Anticoagulant use and associated outcomes in older patients receiving home palliative care: a retrospective cohort study

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Abstract

Background: The benefits and harms of anticoagulants for people near the end of life are not well understood, nor is it known what proportion of patients discontinue these medications. We aimed to characterize anticoagulant use in older recipients of home palliative care and describe patient and provider characteristics, as well as outcomes associated with anticoagulant discontinuation in this group.

Methods: Using linked administrative health databases, we conducted a population-based cohort study of patients aged 66 years and older who initiated home palliative care in Ontario from 2010 to 2018. We calculated the prevalence of anticoagulant use. We used multilevel logistic regression models to assess patient (e.g., sociodemographic, comorbidities) and physician (e.g., demographic, training, practice) factors associated with anticoagulant discontinuation after initiation of home palliative care. We defined discontinuation as either primary (no anticoagulant claim within 1.5 times the days' supply of the previous prescription) or secondary (no subsequent anticoagulant claim at any time after the index date). In secondary analyses, we used cause-specific hazards regression to explore subsequent thrombotic and bleeding events associated with anticoagulant discontinuation, and multivariable logistic regression for location of death.

Results: We identified 98 089 recipients of home palliative care, of whom 15.5% were taking anticoagulants at the time of the first palliative care visit. Depending on the definition of discontinuation, 18.0% to 24.4% of patients discontinued anticoagulants after the first home palliative care visit. Compared with warfarin, use of a direct oral anticoagulant (adjusted odds ratio [OR] 0.49, 95% confidence interval [CI] 0.43–0.56) and low-molecular-weight heparin (adjusted OR 0.56, 95% CI 0.47–0.66) were associated with a lower likelihood of discontinuation. Few patient or physician characteristics — and no comorbidities or indications for therapeutic anticoagulation — were associated with discontinuation. Anticoagulant discontinuation after beginning home palliative care was associated with similar rates of thrombosis (adjusted hazard ratio [HR] 1.06, 95% CI 0.81–1.39), lower rates of bleeding (adjusted HR 0.75, 95% CI 0.62–0.90) and a higher likelihood of a home death (adjusted OR 1.22, 95% CI 1.09–1.36) compared with continuing anticoagulation.

Interpretation: Among recipients of home palliative care in Ontario, anticoagulant use is common, and discontinuation is not influenced by comorbidities or indication for anticoagulation. Physician preference may play an important role; patients should be made aware of their options toward the end of life and supported in shared decision-making.

Toward the end of life, patients with advanced disease and their clinicians often consider stopping medications that are not contributing to symptom relief or improving quality of life.[1–4] Home-visiting palliative care physicians care for such patients, who frequently wish to avoid complications from medical interventions and hospital admissions, and prefer to die at home.[5–9] For this reason, the initial home visit involves a comprehensive assessment of the risks and benefits of all medications, including anticoagulants.[4]

Because older age, cancer and other comorbidities increase the risk of atrial fibrillation and venous thromboembolism, patients receiving palliative care frequently have indications for anticoagulants; decisions about whether to continue or stop these medications are challenging.[10] For most patients, clinical guidelines informed by randomized controlled trials recommend long-term anticoagulation to reduce morbidity and mortality from cardioembolic stroke in patients with atrial fibrillation[11–13] and to prevent recurrent events and premature death in patients

with venous thromboembolism.[14–21] Guidelines emphasize that beginning or continuing anticoagulation should be a shared decision that considers patient preferences and the risks of bleeding associated with anticoagulant use.[11–21] However, because no high-quality studies have considered patients receiving palliative care, the benefits and risks of anticoagulation near the end of life are not known.[10,22–24]

Recent articles have highlighted the importance of studying anticoagulant use in patients with limited life expectancy[25–28] to gain a better understanding of anticoagulant practices, the factors influencing the decision to continue or stop anticoagulants, the outcomes associated with those decisions, and the importance of shared decision-making. However, the characteristics of anticoagulant use in a population-based home palliative care cohort are unknown.

We aimed to study the epidemiology of anticoagulant use among older recipients of home palliative care in Ontario, characterize patient and provider factors associated with their discontinuation, and compare subsequent clinical and health care outcomes between patients who discontinued and those who continued anticoagulants.

Methods

Study design and setting

Using linked health administrative data at ICES, we conducted a retrospective, population-based observational cohort study of older (≥ 66 yr) people in Ontario for whom physician-based home palliative care was initiated from 2010 to 2018.

All Ontario residents have publicly administered insurance for hospital care and physician services, and those aged 65 years or older receive publicly funded prescription medication coverage for most drugs. Multidisciplinary and predominantly physician-led community-based teams provide home palliative care for people in Ontario with advanced life-limiting illnesses (typically those with anticipated prognoses < 6 mo, accompanied by functional decline).[7] These physicians generally have advanced training in palliative care, and although they could have completed their initial training in any medical or surgical specialty, most hold their primary certification as family physicians.[29]

We reported our study using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[30]

Data sources

A detailed description of the databases and the specific codes we used in the study can be found in Appendix 1, Supplemental Tables 1 and 2 (available at www.cmaj.ca/lookup/doi/10.1503/cmaj.220919/tab-related-content). We ascertained vital statistics and sociodemographic information from the Registered Persons Database[31] and immigration status from the Immigrant, Refugees and Citizenship Canada Permanent Residents Database.[32,33] In the Ontario Health Insurance Plan database, we identified claims for home palliative care visits by physicians, which are unique to the provision of palliative home care.[8,29,34,35] Use of these service claims has been adopted by the Canadian Institute for Health Information (CIHI), the Ontario Ministry of Health and the Ontario Ministry for Long-Term Care to identify the provision of palliative care services, and the 3 service codes we used (Appendix 1, Supplemental Table 2) are exclusive to a home palliative care visit by a physician.

We ascertained anticoagulant and other prescription medication use from the Ontario Drug Benefit Plan (ODB) database, which contains records of all outpatient prescriptions covered by Ontario's publicly funded drug plan dispensed to individuals aged 65 years or older, with an error rate of < 1%.[36] We obtained diagnostic and procedural information about hospital and emergency visits from the CIHI Discharge Abstract Database, National Ambulatory Care Reporting System and Same Day Surgery databases, which are widely used and have been assessed for completeness and accuracy in encoding exposures, outcomes and comorbidities.[37]

We determined diagnoses of cancer, congestive heart failure, chronic obstructive pulmonary disease, dementia, diabetes mellitus, hypertension and renal disease using previously developed algorithms that use diagnosis codes and drug-dispensing data to ascertain these conditions.[38–40] Finally, we obtained physician demographics and practice characteristics from the ICES Physician Database and the Corporate Provider Database.[29,41] A detailed description of the databases and the specific codes can be found in Appendix 1, Supplemental Tables 1 and 2.

Study population

We included all people in Ontario aged 66 years and older whose first home palliative care visit by a physician occurred between Jan. 1, 2010, and Dec. 31, 2018. The first physician home visit marked the index date, and individuals were followed until death or the end of the study observation period (Dec. 31, 2019).

Among these individuals, we applied additional criteria to create a cohort to investigate anticoagulant discontinuation. This cohort included only active anticoagulant users at the index date, defined as individuals with an anticoagulant claim with a duration overlapping the index date. We further excluded patients who died within the early mortality observation window, a period after the date of the index anticoagulant claim (the most recent claim before or on the index date) that would not allow assessment of discontinuation and subsequent outcomes, defined as 1.5 times the days' supply of the index anticoagulant claim and a minimum 7-day gap after supply expiry[36] (Appendix 1, Supplemental Figure 1).

Outcomes

We studied the point prevalence of anticoagulant use at the index date and characteristics of anticoagulant claims among anticoagulant users after initiation of home palliative care. We classified anticoagulant medications into 3 groups: warfarin, direct oral anticoagulants (DOACs) and low-molecular-weight heparins (LMWHs); see Appendix 1, Supplemental Table 3 for specific agents.

We studied anticoagulant discontinuation after initiation of home palliative care, defined as no subsequent anticoagulant claim within 1.5 times the days' supply or a 7-day gap from supply expiry of the previous anticoagulant claim — whichever

was longer — as the primary study outcome[36] (Appendix 1, Supplemental Figure 1). We also considered this as an exposure in secondary analyses.

As our primary definition of discontinuation did not preclude the possibility of a subsequent anticoagulant claim beyond this initial window, we also studied a secondary definition of discontinuation, which included only those who permanently stopped (i.e., no anticoagulant prescriptions after the index claim), post hoc.

We examined both patient and physician characteristics as potential predictive variables influencing the decision to discontinue anticoagulants. Patient sociodemographic characteristics included income quintile, rural residence and immigration status. With respect to clinical characteristics, we studied indications for anticoagulation (e.g., atrial fibrillation, venous thromboembolism) and diagnoses and risk factors routinely incorporated into thrombotic and bleeding risk assessment, such as cancer, congestive heart failure, and previous stroke and previous bleeding.[11–21,42–46]

Physician variables included sex, year of graduation, training (e.g., primary specialty certification, Canadian v. international medical graduate) and practice characteristics (e.g., rural v. urban). To denote palliative care specialists, we used a previously validated definition of 10% or more of service claims for palliative care services.[41] We further evaluated discontinuation rates among physicians who cared for 5 or more patients, as a minimum patient volume.

We conducted secondary analyses to assess outcomes occurring after the early mortality observation window associated with anticoagulant discontinuation, including thrombotic events (ischemic stroke, transient ischemic attack and venous thromboembolism),[47–49] bleeding (intracranial, gastrointestinal [upper or lower], or other [primarily genitourinary and respiratory]),[47–49] death and location of death.[8,35] We captured thrombotic and bleeding events using *International Statistical Classification of Diseases and Related Health Problems, 10th revision* (ICD-10) diagnostic codes from hospital admissions and emergency department visits (Appendix 1, Supplemental Table 2). We defined location of death as a binary outcome using discharge disposition variables from the data sources, where death occurred either at home or in a health care facility.[8,35]

Statistical analysis

We used descriptive statistics to summarize patient and provider characteristics and calculated the absolute standardized difference of means to compare these characteristics between patients who discontinued and those who continued anticoagulants. We considered standardized differences greater than 0.1 to reflect meaningful differences between groups.[50]

To account for the hierarchical nature of our data, we constructed a multilevel logistic regression model[51] for anticoagulant discontinuation in which the physician was included as a random intercept and all patient and physician variables were included as covariates. In this model, which included all patients taking anticoagulants and who had no missing baseline variables, we calculated the intraclass correlation coefficient to interpret the contextual variance and heterogeneity in discontinuation related to clustering of patients by physician.[51] Among physicians who cared for 5 or more patients, we calculated the mean provider-level anticoagulant discontinuation rate by quintile (lowest to highest discontinuation rate).

For the secondary analyses, we first described crude outcome rates by discontinuation status, reporting incidence rates per 100 person-years of follow-up and Wald 95% confidence intervals (CIs). We then fit cause-specific hazards regression models to calculate adjusted hazard ratios (HRs) for subsequent thrombosis and bleeding, treating mortality as a competing risk. Among patients who died within the study period, we used multivariable logistic regression to study the association of anticoagulant discontinuation with location of death. We adjusted these models for all measured patient sociodemographic and clinical characteristics.

As post hoc sensitivity analyses, we repeated the multilevel logistic regression model and secondary analyses after excluding patients who underwent hip or knee arthroplasty within 30 days before the index anticoagulant claim.

Ethics approval

The use of data in this study was authorized under section 45 of Ontario's *Personal Health Information Protection Act* and approved by the Toronto Academic Health Science Network research ethics board.

Results

We identified 130 852 people in Ontario who received at least 1 home palliative care visit by a physician during the study period (Figure 1). After exclusions, 98 089 (75.0%) individuals met our inclusion criteria for the study of anticoagulant prevalence, 8687 of whom were taking anticoagulants at the index date and survived the early mortality observation window. These patients comprised the cohort for the analysis of anticoagulant discontinuation.

Prevalence of anticoagulant use

Among the cohort of older people in Ontario who began home palliative care, 15.5% (15 195/98 089) were taking an anticoagulant at the index date, with a similar distribution among warfarin (n = 5149, 5.2%), DOACs (n = 5008, 5.1%) and LMWHs (n = 5038, 5.1%). After initiation of home palliative care and including the index anticoagulant claim, the median number of anticoagulant claims per patient was 2 (interquartile range [IQR] 1–6), with a median supply dispensed per anticoagulant claim of 7 (IQR 7–14) days.

Anticoagulant discontinuation

A total of 8687 patients taking anticoagulants at the index date survived the early mortality observation window. Using our primary definition of anticoagulant discontinuation, 2123 (24.4%) discontinued therapy after beginning home palliative care, and using our secondary definition (i.e., no anticoagulant prescriptions after the index anticoagulant claim), 1445 (18.0%) discontinued

therapy (Table 1). Using either definition, patients who discontinued anticoagulants were more likely to have been treated with warfarin, more likely to have had a recent hip or knee arthroplasty and less likely to be taking DOACs on bivariate analyses (Table 1).

We included 8156 (93.9%) patients with complete data on baseline characteristics who received care from 2024 physicians in the multilevel logistic regression model. After adjustment for patient and physician characteristics, female sex (odds ratio [OR] 0.86, 95% CI 0.78–0.96) and use of a DOAC (OR 0.49, 95% CI 0.43–0.56) or LMWH (OR 0.56, 95% CI 0.47–0.66), compared with warfarin use, were associated with a lower likelihood of discontinuation, using our primary definition (Table 2).

Recent hip or knee arthroplasty remained a strong predictor for discontinuation (OR 13.71, 95% CI 5.69–33.03). No other patient variables were associated with discontinuation in the multilevel model (Table 2). The results of the multilevel model were unchanged after exclusion of patients with a recent hip or knee arthroplasty (Appendix 1, Supplemental Table 4). Treatment by a palliative care specialist (i.e., those with ≥ 10% of service claims for palliative care services) was the only physician characteristic variable associated with anticoagulant discontinuation (OR 1.18, 95% CI 1.04–1.33).

The results of multilevel analyses were essentially the same using our secondary definition of discontinuation (Table 2). Among the 361 physicians who cared for 5 or more patients in

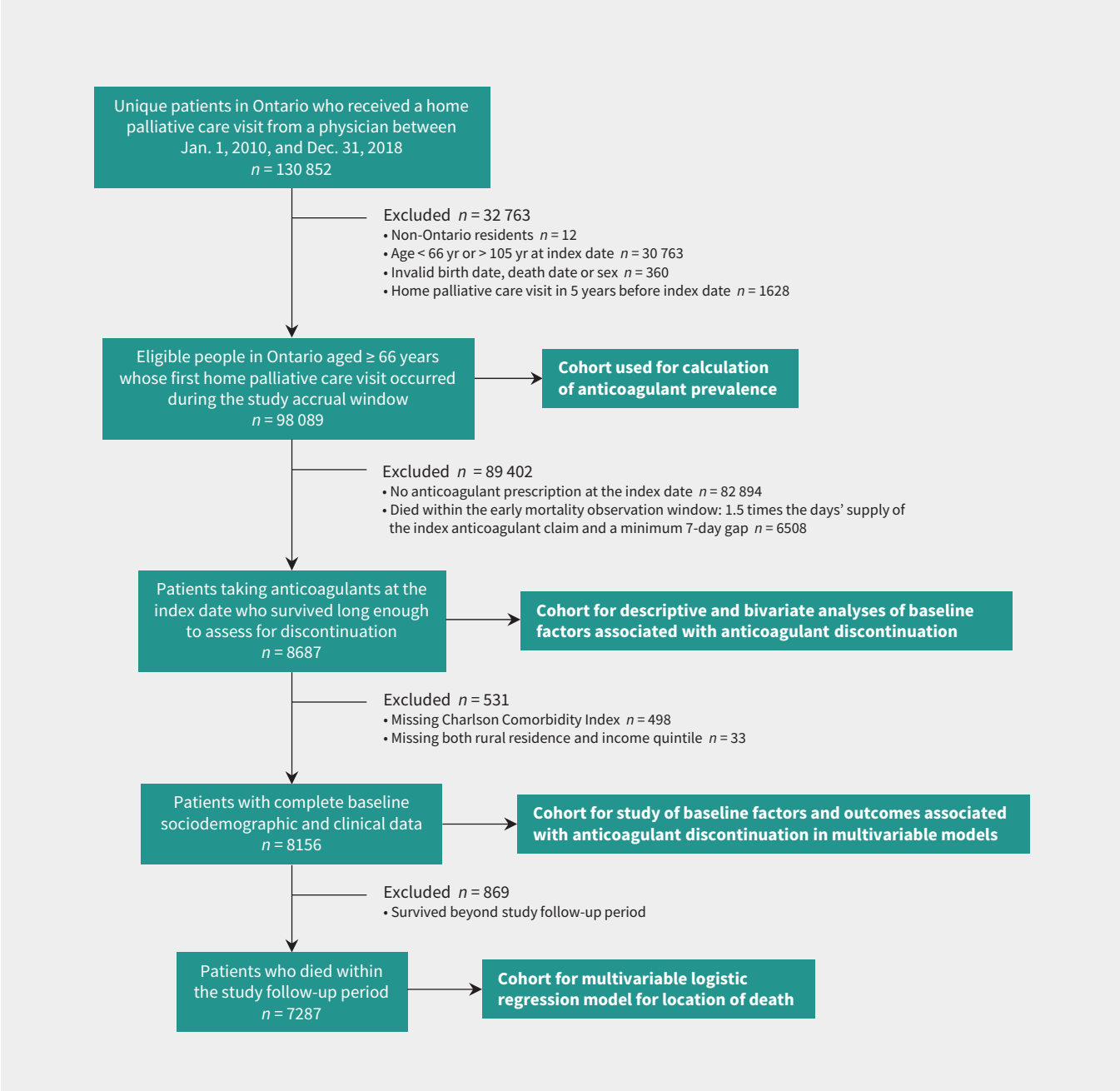

Figure 1: Description of study cohorts.

our cohort (n = 5855 patients), the mean ± standard deviation discontinuation rate ranged from 0.07 ± 0.06 in the first quintile (lowest discontinuation rate) to 0.49 ± 0.09 in the fifth quintile (highest discontinuation rate).

Outcomes associated with anticoagulant discontinuation

We followed the cohort of 8156 patients described above (i.e., those taking anticoagulants with complete baseline data) for a median of 111 (IQR 32–400) days to assess rates of bleeding and

Table 1 (part 1 of 2): Baseline patient and provider characteristics of patients taking anticoagulants who discontinued versus continued anticoagulants after initiation of home palliative care (n = 8687)

Characteristic	No. (%) of patients by anticoagulation group*			Standardized difference (v. continuation group)	
	Continuation n = 6564 (75.6%)	Discontinuation by primary definition† n = 2123 (24.4%)	Discontinuation by secondary definition† n = 1445 (18.0%)	Discontinuation by primary definition†	Discontinuation by secondary definition†
Patient characteristics					
Age, yr, mean ± SD	81.2 ± 8.2	81.2 ± 8.2	81.1 ± 8.4	< 0.01	0.02
Sex (male)	3051 (46.5)	1068 (50.3)	739 (50.8)	0.08	0.09
Income quintile‡					
First (lowest)	1340 (20.4)	390 (18.4)	261 (17.9)	0.05	0.06
Second	1376 (21.0)	445 (21.0)	286 (19.7)	< 0.01	0.03
Third	1291 (19.7)	417 (19.6)	296 (20.3)	< 0.01	0.02
Fourth	1195 (18.2)	400 (18.8)	276 (19.0)	0.02	0.02
Fifth (highest)	1337 (20.4)	463 (21.8)	331 (22.7)	0.04	0.06
Rural residence‡	596 (9.1)	222 (10.5)	166 (11.4)	< 0.01	0.08
Recent immigrant§	69 (1.1)	16 (0.8)	12 (0.8)	0.03	0.02
Index anticoagulant					
Warfarin	2073 (31.6)	924 (43.5)	560 (38.5)	0.25	0.15
Direct oral anticoagulant	2445 (37.2)	575 (27.1)	426 (29.3)	0.22	0.17
Low-molecular-weight heparin	2036 (31.0)	624 (29.4)	469(32.2)	0.04	0.03
Indication for anticoagulation¶					
Atrial fibrillation	3475 (52.9)	1084 (51.1)	718 (49.3)	0.04	0.07
Venous thromboembolism	1080 (16.5)	323 (15.2)	208 (14.3)	0.03	0.06
Mechanical heart valve	69 (1.1)	19 (0.9)	11 (0.8)	0.02	0.03
≥ 2 of the above indications	306 (4.7)	87 (4.1)	52 (3.6)	0.03	0.05
Comorbidities and risk factors¶					
Cancer	5089 (77.5)	1677 (79.0)	1171 (80.5)	0.04	0.07
Congestive heart failure	2905 (44.3)	954 (44.9)	621 (42.7)	0.01	0.03
Hypertension	5411 (82.4)	1721 (81.1)	1166 (80.1)	0.04	0.06
Diabetes mellitus	2383 (36.3)	763 (35.9)	514 (35.3)	< 0.01	0.02
Previous stroke or transient ischemic attack	628 (9.6)	181 (8.5)	111 (7.6)	0.04	0.07
Coronary artery disease	1489 (22.7)	482 (22.7)	326 (22.4)	< 0.01	0.01
Peripheral arterial disease	292 (4.4)	108 (5.1)	60 (4.1)	0.03	0.02
Renal disease	1669 (25.4)	612 (28.8)	388 (26.7)	0.08	0.03
Liver disease	147 (2.2)	54 (2.5)	39 (2.7)	0.02	0.03
Previous bleeding**	1696 (25.8)	570 (26.8)	393 (27.0)	0.02	0.03
Recent hip or knee arthroplasty††	7 (0.1)	22 (1.0)	18 (1.2)	0.12	0.14
Chronic obstructive pulmonary disease	1618 (24.6)	526 (24.8)	339 (23.3)	< 0.01	0.03
Dementia	617 (9.4)	177 (8.3)	119 (8.2)	0.04	0.04
NSAID or antiplatelet agent use‡‡	434 (6.6)	147 (6.9)	114 (7.8)	0.01	0.05
Charlson Comorbidity Index, mean ± SD	3.6 ± 2.8	3.8 ± 2.8	3.8 ± 2.8	0.05	0.07

Table 1 (part 2 of 2): Baseline patient and provider characteristics of patients taking anticoagulants who discontinued versus continued anticoagulants after initiation of home palliative care (*n* = 8687)

Characteristic	No. (%) of patients by anticoagulation group*			Standardized difference (v. continuation group)	
	Continuation *n* = 6564 (75.6%)	Discontinuation by primary definition† *n* = 2123 (24.4%)	Discontinuation by secondary definition† *n* = 1445 (18.0%)	Discontinuation by primary definition†	Discontinuation by secondary definition†
Treating physician characteristics					
Sex (male)	3652 (55.6)	1162 (54.7)	781 (53.7)	0.02	0.04
Graduation year					
2010 or later	783 (11.9)	261 (12.3)	199 (13.7)	0.04	0.05
2000–2009	1740 (26.5)	525 (24.7)	366 (25.2)	0.01	0.03
1990–1999	1317 (20.1)	406 (19.1)	265 (18.2)	0.02	0.05
1980–1989	1403 (21.4)	466 (22.0)	327 (22.5)	0.04	0.03
1979 or earlier	1321 (20.1)	465 (21.9)	298 (20.5)	0.01	0.01
International medical graduate	613 (9.3)	199 (9.4)	52 (3.6)	< 0.01	0.01
Primary certification in family medicine	6169 (94.0)	1972 (92.9)	1349 (92.7)	0.04	0.05
Rural practice	447 (6.8)	167 (7.9)	122 (8.4)	0.04	0.06
Palliative care specialist§§	3804 (58.0)	1295 (61.0)	915 (62.9)	0.06	0.10

Note: NSAID = nonsteroidal anti-inflammatory drug, SD = standard deviation.
*Unless otherwise noted.
†Among recipients of home palliative care taking anticoagulants at the index date, we evaluated 2 different definitions of discontinuation. The primary definition was no subsequent anticoagulant claim within 1.5 times the days' supply with a minimum 7-day gap from supply expiry of the previous claim. The secondary definition was no anticoagulant claim at any time after the index anticoagulant claim. Standardized differences > 0.1 were considered to be meaningful differences between groups.[50]
‡Census-based definitions of neighbourhood income quintile and community size based on postal codes (ascertained from the Registered Persons Database).
§Immigrated to Canada within 10 years before the index date.
¶Indications for anticoagulation and baseline comorbidities or risk factors occurred before or on the date of the index anticoagulant claim.
**Within 1 year before the index anticoagulant claim.
††Within 30 days before the index anticoagulant claim.
‡‡Within 6 months before the index anticoagulant claim.
§§Providers were considered palliative care specialists if ≥ 10% of their claims were for palliative care services.[41]

thrombotic events (Table 3). Discontinuation was associated with similar rates of thrombotic events (adjusted HR 1.06, 95% CI 0.81–1.39), lower rates of bleeding (adjusted HR 0.75, 95% CI 0.62–0.90) and increased mortality (adjusted HR 1.35, 95% CI 1.28–1.42), compared with those who continued their anticoagulant.

Of the 7287 decedents, 3997 (54.9%) died at home and 3290 (45.1%) died in a health care facility. Within this cohort, discontinuation was independently associated with a higher odds of a home death (adjusted OR 1.22, 95% CI 1.09–1.36).

Exclusion of patients with a recent hip or knee arthroplasty did not materially change the results of the analyses of outcomes associated with anticoagulant discontinuation (Appendix 1, Supplemental Table 5).

Interpretation

Among older patients referred for home palliative care in Ontario, anticoagulant use was common (15.5%), and 1 in 4 patients subsequently discontinued these medications. Few patient or physician factors, and no indications for therapeutic anticoagulation or comorbidities, were associated with the likelihood of discontinuation. Among palliative care physicians, anticoagulant practices ranged widely — the mean discontinuation rate in the highest quintile was 7-fold that of the lowest quintile. Anticoagulant discontinuation was associated with a lower subsequent risk of bleeding without an increased risk of thrombotic events. Overall survival was poorer among those who discontinued anticoagulants; these patients were more likely to die at home than in a health care facility.

The prevalence of therapeutic anticoagulant use at the time of enrolment in palliative care in our study is similar to the rates of 14%–33% reported in other cohorts.[25,27,52–55] However, previous studies focused primarily on inpatient settings and did not consistently differentiate between therapeutic and transient prophylactic indications for anticoagulation.[25,27,52–55]

Aside from the small number of patients who had undergone recent orthopedic surgery (0.3%), analysis of outpatient prescription claims in our study suggests that most patients received anticoagulation for therapeutic reasons and not as transient thromboprophylaxis.[56] The prevalence of 15.5% in our population-based cohort therefore represents an estimate of therapeutic anticoagulant use among older people initiating home palliative care in Ontario.

Our finding that clinical indications and comorbidities known to influence thrombotic and bleeding risk[11–21,42–46] were not associated with anticoagulant discontinuation suggests that decisions to stop were influenced by physician or patient

preference (a hypothesis supported by the wide range in practice among physicians), or by unmeasured confounders — in particular, those that could affect prognosis.

Some patient factors associated with discontinuation were not surprising. We expected patients who had had recent orthopedic surgery to discontinue anticoagulants because postoperative thromboprophylaxis is transient.[56] The lower likelihood of discontinuing a DOAC or LMWH than warfarin is likely explained by patients' preferences to avoid the frequent blood work and dose adjustments required to maintain therapeutic levels of warfarin — an inconvenience perceived to outweigh the daily injections associated with LMWH in qualitative studies.[57,58] Why male patients were more likely to discontinue anticoagulants than female patients was not clear.

Table 2 (part 1 of 2): Estimated odds ratios for patient and physician variables in the multilevel logistic regression model for anticoagulant discontinuation, by discontinuation definition*

Variable	Odds ratio (95% CI)	
	Discontinuation by primary definition*	Discontinuation by secondary definition*
Patient characteristics		
Age, yr (continuous variable, older)	1.00 (0.99–1.01)	1.00 (1.00–1.01)
Sex (female v. male)	0.86 (0.78–0.96)	0.85 (0.75–0.96)
Income quintile		
First (lowest)	0.86 (0.73–1.02)	0.80 (0.66–0.97)
Second	0.96 (0.82–1.13)	0.86 (0.71–1.03)
Third	0.94 (0.80–1.11)	0.91 (0.76–1.10)
Fourth	0.96 (0.81–1.13)	0.92 (0.76–1.11)
Fifth (highest)	1.00 (Ref.)	1.00 (Ref.)
Urban residence (v. rural)	0.94 (0.74–1.19)	0.86 (0.65–1.13)
Recent immigrant† (v. long-standing resident)	0.77 (0.43–1.37)	0.82 (0.42–1.58)
Index anticoagulant		
Warfarin	1.00 (Ref.)	1.00 (Ref.)
Direct oral anticoagulant	0.49 (0.43–0.56)	0.59 (0.51–0.69)
Low-molecular-weight heparin	0.56 (0.47–0.66)	0.69 (0.56–0.83)
Indication for anticoagulation‡		
Atrial fibrillation	0.87 (0.77–1.00)	0.86 (0.74–1.01)
Venous thromboembolism	0.88 (0.76–1.03)	0.76 (0.64–0.91)
Mechanical heart valve	0.73 (0.43–1.24)	0.67 (0.35–1.29)
Comorbidities and risk factors‡ (v. none)		
Cancer	1.11 (0.96–1.27)	1.11 (0.96–1.27)
Congestive heart failure	0.95 (0.84–1.09)	0.95 (0.81–1.10)
Hypertension	0.89 (0.77–1.02)	0.88 (0.74–1.04)
Diabetes mellitus	0.94 (0.84–1.06)	0.94 (0.82–1.07)
Previous stroke or transient ischemic attack	0.93 (0.78–1.12)	0.82 (0.66–1.03)
Coronary artery disease	0.94 (0.83–1.08)	0.99 (0.85–1.16)
Peripheral arterial disease	1.14 (0.90–1.44)	0.94 (0.70–1.26)
Renal disease	1.12 (0.99–1.27)	1.04 (0.90–1.21)
Liver disease	1.17 (0.84–1.63)	1.27 (0.87–1.85)
Previous bleeding§	0.98 (0.87–1.10)	1.01 (0.88–1.16)
Recent hip or knee arthroplasty¶	13.71 (5.69–33.03)	15.71 (6.27–39.39)
Chronic obstructive pulmonary disease	1.00 (0.89–1.14)	0.93 (0.81–1.08)
Dementia	0.95 (0.78–1.15)	0.95 (0.75–1.19)
NSAID or antiplatelet agent use**	1.03 (0.84–1.27)	1.16 (0.92–1.47)
Charlson Comorbidity Index (continuous variable, greater)	1.02 (1.00–1.04)	1.03 (1.00–1.05)

Table 2 (part 2 of 2): Estimated odds ratios for patient and physician variables in the multilevel logistic regression model for anticoagulant discontinuation, by discontinuation definition*

Variable	Odds ratio (95% CI)	
	Discontinuation by primary definition*	Discontinuation by secondary definition*
Physician characteristics		
Sex (female v. male)	1.07 (0.94–1.21)	1.08 (0.94–1.25)
Graduation year		
2010 or later	1.01 (0.82–1.26)	1.13 (0.88–1.45)
2000–2009	0.90 (0.75–1.09)	0.97 (0.78–1.20)
1990–1999	0.90 (0.75–1.09)	0.90 (0.72–1.13)
1980–1989	0.99 (0.83–1.19)	1.06 (0.86–1.31)
1979 or earlier	1.00 (Ref.)	1.00 (Ref.)
Primary certification (other specialty v. family medicine)	1.19 (0.88–1.63)	1.23 (0.84–1.79)
Urban practice (v. rural)	0.81 (0.61–1.09)	0.78 (0.56–1.10)
Palliative care specialist†† (v. generalist)	1.18 (1.04–1.33)	1.28 (1.10–1.48)

Note: CI = confidence interval, IQR = interquartile range, NSAID = nonsteroidal anti-inflammatory drug, Ref. = reference category.
*Multilevel logistic regression model for anticoagulant discontinuation including patient and physician variables. In the model for primary discontinuation, 8156 patients and 2024 physicians were included (498 patients were excluded because of missing Charlson Comorbidity Index and 33 were excluded for missing both rural residence and income quintile). The median number of patients per physician was 1 (IQR 1–3) and the mean discontinuation rate by physician was 23.7% (95% CI 14.6–36.1). The intraclass correlation coefficient was 0.027, indicating low proportional variance in discontinuation attributable to clustering of patients by physician. For the model employing the secondary definition of discontinuation, 7532 patients and 1944 physicians were included (498 patients were excluded because of missing Charlson Comorbidity Index and 33 were excluded for missing both rural residence and income quintile). The median number of patients per physician was 1 (IQR 1–3) and the mean discontinuation rate by physician was 17.1% (95% CI 8.6–31.2).
†Immigrated to Canada within 10 years before index date.
‡Indications for anticoagulation and baseline comorbidities or risk factors occurred before or on the date of the index anticoagulant claim.
§Within 1 year before the index anticoagulant claim.
¶Within 30 days before the index anticoagulant claim.
**Within 6 months before the index anticoagulant claim.
††Providers were considered palliative care specialists if ≥ 10% of their claims were for palliative care services.[41]

Table 3: Subsequent outcomes associated with anticoagulant discontinuation after initiation of home palliative care

Outcome	Crude incidence rates Incidence (95% CI) per 100 person-years		Multivariable analysis* HR† (95% CI)
	Discontinuation	Continuation	
Thrombotic event‡	5.2 (4.1–6.6)	4.9 (4.3–5.5)	1.06 (0.81–1.39)
Bleeding event§	10.4 (8.7–12.3)	12.7 (11.8–13.7)	0.75 (0.62–0.90)
All-cause mortality	135.9 (129.8–142.3)	95.7 (93.2–98.3)	1.35 (1.28–1.42)
	No. (%) of patients		Odds ratio¶ (95% CI)
Death at home (v. in a health care facility)	1059 (57.6)	2938 (53.9)	1.22 (1.09–1.36)

Note: CI = confidence interval, HR = hazard ratio.
*Covariates included in multivariable analyses: age, sex, income quintile, rural residence, recent immigration, index anticoagulant, atrial fibrillation, previous venous thromboembolism, mechanical heart valve, cancer, congestive heart failure, hypertension, diabetes mellitus, previous stroke or transient ischemic attack, coronary artery disease, peripheral arterial disease, renal disease, liver disease, previous bleeding, recent hip or knee arthroplasty, chronic obstructive pulmonary disease, nonsteroidal anti-inflammatory drug or antiplatelet use, and Charlson Comorbidity Index.
†Cause-specific hazards model (n = 8156) adjusted for baseline patient characteristics. Among 8687 patients in the study cohort, 498 patients were excluded because of missing Charlson Comorbidity Index and 33 were excluded for both missing rural residence and income quintile. Primary discontinuation was the independent variable.
‡Hospital admission or emergency department visit with ischemic stroke, transient ischemic attack or venous thromboembolism (Appendix 1, Supplemental Table 2).
§Hospital admission or emergency department visit with intracranial, gastrointestinal (upper or lower) or other (primarily genitourinary and respiratory) bleeding (Appendix 1, Supplemental Table 2).
¶Multivariable logistic regression model (n = 7287) adjusted for baseline patient characteristics. An additional 869 patients who survived beyond the study follow-up period were excluded from this model. Primary discontinuation was the independent variable.

Our finding that patients treated by palliative care specialists (i.e., those with ≥ 10% of service claims for palliative care services) had a slightly higher likelihood of discontinuing anticoagulation suggests that these physicians might be more comfortable discussing medication discontinuation. Deprescribing is a core element of palliative and end-of-life care training and practice, with which experienced and specialized palliative care clinicians must be familiar.[4,59]

The absence of strong patient- and physician-level predictors for anticoagulant discontinuation and variability in practices among physicians is in keeping with the lack of consensus about whether to continue or discontinue anticoagulants toward the end of life. A recent study showed wide variation in physicians' opinions and uncertainty regarding anticoagulation in such patients.[28] Variations in patients' perceptions of the advantages and risks of continuing anticoagulant therapy would also align with our results.[10,57,58,60]

Despite the advanced age and high prevalence of comorbidities in our cohort, anticoagulant discontinuation was not associated with an increased risk of subsequent thrombotic events, and patients who discontinued anticoagulants were less likely to present with bleeding. Although survival was poorer among those who discontinued, this outcome was strongly susceptible to selection bias: patients with anticipated poor prognoses would be less likely to refill their prescription. We observed that patients who discontinued anticoagulants were more likely to die at home. This likely reflects greater comfort with stopping medications among patients wishing for a home death.

Limitations

We used administrative health data to adjust for many sociodemographic and clinical factors as covariates. However, our study was still prone to unmeasured confounding. We could not capture detailed data with potential therapeutic and prognostic implications, such as performance status (also known as functional status, used to describe a patient's level of physical function as affected by their disease), symptom scores and stage or severity of disease. Similarly, we could not ascertain patient preferences, including advance directives, in the administrative data. We did not analyze data from 2020 onward as we terminated our study at the end of 2019 to avoid potential confounding related to the COVID-19 pandemic.

As noted earlier, we identified home palliative care visits by physicians using service claims unique to the provision of home palliative care in the Ontario Health Insurance Plan. This definition has not been validated but has been adopted by CIHI and the Ontario Ministry of Health and Ontario Ministry of Long-Term Care to identify the provision of palliative care services.

Although the use of a cut-off of 5 or more patients as a minimum patient volume to evaluate discontinuation rates among physicians providing palliative care was arbitrary, it was determined a priori as we expected many physicians in our cohort to provide palliative care to very few patients. Given that the median number of patients per physician in our cohort was 1, the distribution of discontinuation rates by physician if all physicians were included in the analysis would fall to both extremes.

Because the ODB database records prescriptions for Ontarians aged 65 years and older, we were unable to study anticoagulant use among younger patients. As we captured outpatient prescriptions only, we inferred discontinuation exclusively from dates dispensed. The validity of this outcome would be threatened by longer prescriptions; however, most anticoagulant claims in our study were for short dispensing periods (median 7 d).

Some patients who met our primary definition of discontinuation subsequently received an anticoagulant prescription. This led us to develop a secondary definition of discontinuation post hoc, in which patients never filled a subsequent prescription for an anticoagulant. The reasons patients who met our primary definition of discontinuation would have filled a subsequent anticoagulant prescription include development of a new indication for anticoagulation, patient choice to resume anticoagulants, admission to hospital shortly after the index date, or pre-existing excess supply of anticoagulant. It is reassuring that the variables associated with discontinuation were the same with both definitions.

Because DOAC use during the study period was restricted by the ODB to patients who could not tolerate warfarin, some patients who obtained these drugs through private insurance or personal payment would not have been captured; however, many Ontario physicians interpret the ODB eligibility criteria for DOACs liberally.[61]

We likely underestimated the incidence of both thrombosis and bleeding, which we ascertained from disease codes that necessitated hospital encounters and diagnostic investigations that do not consistently occur during end-of-life care. Additionally, death, thrombosis and bleeding were all studied as competing risks, and therefore we did not capture whether thrombosis or bleeding was the cause of death. The only outcome that was tabulated was whichever of the 3 occurred first. Finally, assessment of subsequent events associated with anticoagulant discontinuation was susceptible to confounding, as patients were not randomized to continuation or discontinuation. We therefore cannot draw any causal associations from these results — rather, they are descriptive and hypothesis generating.

Conclusion

In our large population-based cohort study of older people in Ontario receiving home palliative care, therapeutic anticoagulation was common and frequently continued near the end of life. Although anticoagulant practices are undoubtedly multifactorial and nuanced, our findings suggest that preferences of the treating physician and patient may ultimately be determining factors in the decision to discontinue therapy.

We observed a lower risk of bleeding without an associated increase in thrombosis and a higher probability of a home death when anticoagulants were discontinued. Establishing the effectiveness and safety of anticoagulants in palliative care populations, however, requires further study. This, combined with work exploring patients' and physicians' attitudes toward anticoagulant use near the end of life, may provide information to guide decisions on therapy that align with patients' values.

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