

Original Research

Effectiveness of a technological tool associated with pharmaceutical guidance in hospital discharge of patients using warfarin

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Abstract

Background: Warfarin is an anticoagulant considered a high-alert medication by the Brazilian Institute for Safe Practices in the Use of Medicines. The clinical pharmacist advises patients on safety and adherence to this therapy. Lack of patient guidance can lead to undesirable outcomes, from readmissions to deaths. **Objective:** The objective of this study was to evaluate the impact of the use of a technological tool associated with the role of the clinical pharmacist in a tertiary hospital in guiding patients on the use of warfarin. **Method:** Cohort research with 960 patients using warfarin from 2017 to 2020 and discharged from hospital. Information was compared between the period before (G1) and after (G2) the implementation of the technological tool that searches for specific keywords in real-time in the hospital operating system. **Results:** A greater range of patients was advised at hospital discharge, going from 57.4% in G1 to 74.9% in G2 ($p<0.001$). Implementing a technological tool in the hospital system allowed the identification of discharged patients using warfarin in real-time. Internal failures can be avoided by implementing health technologies, as evidenced in our research. Warfarin belongs to a group of high-alert medications; all patients could benefit from technological tools. We understand that despite some perceived limitations, the application achieved the purpose for which it was developed, and its use could, in the future, be extended to other medicines and internal hospital processes. **Conclusion:** Health technologies can benefit patients and healthcare professionals, as demonstrated by the greater scope of patients guided by clinical pharmacists at hospital discharge. Given the scarcity of similar studies, new strategies must be developed for outpatients and home monitoring.

Keywords: pharmacists; warfarin; patient discharge; pharmaceutical services; biomedical technology; information technology

INTRODUCTION

Haemostasis is responsible for preventing and stopping bleeding, which results in the blockage of vascular injury, in addition to maintaining blood fluidity and the integrity of blood vessels. Platelets and clotting factors do not stick to blood vessels. When tissue injury occurs with the release of endothelial proteins and von Willebrand factor, there is adherence, recruitment, and activation of platelets, secretion, and synthesis of vasoconstrictors to stabilize the clot.¹

Thromboembolic events (TE) are among the main causes of mortality and morbidity worldwide and are prevented by anticoagulant medications.^{2,3,4} Warfarin blocks the transformation of oxidized vitamin K into reduced vitamin K, which acts as a coenzyme and prevents and treats venous thromboembolism.^{5,6}

The use of warfarin has been described since 1954 and is often started during hospital admission and prescribed for continued

use after the patient is discharged. From 2009 onwards, the use of anticoagulants in clinical practice was expanded due to new oral anticoagulants (NOACs) or “direct action anticoagulants” (DAA), as called by the International Society of Thrombosis and Hemostasis.⁷ These anticoagulants, unlike warfarin, do not have a narrow therapeutic index, have fewer drug-drug and drug-food interactions, and can be administered in standardized doses without requiring frequent laboratory monitoring, differentiating them from warfarin. Despite this, warfarin remains the anticoagulant most prescribed by doctors in Brazil due to its affordable cost and patient access through the Unified Health System (SUS) programs.^{7,8,9}

The consumption and therapeutic choice of warfarin continue to increase around the world. A study carried out in the United States demonstrated a 45% increase in the dispensing of warfarin tablets between 1998 and 2004.^{10,11}

According to the Institute for Safe Practices in the Use of Medicines (ISMP) in Brazil, medicines containing warfarin require high surveillance due to the high risk of medication errors, leading to significant patient harm.¹² The factors that affect the activity of this drug are important, as deviation from its therapeutic window can result in a greater risk of thrombosis, in the case of subtherapeutic levels, or risk of bleeding, when excessive anticoagulation occurs, the latter of which can lead to adverse events, with risk of morbidity and mortality. Furthermore, there is significant variability in the dose-response relationship. Patients’ understanding of anticoagulant therapy is of fundamental importance for safe

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and effective treatment.^{12,13}

Institutions such as ISMP constantly develop and recommend strategies to avoid errors associated with potentially dangerous medications in hospital and outpatient settings, including promoting patient education that the pharmacist can carry out in a multidisciplinary team.^{13,14}

Innovations in information technologies applied to the health sector to improve patient care and care are essential, as they can bring benefits in monitoring, generation of information, and awareness regarding health care, disease prevention, and health management.¹⁵

Our study was conceived based on the premise that it could be possible to consider that the implementation of a technological tool that identifies patients discharged from hospital using warfarin and triggers an internal alert system for the Clinical Pharmacists team in a tertiary hospital has expanded its performance and contributed to reducing hospitalizations and improving clinical outcomes. The objective of this study was to analyze the impact of using a technological tool associated with the work of the Clinical Pharmacist in a tertiary hospital to increase the number of patients advised on the use of oral anticoagulant – warfarin.

METHOD

The study was approved by the PUC-Campinas Human Ethics Committee (number 5,098,027).

Participants were patients who remained hospitalized at the PUC-Campinas Hospital (Campinas, SP, Brazil) from 2017 to 2020, aged at least 18, continuously using warfarin, and who were discharged from the hospital while still using it.

Study design

Cohort research was conducted in a medium- and high-complexity university hospital in Campinas/SP, Brazil. The hospital operates with strategic lines of care in cardiology, oncology, and bariatric surgery.

The technological tool used in this research is software that searches for specific keywords in real-time within the MV2000® operating system, which are: “hospital discharge,” “warfarin,” and “Marevan” (a term referring to the drug Marevan®, which has warfarin as its active ingredient). These specific keywords are obligatorily entered into patient records by hospital staff. Immediately, the technological tool starts an alert system that sends messages to the smartphones of the hospital’s clinical pharmacists and informs the bed and initials of the patient being discharged from the hospital so that they can carry out pharmaceutical guidance before the patient leaves the hospital. The alert system stops when the clinical pharmacist accesses the operational system and records the guidance provided.

Pharmaceutical guidance

The hospital’s pharmacy service team is responsible for pharmaceutical guidance (FG) for patients discharged. Before implementing the technological tool, this guidance depended on verbal communication. The FG is performed, and the patient

receives a booklet containing essential self-care information.

Patients are informed about the dose and dosage, care in storing the medication, frequent monitoring, changes and bleeding that may occur and how these may be perceived by the patient and family, in addition to information about food and its interactions with warfarin, the use of other medications concomitantly, the performance and scheduling of invasive procedures and the need to communicate the use of this anticoagulant in medical care to any health service.

Data collect

Data were collected from the medical records of patients who met the inclusion/exclusion requirements from January 2017 to October 2020, taking care that the sample analyzed covered the same number of months before and after the implementation of the technological tool (name, dates of start of care and hospital discharge, length of stay, whether the manual/guidance was delivered and if not, what would be the reason identified). Two groups were considered and compared: Group 1 (G1) the pre-implantation group (n=481); Group 2 (G2) the post-implantation group (n=479). Group 3 (G3) comprised the combination of Groups 1 and 2.

Statistical Analysis

The statistical analysis compared the pre- and post-implementation groups of the technological tool implemented on October 17, 2018. Statistical analyses were conducted using the software SPSS V20®, Minitab 16®, and Excel Office 2010®. The significance level was set at 0.05 (5%), and confidence intervals were constructed with 95% statistical confidence. Parametric statistical tests were used, as the normality of the main outcome quantitative variables was tested using the Kolmogorov-Smirnov test (n≥30), concluding that there is a normal distribution.

RESULTS

The results show no statistically significant mean difference between Groups 1 and 2 for length of stay and age at admission (Table 1). However, some differences were noticed in other variables (Table 2).

During the analysis, to verify whether or not there is an association, the distribution of the Total column was compared with the distribution of the other (intermediate) columns. As shown in Table 2, there is a statistically significant difference between the groups in the distribution of the three factors since the values per line analyzed differed from the value in the total column, making it possible to infer the probability of association and statistical dependence.

After the analysis, it can be concluded that there is a statistically significant relationship between “Hospitalization related to Warfarin” and “Readmission” in both groups. In Group 1, the readmission rate was 37.9% among people “Without Warfarin” versus 23.3% among people “With Warfarin” (p-value = 0.009). In Group 2, the readmission rate was 46.8% among people “Without Warfarin” versus 34.9% among people “With Warfarin” (p-value = 0.044).



	Groups	Average	Median	Standard deviation	CV	Min	Max	N	IC	P-valor
Hospitalization time (days)	1	12,61	9	13,56	108%	1	152	481	1,21	0,197
	2	13,76	9	13,90	101%	0	114	479	1,24	
Age at admission (years)	1	58,18	60	16,36	28%	18	97	434	1,54	0,942
	2	58,26	60	15,37	26%	19	92	479	1,38	

Coefficient of Variation (CV), minimum (Min), maximum (Max), sample number (N) and confidence interval (CI). T-Student Test

N		Group 1		Group 2		Total		P-valor
		%	N	%	N	%		
Patient assessment	No	85	17,7%	46	9,6%	131	13,6%	<0,001
	Yes	396	82,3%	433	90,4%	829	86,4%	
Delivery of the guidance manual	No	205	42,6%	120	25,1%	325	33,9%	<0,001
	Yes	276	57,4%	359	74,9%	635	66,1%	
readmission	No	312	64,9%	265	55,3%	577	60,1%	0,003
	Yes	169	35,1%	214	44,7%	383	39,9%	

Caption: Chi-Square Test

DISCUSSION

Software for managing processes and measuring results in hospitals is widespread worldwide and helps with dynamics. Given the high number of professionals who work in these services daily, patients are assisted, and adverse events related to care are prevented.

The National Action Plan for the Prevention of Adverse Drug Events drawn up in the United States in 2015 identified three classes of high-priority medications: anticoagulants, with warfarin as the main representative; hypoglycaemic agents, represented by insulins; and opioid analgesics. These classes are responsible for serious damage, which is considered preventable.¹⁶

In our study, we evaluated the impact of implementing software that helps in the real-time identification of patients discharged from the hospital using warfarin for immediate pharmaceutical guidance before the patient leaves the hospital.

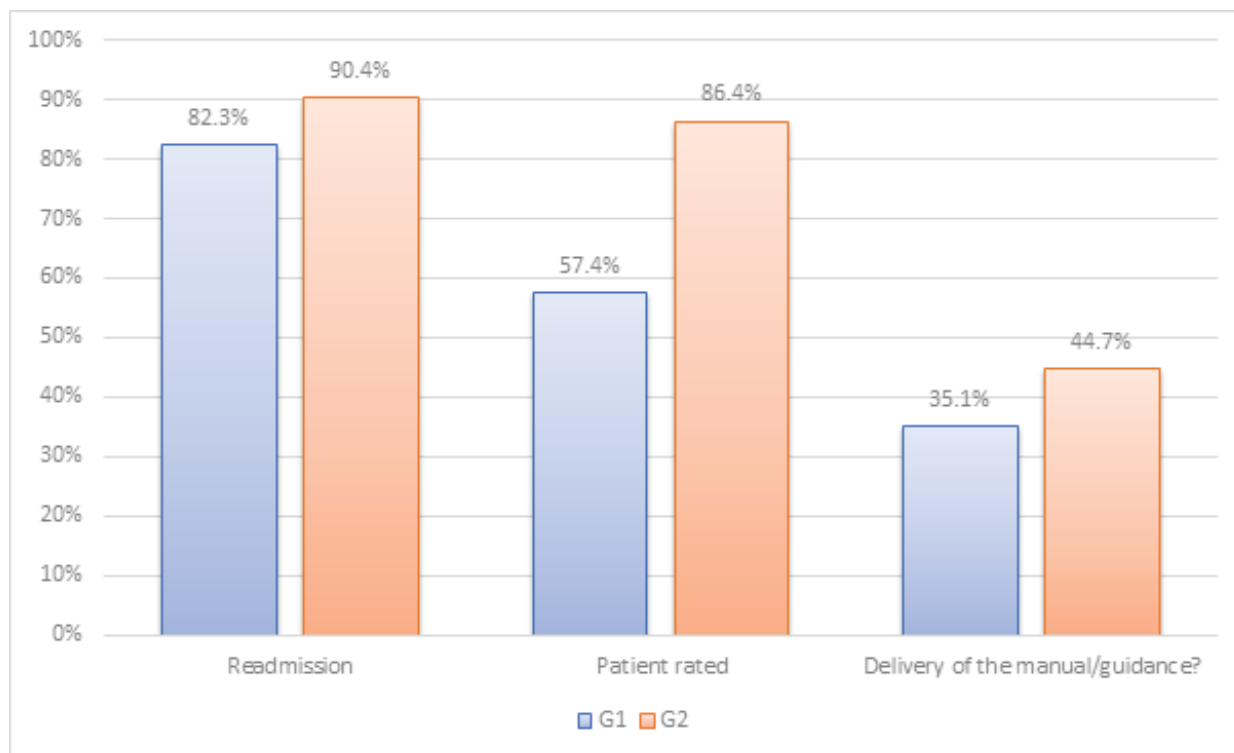
Studies of this nature were carried out in other locations to evaluate the efficiency of using software. Natali et al.¹⁷ carried out a retrospective analysis regarding incorporating a real-time pharmacotherapy alert system that highlighted medication errors. In this study, the authors compared the “pre” and “post” periods of implementation of the alert system, with the “pre” period comprising the clinical pharmacist responding to all alerts. In contrast, the “post” or “intervention” period was restricted to some medications such as darbepoetin, filgrastim, fondaparinux, and warfarin. There was a 36% decrease in the frequency of error verification alerts, allowing us to conclude that the association between the implementation of the system and monitoring by pharmacists made it possible to avoid errors in the verification stage and possible harm to the patient.

In another study, the authors noticed the efficiency of these technological resources. Falconer et al.¹⁸ developed a computational tool with the clinical pharmacy department in New Zealand called the Risk Assessment Tool, which issued a report prioritizing hospitalized patients to prevent adverse drug events. Such patients were classified as low, medium, or high risk, allowing the pharmaceutical team to carry out more timely and targeted interventions. In the first 18 months after implementation, the average number of patients with medication reconciliation increased from 280 to 500. After eight months of this period, 765 high-risk patients were prioritized for discharge services, and 526 medication errors were avoided, 33% of which were errors that would cause moderate to severe harm to patients.

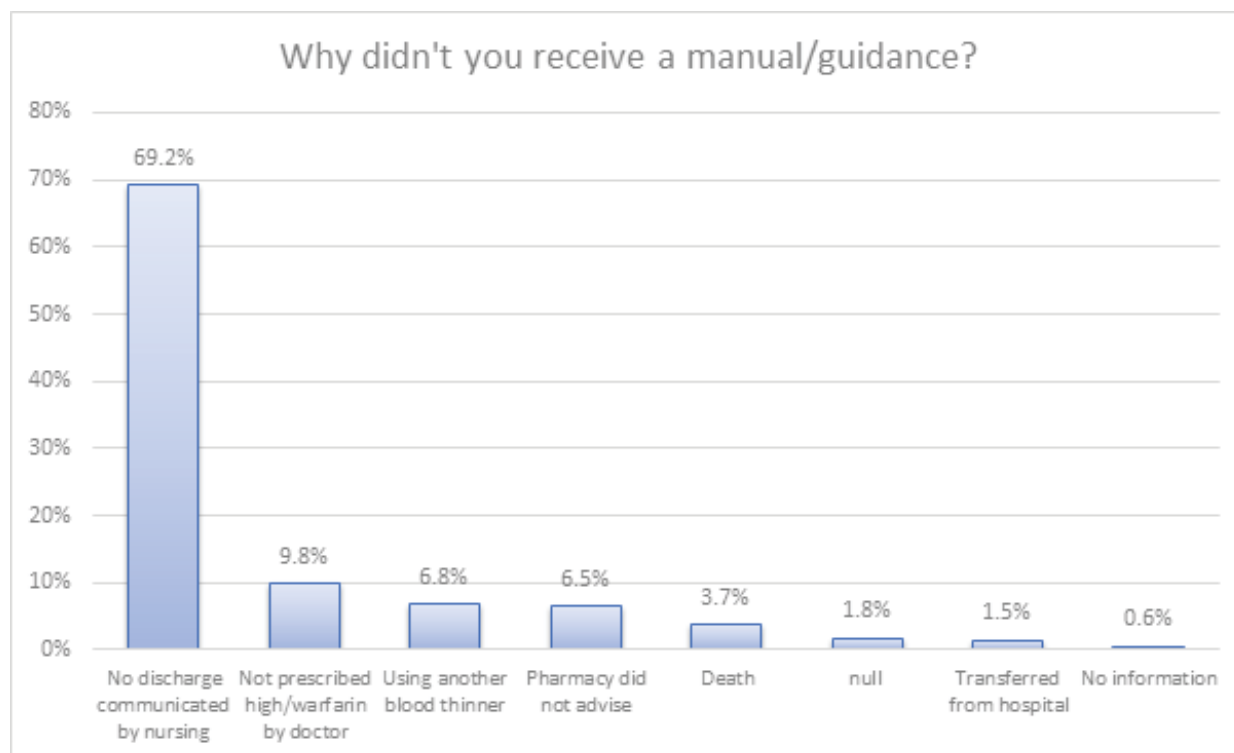
The use of applications during the pandemic was intensified due to restrictions and high demand for health services.¹⁹ Most of the applications were for teleconsultations, which is different from what was evaluated in this work, which was developed to improve the performance of the Pharmacy team. We sought to demonstrate that directly, after the implementation of the technological tool, more patients discharged from hospitals were identified and guided; indirectly, there was a positive impact by increasing the number of patients advised.

In order to identify the factors that could have led to a lack of patient counseling (Graph 2), as was already perceived in the practice of the team involved in patient care, according to the verbal information received, the results demonstrated that 69.2% of the lack of guidance occurred due to “discharge not communicated by nursing” with the index statistically different from all others, followed later by discharge/warfarin not prescribed by the doctor, changed therapy, transfer to other hospitals and patients who died.





Graph 1. Presentation of G1 (Pre-implantation) and G2 (post-implantation) about readmission, patient assessment, and delivery of the guidance manual
Caption: Chi-square test with significance in the first two variables



Graph 2. Reasons in patient records for not receiving the pharmaceutical guidance manual

Table 3. Comparison of Groups 1 (Pre) and 2 (Post) implantation with "Warfarin-related readmission" and "without readmission"								
Readmission		Unrelated to warfarin		Related to warfarin		Total		P-valor
		N	%	N	%	N	%	
Group 1	No	243	62,1%	69	76,7%	312	64,9%	0,009
	Yes	148	37,9%	21	23,3%	169	35,1%	
Group 2	No	209	53,2%	56	65,1%	265	55,3%	0,044
	Yes	184	46,8%	30	34,9%	214	44,7%	

Caption: Chi-square test

That is important data, as it can be variable and depends on the human factor; it is linked to the efficiency of communication on the part of the nursing team to alert that a patient who would continue to use warfarin has been discharged from the hospital. Possible explanations for these failures are the high demand for these professionals in their routine, which is associated with the need for more professionals working in care, resulting in overload. Concerning the medical team, a possible explanation would be the failure to fill out documents/medical records and the hospital discharge prescription itself.

Even with patients not receiving care at the time of hospital discharge, the data demonstrated that 86.4% of patients using warfarin were evaluated during their hospital stay (Group 3).

Regarding receiving guidance, data from Group 1 indicate that of the 396 patients evaluated at some point during hospitalization, 276 received the discharge guidance manual (57.4%). In Group 2, this number was higher: of the 433 patients evaluated at some point during hospitalization, 359 (74.9%) received the discharge guidance manual. Therefore, in Group 2, more patients were reached ($p < 0.001$).

The expectation that all patients would be reached still needs to be met. When analyzing the particularities, it was realized that covering all patients is difficult, given the unpredictability of the therapeutic process of patients admitted to hospitals. They may have their therapy optimized or suspended, be transferred from the hospital, or even achieve unfavorable outcomes.

In both groups, a statistically significant relationship exists between "Hospitalization related to Warfarin" and Readmission, as shown in Table 3. In Group 1, the Readmission rate was 37.9% among people with "No relation to Warfarin" against 23.3% among people with "Related to Warfarin" ($p = 0.009$). In Group 2, the readmission rate was 46.8% among people "Without Warfarin" versus 34.9% among people "With Warfarin" ($p = 0.044$).

The randomized controlled trial²⁰ with 1467 Danish participants demonstrated a reduction in the rate of readmissions within 30 and 180 days after receiving an extended pharmaceutical intervention that comprised a medication review and three patient interviews to provide information regarding dose, introduction or discontinuation of treatments, adverse events, adherence, and cost. Multifaceted clinical pharmacist intervention can reduce the number of emergency room visits and hospital readmissions.²⁰

A study was carried out in another Brazilian hospital in 2003 to demonstrate the evolution of Clinical Pharmacy.²¹ In this study, the number of clinical pharmacists, the number and types of interventions carried out, the acceptance by the medical team of the interventions, and the number of patients per day were evaluated. The interventions analyzed were classified into route of administration, frequency, dose, dilution, description/readability, drug interaction, allergy, infusion time, indication, pharmacovigilance/adverse drug reaction (ADR), home medication reconciliation, anticoagulants, opioids, and hypoglycaemic drugs. They also considered the pharmacist's participation in terms of adherence to institutional protocols such as antibiotic prophylaxis, antibiotic therapy, and serum monitoring of drugs such as vancomycin (vancokinemia), digoxin, and valproic acid. The authors significantly increased the types and numbers of interventions carried out. At the end of the study, it was possible to observe that acceptance by the medical team was 99.5%, which represented an extremely positive impact on patient safety.

During a study from 2010 to 2013 in a tertiary university hospital, 834 pharmaceutical recommendations were categorized and analyzed, and the most frequent ones on dilution, dose adjustment, and monitoring of adverse events were identified.²² Pharmaceutical interventions have been increasingly accepted in the therapeutic context, as their suggestions bring proven clinical and economic benefits.²³

Still, concerning the desired outcomes for this research, it was expected that patients who received guidance from the clinical pharmacist would acquire an understanding regarding the indication, dose, and care and that there would be a reduction in the return to the hospital due to events related to the inappropriate use of this product—medication, in addition to safe outpatient monitoring. The results indicate that there were readmissions, and these depend on factors such as each patient's self-care (nutrition, adherence to treatment, and care in general) and subjective factors that could interfere with treatment and lead to inappropriate medication use.

In the present research, this may have been aggravated by the COVID-19 pandemic period, as part of the data collected for Group 2 was from this period (March to September 2020, that is, around 30% of the period analyzed for this group), a period in which many people sought medical care late. Their health condition could have worsened due to this delay,²⁴ which remains a suggestion for future research, as the technological

tool should also be evaluated in other periods, as the pandemic was a challenge for the hospital and the entire care team and, of course without reducing the sample number of the research.

Some authors,²⁵ when creating an adherence measurement score, demonstrated that the reasons (education, income, inappropriate use, among others) and the prognostic variables (drug interactions, eating habits, clinical conditions, and factors such as stress) are potential interferers in adherence to the drug treatment. However, another author²⁶ had already concluded that initially, one must understand the clinical profile of the patient using oral anticoagulants during hospitalization, as well as their understanding of the health-disease process. Identifying the presence of symptoms of anxiety and depression is also important as some actions can be considered when caring for these patients beyond hospitals and thus achieving treatment adherence.

Warfarin belongs to a group of high-alert medications; all

patients could benefit from technological tools. We understand that despite some perceived limitations, the application achieved its purpose, and its use could, in the future, be extended to other medicines and internal hospital processes.

CONCLUSION

We concluded that the scope of the number of patients advised by clinical pharmacists at the time of hospital discharge was greater due to the implementation of the technological tool. However, in relation to length of stay and reasons for readmission, there were no statistically significant differences, for reasons that could be attributed to the turbulent pandemic period faced.

Health technologies can benefit the population and health professionals, represent new strategies for dealing with outpatients, and create/implement new applications to monitor these patients at home.

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