Research Paper

The Effect of Rewarming on the Cognitive Status of Patients After Open-heart Surgery: A Randomized Clinical Trial

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Citation Haji-Jafari, S., Ahmadi Tafti, S, H., Azizi-Fini, I., Rezaei, M., Atoof, F. 2023. The Effect of Rewarming on the Cognitive Status of Patients After Open-heart Surgery: A Randomized Clinical Trial. *Journal of Client-Centered Nursing Care*, 9(1), pp. 25-34. https://doi.org/10.32598/JCCNC.9.1.305.5

https://doi.org/10.32598/JCCNC.9.1.305.5

Article info:
Received: 06 Sep 2022
Accepted: 15 Nov 2022
Published: 01 Feb 2023

Keywords:
Rewarming, Hypothermia, Cognitive status, Postoperative complications, Thoracic surgery

ABSTRACT

Background: Hypothermia is usually used during cardiac surgery to further protect against cardiac and cerebral ischemia. However, cognitive impairment could be a common complication after open heart surgery. This study aims to determine the effect of rewarming on the cognitive status of patients after open heart surgery.

Methods: The present study was conducted as a double-blind, randomized clinical trial at Tehran Heart Center, Tehran, Iran. In this clinical trial, 80 patients referred for open heart surgery were selected and randomly assigned into the intervention (n=40) and control (n=40) groups. In the intervention group, rewarming the mattress was started after the patient entered the intensive care unit. Warming continued until the patient's body temperature reached the normothermia level (37°C to 37.5°C). The data were collected by demographic-clinical questionnaire and Mini-Mental State Examination at three time points: before, 7 days, and 1 month after the surgery. The data were analyzed in SPSS software, version 16 using descriptive statistics, independent t test, chi-square test, repeated measure ANOVA, and paired t test. The significance level was considered less than 0.05.

Results: The difference between the Mean±SD scores of cognitive status in the intervention group before the surgery (28.73±0.87), 7 days (27.63±1.03), and 1 month after the surgery (28.93±1.21) was significant (P=0.008). The difference between the Mean±SD scores of cognitive status in the control group before the surgery (28.42±1.02), 7 days (26.61±0.86), and 1 month after the surgery (27.85±1.06) was also significant (P=0.042). The results indicated that the mean score of cognitive status improves after 1 month, and it is greater in the intervention group (F=20.37, df=2, P<0.001). Significant differences were observed between the first and second time of measurements (P<0.0001) and also the second and third time of measurements (P<0.0001).

Conclusion: Rewarming patients after open heart surgery improves their cognitive status. Therefore, this procedure can be used as a safe and non-invasive method to prevent cognitive complications by nurses after open heart surgery.

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Highlights

• Cardiovascular diseases are one of the most important causes of death worldwide.

• Open heart surgery is one of the main treatments for coronary artery occlusion, which leads to complications such as cognitive impairment in patients.

• Hypothermia complications are among the factors that cause cognitive impairment in patients undergoing open-heart surgery.

• The results showed that rewarming the patient after open heart surgery can neutralize the effect of preoperative hypothermia on the patient's cognitive status.

Plain Language Summary

Open heart surgery is a standard treatment for coronary artery obstruction. The nature of the surgery and the use of hypothermia during the surgery can cause many complications in the long run, including cognitive impairment. Warming up the body after surgery is initially done in the operating room by a cardiopulmonary bypass machine. But after entering the ward, the patients suffer hypothermia again, which may affect their cognitive status. The results indicated that rewarming the patient after open heart surgery can neutralize the effect of preoperative hypothermia on the patient's cognitive status.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality and morbidity worldwide. Approximately 17.9 million global deaths from CVD were reported in 2015. Ischemic Heart Disease (IHD) and stroke are the top two leading causes of CVD worldwide, and more than 22.2 million individuals will die from CVD by 2030 (Pepera et al., 2022).

The mortality rate from non-infectious diseases such as cardiovascular problems has risen from 66.17% to 68.98% in the Iranian population from 2006 to 2016 (Kazemi et al., 2021). According to other studies in Iran, cardiovascular diseases account for nearly half of all deaths (Rezaei et al., 2022; Sadeghi et al., 2017). Coronary artery obstruction is the leading cause of death among these cardiovascular problems (Izadi-Avanji et al., 2022). Complications of infarction or heart attack cause problems for many patients (Poorzand et al., 2019).

Open heart surgery is one of the most common treatments for patients who have suffered a heart attack. However, like any other surgery, an open heart surgery can have early and late complications. These include hemodynamic instability, infection, cardiac tamponade, non-fusion of the sternum bone, and cognitive impairment (Maghami et al., 2020; Afazel et al., 2017). Cognitive impairment after open heart surgery affects the patient's quality of life (Li et al., 2022; Martirosyan et al., 2020). Despite the progress in heart surgery techniques and effective brain protection strategies, cognitive dysfunction is still significant. Cognitive dysfunction after surgery has been defined as a decrease in a person's cognitive function after surgery and anesthesia compared to the initial level before surgery (Tan and Amoako, 2013). It is more common in patients undergoing heart surgery than in those undergoing other types of surgery. Postoperative cognitive dysfunction (POCD), characterized by impaired attention, concentration, and memory with possible long-term consequences, is a frequent neurological sequela after cardiac surgery. POCD can be classified into two types based on its duration: short-term and long-term. A transient cognitive decline usually lasts up to 6 weeks after a cardiac procedure, affecting 20%-50% of patients, while a subtle decline in cognitive function occurs 6 months after a cardiac procedure, affecting 10%-30% of patients (Bruggemans, 2013; Tan and Amoako, 2013). The occurrence of this disorder after surgery has been reported to be 45%-88% at the time of hospital discharge and 15%-36% six weeks after discharge so the patient may suffer from this disorder for even up to 5 years after surgery (Yang et al., 2022; Bruggemans, 2013). Cognitive dysfunction after surgery leads to frequent visits of patients to medical centers and a decrease in their quality of life, leading to an increase in the health burden. In addition, this condition puts a significant economic burden on the health system and the families of these patients, which is estimated to be 18 billion dollars annually (Sakusic et al., 2018).

Hypothermia during surgery is one of the most important causes of cognitive failure after heart surgery. The duration of hypothermia in surgery plays a major role in determining the neurologic outcomes of patients, but the extent of this effect is still debated (Patel et al., 2015). Since there is no known treatment for cognitive dysfunction after open heart surgery, emphasis is placed on implementing non-invasive nursing intervention strategies, including rewarming to reduce postoperative central nervous system damage (Berger et al., 2018). It is widely believed that rewarming after deep hypothermia induced by a cardiopulmonary bypass (CPB) machine is favorable for rapid patient recovery (Gocoł et al., 2021).

Various studies have been conducted on warming patients, which have entirely focused on the issue of warming during open heart surgery (Saad and Aladawy, 2013; Currey and Botti, 2005). Rewarming has been shown to improve cognitive function (Patel et al., 2015). Some studies have found it helpful to perform non-invasive interventions such as warming the skin during surgery with a hot water mattress or hot compressed air. Some also point to warming the face, knees, and shoulders of patients after surgery as a simple and effective method and consider it effective in preventing the temperature from dropping again (Rajagopalan et al., 2008; Bezerra et al., 2021; Ciğerci et al., 2020).

Various studies have been conducted on the effect of temperature with different degrees during surgery on the cognitive function of patients after surgery. However, studies do not reveal a clear difference between the induction of mild hypothermia or normothermia and their effect on neurocognitive function at discharge and three months later. The results of two studies comparing the effects of normothermia and hypothermia during cardiac surgery on cognitive function after surgery showed a significant improvement in cognitive function in the normothermia group (Shaaban-Ali et al., 2002; Grimm et al., 2000). The results of two other studies comparing the effect of hypothermia and normothermia during heart surgery show that cognitive status improves in the hypothermia group (Kadoi and Goto, 2006; Boodhwani et al., 2006). Meanwhile, the results of some other studies comparing the effect of hypothermia and normothermia on the nervous system function after heart surgery show no difference between the use of these two methods (Grigore et al., 2009; Reinsfelt et al., 2012).

Because most studies focus on rewarming during surgery and few on rewarming after surgery, as well as the conflict between the results of the studies, the present study aims to determine the effect of rewarming on the cognitive status of patients after open heart surgery.

2. Materials and Methods

Study setting and sample

This double-blind, randomized clinical trial was conducted from September to December 2020 at Tehran Heart Center in Tehran-Iran. The initial sample of the study was determined through consecutive sampling. A total of 80 subjects were selected based on the inclusion criteria and randomly allocated into two groups of 40 by generating ten blocks of four using online blocked randomization software (Sealed Envelope Ltd., 2022). In the online randomization site, letter A was assigned to the intervention group and B to the control group. The patients were unaware of being placed in the intervention or control group. In addition, the statistical analyst did not know the names of the groups. The sample size was determined based on mean arterial blood pressure from the study of Murphy (Murphy et al., 2009), in which the Mean±SD arterial blood pressure was 13.5±1.9 and changed to 15.2±0.7 mmHg. Then, with a type I error of 0.05, a type II error of 0.2, an S1 of 1.9, an S2 of 0.7, a µ1 of 13.5, and a µ2 of 15.2, the sample size for each study group was estimated to be 37. However, due to possible attrition, the sample size in each group was increased to 40 (Equation 1).

$$1.\ n=\frac{2(z_{1-\alpha/2}+z_{1-\beta})^2(s_1+s_2)^2}{(\mu_1+\mu_2)^2}=37$$

The potential subjects were elective patients who were candidates for open heart surgery. Other inclusion criteria were having a Mini-Mental State Exam (MMSE) score higher than 24 and not having an intra-aortic balloon before surgery. The exclusion criteria were prolongation of intubation time (more than 12 hours) due to respiratory reasons, resternotomy due to postoperative surgical reasons, having an intra-aortic balloon after surgery, and re-intubation after surgery, patients undergoing reoperation, aortic aneurysm or dissection, death of the patient, return of the patient to the operating room for any reason, and prolongation of surgery for any reason more than five hours. The outcome measure in this study is the changes in mean cognitive function in different time intervals.

Study procedure

As part of a routine cardiac operating room procedure, all patients become hypothermic during cardiac surgery, with their body temperature lowered to 25°C-32°C. Immediately after surgery, the body temperature gradually increases to 36°C, which is the first step to warming the patient in the operating room. All patients undergoing open heart surgery are required to undergo this procedure.

Before the patient entered the intensive care unit, an electric warming mattress was placed on the patient's bed. It was model EU133, the electrical under blanket and heating pad-EmsiG GmbH. The upper surface is made of small woolen fibers, and the lower surface of polyester (dimensions: 80 x 150 cm, power: 75 W, the temperature range: 35°C to 50°C). The blanket performance was examined, and its temperature was set at 37.5°C. The bed was sent to the operating room, and the patient was transferred from the operating room bed to the bed with the electric mattress so that the mattress was placed under the patient from the shoulder to the ankle. This way, rewarming was started immediately after the surgery, and the patient's body temperature was gradually raised to 36°C. Although it was the first step of rewarming and the same for all patients, we did not consider it part of the intervention, and the rewarming time was calculated from the entry of the patients to the ICU till their body temperature reached preoperative normothermic condition (i.e., between 37°C and 37.5°C).

This way, all patients in the intervention group were rewarmed using an electric mattress, but the control group received routine care.

Study instruments

The data were collected using demographic information form (age, gender, education, marital status, occupation, smoking), surgical information form (type of surgery, duration of surgery, duration of the aortic clamp, number of grafts, and duration of intubation), the MMSE, and an axillary temperature probe. MMSE has been translated into different languages and standardized in different cultures. This 30-point test measures different cognitive functions and provides a general assessment of the subject's cognitive status. It is an 11-question measure that tests 5 areas of cognitive function: orientation, registration, attention and calculation, recall, and language. The scoring procedure in this questionnaire is as follows: orientation=10 points, memory=6 points (including recording 3 points and recalling 3 points); attention and calculation=5 points; assessment of language abilities and understanding=8 points. Also, 1 score is given to visual and spatial abilities. The minimum and maximum scores for the MMSE are 0 and 30, respectively. Scores above 24 indicate no cognitive problem, scores between 20 and 23 indicate mild cognitive impairment, scores 10 to 19 indicate moderate impairment, and 0 to 9 indicate severe impairment (Seyedian et al., 2007).

To measure body temperature, an axillary temperature probe connected to a monitor continuously measured and monitored the body temperature of the patients. Before use, the probes were calibrated by a medical equipment engineer. To ensure the accuracy of the thermometer, the measurement results were compared with those of a mercury thermometer for one patient, and the results were identical.

The cognitive status of patients was measured in three time intervals; before the surgery, 7 days, and 1 month after the surgery (Cormack et al., 2012; Nathan et al., 2001). In the third time interval (1 month after the surgery), the patients completed the questionnaires when they returned to the hospital for their cardiac rehabilitation.

The data were entered into SPSS software, version 16 (SPSS Inc., Chicago, IL, USA) and analyzed using descriptive statistics, independent t test, and paired t test. The Kolmogorov-Smirnov test was used to check if the data had a normal distribution. The P value was considered less than 0.05.

3. Results

A total of 100 patients were consecutively assessed for eligibility, of which 8 patients were excluded due to unwillingness to participate in the study, and 12 patients due to lack of eligibility criteria (Figure 1).

The results showed that the Mean±SD ages of the intervention and control groups were 58.71±13.8 and 57.94±9.7 years, respectively. The Mean±SD durations of intubation in the intervention and control groups were 11.33±5.19 and 12.48±5.7 hours, respectively. Most of the subjects in the intervention (65.72%) and control (66.66%) groups were men; the statistical tests did not show any statistically significant difference between the two groups in terms of individual characteristics, including age, sex, type of surgery, tobacco and substance abuse in the past year, underlying diseases, number of grafts, tracheal tube time, CPB time, aortic clamping time, and duration of surgery (P>0.05) (Table 1).

Table 1. Demographic and clinical characteristics of the patients in the intervention and control groups

Variables		No. (%)/Mean±SD		P
		Intervention (n=35)	Control (n=36)	
Sex	Male	23 (65.72)	24(66.66)	0.14
	Female	12 (34.28)	12(33.33)	
Tobacco and substance abuse in the past year	Yes	35 (100)	36(100)	1
	No	0	0	
Type of surgery	CABG	25 (71.42)	23(63.88)	0.43
	Valve replacement	8 (22.85)	12(33.33)	
	Both	2 (5.71)	1(2.77)	
Underlying diseases	HTN	10 (28.6)	8(22.2)	0.71
	Diabetes	6(17.1)	9(25)	
	HTN & Diabetes	15(42.9)	13(36.1)	
	No	4 (11.4)	6(16.7)	
Age (y)		58.71±13.8	57.94±9.7	0.78
Number of grafts		2.4±0.20	2.1±0.12	0.54
Duration of surgery (h)		1.37±0.86	1.38±0.54	0.90
Tracheal tube time (d)		11.33±5.19	12.48±5.7	0.37
CPB time (min)		68.40±35.4	70.08±19.6	0.80
Aortic clamping time (min)		37.68±20.12	44.11±14.90	0.13

CABG: Coronary artery bypass graft; HTN: Hypertension; CPB: Cardiopulmonary bypass.

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In the repeated measures analysis, Mauchly's test illustrated that sphericity was assumed (P>0.05); then, the degrees of freedom were corrected using the sphericity assumed test. The analysis of variance with repeated measures showed significant changes in cognitive status over time (F=20.37, P=0.000). Also, a significant difference was observed between the mean scores of the cognitive status of the two groups (F=18.12, P=0.000). However, the changes in cognitive status at three time points between the two groups were not significant (F=1.12, P=0.330). Moreover, the analysis of variance with repeated measures performed separately for each group showed that the mean scores of cognitive status changed significantly over time in the intervention (F=5.55, P=0.008) and control (F=4.70, P=0.000) groups. The results of the independent t test at three time points showed that before surgery, there was no difference between the two groups in terms of cognitive status, but at the time points of 7 days and 1 month after the surgery, there was a significant difference between the control and intervention groups (P<0.05) (Table 2).

4. Discussion

The results showed that rewarming after cardiac surgery significantly improved the cognitive status of patients 7 days and 1 month after the intervention. Cognitive disorders after heart surgery may occur due to transient hypoxia, cerebral hypoxia, long duration of the aortic clamp, hemoglobin drop during surgery, severe or prolonged drop in arterial blood pressure, and a drop in body temperature during the CPB (Rezamasouleh et al., 2014). Patel et al.'s research showed that slow rewarming after heart surgery could improve cognitive performance (Patel et al., 2015). The results of his research are consistent with the present study. It has been shown that rewarming after heart surgery reduces cognitive impairment and increases memory and attention in patients 1

Table 2. Comparing the mean scores of cognitive status before, 7 days, and 1 month after the heart surgery in the intervention and control groups

Group / Time		Mean±SD Control (n=35)	Mean±SD Intervention (n=36)	Independent t-test
24 hours before the surgery (T1)		28.42±1.02	28.73±0.87	t=1.02, P=0.316
Seven days after the surgery (T2)		26.61±0.86	27.63±1.03	t=3.41, P=0.002
One month after the surgery (T3)		27.85±1.06	28.93±1.21	t=2.15, P=0.038
Time effect in each group		F=4.70, P=0.000	F=5.55, P=0.008	-
Results of repeated measure ANOVA	Within groups		F=20.37, P=0.000	-
	Between groups		F=18.12, P=0.000	-
	Groups×time		F=1.12, P=0.330	-

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week (Cormack et al., 2012; Nathan et al., 2001) and 3 months after surgery (Polderman, 2008; Linassi et al., 2022; Cormack et al., 2012). Also, it is shown in a study that rewarming after coronary artery bypass surgery improves cognitive function in rats (De Lange et al., 2008). In the mentioned study, rats underwent surgery for 90 minutes, and their cognitive function was measured based on brain function and cerebral perfusion.

It has been reported in some studies that surgery using extra-corporeal blood circulation (extra-corporeal) has been found to cause short-term and long-term cogni-

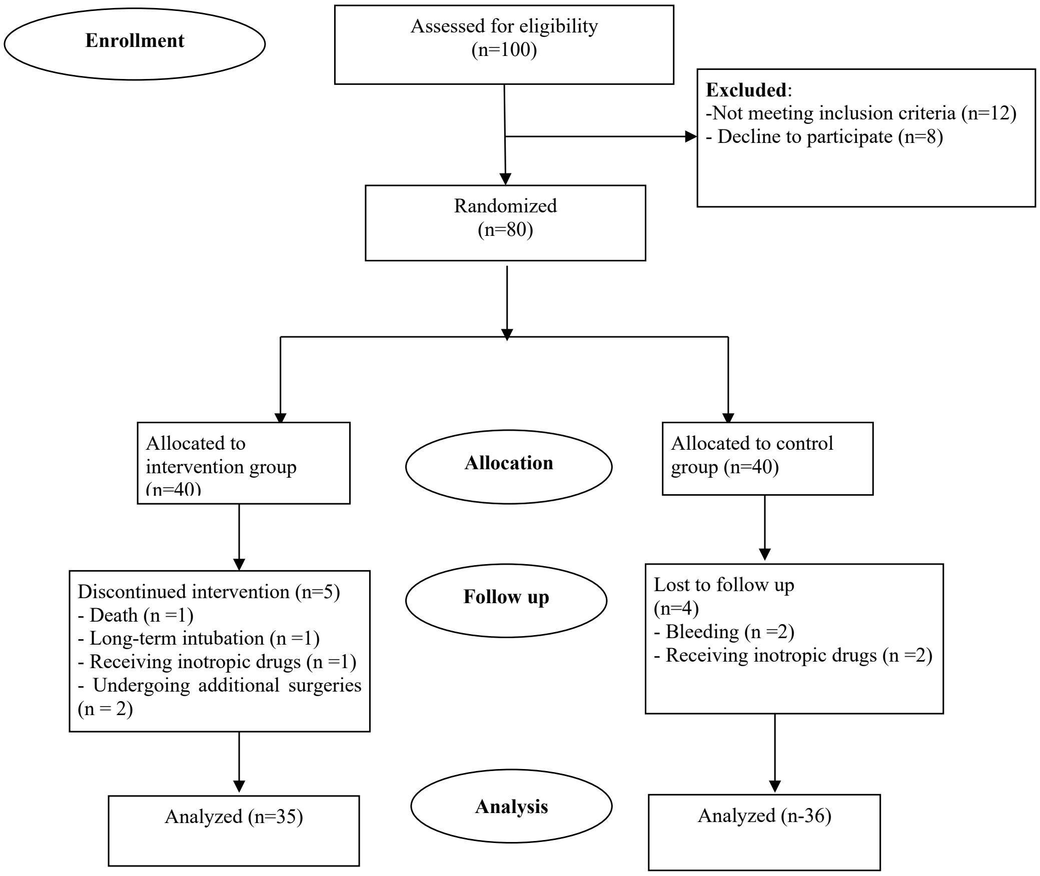

Figure 1. CONSORT flowchart of the study process

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tive dysfunction in 55% of cases (Chernov et al., 2006; Belrose and Noppens, 2019). Therefore, it seems that short-term and long-term complications of cognitive impairment after open heart surgery can be prevented by performing interventions such as rewarming. It is believed that rewarming increases oxygen supply to the brain and improves cognitive status. (Ali et al., 2014; Mohmaed Shaaban et al., 2014; Hu et al., 2016; Sugiura et al., 2021). It has been shown that a CPB machine alone can result in neurological damage. There are several reasons why this complication occurs, including the non-pulsatile blood supply caused by the bypass device, the activation of complements and inflammatory mediators, the activation of platelets, and their accumulation as microemboli (Puthettu et al., 2021).

The prevalence of psychological problems after coronary artery bypass surgery has been emphasized (Burkauskas et al., 2018). Among the cognitive disorders after heart surgery is disorientation to time and place, and disorder in calculating or drawing shapes. Meanwhile, providing oxygen and warming the patient can be effective in solving the neurological disorders of patients after open heart surgery (Burkauskas et al., 2018; Ottens et al., 2017). The findings of these studies are consistent with the present research. In the current study, the MMSE was used to measure the cognitive status of the patients after surgery. This questionnaire includes dimensions of orientation to time and place, performing calculations and drawing shapes, and remembering events. The results showed that patients had disorders in these fields after open heart surgery. However, 1 month after the intervention, these disorders decreased. So that after the intervention, the score of cognitive status in the intervention group increased significantly compared to the control group. Contrary to the present study, Engelman et al. showed no relationship between cognitive status and hyperthermia after open heart surgery. He suggested more studies in this field (Engelman et al., 2019). The results of his research are not consistent with the present study. The inconsistency may be related to the method of warming the patient, the speed of warming, and the tool for measuring the cognitive status. It may also be due to the difference between the measurement time points.

One of the limitations of this study is the possible effects of uncontrollable confounding variables. Another limitation was the impossibility of choosing a specific surgeon for the studied patients, which may have affected the conditions of the samples. Also, hemodynamic changes after cardiac surgery may have affected the results, which were beyond the control of the researchers.

5. Conclusion

The study showed that rewarming patients after open heart surgery improve their cognitive status. Therefore, it can be used as a safe and non-invasive method to enhance the cognitive status of patients after heart surgery by nurses.

Ethical Considerations

Compliance with ethical guidelines

The Ethics Committee of Kashan University of Medical Sciences approved the study (Code: IR.KAUMS.NUHEPM.REC.1398.016). It was also registered in the Iranian Registry of Clinical Trials (IRCT ID: IRCT20100124003146N8). All subjects were informed of the intervention and signed the written informed consent form. They were also assured of data confidentiality and informed that they could withdraw from the study at any time without affecting their treatment. Necessary permissions were also sought from the officials at Tehran Heart Center. We also observed all patients' rights according to the Helsinki Declaration. The subjects were also assured that attending the study would not cost them anything.

Funding

This article was extracted from a Master's thesis Somayeh Haji-Jafari the Research Deputy of Kashan University of Medical Sciences for their financial support (Grant No: 98051).

Authors' contributions

Conceptualization and data curation: Ismail Azizi-Fini and Somayeh Haji-Jafari; Data analysis and software: Fatemeh Atoof; Funding acquisition, resources, and project administration: Ismail Azizi-Fini; Investigation: Ismail Azizi-Fini, Somayeh Haji-Jafari, and Mahboubeh Rezaei; Methodology: Ismail Azizi-Fini and Mahboubeh Rezaei; Supervision and validation, writing, review, and editing: Ismail Azizi-Fini and Seyed Hossein Ahmadi Tafti; Writing the original draft: Ismail Azizi-Fini and Somayeh Haji-Jafari.

Conflict of interest

The authors declared no conflict of interest.

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