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Outpatient management of chronic warfarin therapy at a pharmacist-run anticoagulation clinic during the COVID-19 pandemic

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Abstract
As a result of infection control regulations during the coronavirus disease 2019 (COVID-19) pandemic, anticoagulation clinics have been required to adjust their practices in order to continue providing safe and effective services for their patients. In accordance with a guidance document issued by the Anticoagulation Forum, The Brooklyn Hospital Center (TBHC) anticoagulation clinic in Brooklyn, New York implemented measures including telemedicine follow-ups instead of in-person clinic visits, extending the interval of INR testing, and reviewing eligible candidates for transition from warfarin to direct oral anticoagulants. This study describes the outcomes of one hospital-based clinic location in the 3 months before and after COVID-19 became a significant concern in the New York City area. The primary outcome of time-in-therapeutic range (TTR) for patients receiving warfarin was 60.6 % and 65.8 % in the pre-COVID and post-COVID groups, respectively ($p = 0.21$). For secondary outcomes, there was no difference in percent of therapeutic INRs (51.5 % pre-COVID v. 44.8 % post-COVID, $p = 0.75$) or percent of INRs ≥ 4.5 (2.3 % pre-COVID v. 4 % post-COVID, $p = 0.27$). Based on the data reported in this study, the short-term changes implemented at TBHC's anticoagulation clinic did not appear to cause reductions in safety and efficacy of chronic warfarin therapy management.

Keywords COVID-19 · Vitamin K Antagonist · Anticoagulation Clinic · Warfarin

Highlights

- Due to the COVID-19 pandemic, it was necessary for anticoagulation clinics to implement measures including telemedicine follow-ups instead of in-person clinic visits and extending the interval of INR testing.
- This study describes patient outcomes at one hospital-based clinic location, in the 3 months before and after COVID-19 became a significant concern in the New York City area.
- Based on the data presented, time-in-therapeutic range (TTR) was similar in the pre-COVID and post-COVID period.
- The changes implemented at this anticoagulation clinic suggest that transitioning to virtual care for short periods of time as needed during future outbreaks of COVID-19 may be done with results comparable to usual care.

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Introduction

The end of 2019 brought about a fatal infectious disease which would soon become a global public health crisis. The novel coronavirus disease 2019 (COVID-19) is a viral pneumonia which has been reported to cause massive alveolar damage and progressive respiratory failure [1, 2]. In a time where health systems have shifted much of their attention to the management of patients infected with COVID-19, it remains important for patients with chronic diseases to receive appropriate care. As a result of infection control regulations, such as social distancing and stay-at-home orders, anticoagulation clinics have been required to adjust their

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practices in order to continue providing safe and effective services for their patients [3].

In accordance with a guidance document issued by the Anticoagulation Forum (AC Forum), many anticoagulation clinics have implemented new measures to manage their patients remotely [4]. These measures include the transition of eligible candidates from warfarin to direct oral anticoagulants (DOACs), using telemedicine follow-ups instead of in-person clinic visits, and extending the interval of INR testing. This study describes the care provided during the COVID-19 pandemic at a pharmacist-run anticoagulation clinic in the New York Metropolitan area and evaluates the impact on clinic outcomes.

Methods

This was a retrospective cohort study completed at The Brooklyn Hospital Center (TBHC) in Brooklyn, New York. TBHC is a 464-bed, community teaching hospital, where outpatient anticoagulation services for patients prescribed warfarin are managed by a team of clinical pharmacists working with supervising physicians in accordance with collaborative drug therapy management agreements. The service is offered at a variety of outpatient clinic locations within the hospital's main campus and around the city. Management is primarily done through point-of-care INR testing during face-to-face visits.

In this study, patient outcomes at one hospital-based clinic location were compared in the 3 months before and after COVID-19 became a significant concern in the New York City area. The pre-COVID period is defined as December 2, 2019 to February 28, 2020. As New York State declared a State of Emergency on March 7, 2020, the post-COVID period was considered to be March 2, 2020 to June 2, 2020. Participants were included in statistical analyses if they had a visit with the clinic during both the pre- and post-COVID time periods. A visit was considered to be an encounter where the patient received management and instruction from a clinical pharmacist in response to a newly obtained INR sample. Participants on anticoagulation therapy other than warfarin were excluded.

The electronic medical record was utilized to collect patient data, including demographics, INR results, and visit details. The primary outcome was time-in-therapeutic range (TTR) before and after COVID-19. Acelis Connected Health CoagClinic™ is used by TBHC to track patient outcomes and calculate TTR utilizing the Rosendaal method of linear interpolation [5]. In this study, TTR refers to the proportion of days with INR values between the patient-specific therapeutic INR goal established by their referring provider depending on the indication for anticoagulation (most commonly 2 to 3 or 2.5 to 3.5). As the interval of INR monitoring was extended for many individuals, no time span was excluded from the measurement. Proportion of INRs within range was calculated utilizing the same definition of therapeutic range and is reported as a secondary outcome.

Other secondary outcomes include mean number of visits, mean number of days between visits (counting from the last visit in the previous time period), and proportion of INRs ≥ 4.5 before and after COVID-19. In the post-COVID period, the number of patients requiring referral to the emergency department due to a bleeding episode and the breakdown of patient visit types are reported. Patients with only post-COVID visits (e.g.—new patients during this time) who were excluded from statistical analyses were included in these reports. Patient visits were classified into one of four categories. The first was a point-of-care INR conducted as usual in a face-to-face visit. The other categories were virtual visits with either a venipuncture INR obtained at TBHC one day in advance, a venipuncture INR obtained at an outside laboratory service (e.g.—Quest Diagnostics™), or venipuncture INR obtained through other means. Virtual visits were conducted first as telephone encounters and then as video encounters as clinic telehealth capabilities were implemented.

Statistical analysis

Data were analyzed using SPSS Statistics Software for Mac. Descriptive statistics were utilized for baseline demographics, clinic visit information, and emergency department referrals. Proportion of INRs ≥ 4.5 were assessed utilizing the chi-square statistic. The Wilcoxon signed-rank test for non-parametric, continuous data was used to analyze the difference in TTR, percent of therapeutic INRs, and number of visits between the two groups. P-values of < 0.05 were considered statistically significant.

Results

A previous quality improvement project completed with this same clinic's patient population in September 2019 provided an in-detail assessment of clinic demographics (n = 91). The most prominent indication for anticoagulation treatment was multiple venous thromboembolisms (VTEs) (42 %), followed by atrial fibrillation (37 %), single VTE (17 %), and mitral mechanical valve (14 %). The mean CHA_2DS_2-VASc and HAS-BLED scores for patients with atrial fibrillation were 4.6 and 2, respectively. For patients with a history of VTE, the mean VTE-BLEED score was 2.2. Nearly all patients treated at the clinic are insured through Medicaid and/or Medicare.

During the pre-COVID time period, a total of 340 anticoagulation visits occurred with 100 patients. Following

Table 1 Patient characteristics

Characteristics	N (%) (N = 84)
Female sex	49 (58)
Mean age, years	63
Race/Ethnicity	
Black/African American	64 (76)
White	4 (6)
Hispanic	1 (1.2)
Other	15 (18)
INR Target Range	
2–2.5	3 (4)
2–3	67 (80)
2.5–3	2 (2.4)
2.5–3.5	8 (10)
3–3.5	4 (5)

the onset of COVID, 84 patients received care by the anticoagulation clinic a total of 192 times. As 5 of these patients were new and 1 had not followed up with the clinic during the pre-COVID time period, 78 patients representing 310 of the anticoagulation visits in the pre-COVID time period were included in data analysis. Demographics for the population managed during the COVID time period are presented in Table 1.

The primary outcome of TTR was 60.6 % in the pre-COVID group and 65.8 % in the post-COVID group ($p = 0.21$). For secondary outcomes, the percent of therapeutic INRs was 51.1 % prior to COVID and 44.8 % after COVID ($p = 0.75$). The percent of INRs ≥ 4.5 was 2.3 % in the pre-COVID period and 4 % following COVID ($p = 0.27$).

Patients had a mean of 3.9 and 2.3 clinic visits in the pre-COVID and post-COVID periods, respectively ($p < 0.001$). Prior to COVID, the mean number of days between patient visits was 28.3 (standard deviation [SD] 16.9; interquartile range [IQR] 17.9–32.7) with a median of 28. During COVID, the mean number of days between patient visits was 42.6 (SD 27.8, IQR 20.3–56) with a median of 34. Out of the 84 patients seen, 8 (9.5 %) had a mean of 90 or more days between visits. An additional 11 patients (13.1 %) had a mean of 60–89 days between visits, and 29 patients (35.7 %) were seen on average 30–59 days between visits. The breakdown of patient visit types is presented in Table 2. One patient was referred to the emergency department for a bleeding episode in the post-COVID time period. After being contacted overnight by the resident physician-on-call in response to a critical range INR result returning from the hospital laboratory (5.8), the patient was instructed to come in for further evaluation for reported bleeding while brushing their teeth.

Table 2 Post-COVID clinic visit types

Type of visit	N(%) (N = 192)
Face-to-Face – Point-of-care INR	98 (50.8)
Virtual–Venipuncture INR	
Hospital Laboratory	62 (32.5)
Outside Laboratory	23 (12)
Other	9 (4.7)

Discussion

To date, this study is among the first to report on outpatient management of chronic warfarin patients during COVID-19. Based on the data presented, the changes implemented at TBHC's anticoagulation clinic appear to have resulted in comparable management of patients on warfarin therapy as the primary outcome of clinic TTR was essentially unchanged in the periods before and after the pandemic. Secondary outcomes regarding proportion of therapeutic INRs and INRs ≥ 4.5 were not statistically significant between groups. This differs from results reported by a large anticoagulation service over a 6-week time period (n = 3214 INR samples) in the United Kingdom (UK), which found the proportion of INRs > 8 during the COVID-19 "lockdown" to be significantly greater than the same time period in 2019 [6]. It is possible that due to the relatively small sample size of our clinic, a statistical difference between the pre and post-COVID groups is unable to be detected.

Recommendations made by the AC Forum for management of patients on chronic warfarin therapy during COVID-19 include transitioning eligible patients to DOACs, referring patients to begin INR self-testing, and extending the interval of INR testing up to 12 weeks in patients who have had stable INR results for at least 3 months [4]. Although approximately half of anticoagulation clinic visits at our institution remained in-person, INR monitoring overall occurred less frequently as evidenced by the reduction in mean number of visits per person and a 150 % increase in the mean number of days between visits to an average well above 30. Approximately 40 % of study participants had only one visit over the 3 month study time frame, indicating an extended INR monitoring interval was a strategy frequently utilized by the clinic.

In light of recommendations to consider switching eligible patients to DOAC therapy, a patient review using a standardized template was performed when preparing to transition anticoagulation management to a hybrid virtual care model. Many eligible clinic patients had previously been transitioned to DOAC therapy, causing a slow shift over the past few years in the clinic's demographic to a more complex patient population without data to support DOAC use. This was represented in the patient

review, which indicated that ~ 20 % were likely safe for DOAC transition. Another ~ 60 % were definitively unable to be transitioned to a DOAC (e.g.—mechanical mitral valve, contraindicated drug interaction, renal function outside of package insert recommendations, etc.), and the remainder were of questionable safety (e.g.—body weight > 120 kg) or lacked the necessary data to make a complete assessment.

For the cohort of patients who were clinically eligible for DOAC transition, insurance issues and patient acceptance presented additional barriers. As the clinic manages warfarin patients based on provider referrals, one of the largest challenges during the COVID-19 time period was successfully reaching referring physicians to discuss patient management. Larger health systems may consider addressing this particular barrier within their Pharmacy & Therapeutics Committee by implementing protocols for pharmacists to directly convert appropriate candidates from warfarin to DOAC therapy. Ultimately, nearly all patients in the clinic continued to be successfully managed on their current warfarin therapy as DOAC transition proved to be difficult for our specific patient population.

Another recommended strategy considered by the clinic was implementing a "drive-up" INR point-of-care testing service [4]. This was not thought to be feasible for our institution due to inadequate space for such a service on the hospital campus in downtown Brooklyn. Additionally, the vast majority of patients seen at the clinic do not own a car and typically access care through use of public transit or paratransit services. Providing referrals for self-testing was also found to be impractical due to the processing and training time required, particularly during COVID-19 in the New York City area when self-testing services were inundated with a high number of requests.

Due to factors such as limited resources and complexity of the patient population, the anticoagulation clinic at TBHC elected to focus on strategies of virtual warfarin management while emphasizing ways to minimize patient risk of COVID-19 exposure, such as the use of masks, social distancing, good hand hygiene before and after laboratory/clinic visits, and avoiding busy laboratory times. The most popular model of virtual care selected by clinic patients was having a venipuncture INR obtained at the hospital's outpatient laboratory. The benefit of this model is its elimination of the need to spend time in a public waiting room area or have extended face-to-face contact with a clinician. One-quarter of virtual visits, however, involved the patient obtaining a venipuncture INR at an outside laboratory service. While this provided flexibility for patients who did not live close to the hospital, it was found to be the most time intensive option for clinicians as these outside services did not interface with the electronic medical record. A small number of patients also had INRs collected at "other" locations, which were primarily dialysis centers who agreed to place an order for INR collection during dialysis sessions.

A small number of patients (n = 5) initiated care at the anticoagulation clinic during the post-COVID time period. Three patients hospitalized for reasons unrelated to COVID-19 were initiated on warfarin therapy for the first time during their admissions and referred for outpatient management at discharge. The remaining two patients were referrals from outside providers and had been on warfarin for at least a short time prior to establishing care at the clinic. Data on COVID-19 infection rate for the clinic's patient population was otherwise not collected as it was not reliably available. Screening for COVID-19 symptoms was completed during each patient encounter, including virtual visits, to ensure patients could be referred to appropriate care if necessary.

Limitations of this study include a retrospective design, small sample size likely underpowered to detect a significant difference between groups, and limited patient demographic. Long-standing systemic health and social inequities have led to the primarily Black patient population included in this study to be one of the racial groups most severely affected by COVID-19 [7]. As New York City was additionally the highest risk area for COVID-19 in the United States at the time of this research, the results of this study may not be applicable to other clinics with varying demographics or in different locations. Another significant limitation is that TTR calculations over a short time period such as 3 months may be less informative than 6 or 12 month TTRs. Due to the recent onset of COVID-19, however, it is not yet possible to compare TTRs over a longer time period. Finally, the potential for survivorship bias cannot be eliminated as the study does not adequately capture the pool of individuals seen in the pre-COVID period who did not have a follow up visit in the post-COVID period. Further research is needed to identify the outcomes of these specific patients and reasons for lack of follow-up.

Conclusions

This research indicates the feasibility of managing chronic warfarin patients utilizing a hybrid virtual care model over a 3-month period during the COVID-19 pandemic without apparent reductions in safety and efficacy. Successful implementation of this strategy requires working with patients on an individual basis to determine the plan of care which best fits their medical risk, comfort level, and resources, whether that is transition to a DOAC, continuing face-to-face point-of-care INR monitoring, self-monitoring INR at home, or obtaining a venipuncture INR at a location of their choice. Extending INR monitoring intervals up to 12 weeks for patients with stable INRs should additionally be given routine consideration by anticoagulation clinics as

COVID-19 continues. Ultimately, these study results suggest that transitioning to virtual care as needed during future outbreaks of COVID-19 for patients who must remain on chronic warfarin therapy may be done for short periods of time with results comparable to usual care.

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Declarations

Conflict of interest Briann Fischetti has previously received an investigator sponsored grant from ViiV Healthcare, a company of GSK.

References

1. Ge H, Wang X, Yuan X et al (2020) The epidemiology and clinical information about COVID-19. Eur J Clin Microbiol Infect Dis 39(6):1011–1019. https://doi.org/10.1007/s10096-020-03874-z
2. Xu Z, Shi L, Wang Y et al (2020) Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 8(4):420–422. https://doi.org/10.1016/S2213-2600(20)30076-X
3. Mohammad I, Berlie HD, Lipari M et al (2020) Ambulatory care practice in the COVID-19 era: redesigning clinical services and experiential learning. J Am Coll Clin Pharm. https://doi.org/10.1002/jac5.1276
4. Barnes GD, Burnett A, Allen A et al (2020) Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum. J Thromb Thrombolysis 50(1):72–81. https://doi.org/10.1007/s11239-020-02138-z
5. McAlister FA, Wiebe N, Hemmelgarn BR (2018) Time in therapeutic range and stability over time for warfarin users in clinical practice: a retrospective cohort study using linked routinely collected health data in Alberta, Canada. BMJ Open 8(1):e016980. doi:https://doi.org/10.1136/bmjopen-2017-016980
6. Speed V, Patel RK, Byrne R, Roberts LN, Arya R (2020) A perfect storm: root cause analysis of supra-therapeutic anticoagulation with vitamin K antagonists during the COVID-19 pandemic. Thromb Res 192:73–74. https://doi.org/10.1016/j.thromres.2020.05.024
7. Millett GA, Jones AT, Benkeser D et al (2020) Assessing differential impacts of COVID-19 on black communities. Ann Epidemiol 47:37–44. https://doi.org/10.1016/j.annepidem.2020.05.003