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Cardiac surgery nurses' knowledge of warfarin: evaluation of a training activity

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ABSTRACT

Aims: The aim of this study is to evaluate the effectiveness of the training provided to cardiac surgery nurses regarding warfarin use.

Methods: This pre-test-post-test quasi-experimental study was conducted between June and July 2025 at the department of cardiovascular surgery of a university hospital. The sample consisted of 30 nurses working in the clinic and intensive care unit who volunteered to participate in the study. As part of the research, nurses were educated on warfarin use, and their knowledge was measured before and after the training to evaluate the effectiveness of the training. Data were analysed using SPSS 25.0. Descriptive statistics were calculated, and pre- and post-test scores were compared using the Wilcoxon signed-rank test.

Results: The average age of the nurses participating in the study was 33.30±6.62 years. The average pre-training knowledge score of nurses regarding warfarin use was 15.00±2.74, while the post-training score increased to 18.03±1.29. The average knowledge score of nurses regarding warfarin-drug interactions before training was 13.40±14.40, while after training it was 41.80±10.43, and the average knowledge score regarding warfarin-food-herb interactions increased from 9.73±5.51 to 24.60±11.05. According to the Wilcoxon signed-rank test results, statistically significant increases were observed in nurses' knowledge scores regarding warfarin use and, warfarin–drug interactions, and warfarin–food–herb interactions after the training ($p<0.001$). The large effect sizes indicate that the training had a strong impact across all knowledge domains.

Conclusion: This study found that cardiac surgery nurses had a sufficient level of knowledge regarding warfarin use but insufficient knowledge about drug, food and herb interactions; however, the educational intervention led to statistically significant improvements with large effect sizes across all knowledge domains.

Keywords: Cardiovascular nursing, education, nursing, warfarin

INTRODUCTION

Warfarin is one of the most commonly used anticoagulant drugs in cardiovascular surgery.[1] Warfarin is used to prevent thromboembolic events after mechanical heart valve replacement, in the presence of atrial fibrillation, and after ventricular assist device implantation.[2,3] Warfarin use requires a delicate balance, and improper dosing can lead to life-threatening complications such as bleeding and thromboembolism.[4] Warfarin is further complicated by its numerous interactions with medications, foods, and herbal products.[1,5] These interactions can make it difficult to maintain stable anticoagulation and may increase the likelihood of adverse clinical outcomes.[6] Considering these risks, nurses have a key role in supporting the safe and effective use of warfarin. Successful anticoagulant therapy depends on patient knowledge, medication adherence, and the prevention of food and drug interactions. In this context, nurses have significant responsibilities in the safe use of warfarin. Nurses are responsible for monitoring laboratory values, ensuring coordination and communication with patients, monitoring side effects and complications, and preventing drug interactions to enable patients to use this medication safely and effectively.[1,6] Adequate nurse knowledge regarding warfarin use is directly associated with medication and, consequently, patient safety, whereas insufficient knowledge is linked to an increased occurrence of adverse events.[1] Current evidence indicates that nurse-led monitoring contributes to more stable International Normalized Ratio (INR) levels and helps reduce complications. The roles of cardiac surgery nurses such as monitoring bleeding, interpreting INR values, managing anticoagulation, and educating high-risk patients-contribute to the reduction of complications.[7,8] Studies in the literature also indicate that nurses play an important role in increasing treatment adherence in patients using warfarin, regulating INR value, and preventing complications.[10,11] It is also reported that patients undergoing cardiovascular surgery do not have sufficient knowledge about warfarin.[12,13] This

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situation highlights the need to enhance the knowledge levels of both nurses and patients and underscores the importance of nurse-led patient education programs to ensure safe anticoagulation management.

Researches indicates that nurses' knowledge of warfarin and other anticoagulant medications is insufficient, which may lead to inappropriate patient counselling and adverse clinical outcomes.[9,14-16] Cardiac surgery nurses play a critical role in anticoagulation management.[7,8] However, despite their critical role in the anticoagulation management, the warfarin-related knowledge of cardiac surgery nurses has not been sufficiently addressed in the literature. Accordingly, it is important to determine nurses' knowledge levels and educational needs. Sufficient knowledge about warfarin will contribute to the safe and effective use of the drug. This can increase treatment success and reduce potential complications after cardiac surgery. Therefore, it is important to determine the knowledge of cardiac surgery nurses regarding warfarin and to provide the necessary training. The aim of this study is to evaluate the effectiveness of the training provided to cardiac surgery nurses regarding warfarin use.

Research questions:

- What is the level of knowledge regarding warfarin among cardiac surgery nurses before the training?
- What is the level of knowledge regarding warfarin among cardiac surgery nurses after the training?
- What is the difference between the pre-training and post-training warfarin knowledge levels of cardiac surgery nurses?

METHODS

Ethics

Permission for this study was obtained from the Ege University Medical Researches Ethics Committee (Date: 12.06.2025, Decision No: 25-6T/92), the department and hospital administration. Nurses included in the study were informed about the study and their written consent was obtained. This study was conducted in accordance with ethical principles and the Principles of the Declaration of Helsinki.

Type of Research

This study was a pre-test-post-test quasi-experimental design, conducted between June-July 2025 in the clinic and intensive care unit (ICU) of the department of cardiovascular surgery at a university hospital.

Population and Sample

The population of this study consisted of 51 nurses working in the clinic and ICU of the department of cardiovascular surgery at a university hospital between June —July 2025. The sample consisted of 30 nurses who met the inclusion criteria.

Inclusion criteria:

- Being employed in the clinic or ICU at the time of the study
- Volunteering to participate in the study
- Completing both the pre-test and post-test assessments

Previous participation in training or meetings related to anticoagulant therapy was not defined as an exclusion criterion, as such educational exposure is considered part of routine clinical practice and excluding these participants could have introduced selection bias and limited the generalizability of the findings. In addition, the fact that only one participant had previously received such training was not considered to have a meaningful impact on the overall sample distribution or the statistical results.

Exclusion criteria:

- Not agreeing to participate in the study
- Completing only the pre or post-test assessment

According to the exclusion criteria, ten nurses working in the clinic and ICU did not agree to participate in the study, six nurses were excluded because they completed only the pre-test, and five nurses were excluded because they did not complete the post-test after the training.

Dependent variables: Scores on the warfarin use knowledge test, the warfarin–drug interaction knowledge test, and the warfarin–food–herb interaction knowledge test.

Independent variables: Age, gender, educational level, working unit, years of professional and current unit experience, and participation in any training or meeting related to anticoagulant therapy.

Data Collection Tools

Nurses' sociodemographic and descriptive characteristics form: This form was developed by the researchers through a literature review.[9,16] The form contains a total of seven questions, including three open-ended and four multiple-choice questions. This form was administered only before the education.

Warfarin use knowledge test: This form was developed in line with information from national and international guidelines and research results.[17-19] Each item in the form was phrased as a question that could be answered with "yes", "no", or "I don't know". The form contains a total of 20 questions. Correct responses were scored as 1 point, while incorrect and I don't know responses were scored as 0 points. The lowest possible score from the form is 0, and the highest score from the form is 20. This form was administered before and after the training.

Warfarin-drug interaction knowledge test: This form was developed in line with the literature.[9,20,21] Each item in the form was phrased as a question that could be answered with "interaction present", "interaction absent", or "I don't know". The form contains a total of 50 questions. Correct responses were scored as 1 point, while incorrect and I don't know responses were scored as 0 points. The lowest possible score from the form is 0, and the highest score from the form is 50. This form was administered before and after the training.

Warfarin-food-herb interaction knowledge test: This form was developed in line with the literature.[5,22,23] Each item in the form was structured as a question that could be answered as "reduces anticoagulant effect," "increases anticoagulant effect," "no effect," and "I don't know." The form contains a

total of 40 questions. Correct responses were scored as 1 point, while incorrect and I don't know responses were scored as 0 points. The lowest score obtained from the form is 0 and the highest score obtained from the form is 40. This form was administered before and after the training.

Knowledge tests were assessed using a 70% minimum competency level, a benchmark widely used in clinical education and competency evaluations.[24] Based on this criterion, the cut-off scores were set at 14 out of 20 for the warfarin use knowledge test, 35 out of 50 for the warfarin–drug interaction knowledge test, and 28 out of 40 for the warfarin–food–herb interaction knowledge test. The data collection tools used in this study were developed based on national and international guidelines. Since the items included in these forms were not newly created but were directly derived from evidence-based sources—and because it was necessary to preserve the original names of drug groups and food substances—additional expert opinion was not sought during the development process.

Data Collection and Training

Researchers first explained the purpose of the study to the nurses who agreed to participate. Before the training, data were collected using the nurses' sociodemographic and descriptive characteristics form, a knowledge test on warfarin use, a warfarin-drug interaction knowledge test, a warfarin-food-herb interaction knowledge test form. Subsequently, the training process began. The delivery of this training was approved by the department and was also supported by the charge nurses of the units. The training on warfarin therapy was conducted to increase nurses' knowledge levels regarding warfarin use and to enable them to perform safe practices during the treatment process. The content of the training was created by reviewing current literature,[5,17,25] and included general information on warfarin use, and information on warfarin's interactions with drugs, food, and herbs. A presentation-based instructional method was used during the training sessions, which were delivered by the principal investigator and an assistant researcher. No additional training materials were provided to the participants. The training was conducted in the training hall of the department of cardiovascular surgery. The training was organized in three separate sessions in accordance with the nurses' shift schedules, and each nurse completed the training by attending only one session. Participants were advised not to share the training content with nurses in other groups until all sessions had been completed. Each training session lasted approximately one hour. The training was planned so that both incoming night-shift nurses and day-shift nurses could attend, while ensuring the units were not fully vacated. Appropriate staffing arrangements were made to maintain continuous patient care. Immediately after the training, data were collected using the knowledge test on warfarin use, warfarin-drug interaction knowledge test and warfarin-food-herb interaction knowledge test forms. Filling out the data collection forms took approximately 15-20 minutes for the nurses The research population, sample, and application process are presented in Figure.

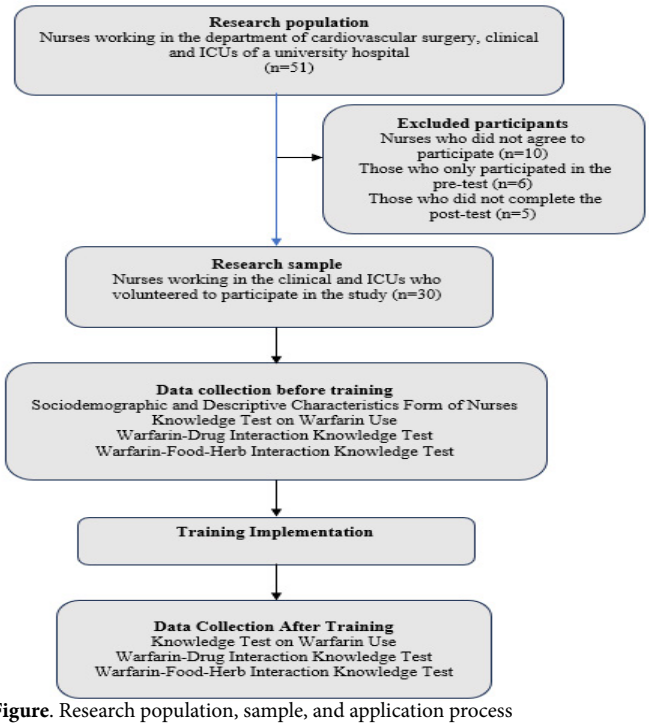


Figure. Research population, sample, and application process

Statistical Analysis

Study data were analysed using the Statistical Package for the Social Sciences (SPSS) Windows 25.0 IBM program. Mean, standard deviation, minimum, maximum, frequency, and percentage values were used in the analysis of descriptive data. Normality assumptions were not met for the total score distributions; therefore, pre- and post-test scores were compared using the non-parametric Wilcoxon signed-rank test. Effect size was reported as r for Wilcoxon signed-rank tests and calculated as $r=|z|/\sqrt{N}$.

RESULTS

Sociodemographic and Descriptive Characteristics

The average age of the nurses participating in the study was 33.30±6.62 years. Of these nurses, 90.0% were female, 83.3% bachelor's degree and 66.7% worked in the ICU. Only 3.3% of the nurses stated that they had attended any training or meeting related to anticoagulant therapy. The average professional working experience of the nurses was determined to be 9.23±7.04 years, and their average working experience in the same unit was 7.53±5.51 years. These findings are presented in Table 1.

Knowledge Regarding Warfarin Use

In this study, the nurses' mean knowledge score on warfarin use increased from 15.00±2.74 (min: 6, max: 19) to 18.03±1.29 (min: 14, max: 20) after training. Regarding the knowledge test results, nurses' understanding of key aspects of warfarin therapy improved following the training. Overall increases were observed in knowledge related to the purpose of warfarin use, its mechanism of action: inhibition of vitamin K–dependent clotting factors, laboratory monitoring parameters (prothrombin time (PT), INR), and the recognition of warfarin-associated complications

Table 1. Sociodemographic and descriptive characteristics of nurses (n=30)

Characteristics	n	%
Age (years)	33.30±6.62 (min: 25; max: 52)	
Gender		
Female	27	90
Male	3	10
Education level		
Bachelor's degree	25	83.3
Master's degree	5	16.7
Working unit		
Clinic	10	33.3
ICU	20	66.7
Participation in any training or meeting related to anticoagulant therapy		
Yes	1	3.3
No	29	96.7
Years of professional experience (year)	9.23±7.04 (min:1; max:29)	
Years of experience in the current unit (year)	7.53±5.51 (min:1; max:20)	
Total	30	100

n: Number; %: Percentage, ICU: Intensive care unit, Min: Minimum, Max: Maximum

and, bleeding. Following the training, improvements were observed in nurses' knowledge related to misconceptions regarding missed doses and restrictions regarding green leafy vegetables, increased awareness of the need for INR testing following major dietary changes, and enhanced knowledge of warfarin contraindications during pregnancy and its safe use during breastfeeding. Following the training, improvements were observed in nurses' knowledge related to before surgery warfarin management, enhanced understanding of target INR ranges for different mechanical valve types, increased awareness of INR monitoring frequency, and improved knowledge regarding the appropriate timing of warfarin intake to support adherence. The detailed distribution of these findings is presented in Table 2.

Warfarin-Drug Interaction Knowledge

In this study, the nurses' mean knowledge score warfarin-drug interactions increased from 13.40±14.40 (min: 0, max: 49) to 41.80±10.43 (min: 10, max: 48) after training. Overall, when

Table 2. Nurses' knowledge regarding warfarin use (n=30)

Questions	Before training			After training		
	Correct	Incorrect	Don't know	Correct	Incorrect	Don't know
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
The purpose of warfarin use is to reduce the tendency of blood to clot, not to completely prevent coagulation.	**28 (93.9)**	0 (0.0)	2 (6.7)	**30 (100.0)**	0 (0.0)	0 (0.0)
Warfarin inhibits the formation of vitamin K–dependent clotting factors.	**24 (80.0)**	2 (6.7)	4 (13.3)	**29 (96.7)**	0 (0.0)	1 (3.3)
The blood test used to measure the time it takes for blood to clot is called the Prothrombin time (PT) or Protime test.	**29 (96.7)**	0 (0.0)	1 (3.3)	**30 (100.0)**	0 (0.0)	0 (0.0)
The International Normalized Ratio (INR) is a standardized way of expressing PT values.	**24 (80.0)**	2 (6.7)	4 (13.3)	**30 (100.0)**	0 (0.0)	0 (0.0)
The warfarin dose is adjusted according to INR test results.	**30 (100.0)**	0 (0.0)	0 (0.0)	**30 (100.0)**	0 (0.0)	0 (0.0)
The main complications related to warfarin are clotting due to underdosage or bleeding due to excessive anticoagulation.	**29 (96.7)**	1 (3.3)	0 (0.0)	**30 (100.0)**	0 (0.0)	0 (0.0)
The most serious bleeding associated with warfarin use is gastrointestinal or intracerebral hemorrhage.	**29 (96.7)**	0 (0.0)	1 (3.3)	**30 (100.0)**	0 (0.0)	0 (0.0)
If a dose is missed during warfarin therapy, a double dose should be taken.	27 (90.0)	**0 (0.0)**	3 (10.0)	3 (10.0)	**27 (90.0)**	0 (0.0)
Green leafy vegetables should be strictly avoided while using warfarin.	18 (60.0)	**12 (40.0)**	0 (0.0)	7 (23.3)	**23 (76.7)**	0 (0.0)
If there are significant dietary changes lasting more than seven days, an INR test should be performed.	**27 (90.0)**	0 (0.0)	3 (10.0)	**30 (100.0)**	0 (0.0)	0 (0.0)
Warfarin is not recommended during pregnancy.	**23 (76.7)**	0 (0.0)	7 (23.3)	**29 (96.7)**	1 (3.3)	0 (0.0)
There are no known adverse effects of breastfeeding while taking warfarin.	**9 (30.0)**	10 (33.3)	11 (36.7)	**21 (70.0)**	8 (26.7)	1 (3.3)
It is important to carry warfarin while traveling.	**30 (100.0)**	0 (0.0)	0 (0.0)	**30 (100.0)**	0 (0.0)	0 (0.0)
Warfarin may need to be discontinued before surgery, tooth extraction, or other medical procedures.	**29 (96.7)**	1 (3.3)	0 (0.0)	**29 (96.7)**	1 (3.3)	0 (0.0)
Warfarin should be discontinued 3–5 days before cardiac or non-cardiac surgery.	**25 (83.3)**	4 (13.3)	1 (3.3)	**29 (96.7)**	0 (0.0)	1 (3.3)
Warfarin should be started two days after prosthetic valve replacement.	**10 (33.3)**	12 (40.0)	8 (26.7)	**22 (73.3)**	6 (20.0)	2 (6.7)
In mechanical prosthetic valves such as the aortic valve, the INR value should be between 2.0–3.0.	**21 (70.0)**	0 (0.0)	9 (30.0)	**30 (100.0)**	0 (0.0)	0 (0.0)
In other mechanical valve replacements and high-risk cases, INR values should be maintained between 2.5–3.5.	**18 (60.0)**	1 (3.3)	11 (36.7)	**30 (100.0)**	0 (0.0)	0 (0.0)
INR should be measured weekly until the target INR level is achieved, and once every four weeks thereafter.	**20 (66.7)**	8 (26.7)	2 (6.7)	**26 (86.7)**	3 (10.0)	1 (3.3)
Patients can take warfarin in the morning or evening, depending on when it is easiest for them to adhere to regular use.	**16 (53.5)**	13 (43.3)	1 (3.3)	**19 (63.3)**	11 (36.7)	0 (0.0)

Correct answers are shown in bold. n: Number; %: Percentage. Percentages are calculated based on the total sample (n=30) and may not total 100 due to rounding

the knowledge test questions were analysed, a remarkable improvement was observed in nurses' awareness of drug–warfarin interactions after the training. The proportion of nurses who correctly identified interaction potential increased notably for several drugs. In particular, following the training, correct response rates increased to 90% or higher for various medications. This improvement was observed across multiple drug classes, including analgesics and anti-inflammatory agents, antibiotics, antifungals, antiepileptics, psychotropic medications, cardiovascular drugs, anticoagulants, and hormone-related agents. Detailed drug-specific results and full percentage distributions are presented in Table 3.

Knowledge of Warfarin-Food-Herb Interactions

In this study, the nurses' mean knowledge score warfarin-food-herb interactions increased from 9.73±5.51 (min: 0, max: 18) to 24.60±11.05 (min: 0, max: 39) after training. Following the training, nurses' knowledge regarding vegetables, beverages, and dietary supplements associated with warfarin interactions showed notable improvement. Increased awareness was observed for green leafy vegetables, including spinach, broccoli, and parsley, as well as fruits and foods including avocado, blueberry, pomegranate juice, grapefruit. Improvements were noted for beverages, including green

Table 3. Nurses' knowledge on warfarin–drug interactions (n=30)

Drug	Before training			After training		
	Interaction	No interaction	Don't know	Interaction	No interaction	Don't know
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Paracetamol (acetaminophen)	**8 (26.7)**	16 (53.3)	6 (20.0)	**28 (93.3)**	2 (6.7)	0 (0.0)
Allopurinol	**6 (20.0)**	8 (26.7)	16 (53.3)	**27 (90.0)**	0 (0.0)	3 (10.0)
Carbamazepine	**8 (26.7)**	4 (13.3)	18 (60.0)	**28 (93.3)**	1 (3.3)	1 (3.3)
Ofloxacin	**12 (40.0)**	4 (13.3)	14 (46.7)	**29 (96.7)**	0 (0.0)	1 (3.3)
Oral contraceptives	**15 (50.0)**	4 (13.3)	11 (36.7)	**29 (96.7)**	1 (3.3)	0 (0.0)
Erythromycin	**10 (33.3)**	4 (13.3)	16 (53.3)	**29 (96.7)**	1 (3.3)	0 (0.0)
Ibuprofen	**15 (50.0)**	3 (10.0)	12 (40.0)	**29 (96.7)**	1 (3.3)	0 (0.0)
Ethanol	**7 (23.3)**	3 (10.0)	20 (66.7)	**27 (90.0)**	3 (10.0)	0 (0.0)
Fluconazole	**6 (20.0)**	7 (23.3)	17 (56.7)	**30 (100.0)**	0 (0.0)	0 (0.0)
Griseofulvin	**5 (16.7)**	4 (13.3)	21 (70.0)	**29 (96.7)**	0 (0.0)	1 (3.3)
Metronidazole	**7 (23.3)**	7 (23.3)	16 (53.3)	**29 (96.7)**	0 (0.0)	1 (3.3)
Miconazole	**5 (16.7)**	5 (16.7)	20 (66.7)	**26 (86.7)**	0 (0.0)	4 (13.3)
Antacids	6 (20.0)	**8 (26.7)**	16 (53.3)	9 (30.0)	**18 (60.0)**	3 (10.0)
NSAIDs	**11 (36.7)**	8 (26.7)	11 (36.7)	**29 (96.7)**	0 (0.0)	1 (3.3)
Salicylates	**18 (60.0)**	6 (20.0)	6 (20.0)	**28 (93.3)**	0 (0.0)	2 (6.7)
Thrombolytics (alteplase, reteplase, tenecteplase, urokinase)	**19 (63.3)**	3 (10.0)	8 (26.7)	**28 (93.3)**	1 (3.3)	1 (3.3)
Tramadol	**8 (26.7)**	10 (33.3)	12 (40.0)	**29 (96.7)**	0 (0.0)	1 (3.3)
Vitamin K	**26 (86.7)**	2 (6.7)	2 (6.7)	**29 (96.7)**	0 (0.0)	1 (3.3)
Zafirlukast	**7 (23.3)**	4 (13.3)	19 (63.3)	**25 (83.3)**	1 (3.3)	4 (13.3)
Amiodarone	**10 (33.3)**	12 (40.0)	8 (26.7)	**27 (90.0)**	1 (3.3)	2 (6.7)
Azathioprine	**7 (23.3)**	5 (16.7)	18 (60.0)	**25 (83.3)**	1 (3.3)	4 (13.3)
Cefazolin	**4 (13.3)**	14 (46.7)	12 (40.0)	**27 (90.0)**	1 (3.3)	2 (6.7)
Chloramphenicol	**5 (16.7)**	6 (20.0)	19 (63.3)	**25 (83.3)**	1 (3.3)	4 (13.3)
Disulfiram	**5 (16.7)**	3 (10.0)	22 (73.3)	**25 (83.3)**	1 (3.3)	4 (13.3)
Ezetimibe	**3 (10.0)**	5 (16.7)	22 (73.3)	**23 (76.7)**	3 (10.0)	4 (13.3)
Fenofibrate	**9 (30.0)**	3 (10.0)	18 (60.0)	**26 (86.7)**	1 (3.3)	3 (10.0)
Flutamide	**3 (10.0)**	3 (10.0)	24 (80.0)	**24 (80.0)**	1 (3.3)	5 (16.7)
Fluvastatin	**3 (10.0)**	3 (10.0)	24 (80.0)	**24 (80.0)**	1 (3.3)	5 (16.7)
Fluvoxamine	**3 (10.0)**	3 (10.0)	24 (80.0)	**24 (80.0)**	1 (3.3)	5 (16.7)
Gemfibrozil	**3 (10.0)**	4 (13.3)	23 (76.7)	**24 (80.0)**	1 (3.3)	5 (16.7)
Glucagon	**5 (16.7)**	6 (20.0)	19 (63.3)	**24 (80.0)**	2 (6.7)	4 (13.3)
Heparin	**24 (80.0)**	1 (3.3)	5 (16.7)	**28 (93.3)**	0 (0.0)	2 (6.7)
Influenza vaccine	**10 (33.3)**	6 (20.0)	14 (46.7)	**25 (83.3)**	3 (10.0)	2 (6.7)

The table continues

Table 3. Nurses' knowledge on warfarin–drug interactions (n=30) (The table continues)

Lovastatin	**6 (20.0)**	9 (30.0)	15 (50.0)	**26 (86.7)**	3 (10.0)	1 (3.3)
Methylphenidate	**2 (6.7)**	3 (10.0)	25 (83.3)	**28 (93.3)**	1 (3.3)	1 (3.3)
Nafcillin	**3 (10.0)**	3 (10.0)	24 (80.0)	**25 (83.3)**	2 (6.7)	3 (10.0)
Paroxetine	**5 (16.7)**	4 (13.3)	21 (70.0)	**27 (90.0)**	1 (3.3)	2 (6.7)
Phenytoin	**6 (20.0)**	4 (13.3)	20 (66.7)	**26 (86.7)**	1 (3.3)	3 (10.0)
Propafenone	**7 (23.3)**	4 (13.3)	19 (63.3)	**23 (76.7)**	4 (13.3)	3 (10.0)
Propoxyphene	**4 (13.3)**	3 (10.0)	23 (76.7)	**24 (80.0)**	1 (3.3)	5 (16.7)
Propranolol	**7 (23.3)**	5 (16.7)	18 (60.0)	**26 (86.7)**	1 (3.3)	3 (10.0)
Quinine	**8 (26.7)**	3 (10.0)	19 (63.3)	**26 (86.7)**	1 (3.3)	3 (10.0)
Raloxifene	**3 (10.0)**	3 (10.0)	24 (80.0)	**24 (80.0)**	3 (10.0)	3 (10.0)
Ranitidine	**5 (16.7)**	3 (10.0)	22 (73.3)	**26 (86.7)**	2 (6.7)	2 (6.7)
Rifampin	**7 (23.3)**	3 (10.0)	20 (66.7)	**27 (90.0)**	1 (3.3)	2 (6.7)
Sertraline	**10 (33.3)**	4 (13.3)	16 (53.3)	**27 (90.0)**	1 (3.3)	2 (6.7)
Simvastatin	**5 (16.7)**	3 (10.0)	22 (73.3)	**23 (76.7)**	1 (3.3)	6 (20.0)
Sucralfate	**7 (23.3)**	3 (10.0)	20 (66.7)	**25 (83.3)**	1 (3.3)	4 (13.3)
Tamoxifen	**4 (13.3)**	3 (10.0)	23 (76.7)	**24 (80.0)**	1 (3.3)	5 (16.7)

Correct answers are shown in bold. n: Number; %: Percentage. Percentages are calculated based on the total sample (n=30) and may not total 100 due to rounding

tea, caffeinated drinks, and alcohol. In addition, knowledge related to herbal products and dietary supplements also improved after the training. Detailed item-level results and percentage distributions are presented in Table 4.

Pre- and Post-Training Differences in Knowledge Domains Assessed by the Wilcoxon Signed-Rank Test

A pronounced effect emerged for warfarin use knowledge. Median performance increased from 15.5 to 18.0 (mean=15.00→18.03); the Wilcoxon test yielded W=2.0, z=–4.74, p<0.001, with r=0.87. This very large effect demonstrates a marked strengthening of participants' understanding of dosing, monitoring, and safe administration practices.

A similarly consistent and substantial enhancement was observed across all three knowledge domains following the educational intervention. For warfarin–drug interaction knowledge, the median score rose from 8.5 to 47.0 (mean=13.40→41.80). The Wilcoxon signed-rank test confirmed this improvement with W=12.5, z=–4.53, p<0.001, and an effect size of r=0.83, indicating a very large practical impact on participants' ability to identify clinically relevant warfarin–drug interactions.

Finally, warfarin-food-herb interaction knowledge exhibited a substantial median gain from 9.5 to 24.5 (mean=9.73→24.60). The corresponding statistics (W=22.5, z=–4.32, p<0.001, r=0.79) again signify a large effect, underscoring appreciable growth in recognising food and herb factors that modulate warfarin efficacy. Given that all p-values are well below 0.001 and each effect size exceeds the conventional threshold for a large effect (r≥0.50), the intervention can be deemed highly effective in enhancing multidimensional warfarin-related knowledge among healthcare professionals. These findings are presented in Table 5.

DISCUSSION

Warfarin, a vitamin K antagonist, is one of the most commonly used oral anticoagulants worldwide.[26] The most significant challenges with warfarin are the prevalence of complications such as bleeding and side effects due to drug-food interactions.[1] To prevent these adverse events, nurses' knowledge and awareness regarding warfarin therapy are important for supporting safe warfarin treatment.[1,27]

Warfarin Use and Management

In this study, it was determined that nurses' knowledge regarding warfarin use before the training was at a sufficient level, however, the training significantly strengthened their understanding of warfarin use and safety, particularly in terms of knowledge and clinical application. This finding indicates that nurses' knowledge of clinical practices related to warfarin therapy—such as dose adjustment, INR monitoring, and safe medication administration—has been strengthened. However, these findings show that advances in knowledge regarding clinical practice rather than changes in patient outcomes. Adequate knowledge of warfarin is critically important for patient safety in cardiac surgery patients who are at risk of bleeding and thromboembolic events. A study indicated that cardiac nurses' information in a knowledge test, which also included questions on anticoagulant use and management, was slightly above average and insufficient.[16] Another study reported that cardiovascular nurses' knowledge and practices in a knowledge test, which also contained questions on warfarin management, were slightly above the median.[1] Accordingly, these findings suggest that nurses' knowledge regarding warfarin use and management may not be optimal level, highlighting the necessity of educational interventions. However, comparisons with previous studies should be interpreted with caution due to differences in study design, sample characteristics, and assessment tools. Nurses' improving their knowledge and practices regarding

Table 4. Nurses' knowledge on warfarin–food–herbal interactions (n=30)

Food/herb	Before training				After training			
	Increases anticoagulant effect	Decreases anticoagulant effect	No effect	Don't know	Increases anticoagulant effect	Decreases anticoagulant effect	No effect	Don't know
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Fresh/frozen/boiled spinach	7 (23.3)	**20 (66.7)**	0 (0.0)	3 (10.0)	2 (6.7)	**26 (86.7)**	0 (0.0)	2 (6.7)
Raw lettuce	6 (20.0)	**19 (63.3)**	0 (0.0)	5 (16.7)	3 (10.0)	**26 (86.7)**	0 (0.0)	1 (3.3)
Kale	6 (20.0)	**15 (50.0)**	0 (0.0)	9 (30.0)	4 (13.3)	**23 (76.7)**	0 (0.0)	3 (10.0)
Broccoli	5 (16.7)	**20 (66.7)**	0 (0.0)	5 (16.7)	3 (10.0)	**26 (86.7)**	0 (0.0)	1 (3.3)
Brussels sprouts	5 (16.7)	**16 (53.3)**	0 (0.0)	9 (30.0)	4 (13.3)	**23 (76.7)**	0 (0.0)	3 (10.0)
Parsley	5 (16.7)	**19 (63.3)**	1 (3.3)	5 (16.7)	3 (10.0)	**25 (83.3)**	0 (0.0)	2 (6.7)
Zucchini	4 (13.3)	**11 (36.7)**	2 (6.7)	13 (43.3)	5 (16.7)	**20 (66.7)**	3 (10.0)	2 (6.7)
Grapefruit	**16 (53.3)**	4 (13.3)	1 (3.3)	9 (30.0)	**18 (60.0)**	11 (36.7)	0 (0.0)	1 (3.3)
Avocado	3 (10.0)	**13 (43.3)**	2 (6.7)	12 (40.0)	2 (6.7)	**25 (83.3)**	1 (3.3)	2 (6.7)
Blueberry	**10 (33.3)**	4 (13.3)	1 (3.3)	15 (50.0)	**24 (80.0)**	5 (16.7)	0 (0.0)	1 (3.3)
Mango	**9 (30.0)**	3 (10.0)	2 (6.7)	16 (53.3)	**18 (60.0)**	7 (23.3)	0 (0.0)	5 (16.7)
Pomegranate juice	**17 (56.7)**	3 (10.0)	0 (0.0)	10 (33.3)	**24 (80.0)**	5 (16.7)	0 (0.0)	1 (3.3)
Cranberry	15 (50.0)	**3 (10.0)**	1 (3.3)	11 (36.7)	11 (36.7)	**15 (50.0)**	0 (0.0)	4 (13.3)
Goji berry	13 (43.3)	**3 (10.0)**	0 (0.0)	14 (46.7)	11 (36.7)	**12 (40.0)**	0 (0.0)	7 (23.3)
Red clover	10 (33.3)	**4 (13.3)**	0 (0.0)	16 (53.3)	10 (33.3)	**16 (53.3)**	0 (0.0)	4 (13.3)
Peas	15 (50.0)	**6 (20.0)**	0 (0.0)	9 (30.0)	18 (60.0)	**11 (36.7)**	0 (0.0)	1 (3.3)
Alcohol	**13 (43.3)**	**9 (30.0)**	0 (0.0)	8 (26.7)	**15 (50.0)**	**13 (43.3)**	0 (0.0)	2 (6.7)
Green tea	**8 (26.7)**	15 (50.0)	0 (0.0)	7 (23.3)	**15 (50.0)**	13 (43.3)	0 (0.0)	2 (6.7)
High-dose caffeine and caffeinated drinks	**8 (26.7)**	6 (20.0)	3 (10.0)	13 (43.3)	**20 (66.7)**	6 (20.0)	1 (3.3)	3 (10.0)
Low-dose caffeine and caffeinated drinks	7 (23.3)	**4 (13.3)**	5 (16.7)	14 (46.7)	5 (16.7)	**17 (56.7)**	5 (16.7)	3 (10.0)
Bee pollen	**4 (13.3)**	1 (3.3)	2 (6.7)	23 (76.7)	**18 (60.0)**	3 (10.0)	1 (3.3)	8 (26.7)
Coenzyme Q10	**2 (6.7)**	3 (10.0)	1 (3.3)	24 (80.0)	**21 (70.0)**	5 (16.7)	1 (3.3)	3 (10.0)
Cannabis	7 (23.3)	**9 (30.0)**	0 (0.0)	14 (46.7)	8 (26.7)	**18 (60.0)**	0 (0.0)	4 (13.3)
Tobacco products	6 (20.0)	**12 (40.0)**	0 (0.0)	12 (40.0)	3 (10.0)	**25 (83.3)**	0 (0.0)	2 (6.7)
Soy	**3 (10.0)**	5 (16.7)	5 (16.7)	17 (56.7)	**16 (53.3)**	9 (30.0)	2 (6.7)	3 (10.0)
St. John's wort	**1 (3.3)**	6 (20.0)	5 (16.7)	18 (60.0)	**23 (76.7)**	2 (6.7)	1 (3.3)	4 (13.3)
Sage	**6 (20.0)**	5 (16.7)	0 (0.0)	19 (63.3)	**23 (76.7)**	5 (16.7)	0 (0.0)	2 (6.7)
Dong quai	3 (10.0)	**1 (3.3)**	0 (0.0)	26 (86.7)	11 (36.7)	**12 (40.0)**	0 (0.0)	7 (23.3)
Ginger	5 (16.7)	**3 (10.0)**	2 (6.7)	20 (66.7)	11 (36.7)	**14 (46.7)**	0 (0.0)	5 (16.7)
Chamomile	9 (30.0)	**0 (0.0)**	1 (3.3)	20 (66.7)	9 (30.0)	**15 (50.0)**	1 (3.3)	5 (16.7)
Chitosan	3 (10.0)	**0 (0.0)**	0 (0.0)	27 (90.0)	5 (16.7)	**16 (53.3)**	0 (0.0)	9 (30.0)
Devil's claw	3 (10.0)	**1 (3.3)**	0 (0.0)	26 (86.7)	7 (23.3)	**15 (50.0)**	0 (0.0)	8 (26.7)
Ginkgo	3 (10.0)	**3 (10.0)**	0 (0.0)	24 (80.0)	7 (23.3)	**14 (46.7)**	0 (0.0)	9 (30.0)
Garlic	8 (26.7)	**3 (10.0)**	3 (10.0)	16 (53.3)	10 (33.3)	**13 (43.3)**	0 (0.0)	7 (23.3)
Ginseng	**7 (23.3)**	4 (13.3)	0 (0.0)	19 (63.3)	**15 (50.0)**	8 (26.7)	0 (0.0)	7 (23.3)
Boldo	2 (6.7)	**0 (0.0)**	0 (0.0)	28 (93.3)	7 (23.3)	**13 (43.3)**	0 (0.0)	10 (33.3)
Echinacea	**3 (10.0)**	1 (3.3)	0 (0.0)	26 (86.7)	**16 (53.3)**	5 (16.7)	0 (0.0)	9 (30.0)
Fenugreek	5 (16.7)	**1 (3.3)**	1 (3.3)	23 (76.7)	11 (36.7)	**13 (43.3)**	0 (0.0)	6 (20.0)
Melilot (yellow sweet clover)	3 (10.0)	**1 (3.3)**	0 (0.0)	26 (86.7)	8 (26.7)	**14 (46.7)**	0 (0.0)	8 (26.7)
Saw palmetto	1 (3.3)	**0 (0.0)**	0 (0.0)	29 (96.7)	7 (23.3)	**16 (53.3)**	0 (0.0)	7 (23.3)

Correct answers are shown in bold. n: Number; %: Percentage. Percentages are calculated based on the total sample (n=30) and may not total 100 due to rounding

Tablo 5. Wilcoxon signed-rank test results

Measure (total score)	Pre-test mean (median)	Post-test mean (median)	Wilcoxon W	z	p	Effect size-r
Warfarin use knowledge	15.00 (15.5)	18.03 (18.0)	2.0	−4.74	< 0.001	0.87
Warfarin–drug interaction knowledge	13.40 (8.5)	41.80 (47.0)	12.5	−4.53	< 0.001	0.83
Warfarin–food–herb interaction knowledge	9.73 (9.5)	24.60 (24.5)	22.5	−4.32	< 0.001	0.79

W: Wilcoxon signed-rank test statistic, z: Standardized test statistic, p: Significance level, r: Effect size. Wilcoxon tests ($r=|z|/\sqrt{N}$)

anticoagulation therapy is crucial for providing optimal care to cardiac patients and minimizing the adverse effects of treatment.[16] In this context, it is recommended that regular training on warfarin be provided and its outcomes evaluated.

In this study, the vast majority of nurses correctly answered the purpose of use (93.9%), the mechanism of action (80%), related to blood tests (96.7%, 80.0%), complications associated with warfarin use (96.7%), and an increase in these rates was observed after training. Regarding not taking a double dose when a warfarin dose is missed, 90% of nurses had incorrect information and 10.0% stated they did not know, whereas after training, the vast majority of nurses were informed on this matter. This is one of the most striking findings. In a study, slightly more than half (57.3%) of cardiovascular nurse,[1] and in another study, slightly more than half (58.0%) of nurses[20] correctly answered that missed anticoagulant doses should be disregarded. When compared with previous studies, the findings of the present study indicate similar deficiencies in missed-dose management knowledge; however, such comparisons should be interpreted cautiously due to methodological and contextual differences. Especially in warfarin use, dose management is of vital importance. Taking a double dose after a missed warfarin dose is not recommended. Excessive dose intake can lead to excessive coagulation and bleeding. Instead, it is stated that the next dose should be taken as usual, and if more than one dose has been missed, a physician should be consulted on how to proceed.[28,29] Accordingly, informing nurses from the most basic to the most detailed information regarding warfarin use is of great importance.

In this study, another striking finding is that nearly half of the nurses (40.0%) believed that consuming green leafy vegetables should be prohibited while using warfarin. Although this information was largely corrected after training, it is still not at the desired level. In a study, half (50.6%) of cardiovascular nurses correctly stated that patients are allowed to eat spinach while taking warfarin, provided they consume the same amount each week.[1] Although similar findings have been reported in previous studies, differences in assessment content and nurses' educational status may explain this findings. Vitamin K, mostly found in green leafy vegetables, reduces the effectiveness of warfarin, which has a narrow therapeutic range, by increasing blood coagulation.[30] It is stated that in warfarin users, daily high intake (more than 250 µg) of vitamin K-rich green leafy vegetables may reduce warfarin effectiveness.[31] It is stated that highly variable consumption of these foods can cause INR variability, increasing the risk of coagulation and bleeding.[30] Instead of avoiding the consumption of green leafy vegetables, it is recommended to consume them in consistent amounts.[31]

In this study, more than half of the nurses (76.7%) knew that warfarin is not recommended during pregnancy, while less than half (30.0%) correctly answered that there is no known contraindication to breastfeeding while using warfarin. In a study, almost half of the nurses (56.8%) correctly answered that warfarin should not be used during pregnancy.[27] Accordingly, it can be understood that nurses' knowledge regarding warfarin use during pregnancy and breastfeeding may be limited. Furthermore, in another study, less than half (35.6%) of cardiovascular nurses correctly answered that it can be safely used in the second and third trimesters of pregnancy.[1] Warfarin is an anticoagulant that easily crosses the placenta.[32] Due to its teratogenic effects, warfarin is generally stated to be avoided during pregnancy, especially during the period of organogenesis.[33] At the same time, in pregnant patients with mechanical heart valve prostheses, planned it is recommended that warfarin be discontinued before birth and replaced with intravenous unfractionated heparin. However, although warfarin use in pregnancy is generally not recommended, its use is recommended in the second and third trimesters to achieve therapeutic INR levels.[34] In this regard, it is recommended that current national and international guidelines be shared with nurses and their knowledge increased.

Slightly more than half of the nurses (53.5%) correctly answered that patients should take warfarin in the morning or evening for easiest adherence, and while there was an increase in this knowledge after training, it was not at the desired level. A study reported that the vast majority of cardiovascular nurses (91.2%) and another study reported that more than half of the nurses (56.3%) correctly answered that the most preferred time to take warfarin is in the evening.[1,27] These findings may reflect differences in institutional routines regarding the timing of warfarin administration. However, studies indicate that warfarin should be taken in the morning or evening, where regular adherence can be most easily achieved.[19] Clinical routine practices may lead to differing opinions among nurses, as warfarin is typically administered in the evenings in clinics. While such practices may establish correct habits, they may also lead to deviations from the literature. In this regard, it is recommended that evidence-based approaches be integrated into nursing education.

Warfarin-Drug Interaction

In this study, it was observed that nurses' knowledge regarding warfarin-drug interactions was quite insufficient before training, however, a significant increase was observed after the training, with the most pronounced improvement detected in the domain of warfarin–drug interaction knowledge. This finding may support nurses' ability to

recognize clinically significant warfarin–drug interactions. Moreover, the marked increase in knowledge observed after the training also indicates the substantial need for education among nurses in this area. A study found that cardiac nurses' knowledge about warfarin-drug interactions was low.[17] In another study, warfarin-drug their knowledge and awareness regarding interactions were reported to be moderate.[27] Studies in the literature suggest that nurses' knowledge levels regarding warfarin may vary and that there may be a need for improvement in certain knowledge areas. Achieving optimal anticoagulation with this agent is clinically challenging due to complex pharmacokinetic and pharmacodynamic profile.[26] Knowledge of warfarin-drug interactions is important for providing the best care to cardiac patients and minimizing the adverse effects of treatment.[16] Nurses' lack of knowledge and incorrect practices can jeopardize drug safety in patients and lead to serious side effects such as bleeding.[1] In this regard, it is recommended that nurses be provided with information about the interaction of warfarin, with other medications, and that these trainings be evaluated in terms of their impact on complications and adverse events.

Some of the most striking findings in this study concerned the interaction of paracetamol and ibuprofen, which are most frequently used in clinics, with warfarin. Nearly half of the nurses (26.7%) correctly answered that paracetamol interacts with warfarin, while half (50.0%) correctly answered the interaction of ibuprofen with warfarin. A study also stated that more than half of the nurses (62.5%) indicated that paracetamol is the safest option for patients using warfarin.[27] In this regard, although the use of paracetamol with warfarin is perceived as safe in clinics, there is a situation that needs attention. The literature states that high-dose (4 g/day) intake of paracetamol increases the anticoagulant effect of warfarin. This situation can pose a clinical risk, and it is recommended to be careful with the intake of paracetamol, which may seem innocent.[35] At the same time, although there are sources[9] suggesting that ibuprofen does not interact with warfarin, it is stated that ibuprofen increases the free fraction of warfarin in plasma, thereby increasing the anticoagulant effect is stated.[21,36] It is important to provide nurses with evidence-based and randomized controlled study results in in-service training.

In this study, few nurses correctly answered the interaction of cardiac drugs such as amiodarone (33.3%), propranolol (23.3%), propafenone (13.3%), and quinidine (26.7%) with warfarin, while there were significant increases in correct answers after training. In one study, very few healthcare professionals (11.1%) correctly answered that warfarin interacts with cardiac drugs.[14] In this study, more than half (60.0%) of the nurses correctly answered the interaction of salicylates, one of the most commonly used agents in cardiac surgery, with warfarin. A study stated that almost half (56.0%) of cardiac nurses correctly answered that aspirin increases the anticoagulant effect of warfarin.[16] Such polypharmacy is common in cardiac surgery patients,[37,38] and it is a necessity to inform nurses about this. This study suggests that education provided to nurses may significantly improve knowledge of warfarin–drug interactions in the context of cardiac surgery.

Warfarin-Food-Herb Interaction

In this study, it was determined that nurses' knowledge regarding warfarin interactions with food and herbal products was insufficient before the training, however, a significant increase was observed after the training, particularly in the domain of food- and herbal product–related interaction knowledge. This finding may support nurses' ability to provide more accurate counselling to patients. Similarly, a study stated indicates that nurses' knowledge of warfarin-food interactions was moderate.[27]

In this study, although not at a sufficient level, at least half of the nurses correctly answered the interaction of green leafy vegetables such as spinach (66.7%), lettuce (563.3%), kale (50.0%), broccoli (66.7%), Brussels sprouts (53.3%), and parsley (63.3%) with warfarin, and these correct answers significantly increased after training. A study have also reported knowledge deficiencies regarding the interaction of vitamin K-rich green leafy vegetables with warfarin is stated.[27] Another study found that more than half of cardiovascular nurses correctly answered that warfarin interacts with broccoli (79.9%) and cabbage (61.9%).[1] Vitamin K is an essential cofactor found especially in green plants and required for the γ-carboxylation of coagulation factors (II, VII, IX, X) in humans. This process enables factors to bind to calcium and initiate coagulation. Warfarin exhibits an anticoagulant effect by inhibiting this mechanism due to its structural similarity to vitamin K.[39] For these reasons, it is recommended that these vitamin K-rich green leafy vegetables, which are abundant in Turkish cuisine, be consumed proportionally by patients using warfarin. In this study, a significant increase was also observed in nurses' insufficient knowledge regarding herbal products (St. John's wort, echinacea, ginseng, ginkgo, etc.). Herbs can alter the anticoagulant effect of warfarin by affecting various parameters in hemostasis. Due to the chemically complex matrix of herbs, they can both increase and decrease the anticoagulant effect of warfarin.[39]

In this study, less than half (26.7%) of the nurses correctly identified the interaction of green tea, one of the most frequently consumed beverages, with warfarin, while the increase in knowledge after training remained limited. In this study, the interaction of grapefruit, a food particularly emphasized in clinics, with warfarin was correctly identified by slightly more than half (53.3%) of the nurses, and an increase was achieved after training. A study found that more than half (73.9%) of nurses correctly answered that warfarin can interact with grapefruit juice, and nearly half (40.9%) with green tea.[27] Another study stated that the majority (66.7%) of healthcare professionals correctly identified the interaction between green tea and warfarin.[14] In this study, less than half of the nurses correctly answered the increasing (43.3%) and decreasing (30.0%) effects of alcohol on anticoagulant activity, while the increase in knowledge after training remained insufficient. In another study, slightly more than half of (58.2%) cardiovascular nurses stated that alcohol users experienced increased anticoagulation.[1] It is stated that moderate/severe alcohol consumption in patients receiving warfarin therapy may increase the risk of major bleeding by enhancing the effect of warfarin.[40] Furthermore, it is stated

that chronic and heavy alcohol consumption may increase the risk of clotting by reducing the effect of warfarin.[41] Accordingly, it is recommended that nurses be aware of the bidirectional interaction of warfarin with alcohol and provide counselling to patients in this regard.

Limitations

This study has several limitations. On of the limitations of this study is that it was conducted at a single centre, preventing generalization, and that it was carried out on a limited population. In addition, items included in the data collection forms were based on information provided in clinical guidelines, and drug–food names were used directly as stated in these sources. Therefore, no additional expert opinion was sought during the development process. This should be considered a limitation when evaluating the content validity of the measurement instruments. Moreover, since the post-test was administered immediately after the training, the study does not provide evidence regarding long-term knowledge retention or the transfer of learning into clinical practice. This should be considered as a limitation when interpreting the results. Another limitation is the absence of a control group in this study makes it difficult to attribute the pre-test and post-test results directly to the training. This has been considered an important limitation in the interpretation of the findings. Additionally, the differences in the educational backgrounds of intensive care and clinic nurses may lead to variability in their levels of knowledge about warfarin, which constitutes a limitation of the study.

CONCLUSION

This study evaluated the effectiveness of training provided to cardiac surgery nurses regarding warfarin use. It was determined that nurses' knowledge of general warfarin use was at a sufficient level, but their knowledge, particularly regarding warfarin's drug and food-herb interactions, was insufficient. Following the educational intervention, statistically significant improvements with large effect sizes were observed across all warfarin-related knowledge domains. The original contribution of this study is that it identifies areas of insufficient knowledge related to warfarin among cardiac surgery nurses and demonstrates that a targeted educational intervention can effectively address these knowledge gaps. From a clinical perspective, increasing nurses' awareness of warfarin therapy is important for safer anticoagulation management. Accordingly, expanding and regularly updating warfarin-related educational programs for nurses is recommended. Future studies conducted in different centres are warranted to further evaluate the effectiveness of such training interventions.

ETHICAL DECLARATIONS

Ethics Committee Approval

Permission for this study was obtained from the Ege University Medical Researches Ethics Committee (Date: 12.06.2025, Decision No: 25-6T/92).

Informed Consent

Written informed consent was obtained from all individual participants prior to their inclusion in the study. Participants were fully informed about the study's aims, procedures, potential risks and benefits, and their rights—including the right to withdraw at any time without consequence. All participants voluntarily signed a written informed consent form.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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Author Contributions

Concept/Design: NCD, TOT, AS, OA; Supervision: NCD; Data Collection and/or Processing: NCD, TOT, AS, OA; Analysis and/or Interpretation: NCD, TOT; Literature Review: NCD; Writing: NCD; Critical Review: NCD.

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