Changes within an anticoagulation clinic during COVID-19

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THE ANTICOAGULANT CLINIC (AC) IS A PHARMACIST-LED ambulatory clinic in Edmonton, Alberta, that manages warfarin therapy for approximately 700 patients across Northern Alberta, the majority of whom have mechanical heart valves. The AC team is composed of clinical pharmacists, secretarial support and, frequently, pharmacy students for clinical preceptorships. All clinical pharmacists have additional prescribing authorization (APA) and manage warfarin independently. Prior to the coronavirus disease 2019 (COVID-19) pandemic, a typical week for the AC involved approximately 350 telephone follow-ups, 2 to 4 intake visits for patients starting warfarin and 3 to 4 perioperative management scenarios.¹ The maximal frequency of international normalized ratio (INR) testing was every 4 weeks for stable patients, consistent with North American practices.² For a very few select stable patients (no warfarin dose adjustments for at least 6 months), a 6-week interval between INRs is considered.

On March 17, 2020, Alberta Premier Jason Kenney declared a state of public health emergency in response to the COVID-19 pandemic.³ With COVID-19, measures targeted at enforcing social distancing for both staff and patients alike were implemented and largely encompassed remote work environments for staff and planned measures to mitigate laboratory use for patients (Table 1). To accomplish this, the AC capitalized on changes occurring within Alberta Health Services specific to a common clinical information system (known as Connect Care) as well as clinical experience combined with literature guidance for mitigating the need for standard laboratory venipunctures for INR testing. Additional measures encompassed planning for the management of patients with suspected or laboratory-confirmed COVID-19, given the inability to assess the INR. As such, the purpose of this article is to describe changes affecting team members and patients within the AC in response to the ongoing COVID-19 pandemic.

Prior to the pandemic, pharmacists were unable to manage patients unless physically present in clinic with access to

paper charts. Staff worked in a shared clinic workspace and completed patient intake visits in person on the hospital ward or in ambulatory clinic space. Secretarial support consisted of fielding clinic phone calls, addressing incoming faxes, coordinating new patient referrals and contacting patients requiring reminders to obtain venipuncture INRs, in addition to other administrative tasks.

In November 2019, Alberta Health Services implemented Connect Care, and this central data repository provided electronic access to health records and a platform on which to order bloodwork and prescriptions, accept or decline referrals and view reports from other health care providers. While the AC staff were still gaining familiarity with electronic charting prior to the COVID-19 outbreak, the pandemic fast-tracked the transition to complete electronic documentation and scheduling, which enabled the implementation of various operational changes.

Using Connect Care was integral in the transition to working remotely for clinic staff, thereby maximizing distancing precautions for the health and safety of the limited pool of trained clinicians. Currently, administrative support is constant in clinic to address telephone/fax queries and perform other tasks. Pharmacists work remotely but have a single pharmacist rotate in clinic each day to maximize social distancing. During the initial stages of the pandemic, the in-clinic pharmacist selectively targeted incoming queries to clinic and tasks related to prescription generation, but over time, these responsibilities have shifted to all pharmacists, both remote and in clinic. Furthermore, while pharmacy student practicums were cancelled at the beginning of the pandemic, students have since returned to the site, following health and safety precautions, and work under the direct supervision of the in-clinic pharmacist. At present, patient follow-ups continue to be completed via telephone, and patient intake visits have also transitioned to telephone with minimal operational difficulties and disruption to clinic workflow.

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TABLE 1 Anticoagulation clinic operational changes due to COVID-19

Factor	Before COVID-19 pandemic	During COVID-19 pandemic
Charting and scheduling	Transitioning from paper-based chart to electronic system	Exclusively electronic
Communication between pharmacists	In person	Secure Chat and telephone
Pharmacist workspace	Clinic workstation	Clinic workstation/home office
Role of in clinic pharmacist	Mainly clinical duties	Clinical and administrative duties; precepting students
Role of pharmacy students	Collaborative teaching with all clinical pharmacists; placements cancelled at the beginning of the COVID-19 outbreak	Returning to clinic with health and safety precautions, teaching with on-site pharmacist only
Patient intake visits	In person	Telephone
Patient follow-up	Telephone	Telephone
Maximum interval between INRs	4 weeks	6-8 weeks where clinically appropriate
Requirements for initiation of POCT	3 cross-checks with venipuncture	1 cross-check with venipuncture
Requirements for continuation of POCT	1 annual cross-check with venipuncture	Requirements waived or held until patient is due for other bloodwork
Management of COVID-19 symptomatology	NA	Empiric warfarin dose adjustments or use of LMWH at discretion of clinical pharmacist
Laboratory INR testing at collection sites	Walk in or appointment	Appointment only, restricted capacity

COVID-19, coronavirus disease 2019; INR, international normalized ratio; LMWH, low molecular weight heparin; NA, not applicable; POCT, point-of-care technology.

While physically distant, the AC team holds daily video-conferences to discuss outstanding issues and relay information to staff working onsite and remotely. Further enhancing electronic communication is the Secure Chat function within Connect Care, which enables instant messaging between users. The ability to clarify issues and relay requests instantaneously has been monumental in maintaining effective communication. Examples of the use of Secure Chat for communication with other health care providers include coordinating referrals for periprocedural bridging with low molecular weight heparin (LMWH) or communicating with inpatient staff to follow up on hospital discharges. In the context of the AC, Secure Chat is most used to address clinical queries and relay administrative tasks to secretarial staff.

Perhaps the single greatest challenge the AC has addressed throughout the COVID-19 pandemic is the restricted capacity of community and hospital labs due to distancing precautions. A memorandum released by Dynalife (the laboratory services provider in Northern Alberta) in March 2020 encouraged health care professionals to cease routine laboratory testing; considering the problematic nature of follow-ups conducted without an INR to guide warfarin therapy, INRs remained essential for dosage guidance. Where appropriate, as defined by having documentation of the patient's previous warfarin maintenance doses and overall responsiveness to warfarin, the

intervals between INRs are extended. For patients having some fluctuation in their warfarin requirements, clinical pharmacists in general have extended the INR interval 1 week longer than what was previously considered standard.

To further mitigate laboratory use, the maximal interval for INR testing was assessed for patients deemed stable on warfarin (at least 3 months of consistent INRs without warfarin dose adjustment) (Table 2).^{4,7} While monthly intervals are considered standard in North America and can result in better anticoagulation control, as evidenced by a greater proportion of time in therapeutic range (TTR),^{2,4} some data support extending INR intervals to as long as 14 weeks, although these data have several methodological limitations.^{4,7} Specifically, a randomized trial having INRs drawn every 4 weeks to assess if warfarin dosing every 4 weeks vs 12 weeks is safe demonstrated TTRs that were noninferior. However, this study was limited by a small sample size of 250 patients and the mandate to still assess patients at 4 weeks, as those in the 12-week arm were still contacted every 4 weeks with sham INRs in range.⁵ A retrospective audit of patients with stable INRs assessing intervals out to 14 weeks found the percentage of INRs within an expanded range of 3 to 4.5 was 76% vs 70% for 6- vs 14-week follow-up intervals.⁶ While the authors advocate a more prolonged follow-up interval, this study inherently selected more stable patients to have longer intervals between INRs and, by

TABLE 2 Frequency of INR testing

Study	Design	Patient population	Findings	Interpretation
Shalev et al. ⁴	Retrospective analysis comparing mean interval between INR tests and TTR	<i>N</i> = 4408, AF on chronic warfarin treatment managed by GP in community setting	TTR 48% for 1- to 3-week(s) INR intervals TTR 45% for 4-week INR interval TTR 41% for 5-week interval (<i>p</i> < 0.0005)	Increased TTR (and therefore better control) seen if INR tests were performed at intervals no greater than 3 weeks. Significantly better TTR obtained when tests done in 7-day multiplications, but risk of bias may favour patients more compliant with recommended INR monitoring.
Schulman et al. ⁵	Randomized, noninferiority trial comparing INRs managed at every 4 vs 12 weeks (INR done every 4 weeks for all with sham INRs reported in the 12-week group at weeks 4 and 8)	<i>N</i> = 250; unchanged warfarin dose × 6 months	Time in INR range: 74.1% ± 18.8% (4 weeks) vs 71.6% ± 20.0%, <i>p</i> = 0.02 for noninferiority Warfarin dose change: 55.6% (4 weeks) vs 37.1% (12 weeks) Extreme INRs: 21.4% (week 4) vs 13.7% (week 12) No difference in bleeding, thromboembolic events or death	Suggests noninferiority to 4- vs 12-week warfarin management for time in range. All patients had INRs drawn every 4 weeks and were contacted by the AC; those in the 12-week group had sham INRs for weeks 4 and 8 (with unblinding for only extreme INR results of <1.5 or ≥4.5); hence, extending testing beyond 4 weeks still mandates contact with the care provider at this interval—need for future study.
Lidstone et al. ⁶	Retrospective analysis calculating percentage of INRs within, above and below therapeutic range for various testing intervals	<i>N</i> > 2000 but exact number not specified	6-week follow-up interval: 70% INRs within therapeutic range (95% CI, 68%-71%) 14-week follow-up interval: 76% of INRs within therapeutic range (95% CI, 75%-81%) 0.94% of INRs were between 5 and 7 for 6-week follow-up compared with 0.67% for 14-week follow-up	Authors report an 8-week interval between INRs to be “unnecessarily strict for stable patients.” Several limitations, including: no outcome events of bleeding or thrombosis reported due to small sample size, 14-week follow-up interval was arbitrarily chosen, expanded INR range accepted (e.g., 3.0-4.5), retrospective design enabled capture of patients with INR stability, thereby promoting extended intervals.
Pengo et al. ⁷	Randomized to INRs at maximum interval of every 4 vs 6 weeks	<i>N</i> = 124; only mechanical valves; unchanged warfarin dose × 2 months	INR >5: 20 times (0.94%) in week 4 vs 29 times (1.67%) for week 6 INR <1.5: 46 times (2.15%) for week 4 vs 28 times (1.61%) for group 6 Total rate (>5 or <1.5): 3.09% every 4 weeks vs 3.27% for every 6 weeks Mean time between INRs: 22.5 ± 9.5 days (1.33/month) for every 4-week group; 24.9 ± 18.1 days (1.20/month) for every 6-week group	If INR outside range, intervals tightened until INRs 2 weeks apart were within range. Reported extremes of INRs as anticipated indicate increased INR variability and are more predictive of bleeding/thrombotic outcomes. Underpowered, study needed to determine if outcomes are affected with different intervals of testing.

AC, anticoagulation clinic; AF, atrial fibrillation; CI, confidence interval; GP, general practitioner; INR, international normalized ratio; TTR, time in therapeutic range.

design, was limited by a small sample size and provided a wider INR range than used in our practice. Lastly, randomizing 124 patients to a maximum of 4 weeks vs 6 weeks of follow-up found that after 2 years, similar proportions of patients in each group had INRs <1.5 or >5 .⁷ Within all these studies, inadequate sample sizes prevented the ability to discern differences in bleeding/thromboembolic outcomes. As such, when applying these data to patients who are stable on warfarin, we have elected to take a moderate approach and extend INR intervals to 6 to 8 weeks, acknowledging the challenges with laboratory access alongside our ability to select patients based on both TTR and assessment of thromboembolic/bleeding risk.

As the pandemic evolved, we have adjusted to reduced lab availability by having patients booking multiple appointments several weeks in advance of an anticipated INR follow-up and encouraging use of the option of checking in on a walk-in basis online with subsequent sending of an alert to the patient's cell phone when nearing the front of the queue. Additionally, in-home INR point-of-care testing has been encouraged, and the uptake of these devices has significantly increased to such an extent that these devices have gone on back order at many community pharmacies.

Unprecedented for the AC clinical pharmacists is managing warfarin for patients with COVID-19 symptomatology. While clinicians had experience managing patients with influenza and other acute illnesses, considerably fewer empiric warfarin

dose adjustments were required, as these patients were usually able to obtain bloodwork within 1 week. For those unable to access lab services due to the requirement to self-isolate, pharmacists empirically adjust warfarin doses based on their assessment of the patient's severity of illness and contact the patient in 3 to 5 days to perform another assessment to guide clinical care. Additionally, the option of switching to an alternative anticoagulant (e.g., LMWH) is assessed on a case-by-case basis. Notably, use of direct oral anticoagulants (DOACs) should be considered, where appropriate, in place of warfarin therapy. Alberta Blue Cross has waived the 2-month warfarin trial requirement prior to granting DOAC coverage for government-sponsored programs.⁸ However, this had little effect on the AC, as pharmacists have always considered DOAC use for all patients referred and within our program to mitigate the need for routine coagulation monitoring with warfarin.

In summary, the AC extensively modified its general operations in response to the COVID-19 pandemic. The most significant changes include adjusting to a remote work environment, transitioning to an electronic charting and scheduling system, mitigating the need for standard laboratory venipuncture testing and managing patients with suspected or confirmed COVID-19. As a result, the AC team has adapted to the pandemic to optimize safety for all while continuing to provide exemplary patient-centred care amid an unprecedented health crisis. ■

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