Time in therapeutic range for virtual anticoagulation clinic versus in-person clinic during the COVID-19 pandemic: a crossover study

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BACKGROUND: COVID-19 infection affects the quality of the medical services globally. The pandemic required changes to medical services in several institutions. We established a virtual clinic for anticoagulation management during the pandemic using the Whatsapp application.

OBJECTIVES: Compare anticoagulation management quality in virtual versus in-person clinics.

DESIGN: A retrospective crossover study

SETTINGS: Specialized cardiac care center

PATIENTS AND METHODS: The study included patients who presented to Prince Sultan Cardiac Center in Riyadh for anticoagulation management during the pandemic from March 2020 to January 2021. We compared time in therapeutic range (TTR) in the same patients during virtual and in-person clinics. All international normalized ratio (INR) measures during the virtual clinic visits and prior ten INR measures from the in-person clinic were recorded. Patients who had no prior follow-up in the in-person clinic were excluded.

MAIN OUTCOME MEASURE: TTR calculated using the Rosendaal method.

SAMPLE SIZE: 192 patients

RESULTS: The mean age was 58.6 (16.6) years and 116 (60.4%) were males. Patients were diagnosed with atrial fibrillation (n=101, 52.6%), mechanical mitral valve (n=88, 45.8%), mechanical aortic valve (n=79, 41%), left ventricular thrombus (n=5, 2.6%) and venous thromboembolism (n=8, 4.2%). Riyadh residents represented 56.7% of the study population (n=93). The median (IQR) percent TTR was 54.6 (27.3) in the in-person clinic versus 50.0 (33.3) (P=.07).

CONCLUSION: Virtual clinic results were comparable to in-person clinics for anticoagulation management during the COVID-19 pandemic.

LIMITATIONS: Number of INR measures during the virtual clinic visits, retrospective nature and single-center experience.

CONFLICT OF INTEREST: None.
The vitamin K antagonist warfarin has a high-risk profile; therefore, it is managed under a specialized anticoagulation management clinic to ensure the efficacy and safety of its clinical use. The COVID-19 pandemic limited all ambulatory healthcare services. The quarantine required application of remote medical services or so-called telehealth. Patients on warfarin requiring regular visits to the anticoagulation clinic to adjust their international normalized ratio (INR) were one of the major challenges during the pandemic era.

Clinical pharmacists were involved in anticoagulation clinics to meet the high demand for anticoagulation management services. Clinical pharmacy services with a telepharmacy practice are well-established worldwide. Pharmacist–managed anticoagulation management services have been shown to be superior to other anticoagulation management services models.

The telehealth model in anticoagulation is an innovative approach for Anticoagulation management and has shown its potential to improve the quality metrics of anticoagulation and the patient outcomes. At the Prince Sultan Cardiac Center, anticoagulation management is a well-established service that has reasonable outcomes. The virtual clinic was started during the COVID-19 pandemic to ensure a high standard of patient anticoagulation management. The patient encounter was conducted virtually, where the pharmacist assessed the INR and planned the new dose. The prescription was processed and delivered to the patients through an ambulatory pharmacy medication delivery program. This study aimed to assess and evaluate the effectiveness of virtual pharmacist-led versus in-person anticoagulation clinics.

PATIENTS AND METHODS
This retrospective crossover study included patients who presented to our virtual clinic for anticoagulation management during the pandemic from July 2020 to January 2021. Prince Sultan Cardiac Center in Riyadh. We included all adult patients aged ≥18 years old who were followed in the virtual anticoagulant clinic. Patients were required to have a minimum of three INR results on separate virtual clinic follow-up appointments and a minimum of ten actual INR results in their previous in-person clinic appointments. We compared the INR readings in the same patients during the in-person and virtual clinics. Demographic data, indications for warfarin therapy, and the INR result in each visit were collected from the electronic records. All patients who had no prior follow-up in the in-person clinic were excluded. The research ethics committee approved the study (Approval No# R20024). The need for patient consent was waived because of the retrospective design.

The virtual clinic was first started using the “WhatsApp” application and phone calls for warfarin dosing adjusting and instructions. The follow-up ranged from 1 to 3 months, depending on the INR result and needed intervention. The patients performed their INR testing outside the hospital and sent it to the anticoagulation clinic through Whatsapp. The clinician received the message and started the visit virtually by verifying the patients’ identity and INR. After that, the clinicians sent the management plan to the patients and recorded it on the electronic encounter.

The study endpoint was the time in therapeutic range (TTR) calculated using the Rosendaal method. Percentage of TTR (TTR%) calculations were conducted for patients using only their actual in-person visits (last ten visits), including the first virtual visit (making it 11 visits total included in the first calculation). Next, TTR% calculations were conducted using only their virtual visit INR test results (approximately 3–4 recent visits). We compared TTR in the same patients during the period of virtual and in-person clinics.

The estimated sample size calculated before the study was 123 patients. The sample size was calculated based on an expected TTR in the in-person clinic of 0.65 and the difference between virtual and actual clinics of 0.05 (standard deviation of 0.2). The Type I error probability associated with this null hypothesis test was .05 and the study power was 0.80.

The distribution of the TTR was tested using the Shapiro-Wilk test and by observation of a histogram, and were not normally distributed so comparisons were made by the Wilcoxon test for paired data. The continuous variables were expressed as mean (standard deviation, SD) or median and 25th to 75th percentile, and the categorical variables as counts and percentages. Stata 16 (Stata Corp- College Station- TX-USA) was used to analyze the data, and a P value of less than .05 was considered statistically significant.

RESULTS
The mean age of the 192 patients was 58.6 (16.6) years and 116 (60.4%) were males. Patients were diagnosed with atrial fibrillation (n=101, 52.6%), mechanical mitral valve (n=88, 45.8%), mechanical aortic valve (n=79, 41%), left ventricular thrombus (n=5, 2.6%) and venous thromboembolism (n=8, 4.2%). Sixty-eight (35.42%) were diabetics, 103 (53.65%) were hypertensives, and 23 (11.98%) had chronic kidney disease. Riyadh residents presented 56.7% of the study population (n=93). For in-person clinic the median
(IQR) TTR% was 54.6 (27.3) and for the virtual clinic the median was 50.0 (33.3) (P= .07) (Figure 1).

DISCUSSION
We evaluated the use of virtual anticoagulation management in the COVID-19 era. The patients in the virtual clinic were in the therapeutic range for 50.0% of the time and for 54.6% of the time in the in-person clinic. There was no statistically significant difference between virtual and in-person clinic TTR. This result showed an overall improvement in anticoagulation management compared to our previous study conducted in Prince Sultan Military Medical City, which showed a lower TTR for in-person clinics of 52%. This TTR for the in-person clinic has been reported in many studies in developing countries. A local study from Saudi Arabia recently reported a virtual clinic TTR <50% in 42.7% of atrial fibrillation patients. The lower TTR reported could be due to a lower sample size (n=124) and shorter study duration (6 weeks).

Telehealth response to emergencies such as the COVID-19 pandemic is ideal for managing patients on a social distancing basis, which significantly impacts the health economy. Our study showed that telehealth has the potential to provide good remote assessment and provision of care during a pandemic that requires quarantine. A pilot study was conducted in a hospital in New York on eight patients to test a program they initiated to improve TTR. The tele-anticoagulation and thrombosis services program showed a mean (SD) improvement in TTR of 45.7% (14.5%) in regular anticoagulation management services and a virtual TTR of 77.9% (9.7%). Telehealth can also serve as a convenient care model when providing routine care for patients in rural and remote areas, which presented a good percentage in our study population (43.3%).

Although the benefits of telehealth are known, the uptake of telehealth is slow and erratic. Factors related to uptake include access to telehealth, clinician willingness, and reorganization of medical care workflow. In our hospital, telehealth application for anticoagulation management was started with the COVID-19 pandemic to reduce patient visits to the hospital, especially during the quarantine. This service was delivered by means of the WhatsApp application and phone calling at the beginning of our study, and we made continuous improvements to the telehealthcare model. Moreover, quarantine and curfew measures during the pandemic could have affected the quality of the services. We believe that these were the explanations for relatively low TTR in the virtual compared to in-person clinics. Additionally, the virtual

| Table 1. Baseline characteristics of the study participants (n=192). |
|---------------------------------------------------------------|
| Age (years) | 58.6 (16.6) |
| Male | 116 (60.42) |
| Atrial fibrillation | 101 (52.6) |
| Mitral valve replacement (mechanical) | 88 (45.83) |
| Aortic valve replacement (mechanical) | 79 (41.15) |
| Left ventricular thrombus | 5 (2.60) |
| Venous thromboembolism | 8 (4.17) |
| Diabetes mellitus | 68 (35.42) |
| Hypertension | 103 (53.65) |
| Chronic kidney disease | 23 (11.98) |
| Ischemic heart disease | 32 (16.67) |
| Heart failure | 21 (10.94) |
| Alkaline phosphatase (U/L) | 87 (68-112) |
| Alanine transaminase (U/L) | 17 (13-23) |
| Creatinine (µmmol/L) | 76 (61-99) |
| Creatinine clearance (mL/min) | 87 (64-121) |
| Riyadh residents | 93 (56.71) |

Data are n (%) or median (IQR), and mean (standard deviation) for age.

Figure 1. Time in therapeutic range during the in-person and virtual anticoagulation clinics (median, interquartile range) (P= .076).
service was first implanted during the pandemic without patient education and before establishing a patient-clinician relationship, which could improve the quality of telemedicine. After the pandemic, we launched an online system for anticoagulation management to increase the quality of the service and ensure patient confidentiality.

Although we have not evaluated the cost of the service directly, the virtual clinic service is expected to lower the cost of care since the patients performed INR testing close to their residency. Additionally, the cost of patient transportation was replaced by the lower cost of prescription delivery. Web-based anticoagulation management was shown to be inexpensive for anticoagulation management in previous research.

In a study from India, the mean TTR significantly improved with the virtual clinic during the COVID-19 pandemic. Before the pandemic, remote anticoagulation services improved the quality of anticoagulation by increasing the TTR and decreasing its variability. These two studies indicate that there is ample space to improve the virtual anticoagulation services and achieve a better TTR than the actual clinics. Several barriers may hinder the delivery of optimal remote anticoagulation services. Individualized approaches to specific patient needs are essential for future service improvement.

The limitation of the study was that the study was retrospective versus a study with prospective randomization. These limitations are justified by the performance of the study during the COVID-19 pandemic, and the virtual clinic was the only service available for those patients. Additionally, it is limited by the few INR results after initiation of the virtual clinic and the relatively short duration of follow-up, which may have affected the TTR; the P-value for comparison of the two methods was marginally non-significant. The P-value could change significantly with more patients in the study or more INR readings. The logistics of the virtual clinic were changed after the end of the lockdown, and to maintain the homogeneity of the included patients and the conditions of follow-up. We limited the study to the duration of the pandemic. The study was a single-center experience, but our center is a tertiary referral center that serves different regions in the country, and this was reflected by the number of patients who presented from outside Riyadh.

In conclusion, our results show that virtual clinic results were comparable to in-person clinics for anticoagulation management during the COVID-19 pandemic. Several factors during the COVID-19 pandemic could have affected the performance of the virtual clinic. Further improvement in performance of the virtual clinic is expected beyond the COVID-19 era.

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