrogate for hospital-level ticagrelor use and observed that hospitals with lower ticagrelor use also had significantly lower use of angiotensin-converting enzyme inhibitors/ angiotensin II receptor blockers, beta blockers, and statins within 90 days post discharge. Accordingly, reasons to explain the slow (to no adoption) of ticagrelor may include lack of awareness of potential benefits of newer agents such as ticagrelor, and the reduced focus on process measures to ensure higher quality of care.

Even though we adjusted for all the known and measurable patient, physician, and hospital factors, we observed substantial hospital variation that the use of ticagrelor varied >2.5 times even after adjustment. This observation suggests that many unmeasured factors still exist that could account for difference in ticagrelor adoption across the hospitals. Those factors may include the hospital formulary system—the prescription

Table 2.   Use of Medications for Secondary Prevention and Adherence Rates of Ticagrelor/Clopidogrel by Quartile of Ticagrelor Use

Characteristics	Quartiles			
	Q1 Low	Q2 Low-medium	Q3 Medium	Q4 High
Hospital ticagrelor use, %	<8.8	8.8 to <20.9	20.9 to <40.0	≥40.0
No. of hospitals	39	38	40	39
No. of patients	1205	3611	5499	13 647
Medication use within 90 d post index episode discharge, n (%)				
ACEi/ARB	883 (73.3)	2764 (76.5)	4319 (78.5)	11 366 (83.3)
Beta blocker	890 (73.9)	2742 (75.9)	4320 (78.6)	10 901 (79.9)
Calcium channel blockers	398 (33.0)	1017 (28.2)	1538 (28.0)	3207 (23.5)
Nitrates	856 (71.0)	2325 (64.4)	3592 (65.3)	8642 (63.3)
Statins	1052 (87.3)	3262 (90.3)	5069 (92.2)	12 906 (94.6)
No. of patients receiving ticagrelor	61	522	1578	8024
Ticagrelor mean PDC±SD	76.7±30.5	78.4±31.2	80.4±29.5	80.9±29.0
Ticagrelor PDC ≥80%, %*	67.2	69.9	72.4	73.1
No. of patients received clopidogrel	1144	3089	3921	5623
Clopidogrel mean PDC±SD	82.5±29.6	85.3±27.0	83.4±28.3	85.9±25.8
Clopidogrel PDC ≥80%, %	76.2	79.3	75.9	79.8

ACEi indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; and PDC, proportion of days covered.

*Not statistically significant.

Table 3. Predictors of Ticagrelor Use

Characteristics	OR	95% CI	P value
Patient characteristics			
Age categories, y			
65–74	1.00		
75–84	0.64	0.60–0.69	<0.001
≥85	0.23	0.21–0.26	<0.001
Men	1.24	1.16–1.32	<0.001
Income quintiles			
1 (lowest)	1.00		
2	1.10	1.00–1.20	0.054
3	1.01	0.92–1.11	0.796
4	1.04	0.94–1.14	0.465
5 (highest)	1.05	0.95–1.16	0.357
Rural resident	0.79	0.71–0.88	<0.001
Cardiovascular comorbidities			
Prior myocardial infarction	1.27	1.08–1.50	0.004
Chronic ischemic heart disease	0.64	0.57–0.73	<0.001
Angina	0.67	0.57–0.79	<0.001
Atrial fibrillation/flutter	0.79	0.63–0.98	0.036
Diabetes	1.04	0.96–1.12	0.378
Heart failure	0.85	0.71–1.02	0.077
Hypertension	0.87	0.81–0.95	0.001
Dyslipidemia	1.04	0.97–1.11	0.278
Peripheral vascular disease	1.08	0.86–1.36	0.492
Cerebrovascular disease	0.80	0.60–1.07	0.139
Ischemic/hemorrhagic stroke/TIA	0.93	0.68–1.28	0.669
Shock	0.77	0.56–1.07	0.119
Medical comorbidities			
Renal disease	0.94	0.76–1.17	0.598
Cancer	1.20	1.01–1.43	0.040
Chronic obstructive pulmonary disease	0.91	0.78–1.07	0.275
Liver disease	1.08	0.69–1.69	0.734
Peptic ulcer disease	1.14	0.87–1.48	0.338
Anemia/blood disease	0.75	0.66–0.86	<0.001
Charlson's Score	0.88	0.84–0.92	<0.001
Prior cardiac invasive procedures			
PCI/CABG	1.35	1.15–1.58	<0.001
Medication use within 90 d prior index episode admission			
ACEi/ARB	1.01	0.94–1.08	0.864
Beta blocker	0.88	0.81–0.95	<0.001
Statins	0.83	0.78–0.90	<0.001

(Continued)

Table 3. (Continued)

Characteristics	OR	95% CI	P value
Physician characteristics			
Specialty of most responsible physician during index hospitalization			
Cardiology	2.80	2.36–3.33	<0.001
Internal medicine	1.48	1.28–1.72	<0.001
Hospital characteristics			
Teaching status	0.62	0.34–1.13	0.121
Volume of myocardial infarction/unstable angina	1.00	1.00–1.00	0.082
Having catheterization laboratory	0.74	0.30–1.81	0.507
Rural	0.49	0.32–0.77	0.002

ACEi indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; CABG, coronary artery bypass grafting; OR, odds ratio; PCI, percutaneous coronary intervention; and TIA, transient ischemic attack.

restriction policies at each hospital may influence prescribing patterns.[18]

Several potential limitations of our study merit consideration. First, given that prescription drug benefits only extend to patients aged ≥65 years in Ontario, we were only able to examine the patterns and factors associated with ticagrelor use in this age group. However, we do not expect that younger patients in Ontario had much higher adoption given the findings of other studies and the fact that hospital factors were highly influential in ticagrelor prescriptions. Second, we did not include prasugrel in our analyses because it is rarely used in Ontario. In our study, we found a usage rate of <0.1% of the overall cohort. Finally, we assessed pharmacy prescriptions and written prescriptions or not medications that patients actually took. However, prior studies have shown a high correlation of these measures with prescription claims.

CONCLUSIONS

In our large population-based study with elderly patients after ACS, a trend of increasing ticagrelor use was observed, yet the rate of usage was suboptimal even in the setting without additional cost burden for the medication selection. We highlighted ticagrelor use substantially varied across hospitals. This hospital-level heterogeneity in ticagrelor prescribing that strongly influenced by prescriber and hospital characteristics rather than patient factors suggests there are significant opportunities to improve medication use by assessing hospital-level barriers as well as providing a standardized approach to prescribe medications.

ARTICLE INFORMATION

Affiliations

School of Pharmacy & Pharmaceutical Sciences, University of California, Irvine, CA, United States (A.F.O.); College of Pharmacy, Western University of Health Sciences, Pomona, CA, United States (C.A.J.); Veterans Affairs Greater Los Angeles Healthcare System, Los Angeles, CA, United States (C.A.J.); ICES, Toronto, Canada (C.A.J., A.C., J.F., P.C.A., D.T.K.); University of Toronto, Ontario, Canada (C.A.J., M.S., P.C.A., D.T.K.); and Schulich Heart Centre, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada (M.S., D.T.K.).

Supplemental Material

Table S1

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SUPPLEMENTAL MATERIAL

Table S1. Hierarchical Predictor Models for Ticagrelor Use.

Characteristics		Model 1		Model 2		Model 3		Model 4	
		OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Intercept		0.29	0.24 - 0.35	0.62	0.49 - 0.78	0.42	0.34 - 0.53	0.47	0.33 - 0.67
Patient Characteristics									
Age categories, years	65 to 74			1.00		1.00		1.00	
	75 to 74			0.63	0.59 - 0.67	0.64	0.60 - 0.69	0.64	0.60 - 0.69
	>= 85			0.22	0.20 - 0.24	0.23	0.21 - 0.26	0.23	0.21 - 0.26
Male				1.27	1.19 - 1.35	1.26	1.18 - 1.34	1.26	1.18 - 1.34
Income quintiles	1 (lowest)			1.00		1.00		1.00	
	2			1.10	1.00 - 1.21	1.10	1.00 - 1.21	1.10	1.00 - 1.20
	3			1.03	0.94 - 1.13	1.02	0.93 - 1.13	1.02	0.93 - 1.12
	4			1.05	0.95 - 1.15	1.04	0.95 - 1.15	1.04	0.94 - 1.15
	5 (highest)			1.06	0.96 - 1.17	1.05	0.96 - 1.16	1.05	0.95 - 1.16
Rural				0.76	0.68 - 0.84	0.77	0.69 - 0.85	0.80	0.72 - 0.90
Cardiovascular comorbidities									
Prior myocardial infarction				1.24	1.05 - 1.45	1.25	1.06 - 1.47	1.24	1.05 - 1.46
Chronic ischemic heart disease				0.65	0.57 - 0.73	0.64	0.57 - 0.73	0.64	0.57 - 0.73
Angina				0.68	0.58 - 0.80	0.68	0.58 - 0.80	0.67	0.57 - 0.79

Atrial fibrillation/flutter	0.78	0.62 - 0.97	0.79	0.63 - 0.99	0.79	0.63 - 0.98
Diabetes	1.04	0.96 - 1.12	1.04	0.97 - 1.13	1.04	0.97 - 1.13
Heart failure	0.80	0.67 - 0.96	0.83	0.69 - 0.99	0.82	0.69 - 0.99
Hypertension	0.85	0.79 - 0.92	0.85	0.79 - 0.93	0.85	0.79 - 0.93
Dyslipidemia	1.05	0.98 - 1.12	1.04	0.98 - 1.11	1.04	0.98 - 1.11
Peripheral vascular disease	1.06	0.85 - 1.33	1.05	0.84 - 1.32	1.06	0.85 - 1.33
Cerebrovascular disease	0.82	0.61 - 1.09	0.82	0.62 - 1.09	0.81	0.61 - 1.07
Ischemic/hemorrhagic stroke/TIA	0.89	0.65 - 1.21	0.90	0.66 - 1.23	0.91	0.67 - 1.25
Shock	0.77	0.56 - 1.06	0.78	0.57 - 1.09	0.78	0.56 - 1.08
Medical comorbidities						
Renal disease	0.92	0.74 - 1.14	0.93	0.74 - 1.15	0.92	0.74 - 1.15
Cancer	1.19	1.00 - 1.42	1.18	0.99 - 1.41	1.18	0.99 - 1.41
Chronic obstructive pulmonary disease	0.89	0.76 - 1.04	0.90	0.76 - 1.05	0.90	0.77 - 1.06
Liver disease	1.14	0.73 - 1.78	1.10	0.70 - 1.71	1.11	0.71 - 1.73
Peptic ulcer disease	1.13	0.87 - 1.47	1.16	0.89 - 1.51	1.16	0.89 - 1.51
Anemia/blood disease	0.74	0.64 - 0.84	0.74	0.65 - 0.85	0.75	0.65 - 0.86
Charlson's Score	0.88	0.84 - 0.92	0.88	0.85 - 0.92	0.88	0.85 - 0.92
Prior Cardiac invasive procedures						
Percutaneous coronary intervention/	1.38	1.18 - 1.62	1.37	1.16 - 1.61	1.37	1.17 - 1.61
Coronary artery bypass grafting						

Medication use within 90 days prior index episode admission						
ACEi/ARB	1.00	0.93 - 1.08	1.01	0.94 - 1.08	1.01	0.94 - 1.08
Beta blocker	0.87	0.81 - 0.94	0.87	0.81 - 0.94	0.87	0.81 - 0.94
Statins	0.83	0.77 - 0.89	0.84	0.78 - 0.90	0.84	0.78 - 0.90
Physician Characteristics						
Specialty of most responsible physician during index hospitalization						
Cardiology			3.22	2.73 - 3.79	2.97	2.50 - 3.52
Internal medicine			1.64	1.42 - 1.89	1.54	1.33 - 1.78
Hospital Characteristics						
Teaching status					0.63	0.35 - 1.13
Volume of MI /UA, mean ± SD					1.00	1.00 - 1.00
Having catheterization lab					0.74	0.30 - 1.81
Rural					0.51	0.32 - 0.79
Random intercept variance	1.22	1.26		1.02		0.94
Standard error	0.17	0.18		0.15		0.14
MOR	**2.87**	**2.92**		**2.62**		**2.53**

Variables in each model:

Model 1: hospital-specific random effects

Model 2: patient characteristics in addition to hospital-specific random effect

Model 3: patient and physician characteristics in addition to hospital-specific random effect

Model 4: patient characteristics, physician and hospital characteristics in addition to hospital-specific random effect

ACEi: angiotensin converting enzyme inhibitors

ARB: angiotensin II receptor blockers

CI: confidence interval

MI: myocardial infarction

MOR: median odds ratios

SD: standard deviation

TIA: transient ischemic attack

UA: unstable angina