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Original Article

The effect of cryotherapy application before versus after subcutaneous anticoagulant injection on pain intensity and hematoma formation: A quasi-experimental design

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ABSTRACT

Objective: To investigate the effect of cryotherapy application before versus after subcutaneous anticoagulant injection (SCAI) on pain intensity and hematoma formation.

Methods: A quasi-experimental design was utilized. A convenient sample of 105 adult patients, who were admitted to one of the biggest teaching hospitals in Cairo and receiving SCAI, were recruited over a period of six months. Patients were randomly allocated into three groups: A Control group who received the routine hospital care (G1, $n = 35$) and two intervention group who received cryotherapy for 5-min (G2: cryotherapy applied before SCAI, $n = 35$; G3: cryotherapy applied after SCAI, $n = 35$). Demographic and medical history data sheet, Pain Numeric Rating Scale and Hematoma Formation and Size Assessment Scale were used to collect the data.

Results: The pain intensity among the patients in the two intervention groups (G2: Median = 1.0; G3: Median = 0) was significantly lower than in the control group (G1, Median = 3.0). No significant difference was found between G2 and G3 ($P = 0.728$). Applying cryotherapy after SCAI (G3) decreased the frequency of hematoma formation (48hrs = 31.4% & 72hrs = 28.5%) compared to applying it before injection (G2, 100%) or not applying it (G1, 100%). The size of hematoma in G3 was smaller than that in G2 ($P < 0.01$).

Conclusion: Applying cryotherapy significantly decreased pain intensity and hematoma occurrence/size. Applying cryotherapy after injection was more effective in preventing hematoma formation and decreasing its size than applying it before injection.

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1. Introduction

Anticoagulant is frequently prescribed as prophylaxis or treatment for venous thromboembolism. However, subcutaneous injections (SCI) of anticoagulant often cause complications such as pain and hematoma at the injection site. Previous studies indicated that complications of subcutaneous anticoagulant injections (SCAI) such as hematomas and pain increased the patients' physical and psychological discomfort [1]. Moreover, it may result in the patients' distrust in nurses' competency, which may consequentially result in the avoidance of future injections [1,2].

Hematomas occur frequently because of local tissue injury that follows the administration of an anticoagulant solution [3]. It may lead to anxiety, body image disturbance and rejection of the treatment in patients. Moreover, it can also reduce the opportunities for site rotation for future subcutaneous injections [2,4]. Therefore, nurses should consider the factors that minimize subcutaneous injection complications, including the intensity of site pain and hematoma formation [5].

Several nursing measures have been found to be essential to avoid the occurrence of hematomas and local pain intensity during injection; such as the injection site, injection angle, aspiration before the injection, needle's size, duration of injection, use of an air bubble, and the application of cryotherapy [5–7]. Additionally, injections in the lower abdominal wall, the insertion of the needle into the tissue at a 90° angle, grasping the tissue of injection and injecting the drug without aspirating have been found effective in

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reducing pain and hematoma formation [6].

“Cryotherapy” is a Greek word that means cure-using cold. Cryotherapy aims to reduce inflammation, decrease spasm and pain and stimulate blood vessel constriction (vasoconstriction), so it can increase the survival of cells. It is currently debated whether applying cryotherapy at the injection site is effective in decreasing pain intensity and hematoma size [5,8,9]. Cold has a physiological effect that can avoid SCAI related complications by increasing vasoconstriction at the injection site and the inflammatory process. These physiological changes decrease the incidence and size of hematomas. Cold also prevents the intensity of pain through its effect on sensory nociceptors by decreasing the conduction time and the synaptic activity in peripheral nerves. When heat in the nerves is reduced, a decrease in the sensory and motor conduction velocities is observed; thus, the intensity of pain is prevented [3,9,10].

The SCAI is a frequently performed nursing task. The incidence of local hematomas as a result of SCAI varies considerably, as reported in previous studies, where it ranged from 20.6% to 88.9% after SCAI [2,11]. It is really a serious problem, especially for those patients who are scheduled for SCAI over a long time or those who had other SCI, since it can reduce the opportunities for site rotation for future subcutaneous injections as well as affect nurses' quality of care. Therefore, it was crucial to investigate methods to decrease hematoma formation. There is a growing research interest to investigate the effect of cryotherapy application before and after SCAI on pain intensity and incidence of hematoma formation [3,7,12–14]. However, the findings are still contradictory, and there is not enough supporting evidence for the effectiveness of cryotherapy as well as too many methodological limitations and not enough details about the procedure or comparison between the two methods. In addition, there was no available research before conducting the current study, which compared the application of cryotherapy before versus after SCAI in order to prove which time is most effective in reducing pain intensity and the incidence of hematoma formation. Cryotherapy is a safe, noninvasive, pain free, easy to self-administer therapy. It can enhance patients' sense of control over their management of side effects, is cost effective and improves the quality of life. It is also an innovative idea to involve patients in their own care to play a major role in relieving their distressing symptoms through a simple procedure like cryotherapy.

Therefore, this study aimed to investigate the effect of cryotherapy application before versus after SCAI on pain intensity and hematoma formation. In order to accomplish this study aim, five hypotheses were formulated:

H1. The study group who received cryotherapy will have a significant lower pain intensity than the control group who received routine hospital care.

H2. There will be a difference between applying cryotherapy before versus after SCAI on pain intensity among the intervention groups.

H3. The study group who received cryotherapy will have a significant lower incidence of hematoma formation compared with the control group who received routine hospital care.

H4. The study group who received cryotherapy will have a significant smaller size of hematoma than the control group who received routine hospital care.

H5. There will be a difference between applying cryotherapy before versus after SCAI on hematoma formation and size among the intervention groups.

2. Material and methods

2.1. Study design

A quasi-experimental design was utilized to accomplish this study's purpose.

2.2. Participants and sample size

The study participants were adult male and female patients who were receiving SCAI. In total, 133 who met the inclusion criteria over a period of six months (January to June 2017) were invited to participate in the study. Patients were eligible to participate if they were 18 years or older, were alert to be able to express pain, agreed to give informed consent, and received subcutaneous injection of 40 mg enoxaparin with the volume of 0.4 or 60 mg enoxaparin with the volume of 0.6 ml once per day. Patients who had any of the following criteria were ineligible to participate: (1) discharge earlier than 72hrs, (2) any impairment in coagulation profiles such as thrombocytopenia, prothrombin time, platelets count, International Normalized Ratio, (3) Liver function disturbance, (4) Scar tissues or old hematomas at the site of injection, and sensory alteration.

The study sample was calculated based on a pilot study of 12 patients with considering $r = 1$ (equal sample size for each group), $\alpha = 5\%$ and power at 90% were computed using the following formula:

$$N = \frac{(r + 1)(Z_{\alpha/2} + Z_{1-\beta})^2 \sigma^2}{rd^2}$$

Where the σ and d are the standard deviation and difference of means of two groups, $N = (1 + 1)(1.96 + 0.84)^2 (1.2)^2 / [1 \times (1.6 - 1.4)^2]$.

Then, for 90% of statistical power, the sample size for each group would be 21. An extra, 10–20% of subjects were required to allow for the adjustment of withdrawals, missing data, lost to follow-up [15]. After calculating the required sample size, a block randomization technique was used to allocate the patients into either intervention group (pre or post cryotherapy) or control group, to ensure a close balance of each group size [16]. This technique was used to insure every patient had an equal probability of being assigned to any of the three groups, and to control an unbiased representation of the groups.

Out of 133 patients who were invited and met the inclusion criteria, 128 accepted to participate with a response rate of 96.24% at the baseline phase. Only 105 patients participated three times (response rate 82.03%) and were involved in the data analysis. Based on this sample ($n = 105$), three groups were investigated in this study: (1) Control group [G1, $n = 35$], who received routine hospital care (RHC) and (2) two intervention groups [G2, $n = 35$ & G3, $n = 35$], who followed RHC alongside 5 min cryotherapy application. G2 received 5 min cryotherapy before SCAI, and G3 received cryotherapy after SCAI (Fig. 1).

2.3. The study setting

The study was conducted in the medical, surgical, cardiovascular and orthopedic wards ($n = 8$ wards) in one of the biggest Teaching Hospitals in Cairo City, Egypt. These wards were selected because admitted patients were usually receiving SCAI as a prophylaxis or treatment medicine.

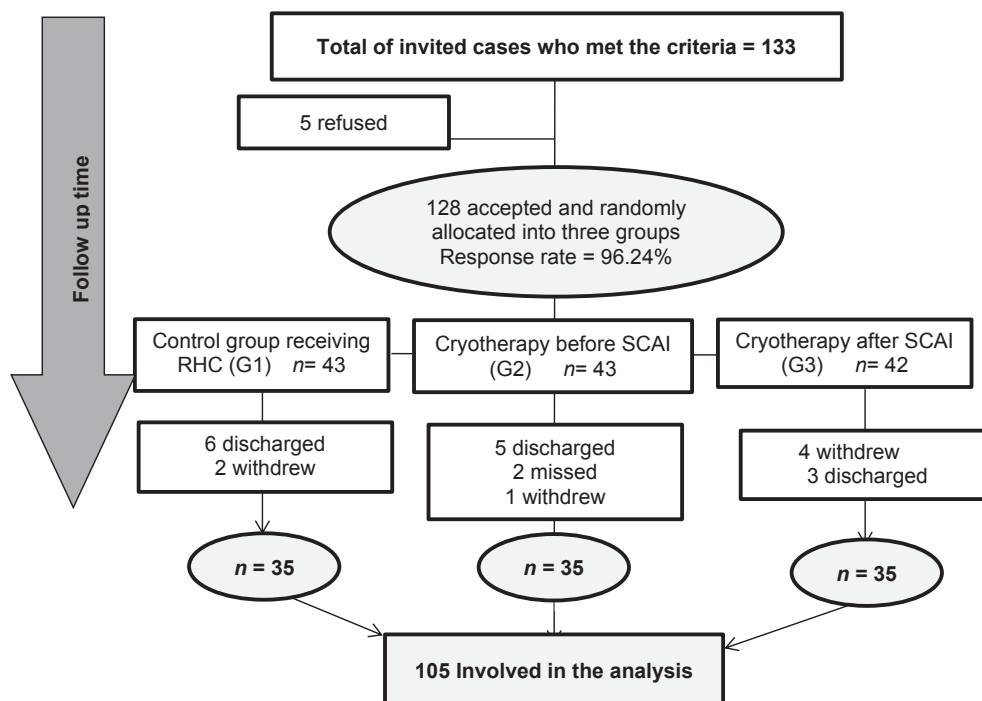


Fig. 1. Sample flowchart.

2.4. Instruments

One questionnaire and two scales were used to collect the data:

A Demographic and Medical History Data Sheet was designed by the researchers to collect the baseline characteristics and medical history data of the participants such as age, gender, marital status, education, employment status and medical diagnosis.

The Pain Numeric Rating Scale (PNRS) is a single 11-point numeric scale in which respondents select a number from zero (no pain) to 10 (severe pain) to reflect the intensity of their pain. The scale has a high test–retest reliability in both literate and illiterate patients ($r=0.96$ & 0.95 , respectively) [17]. Therefore, PNRS was used in this study to assess the pain intensity as perceived by the participants. The participants were requested to select the number that represented their pain intensity most closely.

Hematoma Formation and Size Assessment Scale (HFSAS): A hematoma is generally defined as a collection of blood outside of blood vessels due to an injury to the blood vessel wall [5,8]. Thus, hematomas were observed after the SCAI in the control group and the two intervention groups after 48hrs and 72hrs for assessing their occurrence and size. The presence or absence of hematomas at injection sites was recorded by observing any discoloration of the injection site (pink, red, blue, purple, pale green, yellow and brown). Previously, it was noticed that the hematoma peak occurred at 48hrs and the beginning of healing at 72hrs after injection [18]. Thus, hematomas in this study were recorded at 48hrs and 72hrs after SCAI by observing any discoloration at the injection site. A transparent ruler scale was used to measure the total hematoma size in millimeters and the measurement unit was converted into centimeter during data analysis and interpretation [4].

2.5. Procedure of data collection

The study was conducted in three phases:

2.5.1. Assessment phase

One of the researchers (2nd researcher) interviewed the eligible participants and explained the study aims in order to obtain their informed consent and collect the demographic and medical baseline data. At this phase, all patients who were willing to participate in the study were assessed for deciding the site of SCAI. The injection site was selected on the consideration that it should be free from any scars or hematoma before the intervention. The side of the upper (left or right) arm was selected for injection. It is area located between (4 fingers of hand below) the shoulder and (4 fingers of hand above) the elbow.

2.5.2. Intervention phase

At this phase, the first researcher applied the cryotherapy by using an ice pack in plastic sac for 5 min for the two intervention groups (G2 immediately before injection, and G3 immediately after anticoagulant injection). Ice pack was prepared by placing ice cubes of frozen water inside a small plastic sac. An individualized plastic ice pack was labeled with each participant's name to avoid the risk of cross infection.

For controlling confounders that have been shown in previous studies as factors for increasing pain sensation and hematoma formation [5–7,19], the two study and control groups received the same injection technique. For instance, the anticoagulant dose was slowly injected over a period of 30 s using a syringe ready for injection, with insertion angle of 90° , with no aspiration before the injection, and by holding the skin of the injection site between the thumb and index finger, since these techniques can reduce pain intensity and hematoma formation [6,7]. After injection, a piece of cotton was placed on the injection site and was then removed without rubbing. A Kenko sports chronometer was used to measure the duration of the injection. A circle was drawn around the injection site (at the selected arm) on all participants in order to ensure it will not be selected again for the following injection, and to assess the occurrence and size of the hematoma. Additionally, the nurses were informed not to inject the selected arm through the study period. Moreover, the patients were instructed not to

affect the injection site (itch, touch & massage).

2.5.3. Evaluation phase

The second researcher reassessed the pain immediately after the needle was withdrawn among the G1 and G2 participants, while in the G3 pain was measured 5 min after applying cryotherapy using the PNRS. Hematomas were assessed for the three groups after 48hrs and 72hrs by the second researcher as well using the HFSAS.

2.6. Data analysis

The Statistical Package for the Social Sciences (SPSS) version 20 (IBM: Armonk, New York, United States) was utilized for data entry, tabulation and analysis. Descriptive statistics were computed to summarize the patients' demographic and medical data. A nonparametric statistical ANOVA test (i.e. Kruskal-Wallis Test) was conducted to explore the impact of the interventions on perception of pain intensity and hematoma formation/size. If the output of the Kruskal-Wallis Test was statistically significant, the independent-sample Mann-Whitney Test was used to find which of the three groups was statistically different. Mann-Whitney Test was used with Bonferroni correction to control type 1 error with all effects were reported at a 0.0167 level of significant. To compare the categorical variables, Chi-square was used. The statistical level of significance was set at $P < 0.05$.

2.7. Ethical considerations

Official approval and permissions from the director of the hospital and the heads of the departments were obtained. The study was conducted in accordance with the Helsinki Declaration. All the participants gave informed consent after being given full explanations about the study's aims and benefits. It was emphasized that participation in the study was voluntary. The confidentiality of patients was assured through coding of all data. In addition, the participants were informed that they could refuse or withdraw from the study at any time without giving any reason.

2.8. Pilot study

A pilot study was conducted before starting the main study data collection on 12 patients to assess the recruitment feasibility, the applicability of the tools and to estimate the required sample size. Participants who took part in the pilot study were included in the main study sample since there was no difference in the recruitment process. The results of the pilot study confirmed that the study was feasible.

3. Results

3.1. Descriptions of the samples in the three groups

Regarding the characteristics of the entire studied sample ($n = 105$), the age was (45.45 ± 10.75) ranged from 20 to 70 years, a higher percentage of the participants were males (62.9%), educated (91.4%), married (85.7%), unemployed (51.4%), and had a fracture (42.9%).

Table 1 shows demographic characteristics of patients in the three groups. There is no statistically significant differences at baseline demographic characteristics among the three groups.

Percentage distribution of the medical diagnosis of the three groups are shown in Fig. 2. Fracture and heart disease were the most prevalent diagnoses in the three groups ($\geq 40\%$ & $\geq 25\%$ respectively).

3.2. Pain intensity

The Median (P_{25}, P_{75}) of the pain intensity is presented in Table 2. The nonparametric statistical test (i.e. Kruskal-Wallis Test) was used to compare the pain intensity among the three groups. As noted, there was a statistically significant difference in the pain intensity among the three groups ($P = 0.000$) (Table 3). Using the Post-hoc test (Mann-Whitney Test) with Bonferroni correction indicated that the pain intensity among the two intervention groups ($P \leq 0.001$) was significantly lower than in the control group. However, there was no statistically significant difference in pain intensity between the two intervention groups (G2 & G3) ($Z = 0.34, P = 0.728$) (Table 3).

3.3. Hematoma formation and size

The results revealed a statistically significant difference in hematoma formed across the three different groups at 48hrs and 72hrs ($P < 0.01$). The frequency of hematomas in G3 was 31.4% at 48hrs and 28.5% at 72hrs, while it was 100% in both group G2 and control group G1 (Table 4).

The Median (P_{25}, P_{75}) of the hematoma size among the three groups at 48hrs and 72hrs is presented in Table 2. The nonparametric statistical test (i.e. Kruskal-Wallis Test) was used to compare the hematoma size among the three groups. Table 3 shows that there was a statistically significant difference in hematoma size among the three groups at 48hrs and 72hrs ($P < 0.01$). The comparison using post-hoc test showed that the hematoma size in the control group (G1) was significantly larger than in the two intervention groups (G2 & G3). There was also a statistically significant difference between the two intervention groups, where G3 had a smaller size of hematoma than G2 ($P < 0.01$).

4. Discussions

The SCAI is a regularly administered medicine that aims to inhibit blood coagulation. The SCAI often causes pain and hematoma at the injection site [1].

In this study, about two thirds of the participants were males, the majority was educated and most of them were married. Nearly half of them were unemployed, their mean age was 45.34 ± 9.61 , and approximately two fifths of the study participants had fractures. A previous study [12], which examined the impact of cold therapy on pain and hematomas on the injection site of enoxaparin, similarly showed that the mean age of the participants was 47.5 ± 20.7 , and the majority of them were males. The comparison between the control and the intervention groups' demographic characteristics showed no significant differences at baseline that might affect the findings; this means that the three groups of the study were homogenous groups.

Regarding pain, the pain intensity score in the control group and the two intervention groups, interestingly, seemed mild to moderate. One of the most likely reasons for this is that the researcher followed a certain subcutaneous injection technique, which has been scientifically proven by previous research [5–7] that it is effective in decreasing pain and hematoma. This was highlighted in the methodology and the researcher applied this technique to the entire study sample (control and intervention groups).

In addition, the study's findings concluded that the two intervention groups who received cryotherapy had significantly lower score of pain intensity than the control group. This result may be due to the cooling and analgesic effects of applying ice to the skin, causing a numbing sensation and relieving pain.

Moreover, the results reveal that there was no significant difference between participants who received cryotherapy before

Table 1
Demographic characteristics of the participants(n = 105).

Characteristics	Control group (G1,n = 35)		Intervention group (G2,n = 35)		Intervention group (G3,n = 35)		χ^2	P
	n	%	n	%	n	%		
Age (years)							1.86	0.76
18–35	3	8.6	6	17.1	4	11.4		
36–59	27	77.1	24	68.6	24	68.6		
≥60	5	14.3	5	14.3	7	20		
Gender							1.71	0.76
Male	25	71.4	20	57.1	21	60		
Female	10	28.6	15	42.9	14	40		
Education							4.44	0.35
Educated	19	54.3	23	65.7	21	60		
Uneducated	16	45.7	12	34.3	14	40		
Employment status							2.06	0.36
Employed	20	57.1	14	40	17	48.6		
Unemployed	15	42.9	21	60	18	51.4		
Marital status							0.47	0.79
Married	30	85.7	31	88.6	29	82.9		
Unmarried	5	14.3	4	11.4	6	17.1		

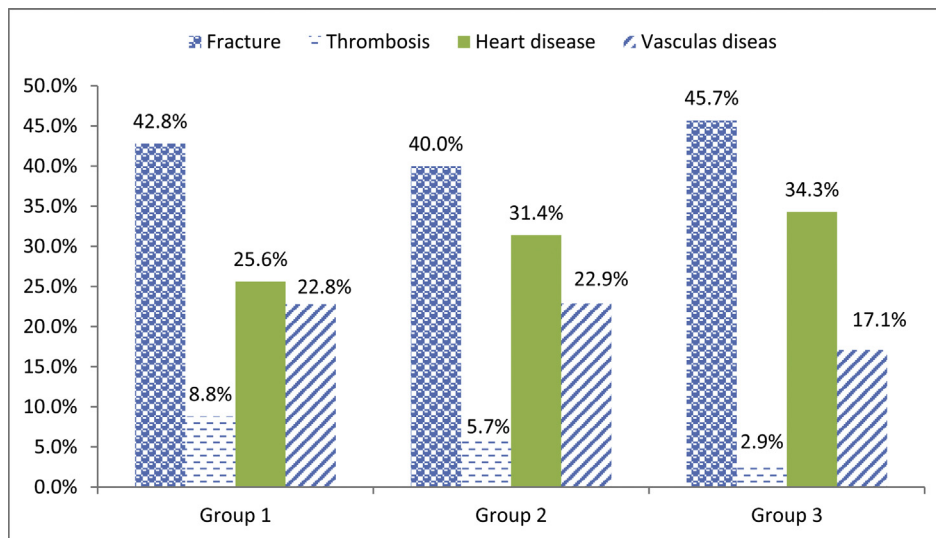


Fig. 2. Distribution of the medical diagnosis of the control and the two intervention groups (n = 105).

Table 2
Pain intensity and hematoma size among control group and intervention groups [Median(P₂₅, P₇₅)].

Groups	Pain Intensity	Hematoma Size(cm, after 48hrs)	Hematoma Size(cm, after 72hrs)
Control group (G1, n = 35)	3.0(3.0, 4.0)	4.0(4.0, 4.0)	1.0(1.0, 5.0)
Intervention group (G2, n = 35)	1.0(1.0, 1.0)	2.0(1.0, 2.0)	1.0(1.0, 1.0)
Intervention group (G3, n = 35)	0(0, 4.0)	0(0, 1.0)	1.0(0, 1.0)

SCAI and those who received it after SCAI. This finding rejected the second research hypothesis. This result may be due to the fact that the cold application in general whatever the time of application (before or after injection) relieves the pain as a result of a reduction of neural transmission speed during or directly after the injection. The cold application has a local anesthetic effect that may suppress the injection pain. This finding is congruent with those of previous studies [4,9,12,14,20], which examined the effects of ice application on pain, and concluded that ice had a significant effect in reducing pain intensity.

Regarding hematoma occurrence and size after 48hrs and 72hrs, the cryotherapy groups had a significant lower incidence of hematoma formation compared with that of the control group, who

received only routine hospital care. In addition, patients who received cryotherapy after SCAI had a significantly lower prevalence of hematoma formation than the control group as well as the group who received cryotherapy before SCAI. Thus, it seems that applying cryotherapy after SCAI might be more effective in decreasing the frequency of hematoma occurrence than applying it before SCAI. This may be due to the vasoconstriction effect of the ice application immediately on the injected area, which decreases or stops the bleeding at the injection site. These findings support the third research hypothesis.

Furthermore, the difference of the hematoma mean size was statistically significant between the three studied groups. The control group had a significantly larger size of hematoma than the

Table 3
Comparison of pain intensity and hematoma size among control group and intervention groups ($n = 105$).

Groups	Mean Rank		
	Pain Intensity	Hematoma Size (after 48hrs)	Hematoma Size (after 72hrs)
Control group (G1)	77.51	86.43	72.06
Intervention group (G2)	35.30	48.46	59.29
Intervention group (G3)	46.19	24.11	27.66
H-value	38.18*	77.08*	50.58*
Comparison (Mann-Whitney Test)	Z-value		
G1 vs. G2	7.32*	7.05*	3.11*
G1 vs.G3	3.23*	7.14*	5.94*
G2 vs. G3	0.34	5.19*	5.55*

Note: * $P < 0.01$.

Table 4
Frequency and percentage distribution and chi-square of hematoma formed after 48hrs and 72hrs among the three groups.

Groups	Hematoma formed at 48hrs(Yes)	Hematoma formed at 72hr(Yes)
	n (%)	n (%)
Control group(G1)	35 (100)	35 (100)
Intervention group(G2)	35 (100)	35 (100)
Intervention group G3)	11 (31.4)	10 (28.5)
χ^2	61.63	65.00
P	<0.001	<0.001

two intervention groups. Moreover, patients who received cryotherapy after SCAI had a significantly smaller size of hematoma after 48hrs and 72hrs than the control group and G2 who received cryotherapy before SCAI. The researchers attribute this finding to the physiological effects of ice, which include increased vasoconstriction at the injection site; these physiological changes may contribute to decrease the occurrence and size of hematoma. As previous studies show the ice pack application also reduces the initial inflammatory response at the injection site, thus minimizing the barriers to healing and facilitating tissue repair [8,9]. Consequently, these results support the fourth and fifth research hypotheses.

This study findings are supported by several previous studies that examined the effectiveness of cryotherapy application before injection on hematoma formation [4,12] as well as after injection [7,12,21]. Five minutes of cold administration applied locally (before & after injection) was found effective not only in decreasing the intensity of pain but also in reducing the occurrence of hematoma [7]. Additionally, the effect of applying cold versus cold-hot packs on the size of bruising after 24, 48 and 72 h after SCAI was recently investigated in 180 patients with coronary heart disease. The results show that the cold-hot groups had a significantly smaller size of bruising than the only cold or control groups after 48 and 72 h [21]. However, other studies reported contradictory findings, where no significant effect was observed on hematoma formation after the 5-min application of cryotherapy before or after injection [11]. The mechanism of cryotherapy effects is often contradictory as the published results show [13]. However, most of the published study findings [7,12,21] support the current study results, particularly the 4th and 5th research hypotheses. Thus, this study finding is contributing to current knowledge that will support nurses' application of cryotherapy on patients receiving SCAI.

5. Conclusion

It can be concluded from these study results that the application of cryotherapy might significantly decrease pain intensity.

Cryotherapy as a non-invasive and inexpensive technique could also be effective for decreasing the incidence of hematoma formation and size. However, the study results prove that the application of cryotherapy after SCAI might be more effective in decreasing the incidence and size of hematoma than the application of cryotherapy before SCAI. In conclusion, the research findings support four (1st, 3rd, 4th & 5th) research hypotheses and rejected only one hypothesis (2nd).

6. Recommendations of the study

Based on these study results, the following recommendations are proposed:

The application of cryotherapy is recommended to be endorsed as a nursing practice for patients who are scheduled for SCAI.

Further studies may be needed to determine the stability of the effect of cryotherapy on pain intensity and hematoma occurrence in patients who receive SCAI.

Further studies are essential to illuminate the effect of cryotherapy application twice, both before and after SCAI for each patient, on pain intensity and hematoma formation.

A replication of this study for a larger sample from various settings in many hospitals is required to generalize the results.

7. Implications for nursing practice

The study findings have implications for clinicians and nursing research. Pain and hematoma are the most frequently reported patients' complaints due to SCAI. Looking for effective and safe applicable management techniques is one of the primary and crucial duties of nurses. Thus, nurses can use the cryotherapy technique before subcutaneous injection to decrease pain intensity, and after injection to reduce hematoma formation. Raising nurses' awareness about the appropriate technique of anticoagulant injections and the factors that can relieve its related adverse effects is highly recommended.

Conflicts of interest

No conflict of interest.

Author contributions

DS and NY planned and designed the study. DS and NY collected the data, NY analyzed the data. DS and NY interpreted the results. NY drafted the manuscript and all authors contributed substantially to its revision.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.ijnss.2018.07.006>.

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