The coronavirus disease 2019 (Covid-19) pandemic has challenged health care systems to implement strategies to limit the spread of disease while continuing to provide essential health care services to the patients they serve. This case study describes how Atrium Health’s Sanger Heart & Vascular Institute designed and implemented a clinical protocol to minimize Covid-19 exposure for 2,312 high-risk patients receiving vitamin K antagonist (VKA) therapy. Patients either (1) were actively converted to a direct oral anticoagulant agent according to appropriate indications or (2) had their international normalized ratio (INR) testing intervals extended according to clinical guidelines. In addition, mobile INR testing capabilities were established so that patients requiring ongoing VKA management could do so in a manner that reduced in-person contact. Given the potential for further Covid-19 surges, patients continuing to require VKA therapy are being actively transitioned from on-site testing to home INR monitoring.

**KEY TAKEAWAYS**

- Effecting rapid transformation in care delivery while ensuring patient safety requires detailed planning.
- Forming dedicated teams, each with specific roles and assigned responsibilities, is essential to achieve meaningful transformation.
Utilizing available information sources to identify opportunity and to assess outcomes is vital in supporting a large-scale change effort.

Issues such as cost (including costs directly incurred by the patients), convenience, preference, and access will limit that which is achievable with any “real world” change effort, even when those concerns are identified and addressed prospectively.

Outcomes that are <100% of the defined opportunity may nevertheless be meaningful.

The Challenge

Cardiovascular patients receiving vitamin K antagonist (VKA) therapy, commonly known as warfarin, are at high risk for severe illness from Covid-19.\(^1,2\) Care of these patients typically includes in-office visits to acquire blood samples for international normalized ratio (INR) testing (a measure of the time it takes for blood to clot), for VKA dosing management. The cadence of these dosing visits varies by patient and clinical condition, but it is not unusual for weekly visits to be required when initiating or adjusting VKA therapy.

These in-person encounters increase the exposure of this high-risk group to Covid-19. When clinically appropriate, changing from VKA therapy to a direct oral anticoagulant (DOAC) agent can reduce potential Covid-19 exposure, as considerably fewer blood samples are required for DOAC management. Despite demonstrated superior efficacy of DOAC agents to VKA therapy in many clinical conditions, the relative novelty of DOAC agents and concerns regarding their costs have served as barriers to their broader-scale adoption across health systems.

The Goal

With the outbreak of the Covid-19 pandemic and institution of “shelter in place” restrictions, we at Sanger Heart & Vascular Institute (SHVI) strove to maintain the safe continuation of anticoagulation management for our 2,312 patients on VKA therapy. While the indications for and dosing of VKA agents are diagnosis-specific, the most common indications in our patient population were for (1) management of atrial fibrillation/flutter (Afib/Afl) and (2) chronic management of deep vein thrombosis or pulmonary embolism (DVT/PE).

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The clinical non-inferiority (if not superiority) of DOAC agents relative to VKA therapy in these cohorts is well accepted.\(^3\) In addition, recognizing that utilization of our ambulatory care team had decreased markedly consequent to self-quarantine behaviors, we reasoned that devoting clinical staff time to a broad-scale medication conversion effort during the pandemic would optimize
use of these staff resources. Accordingly, we formulated a plan to convert VKAs to DOACs in appropriately selected patients. If conversion to DOACs was deemed inappropriate, a plan was formulated instead to increase the interval between INR testing in accordance with best practice protocols.4,5

The Team

Twelve registered nurses (RNs), two medical assistants (MAs), and two advanced practice providers (APPs), led by the SHVI Director of Nursing (KG) and Physician Director of Medical Education (RM), were organized into three teams: Conversion, Compliance, and Continuation. The Conversion team (7-10 RNs and APPs) was responsible for recommending the specific transition details from VKAs to DOACs for each patient eligible for DOAC transition. The Compliance team (one RN and two MAs) engaged in insurance authorization and other patient-assistance activities as needed for those patients identified as candidates for conversion to a DOAC agent. The Continuation team (four VKA RNs and one APP) was responsible for reviewing the records of those patients not transitioned to DOAC therapy to determine if subsequent INR testing could be safely conducted on a less frequent basis.

The Execution

By March 23, 2020, the SHVI clinical informatics team, through a search of the electronic health record (EHR), identified 2,312 patients who were being managed with VKAs at 17 SHVI care locations. The primary care and/or SHVI providers for these patients were notified of the planned DOAC conversion through clinical messaging within the EHR or by secure email. This communication provided the rationale for the conversion effort and detailed description of the conversion protocol. All team members then worked to evaluate the individual records of these VKA patients to determine each patient’s eligibility for DOAC conversion. A clinical database of these patients was developed.

The Conversion team further reviewed the EHR of all patients deemed appropriate for DOAC conversion and recommended the specific transition details in accordance with the SHVI conversion protocol (Figure 1). This information was documented on a standard “transition template” within the EHR. The completed transition template was sent securely within the EHR to inform the primary provider of intended conversion. The primary provider was given the opportunity to refuse conversion; DOAC conversion proceeded unless specifically halted by the primary provider.
The Conversion team was also responsible for patient education on DOAC use. SHVI elected to utilize apixaban therapy as the primary DOAC to simplify the conversion process, as the safety and efficacy of apixaban therapy are well established.\textsuperscript{6-8} Apixaban was utilized unless otherwise contraindicated by prior drug allergy/sensitivity, patient insurance restrictions, or preference of the patient or primary provider. As indicated in Figure 1, other DOACs such as Rivaroxaban were offered if the patient was allergic to apixaban. If on review a DOAC contraindication was identified
or if the patient (or primary provider) elected not to proceed with DOAC conversion, VKA therapy was continued and the Continuation team notified via the EHR.

After communication and education were provided to the patient, a prescription was submitted to the pharmacy on behalf of patient’s SHVI provider to facilitate future refills. In conjunction with Atrium Health Pharmacy Services and the manufacturer, pharmaceutical samples were provided to facilitate the initiation of DOAC conversion. To minimize patient in-person contact solely for the purposes of INR assessment, the patient was instructed to discontinue VKA therapy for 4 days, then to begin DOAC therapy on the morning of the 5th day. This time frame was established to minimize the risk of bleeding while also balancing the risks of not being anticoagulated. Pre-conversion assessment of INR was performed upon recommendation of the primary provider but was not mandated.

“The primary provider was given the opportunity to refuse conversion; DOAC conversion proceeded unless specifically halted by the primary provider.”

The Compliance team worked in concert to ensure that patients transitioned to a DOAC agent were able to safely continue long-term DOAC therapy. This team initiated any prior authorization and facilitated in preparing patient assistance forms. For those patients who could not continue DOACs due to cost or other reasons, the team facilitated the resumption of VKA therapy.

The Continuation team reviewed the record of INR values of VKA patients for the preceding 3, 6, and 9 months. According to documented safety standards in care (Figure 2), appropriate extension of INR testing intervals was initiated on April 1, 2020. For VKA patients, drive-up point of care (POC) INR testing at numerous care locations was instituted to further minimize Covid-19 exposure. Drive-up testing protocols were developed in compliance with Clinical Laboratory Improvement Amendments (CLIA) standards. Notably, protocols emphasized strict adherence to the environmental requirements for maintaining the accuracy of POC INR strips (ambient temperature range of 59°–90°F). Clinical encounters outside the temperature range occurred within the usual office setting.
SHVI Protocol for Extending INR Testing Interval in Patients on Vitamin K Antagonist Therapy

As of April 1, 2020, 2312 patients within our system were on VKA therapy. Table 1 shows their eligibility criteria for conversion to apixaban. Of all patients on VKAs therapy, 29% had a contraindication for DOAC use, 6% had history of acute DVT/PE for which VKA was recommended, and 1.5% were on high-risk medications or had documented allergy to apixaban. The remaining 63% were eligible for conversion to DOAC. Between April 1 and May 15, 2020, our team converted 30% of these eligible patients to a DOAC agent (Table 1). For the remaining 70% of eligible patients who were not converted to DOAC therapy, our team examined the reasons for non-conversion (Table 1).

As of December 1, 2020, we reviewed the medical records of those 437 patients converted to DOAC therapy to assess their compliance with the new agent. We found that 74% had maintained DOAC therapy. Cost was the main reason cited for conversion back to VKA. We also reviewed the number of office visits in February 2020 that were conducted solely for in-office INR evaluation and compared those similar visits in November 2020. The number of such visits decreased by 65%.

Hurdles

There are many challenges that may affect uptake of new medication changes. In our case study, the primary obstacle to conversion was cost, as cited by the 21% of patients eligible for conversion who continued their current VKA regimen. This percentage may be even higher; the lack of conversion due to “patient preference” was 49%. Insurance coverage plans for patients varied in their support for DOAC agents. Dedicated staff, such as the Continuation team in this study, are essential for navigating complex drug coverage issues.
We also reviewed the number of office visits in February 2020 that were conducted solely for in-office INR evaluation and compared those similar visits in November 2020. The number of such visits decreased by 65%.

A large-scale clinical care conversion effort like this one is resource intensive. It requires redirection of clinical staff time. This redirection happened to be possible in this case owing to the unique circumstance of the Covid-19 pandemic, which freed staff time because some clinical services were suspended. We recognize that future broad-scale change efforts within our health system will likely require additional staff resources, as it is unlikely such clinical redeployment will be practicable once all staff resume their normal schedules.

Next Steps

We will reevaluate the 324 patients who were converted to a DOAC agent and compare them to those of the original cohort who remain on VKA therapy. Primary end points will include major acute clinical events at 90 days after DOAC conversion. The specific components of this composite end point include hospitalization for DVT/PE, embolic events, and major bleeding events requiring hospitalization or transfusion. Secondary end points at 90 days after conversion will include minor bleeding and Covid-19 status. Quality-of-life surveys will be conducted at 6–9 months.

In response to the ongoing Covid-19 pandemic, SHVI continues to offer additional opportunities to reduce potential in-office exposure. All patients remaining on a VKA are being evaluated for conversion to home INR management. SHVI plans to manage the INR values obtained at our 17
care locations by a centralized virtual team of RNs. Patients on VKA therapy who do not undergo home testing will continue to be managed in the office setting.

The circumstances surrounding the Covid-19 pandemic provide a unique opportunity to rethink care delivery for cardiovascular patients. Our case study describes one such care domain — namely, anticoagulation management — that could be transformed through judicious application of process and resources. Applying this approach to reexamine other entrenched care practices (e.g., ED referral for diuretic treatment; prolonging hospitalization owing to lack of home-based care options) could potentially yield similar clinical gains.

Where to Start

We recommend that health systems begin by assessing the clinical infrastructure and workflows associated with current care of patients. Any opportunity to increase effectiveness of the ambulatory delivery of that care should be examined, as such gains will serve to mitigate the strains on health systems incurred by the Covid-19 pandemic. Implementing any safe and effective transformation in care will require both thoughtful planning and new (or reallocation of) resources. Patient engagement will be essential for implementing and sustaining any change from baseline approaches to care and therefore must be specifically addressed. In addition, given the inherent complexity of such efforts, strong clinical and administrative leadership is crucial if this type of rapid, large-scale transformation in care delivery is to be achieved.

It is worth emphasizing that the “call to action” associated with a public health emergency, like the Covid-19 pandemic, affords health systems an especial opportunity to effect transformation in care delivery: meaningful changes that would have taken a much longer amount of time, or might never have happened at all, under normal circumstances.

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