



The effects of thermotherapy and cryotherapy on pain and fear during intravenous cannulation: a systematic review and meta-analysis

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Purpose: Intravenous (IV) cannulation is a common hospital procedure that often causes pain and discomfort, leading to injection-related fear. Therefore, effective strategies for alleviating IV-related pain are necessary. To investigate the impact of thermotherapy and cryotherapy on pain and fear associated with IV cannulation, we reviewed randomized controlled trials. **Methods:** PubMed, Embase, Cochrane, CINAHL, Research Information Service System, DBpia, NSDL, and the Korean Studies Information Service System were searched for studies available in databases as of December 31, 2024. The study participants were individuals who underwent IV line (angio-needle) insertion. The intervention group received thermotherapy or cryotherapy for pain management, and the comparison group received no treatment or placebo. The outcome variables were pain and fear. **Results:** Significantly lower pain levels were observed in the thermotherapy and cryotherapy groups compared to the control group. The effect size of thermotherapy was shown by a standardized mean difference (SMD) of -0.68 , while the SMD for cryotherapy was -0.93 . No significant difference was found between thermotherapy and cryotherapy ($p = .430$). The effect of thermotherapy and cryotherapy on IV-related fear was also significant (SMD = -1.74 ; $p = .005$). **Conclusion:** This meta-analysis confirms that both thermotherapy and cryotherapy are effective in reducing IV-related pain and fear, with no significant difference between the two approaches. However, thermotherapy may offer additional benefits, such as reducing IV insertion time and improving patient satisfaction. These findings suggest that thermotherapy and cryotherapy are viable non-pharmacological options for IV-related pain and fear management.

Key Words: Cryotherapy; Thermotherapy; Pain; Fear; Injections, intravenous

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INTRODUCTION

Intravenous (IV) cannulation is one of the most common procedures performed for diagnostic or therapeutic purposes when patients visit or are admitted to a hospital. It is performed in approximately 60%~70% of hospitalized patients [1] and serves various purposes during hospitalization, such as blood sampling for tests, medication administration, continuous fluid therapy, blood transfusion, and preparation for emergencies [2-

4]. Despite being a routine procedure, needle insertion often evokes pain and negative memories, especially from early-life experiences [5-7] compounded by the necessity to endure it for medical care. This pain represents a complex integration of physical, psychological, and social experiences and emotions [7,8]. Notably, younger children, older individuals, or those requiring repeated injections may experience persistent discomfort associated with needle insertion [5, 9-10].

Advancements in hospital-based treatment methods have led

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to significant progress in diagnostic and therapeutic procedures, including research aimed at alleviating pain during needle insertion. Needle-free injection systems, designed to administer medication without the use of needles, have been reported to cause less pain [11] and are particularly utilized in dental anesthesia [12]. However, while these systems are effective for intramuscular or intradermal injections, they are not yet applicable for IV cannulation, which still relies on conventional needle use.

IV cannulation often induces pain and discomfort, and fear of needles can lead some patients to refuse treatment [5,9,10]. As small-gauge needles (22~24G) are typically utilized in simple procedures such as blood sampling or venipuncture, these are less uncomfortable. Meanwhile, the insertion of an IV catheter for prolonged medication administration or blood transfusion can cause greater discomfort due to the complexity of the procedure, the insertion site, and the use of larger needles [13,14]. Such pain may lead to psychological issues, such as anxiety and fear, in patients [15] and increase the workload of the nurses. Ideally, IV cannulation with devices such as IV catheters should be successful with minimal attempts [16]; however, it is not feasible to guarantee this outcome in every procedure. Therefore, effective interventions to temporarily alleviate pain during IV insertion are necessary. These interventions are considered to not only contribute to the patient's emotional stability but also play an important role in improving nursing efficiency [17,18].

Various randomized controlled trials have applied methods such as virtual reality devices [19], vibratory stimulation [20], topical anesthetic creams [20,21], thermotherapy, and cryotherapy [22,23] to alleviate pain, anxiety, and fear during IV cannulation. Among these, cryotherapy and thermotherapy are independent nursing interventions that can be easily applied in clinical settings, and directly implement the pain control mechanisms described by the Gate Control Theory [24-26]. Unlike topical anesthetic creams, which may have delayed onset and potential side effects, thermotherapy and cryotherapy are safe, low-cost, and immediately applicable interventions that can be initiated by nurses without a physician's order. In addition to their physiological effects, thermotherapy and cryotherapy may reduce fear by providing a soothing sensory stimulus, which distracts attention from the procedure and enhances the patient's sense of comfort and control [27]. Cryotherapy reduces blood flow and inhibits the release of neurotransmitters, inducing a local anesthetic effect to alleviate pain, while thermotherapy promotes vasodilation in both peripheral and systemic

blood vessels, enhancing blood flow [25,28]. This increase in blood flow activates tissue metabolism, reduces vascular tension, and suppresses the terminal branches of the autonomic nervous system, ultimately decreasing pain [29].

The use of thermotherapy and cryotherapy for pain management during IV catheter insertion initially involved simple applications such as ice packs or hot packs [30]. Over time, these methods have evolved into various forms of thermal and cryotherapy applications. Specifically, the application of cryotherapy has advanced to include methods such as cold spray, vibration devices combined with cryotherapy (e.g., Buzzy[®] device), or thermoelectric element devices providing thermotherapy or cryotherapy [31,32]. Thermotherapy and cryotherapy have not only been implemented in diverse ways but have also been assessed using various outcome measures including pain, stress, anxiety, fear, and blood flow velocity.

Systematic reviews and meta-analyses have examined whether thermotherapy and cryotherapy are effective methods for alleviating IV injection-related pain [33,34]. A previous meta-analysis evaluating vapor coolants (cold spray) reported that their application was effective in alleviating pain during IV cannulation [34,35]. Another study [33] demonstrated that these coolants were more effective for venous puncture than arterial puncture and were particularly beneficial for adults than for children. In a meta-analysis of studies using the Buzzy[®] device, which combines vibration and cold stimuli, significant reductions in pain and anxiety were observed in pediatric patients undergoing venipuncture [34]. Similarly, meta-analyses of interventions combining vibration and cryotherapy reported significant effects [35]. However, when thermoelectric element devices were used to provide cryotherapy and thermotherapy, no significant differences in venipuncture pain and anxiety were observed [32]. On the other hand, cryotherapy applied in the form of a tourniquet resulted in significantly lower pain levels compared to those in the control group [31].

These therapies aim to alleviate pain as well as to reduce anxiety and fear during the procedure. However, the outcomes vary with intervention type and application method [33]. Theoretically, thermotherapy has the potential to alleviate pain; however, few meta-analyses have independently examined its effects.

There is a need for additional well-designed studies that explore the separate impacts of thermotherapy and cryotherapy on pain and fear during IV cannulation, contributing to evidence-based combined approaches. This study aimed to systematically evaluate the independent effects of thermotherapy and cryotherapy on IV-related pain and fear.

METHODS

To objectively evaluate the effectiveness of thermotherapy and cryotherapy for pain and fear management during IV catheter insertion, our study followed the process of literature searching and study selection in accordance with the guidelines developed by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) group [36], and was registered with PROSPERO (CRD42024567711). Additionally, as a meta-analysis utilizing previously published data, it was exempted from ethical review (GU-202407-HRc-05).

1. Inclusion and exclusion criteria

This study used the PICO-SD framework. P (Population): individuals who underwent IV line insertion; I (Intervention): thermotherapy and cryotherapy for pain management; C (Comparison): no treatment or placebo; O (Outcome): pain and fear; SD (Study Design): randomized controlled trials.

Studies published in Korean or English that focused on heat or cold therapy during venipuncture procedures were included into this study. Priority was given to studies measuring pain during venipuncture or immediately after the procedure, rather than before the intervention began or after it ended. Only studies involving IV line insertion with an angio needle were included, while those involving simple venipuncture procedures, defined as procedures for collecting blood specimens using a standard hypodermic needle without an angiocatheter, were excluded. Preclinical or animal studies, studies not published in Korean or English, studies without full texts, non-experimental designs, studies combining pharmacological interventions with heat or cold therapy, or studies combining heat or cold therapy with other interventions such as vibration therapy were excluded. We included in the qualitative synthesis all studies that reported outcome data in any form (e.g., median with range, categorical data, or mean $\pm$ standard deviation [SD]), and only those that provided values in mean $\pm$ SD were included in the quantitative synthesis.

2. Search strategy and data sources

The literature search encompassed studies published from the earliest available date in each database to December 31, 2024. Searches were performed using international databases such as PubMed, CINAHL, Cochrane, and EMBASE, alongside domestic databases including DBpia, NDSL, Korean Studies Information Service System, and Research Information Service System. To ensure comprehensive coverage, gray literature such

as theses, news articles, and presentation materials was manually searched using Google Scholar.

The search strategy incorporated both MeSH terms and text words, employing AND/OR operators and truncation techniques. For participants, search terms included “venipuncture,” “injections,” “intravenous,” “IV,” “intravenous catheter,” “intravenous cannulation,” and “intravenous cannula.” For intervention, terms related to hot and cold therapy were used, such as “hot,” “warm,” “heat,” “ice,” “cold,” “vapor coolant,” “cryotherapy,” and “thermotherapy.” For outcome, terms such as “pain” and “fear” were utilized to identify relevant studies.

Considering the lack of MeSH functionality in some domestic databases, additional Korean terms were employed, including “venipuncture,” “intravenous access,” “IV,” and “fear.” This strategy ensured thorough identification of relevant studies across all selected databases (Appendix 1).

3. Data extraction

Bibliographic data were organized in Microsoft Excel. Duplicate records were removed based on title and author information. Titles and abstracts were independently screened by two researchers in the first round of screening following the specified criteria for inclusion and exclusion. The full texts of the studies that passed the first round of screening were then reviewed by the same researchers in the second round of screening, and reasons for exclusion (e.g., animal studies, language, study design, statistical data, interventions involving pharmacotherapy, or combined interventions involving non-thermal modalities) were recorded.

Studies that applied both thermotherapy and cryotherapy within a single group were excluded, while studies that applied them separately in independent groups were included.

Consistency at each stage was ensured through cross-checks, and disagreements between researchers were resolved through thorough discussion until a consensus was reached. Although a third reviewer was available to resolve any discrepancies, no disagreements occurred between the two researchers during data extraction.

A coding book was developed to record general characteristics of the studies, including study participants, country of sampling, participant sex and age, sample size, and intervention details for experimental and control groups (e.g., type of intervention, duration of application). Outcome variables such as pain and fear scores were extracted for effect size analyses. Data coding was independently performed by two researchers, and discrepancies were resolved through a joint review of the origi-

nal texts, to finalize the coding. The process of study selection and exclusion was visualized using a PRISMA flow diagram (Figure 1).

4. Quality assessment

The Cochrane Risk of Bias 2 tool [37] was utilized for quality assessment. This tool evaluates the risk of bias across five domains, including the randomization procedure, adherence to intended interventions, completeness of outcome data, accuracy of outcome measurement, and selective reporting of results [37,38]. Quality assessment was independently performed by two researchers. In cases of disagreement, the researchers engaged in thorough discussions, and if consensus could not be

reached, the decision was finalized by consulting a third researcher (Figure 2).

5. Statistical analysis

The systematic analysis, synthesis, statistical integration, and reporting of results for the selected studies were conducted in accordance with the guidelines provided by Cochrane [39]. The meta-analysis of studies that applied thermotherapy and cryotherapy to measure pain and fear as outcome variables was performed using the Cochrane Review Manager software version 5.4 (The Cochrane Collaboration, London, UK). In this study, the characteristics of the participants and interventions (included first author, country, age, sex, IV needle gauge, intervention

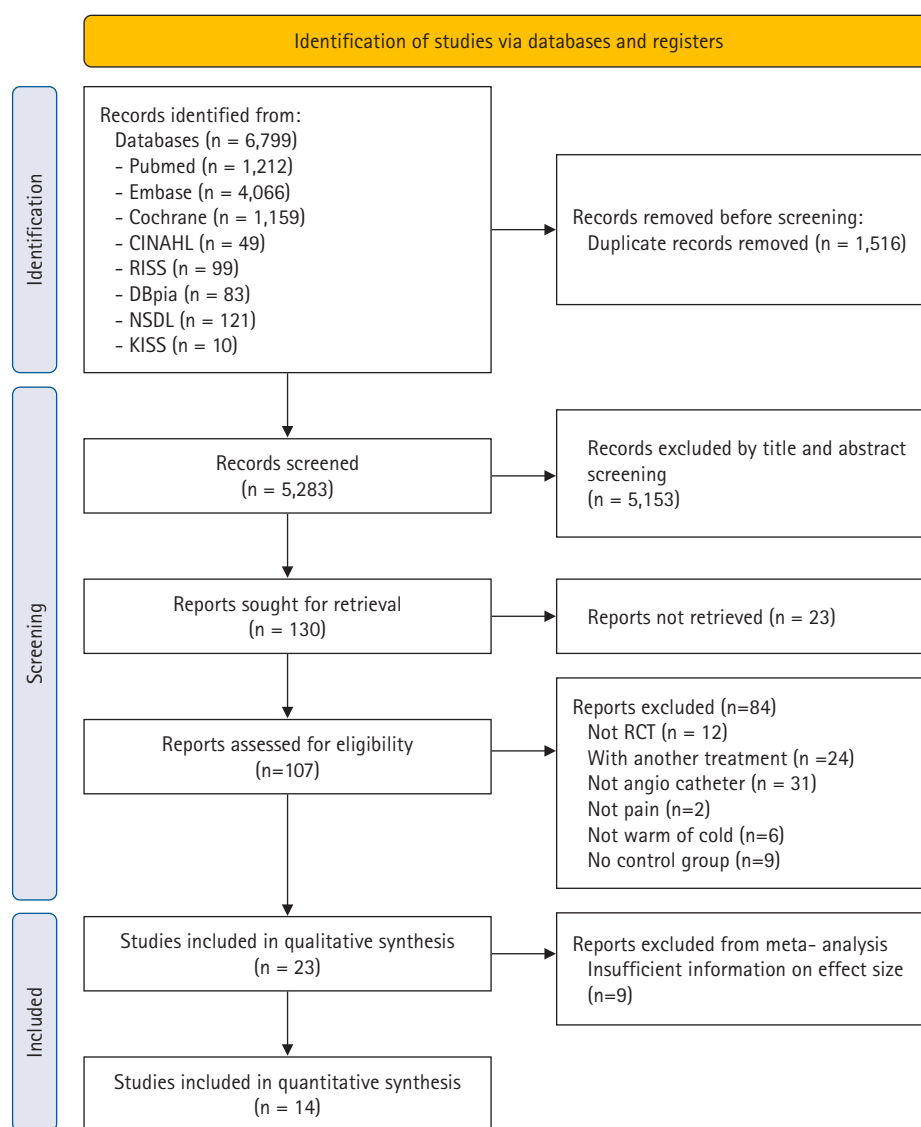


Figure 1. Flow chart of study selection process.

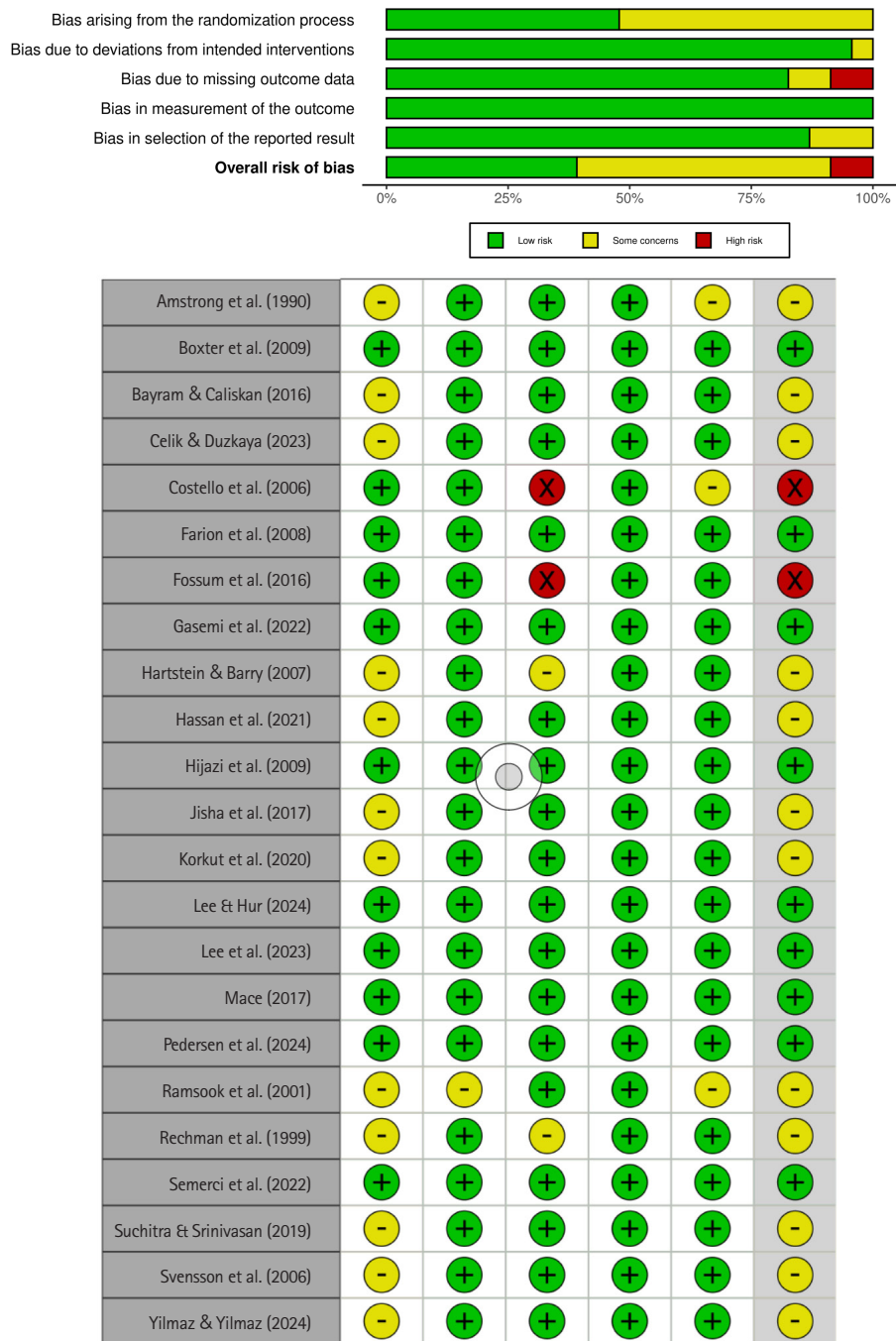


Figure 2. Risk of bias of the included studies.

time, intervention temperature, main outcome measure, baseline outcome, post outcome, and author's conclusion) were extracted. The primary outcome variable was pain measured during IV catheter insertion, and the effect size was calculated using the mean and SD, expressed as the standardized mean difference (SMD) 95% confidence interval (CI).

We followed the methodological guideline of the Higgins' I^2

statistic to assess heterogeneity among studies. An I^2 value of 25% or lower was interpreted as low heterogeneity, 75% or higher as substantial heterogeneity, and values in between as moderate. In general, when the I^2 value exceeded 50%, a random-effects model was applied [40,41].

Subgroup analyses were planned to explore potential sources of heterogeneity in pain outcomes only, as fear outcomes were

reported in too few studies to allow for meaningful subgroup analysis. The subgroup analyses were conducted based on intervention type (heat vs. cold), management methods (cold spray, other cold therapies, heat therapy), and participant age.

RESULTS

1. Characteristics of included studies

In this study, 23 studies were reviewed to evaluate the effects of thermotherapy and cryotherapy on pain management during IV cannulation. Among these, 9 (39.1%) studies were conducted in North America (United States of America, 8; Canada, 1), 11 (47.8%) in Asia (India, 2; Korea, 2; Turkey, 5; Malaysia, 1; Iran, 1), and 3 (13.0%) in Europe and Oceania (Sweden, 1; Australia, 1; Denmark, 1). Regarding the target populations, 10 (43.5%) studies focused on adult participants, 7 (30.4%) on children, and 6 (26%) did not report participant age. Regarding needle gauges for IV cannulation, 18G needles were used in four (17.4%) studies, 20G needles in five (21.7%), < 22G in nine (39.1%), and unspecified gauge number or various gauges used in five (21.7%).

Among these studies, six multi-arm studies (A4, A12, A13, A14, A15, and A23) included two experimental groups and one control group. As a result, 29 comparisons were performed in the qualitative analysis. Of the 29 comparisons, in terms of interventions, 20 (66.6%) studies involved cryotherapy, including 13 (43.3%) utilizing sprays and 7 (24.1%) using ice cubes or gel packs. In contrast, nine (31.0%) studies employed heat therapy, including thermal energy equipment such as electric devices, bands, pillows, or pads, and hot packs. For the control groups, 12 (41.4%) studies used placebo interventions, while 17 (58.6%) provided no treatment as a comparator. From the 23 reviewed studies (29 comparisons in total), the final meta-analysis included 14 studies (19 comparisons) in which effect sizes were confirmed.

Table 1 summarizes the characteristics of all studies included in the qualitative synthesis. Studies without sufficient outcome data for effect size estimation were excluded from the final meta-analysis (14 studies, 19 comparisons). Appendix 2 provides a list of all studies reviewed in the systematic review.

2. The effect of heat and cold interventions on IV pain

The pooled overall effect size of the 14 studies that evaluated the impact of heat and cold interventions on IV pain was -0.85 (95% CI, -1.21 to -0.50), with a significant difference ($Z = 4.73$, $p < .001$). The heterogeneity test showed high heteroge-

neity among the studies (Higgins' $I^2 = 86\%$), prompting the use of a random-effects model to analyze the effect size.

Subgroup analysis showed that heat interventions had an effect size [SMD (95% CI)] of -0.68 (-1.08 to -0.29), with $Z = 3.37$ ($p < .001$), and cold interventions had an effect size of -0.93 (-1.38 to -0.47), with $Z = 3.97$ ($p < .001$). No significant difference was found between thermotherapy and cryotherapy ($p = .430$) (Figure 3).

3. Comparison of pain management methods

The subgroup analysis further explored the effects of different hot and cold therapy methods. The results showed that cold spray (SMD = -1.11 ; 95% CI, -1.94 to -0.28 ; $Z = 2.63$; $p = .009$), other cold therapies such as ice packs and electric bands (SMD = -0.75 ; 95% CI, -1.02 to -0.47 ; $Z = 5.29$; $p < .001$), and heat application (SMD = -0.68 ; 95% CI, -1.08 to -0.29 ; $Z = 3.37$; $p < .001$) all demonstrated significant effects. No significant differences were observed among the cold spray, other cold therapies, and heat therapy subgroups ($p = .660$), indicating comparable effectiveness among these interventions (Appendix 3).

4. Effectiveness of interventions based on age

The subgroup analysis was conducted to evaluate the effectiveness of interventions based on the participants' age groups. For children aged under 19 years, the interventions resulted in an SMD of -1.20 (95% CI, -2.06 to -0.35), with $Z = 2.76$ ($p = .006$). For adults aged 19 years or older, the interventions showed an SMD of -0.77 (95% CI, -1.03 to -0.51), with $Z = 5.73$ ($p < .001$). The group with no reported age showed an SMD of -0.41 (95% CI, -0.98 to 0.15), with $Z = 1.45$ ($p = .150$). There was no significant difference among the three groups ($p = .290$) (Appendix 4).

5. The effect of heat and cold interventions on IV-related fear

Of the 23 included studies, three reported measurable outcomes for fear. Of these, two studies were multi-arm designs, resulting in a total of five datasets analyzed. The pooled effect size SMD (95% CI) was -1.74 (-2.95 to -0.54), with a significant difference ($Z = 2.84$, $p = .005$). These findings indicate that both heat and cold interventions significantly reduce fear associated with IV procedures (Figure 4).

6. Publication bias

Of the 23 included studies in this systematic literature review,

Table 1. Summary of the Effects of Heat or Cold Therapy on Pain during IV Cannula Insertion

Study	First author (year) Country	Age Sex (M/W)	I (No.)	IV size Intervention time Spraying distance Temperature	C (No.)	Main outcome measures	Baseline	Post test (M ± SD) (med [min~max])	Author's conclusion
A1	Armstrong et al. (1990) United Kingdom	NR 0/80	Vapocoolant spray (ethyl chloride) (40)	20G 10 seconds 8 inches N/A	No treatment (40)	Pain	NR	I: 1.80 ± 2.10 C: 3.80 ± 2.10	Ethyl chloride significantly reduced the pain of venipuncture
A2	Baxter et al. (2009) USA	I: 26~55 C: 26~55 I: 8/6 C: 8/6	Vapocoolant spray (14)	22G 5 seconds 5~10 cm N/A	No treatment (14)	Pain Fear	NR	I: 1.1 [0~9.8] C: 3.1 [0~9.9] I: 0.65 [0~4.5] C: NR	Compared with no intervention, vapocoolant did not reduce pain significantly
A3	Bayram & Caliskan (2016) Turkey	I: 55.22 ± 14.59 C: 54.0 ± 10.23 I: 21/19 C: 25/15	Moist heating pad (40)	22G 10 minutes N/A 52°C (126°F)	No treatment (40)	Pain	I: 1.05 ± 1.58 C: 1.67 ± 2.30	I: 0.8 ± 1.65 C: 2.82 ± 2.57	Local application of heat results in vasodilation, making intravenous catheter insertion easier and decreasing patients' pain
A4a	Celik & Duzkaya (2023) Turkey	I: 10.72 ± 2.80 C: 11.22 ± 2.74 I: 16/16 C: 14/18	Cold spray (32)	24G 5 seconds 15 cm NR	No application (32)	Pain	I: 7.19 ± 2.74 C: 5.97 ± 1.77	I: 2.63 ± 1.43 C: 7.59 ± 1.10	The pain and fear scores of the children in the control group were higher than the scores of those in the spray groups
A4b	Celik & Duzkaya (2023) Turkey	I: 10.06 ± 2.99 C: 11.22 ± 2.74 I: 21/11 C: 14/18	Ice gel bag (32)	24G 5 seconds 15 cm NR	No application (32)	Fear Pain	I: 4.09 ± 0.86 C: 2.91 ± 1.06 I: 7.19 ± 2.04 C: 5.97 ± 1.77	I: 1.78 ± 0.55 C: 3.81 ± 0.69 I: 6.75 ± 2.29 C: 7.59 ± 1.10	The pain and fear scores of the children in the control group were higher than the scores of those in the ice groups
A5	Costello et al. (2006) USA	I: 12.7 ± 2 C: 13.2 ± 3 I: 15/22 C: 21/221	Vapocoolant spray (ethyl vinyl chloride) (37)	22G 5 seconds NR N/A	No application (42)	Fear Pain	I: 3.72 ± 0.85 C: 2.91 ± 1.06 NR	I: 3.31 ± 1.20 C: 3.81 ± 0.69 I: 34 ± 26 C: 31 ± 25	Vapocoolant spray failed to measurably reduce pain associated with intravenous cannulation when compared to receiving no intervention
A6	Farion et al. (2008) Canada	I: 9.4 ± 2.1 C: 9.2 ± 2.0 I: 23/17 C: 19/21	Vapocoolant spray (1,1,1,3,3-pentafluoropropane and 1,1,1,2-tetrafluoroethane) (40)	22~24G 4~10 seconds 8~18 cm N/A	Placebo spray (normal saline) (40)	Pain	NR	I: 36.90 ± 27.50 C: 56.10 ± 31.90	The use of vapocoolant spray significantly reduced pain compared to placebo

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Table 1. Continued

Study	First author (year) Country	Age Sex (M/W)	I (No.)	IV size Intervention time Spraying distance Temperature	C (No.)	Main outcome measures	Baseline	Post test (M ± SD) (med [min~max])	Author's conclusion
A7	Fossum et al. (2016) USA	NR NR	Vapocoolant spray (ethyl chloride) (38)	20G 5~8 seconds NR 36°F	Placebo spray (sterile water) (38)	Pain	NR	I: 2 [1~4] C: 4 [2~5]	Topical ethyl chloride was more effective than placebo in reducing pain during venous catheterization
A8	Ghasemi et al. (2022) Iran	NR 13/18	Vapocoolant spray (31)	22G 5 seconds 25 cm N/A	No treatment (31)	Pain	NR	I: 4.19 ± 0.65 C: 4.41 ± 0.71	During and after the cannulation, the pain was significantly lower in the vapocoolant measurement than in control and music
A9	Hartstein & Barry (2007) USA	NR NR	Vapocoolant spray(1,1,1,3,3-pentafluoropropane and 1,1,1,2-tetrafluoroethane) (47)	22~18G 2~4 seconds 7~12 cm 36°F	No application (45)	Pain	NR	I: 2.80 ± 2.59 C: 2.80 ± 2.53	This study reported no significant difference in pain perception with the use of skin coolant prior to IV placement
A10	Hassan et al. (2021) Malaysia	I: 9.57 ± 1.49 C: 9.20 ± 1.45 I: 19/11 C: 20/10	Ice compression (ice cube) (30)	22G 2 minutes N/A N/A	Without any analgesics (30)	Pain	NR	I: 31.2 ± 19.16 C: 49.77 ± 14.80	Ice compression is an effective intervention to reduce pain during venipuncture and IV cannulation among primary school children
A11	Hijazi et al. (2009) Australia	I: 59.9 ± 19.0 C: 56.3 ± 20.0 I: 57/46 C: 52/46	Vapocoolant spray (propane, butane, and pentane blend) (103)	22~18G 2 seconds 12 cm N/A	Placebo spray (pure water) (98)	Pain	NR	I: 12 [5~40] C: 36 [29~51]	Topical alkane vapocoolant spray is effective, acceptable, and safe in reducing pain with peripheral intravenous cannulation in adult
A12a	Jisha et al. (2017) India	NR NR	Dry heat application	NR 7 minutes N/A	Placebo spray (sterile water)	Pain	NR	I: 1 [NR] C: 7 [NR]	Dry heat applications significantly reduced pain compared to the control group
A12b	Jisha et al. (2017) India	NR NR	Moist heat application (wrapping a moist towel)	NR 7 minutes N/A	NR	Pain	NR	I: 5 [NR] C: 7 [NR]	Moist heat applications significantly reduced pain compared to the control group
A13a	Korkut et al. (2020) Turkey	I: 48.8 ± 14.6 C: 30.23 ± 7.8 I: 22/8 C: 24/6	Cold pack (30)	110~115°F 20G 60 seconds N/A NR	No applications (30)	Pain	I: 0.1 ± 0.5 C: 0 ± 0	I: 1.1 ± 1.4 C: 2.2 ± 1.9	Applying local cold application before IV insertion reduced both pain and anxiety levels of the patients

(Continued to the next page)

Table 1. Continued

Study	First author (year) Country	Age Sex (M/W)	I (No.)	IV size Intervention time Spraying distance Temperature	C (No.)	Main outcome measures	Baseline	Post test (M ± SD) (med [min~max])	Author's conclusion
A13b	Korkut et al. (2020) Turkey	I: 56 ± 7.5 C: 30.23 ± 7.8	Hot pack (30)	20G 60 seconds N/A NR	No applications (30)	Pain	I: 0.1 ± 0.4 C: 0 ± 0	I: 0.7 ± 1.1 C: 2.2 ± 1.9	Applying local hot application before IV insertion reduced both pain and anxiety levels of the patients
A14a	Lee & Hur (2023) Korea	I: 21/9 C: 24/6 I: 45.9 ± 13.4 C: 49.8 ± 14.4	Warm electric pad (20)	18G 10~30 seconds NA 40~45°C	Placebo application (19)	Fear Pain	I: 0.6 ± 1.1 C: 0.3 ± 0.8 I: 0.00 C: 0.00	I: 0.2 ± 0.5 C: 1.6 ± 1.4 I: 4.25 ± 2.45 C: 5.26 ± 2.08	The thermoelectric tourniquet has no significant effect on relieving intravenous injection pain
A14b	Lee & Hur (2023) Korea	I: 8/12 C: 7/12 I: 47.6 ± 13.2 C: 49.8 ± 14.4	Cold electric pad (20)	18G 10~30 seconds NA 0~10°C	Placebo application (19)	Pain	I: 0.08 ± 0.34 C: 5.3 ± 2.1	I: 3.43 ± 2.07 C: 5.26 ± 2.08	The thermoelectric tourniquet has the effect of relieving intravenous injection pain in cold therapy
A15a	Lee et al. (2022) Korea	I: 51.8 ± 14.6 C: 48.4 ± 12.5 I: 9/20 C: 13/17	Warm electric pad (29)	18G 5~60 seconds NA 40~45°C	Placebo application (30)	Pain	NR	I: 3.31 ± 1.65 C: 5.00 ± 1.88	Heat therapy applied with thermoelectric tourniquet during venipuncture exerted pain-relief and stress-reduction effects
A15b	Lee et al. (2022) Korea	I: 45.5 ± 14.0 C: 48.4 ± 12.5 I: 15/14 C: 13/17	Cold electric pad (29)	18G 5~60 seconds NA 0~10°C	Placebo application (30)	Pain	NR	I: 4.24 ± 1.33 C: 5.00 ± 1.88	Cold therapy applied with thermoelectric tourniquet during venipuncture exerted pain-relief and stress-reduction effects
A16	Mace et al. (2017) USA	I: 43.0 ± 16.6 C: 42.7 ± 16.6 I: 56/94 C: 64/86	Vapocoolant spray (1,1,1,3,3-pentafluoropropane and 1,1,1,2-tetrafluoroethane) (150)	18~22G 4~10 seconds 3~7 inches N/A	Placebo spray (sterile water) (150)	Pain	NR	I: 1 [0~3] C: 3 [1.2~5]	Vapocoolant spray was effective in significantly relieving the pain of PIV cannulation in adults
A17	Pedersen et al. (2024) Denmark	I: 61 C: 63.5 I: 33/31 C: 35/29	Cryospray (Chloroethyl spray) (64)	20G 4 seconds (2 times, 2 seconds) 15~20 cm N/A	Placebo spray (normal saline) (64)	Pain	I: 0 [0~0] C: 0 [0~2.5]	I: 1 [0~3] C: 3 [2~5]	Patients reported lower pain scores and a greater preference for cryospray in future procedures

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Table 1. Continued

Study	First author (year) Country	Age Sex (M/W)	I (No.)	IV size Intervention time Spraying distance Temperature	C (No.)	Main outcome measures	Baseline	Post test (M ± SD) (med [min~max])	Author's conclusion
A18	Ramsook et al. (2001) USA	I: 9 C: 10 I: 50/64 C: 51/57	Vapocoolant spray (ethyl chloride) (114)	NR 5 seconds 6 inches N/A	Placebo spray (alcohol) (108)	Pain	NR	I: 4 [NR] C: 6 [NR]	Vapocoolant spray showed no benefit in reducing IV cannula insertion pain
A19	Richman et al. (1999) USA	I: 8.50 ± 2.27 C: 8.33 ± 2.12 I: 25/25 C: 28/24	Ice pack (28)	18G 10 minutes N/A NR	No treatment (28)	Pain	NR	I: 27.50 ± 15.90 C: 34.20 ± 21.60	Pretreatment with ice did not reduce overall mean pain scores from IV catheter insertion
A20	Semerici et al. (2022) Turkey	I: 8.50 ± 2.27 C: 8.33 ± 2.12 I: 25/25 C: 28/24	Cold spray (chloromethyl ethyl spray) (50)	24G 5 seconds 15 cm N/A	Routine practice (52)	Pain	NR	I: 1.10 ± 1.39 C: 6.31 ± 2.29	Cold spray was more effective than standard care in reducing the level of pain, and fear in children ages 5~12 years during venipuncture
A21	Suchitra et al. (2019) India	NR I: 22/20 C: 20/22	Electric heating pad (42)	24~26G 10 minutes N/A 40°C	No heat application (42)	Pain	NR	I: 0.89 ± 0.92 C: 3.42 ± 0.72	Dry heat before IV insertion improves venipuncture ease and reduces perceived pain
A22	Svensson et al. (2006) Sweden	I: 49 C: 49 I: 31/30 C: 40/24	Local warming pillow (61)	18G 60 seconds N/A 39~40°C	No warming (64)	Pain	NR	I: 1.74 [0.1~4.8] C: 2.01 [0.3~7.2]	Local warming before peripheral IV insertion appears not to have any pain reducing effect
A23a	Yilmaz & Yilmaz (2024) Turkey	I: 53.20 ± 11.15 C: 53.10 ± 13.51	Cold gel pack application (30)	20G 1 minute N/A NR	No treatment (30)	Pain	NR	I: 30.50 ± 16.78 C: 48.36 ± 24.02	One-minute local cold application reduced pain during peripheral IV catheterization
A23b	Yilmaz & Yilmaz (2024) Turkey	I: 53.20 ± 11.15 C: 53.10 ± 13.51	Dry hot pack application (30)	20G 1 minute N/A 40~42°C	No treatment (30)	Pain	NR	I: 48.66 ± 17.16 C: 48.36 ± 24.02	One-minute local warm application reduced pain during peripheral IV catheterization

NR = Not reported; N/A = Not applicable; M = Men; W = Women; I = Intervention group; C = Control group; IV = Intravenous; G = Gauge; M = Mean; SD = Standard deviation; Med = Median; min = Minimum; max = Maximum.

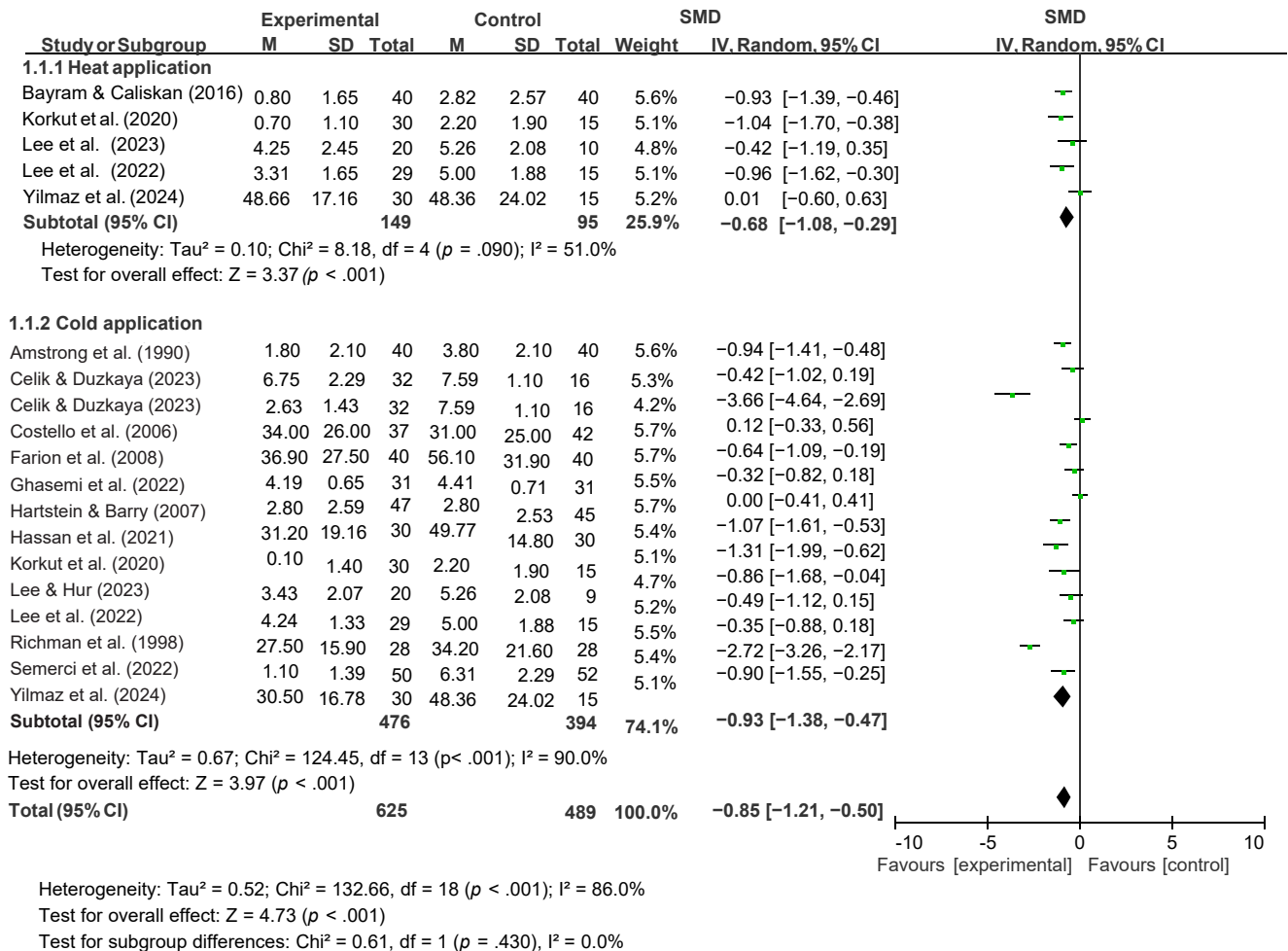


Figure 3. The effect of heat and cold intervention on intravenous pain.

M = Mean; SD = Standard deviation; IV = Inverse variance; CI = Confidence interval; SMD = Standardized mean difference.

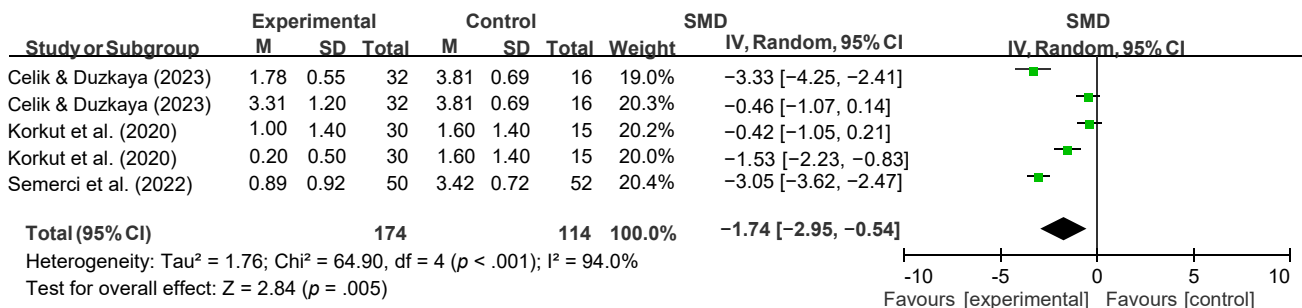


Figure 4. The effect of heat and cold intervention on intravenous-related fear.

M = Mean; SD = Standard deviation; IV = Inverse variance; CI = Confidence interval; SMD = Standardized mean difference.

we assessed publication bias for 14 studies with available effect size estimates. The funnel plot shows that the studies are dispersed near the estimated effect size, with larger studies clustered at the top of the plot and smaller studies displaying great-

er variability, resulting in a wider distribution. The symmetrical shape of the funnel plot suggests no significant publication bias among the included studies (Appendix 5).

DISCUSSION

We conducted a systematic review and meta-analysis to establish evidence on the effectiveness of thermotherapy and cryotherapy in alleviating pain and fear during IV cannulation. A total of 23 studies were included in the qualitative analysis, and 14 studies were selected for meta-analysis. The results showed that when comparing 625 participants in the intervention group and 489 in the control group, both thermotherapy and cryotherapy were effective in reducing pain ($SMD = -0.85$). The effect size of thermotherapy, expressed as SMD , was -0.68 , while that of cryotherapy was -0.93 , indicating that both interventions were effective in pain relief, with no significant difference between the two. According to Cohen's criteria, these effect sizes correspond to a large effect, suggesting that thermotherapy and cryotherapy are suitable non-pharmacological interventions for clinical application in pain management during IV cannulation [42]. Randomized controlled trials, systematic reviews, and meta-analyses conducted to date have aimed to determine the effectiveness of thermotherapy and cryotherapy. Primarily, studies examining the effectiveness of cold therapy have demonstrated its efficacy when applied in various forms, including vapor coolants [34], Buzzy[®] device [20], and thermoelectric element tourniquets [31]. Considering these findings along with the results of this meta-analysis, it can be concluded that cryotherapy is an effective method for alleviating pain during IV puncture. Various studies have examined temperature conditions of cryotherapy; in one study, the Cool-sense device provided a temperature range of 12°C to -2°C for 3 to 5 seconds [23], and in another, a thermoelectric element tourniquet [31] provided a cooling temperature of $0\sim 10^{\circ}\text{C}$ for 10~30 seconds. Meanwhile, cold spray instantly evaporates upon contact with the skin, reducing the surrounding temperature to as low as -20°C . It is also used in minor surgical procedures requiring partial anesthesia. However, a major drawback of this method is that it can cause severe pain during the thawing process [43]. Cold spray shows significant effects even with an application time of approximately 10 seconds, but it has limitations regarding the areas of the skin where it can be applied [43-45].

These findings suggest that cold therapy is significantly effective in reducing pain during IV needle insertion when applied for less than one minute. In contrast, a study reported that applying cold therapy for 10 minutes did not alleviate pain and instead increased discomfort [46]. Considering this, cryotherapy appears to be most effective when applied for a short dura-

tion at temperatures below $10\sim 12^{\circ}\text{C}$ during IV procedures. Therefore, careful consideration of the appropriate temperature and application time is necessary.

In this meta-analysis, in studies in which thermotherapy was applied, dry or moist heat, such as hot packs, moist towels, and electric pads, was applied at temperatures ranging from 40 to 60°C [31,32]. Studies in which heat therapy was applied for 7 to 10 minutes demonstrated significant pain reduction, whereas studies with an application time of approximately one minute showed varying effects [31,32]. These findings suggest that, similar to cold therapy, the effectiveness of heat therapy may also be influenced by the duration of application.

Thermotherapy and cryotherapy are based on the gate control theory of pain [47,48]. Thermotherapy provides anesthetic and sedative effects by interfering with pain transmission. When applied locally, it increases blood flow and facilitates the removal of metabolic byproducts, thereby alleviating pain. Additionally, it promotes psychological relaxation, effectively reducing tension [49]. Cryotherapy, on the other hand, has been reported to potentially increase pain due to vasoconstriction [50]. However, it also reduces the sensitivity of nerve terminals, induces numbness, and provides immediate pain relief [47]. Based on this theoretical foundation, both thermotherapy and cryotherapy in this study appear to be effective in reducing pain during IV catheter insertion.

Pain is greatly influenced by subjective experiences [50]. In this study, the comparison of thermotherapy and cryotherapy showed that both methods are effective in alleviating pain. However, thermotherapy has been shown to shorten IV insertion time and increase patient satisfaction, whereas cryotherapy, despite reducing pain, has been associated with lower patient satisfaction [23]. Additionally, prolonged application of cryotherapy has been reported to cause discomfort and had no significant effect on pain relief [46]. Considering these findings, future research should not only explore various intervention methods but also allow individuals to choose between thermotherapy and cryotherapy based on their subjective preferences. This approach would help assess the impact of personal choice on psychological stability and pain relief outcomes.

In this study, the subgroup analysis by age demonstrated that the intervention was effective across all age groups. When applied to participants under the age of 19 years, the effect size was significant ($SMD = -1.20$; 95% CI, -2.06 to -0.35), as well as in adults aged ≥ 19 years ($SMD = -0.80$; 95% CI, -1.04 to -0.55). However, the effect size for the "no reported age" group was not significant ($SMD = -0.41$; 95% CI, -0.98 to 0.15). No signifi-

cant difference was observed between the groups ($p = .280$). These findings suggest that thermotherapy and cryotherapy are effective in reducing pain associated with IV cannulation, regardless of age. However, rather than applying a generalized intervention, it is necessary to implement interventions that are specific to individual characteristics such as age and sex.

In this study, the effect of thermotherapy and cryotherapy on IV-related fear was analyzed based on three papers (five studies), revealing an overall effect size of -1.74 (-2.95 to -0.54). This finding suggests that thermotherapy and cryotherapy are not only effective in reducing pain but also in alleviating psychological stress associated with IV procedures.

Additionally, this study analyzed cold sprays as well as various cold therapy methods (e.g., gel bags, ice cubes) and compared the effects of thermotherapy and cryotherapy, clearly presenting their respective effectiveness. This analysis provides a more detailed examination of the clinical applicability of thermotherapy and cryotherapy and may contribute to proposing future implementation strategies. This study highlights that thermotherapy and cryotherapy are simple, non-invasive, and cost-effective methods for managing IV-related pain and fear. In particular, thermotherapy and cryotherapy can serve as valuable alternatives for pediatric patients, for whom medication use may be limited. While these interventions are generally safe, clinicians should be aware of potential adverse effects such as skin irritation, cold-induced discomfort, or thermal burns, depending on the temperature and duration of application. Therefore, appropriate safety measures and individualized precautions should be considered when implementing these methods in clinical settings.

The significance of this study is its distinct approach compared to previous research. Unlike prior studies, this study exclusively evaluated the pure effects of thermotherapy and cryotherapy by excluding mixed-intervention studies that incorporated medications or distraction techniques. Additionally, only studies with a control group were included in the analysis, ensuring a more rigorous assessment. Among the 23 included studies, 12 were rated as having some concerns, nine as low risk, and two as high risk in the overall quality assessment. The high proportion of studies with some concerns was mainly due to the inherent difficulty of blinding participants and personnel, given the nature of the interventions. In addition, studies that did not report outcome data sufficiently were assessed as high risk. Therefore, future research should aim to improve methodological rigor through better blinding procedures and more complete outcome reporting. Another limitation of this

study is the challenge in providing sufficient evidence due to the limited number of studies applying only thermotherapy or cryotherapy during IV puncture. Additionally, the sub-analysis by age group lacked sufficient studies for each age category. Furthermore, the number of studies in which thermotherapy was applied during IV catheter insertion was limited, which restricts the generalizability of the results.

Therefore, we suggest that thermotherapy may have similar or even greater effects compared to cryotherapy, emphasizing the need for well-designed randomized controlled trials in the future. Future research should assess its effectiveness across various clinical settings, compare and analyze different tools and methods used in thermotherapy and cryotherapy, and propose an optimal intervention strategy.

CONCLUSION

This systematic review and meta-analysis provides important evidence supporting the effectiveness of thermotherapy and cryotherapy in managing pain and fear associated with IV procedures. Both interventions showed large effect sizes in reducing pain and fear, with no significant difference between them. Given their non-invasive, cost-effective nature and applicability across age groups, thermotherapy and cryotherapy can be actively utilized in clinical practice, particularly for patients where pharmacological interventions are limited or less desirable. Future studies should further investigate their comparative effectiveness, optimal application conditions, and patient preferences to develop tailored pain management strategies.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

AUTHORSHIP

JH, MHH and KYK contributed to the conception and design of this study; JH, MHH and KYK curated the data; JH and

MHH performed formal (statistical) analysis and interpretation; MHH and YJL acquired funding; JH and MHH developed the methodology; JH, MHH and YJL administered the project; JH and KYK prepared the visualization; JH and MHH drafted the manuscript; JH and BSK critically revised the manuscript; JH and MHH conducted the investigation; JH and KYK provided resources; JH and MHH handled the software; JH, MHH and YJL supervised the study; JH, MHH and KYK validated the findings. All authors have read and approved the final manuscript.

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DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Appendix 1. Literature Search Strategy

1. PubMed: 1212 Results
#1(("phlebotomy"[MeSH Terms] OR "phlebotomy"[All Fields] OR "venipuncture"[All Fields] OR "venipunctures"[All Fields] OR ("injections, intravenous"[MeSH Terms] OR ("injections"[All Fields] AND "intravenous"[All Fields]) OR "intravenous injections"[All Fields] OR "injections intravenous"[All Fields]) OR "iv"[All Fields]) OR (("intravenous"[All Fields] OR "intravenously"[All Fields] OR "intravenous"[All Fields] OR "intravenously"[All Fields]) AND ("catheter s"[All Fields] OR "catheters"[MeSH Terms] OR "catheters"[All Fields] OR "catheter"[All Fields])) OR (("intravenous"[All Fields] OR "intravenously"[All Fields] OR "intravenous"[All Fields] OR "intravenously"[All Fields]) AND ("canulated"[All Fields] OR "canulation"[All Fields] OR "canule"[All Fields])) OR (("intravenous"[All Fields] OR "intravenously"[All Fields] OR "intravenous"[All Fields] OR "intravenously"[All Fields]) AND ("cannula"[MeSH Terms] OR "cannula"[All Fields] OR "cannulae"[All Fields] OR "cannulas"[All Fields] OR "cannula s"[All Fields]))
#2(("hot"[All Fields] OR "warm"[All Fields] OR ("hot temperature"[MeSH Terms] OR ("hot"[All Fields] AND "temperature"[All Fields]) OR "hot temperature"[All Fields] OR "heat"[All Fields]) OR ("ice"[MeSH Terms] OR "ice"[All Fields]) OR ("common cold"[MeSH Terms] OR ("common"[All Fields] AND "cold"[All Fields]) OR "common cold"[All Fields] OR "cold"[All Fields] OR "cold temperature"[MeSH Terms] OR ("cold"[All Fields] AND "temperature"[All Fields]) OR "cold temperature"[All Fields]) OR ("vapocoolant"[All Fields] OR "vapocoolants"[All Fields]) OR "cryotherapy"[MeSH Terms] OR "cryotherapy"[All Fields] OR "cryotherapies"[All Fields]) OR ("hyperthermia, induced"[MeSH Terms] OR ("hyperthermia"[All Fields] AND "induced"[All Fields]) OR "induced hyperthermia"[All Fields] OR "thermotherapy"[All Fields] OR "thermotherapies"[All Fields]))
#3(("pain"[MeSH Terms] OR "pain"[All Fields] OR ("fear"[MeSH Terms] OR "fear"[All Fields]))
#4 #1 AND #2 AND #3
2. Embase: 4066 Results
#1 ('venipuncture'/exp OR venipuncture OR 'injections, intravenous'/exp OR 'injections, intravenous' OR (('injections,'/exp OR injections,) AND intravenous) OR iv OR 'intravenous catheter'/exp OR 'intravenous catheter' OR (intravenous AND ('catheter'/exp OR catheter)) OR 'intravenous cannulation' OR (intravenous AND cannulation) OR 'intravenous cannula'/exp OR 'intravenous cannula' OR (intravenous AND ('cannula'/exp OR cannula)))
#2 (hot OR warm OR 'heat'/exp OR heat OR 'ice'/exp OR ice OR 'cold'/exp OR cold OR 'vapocoolant'/exp OR vapocoolant OR 'cryotherapy'/exp OR cryotherapy OR 'thermotherapy'/exp OR thermotherapy)
('pain'/exp OR pain OR 'fear'/exp OR fear)
#4 #1 AND #2 AND #3
3. Cochrane: 1159 Results
((('venipuncture) OR (Injections, intravenous) OR (IV) OR (intravenous catheter) OR (intravenous cannulation) OR (intravenous cannula)) AND ((Pain) OR (fear)) AND ((hot) OR (warm) OR (heat) OR (ice) OR (cold) OR (vapocoolant) OR (cryotherapy) OR (thermotherapy))) in Title Abstract Keyword
4. CINAHL: 49 Results
((('venipuncture) OR (Injections, intravenous) OR (IV) OR (intravenous catheter) OR (intravenous cannulation) OR (intravenous cannula)) AND ((Pain) OR (fear)) AND ((hot) OR (warm) OR (heat) OR (ice) OR (cold) OR (vapocoolant) OR (cryotherapy) OR (thermotherapy)))

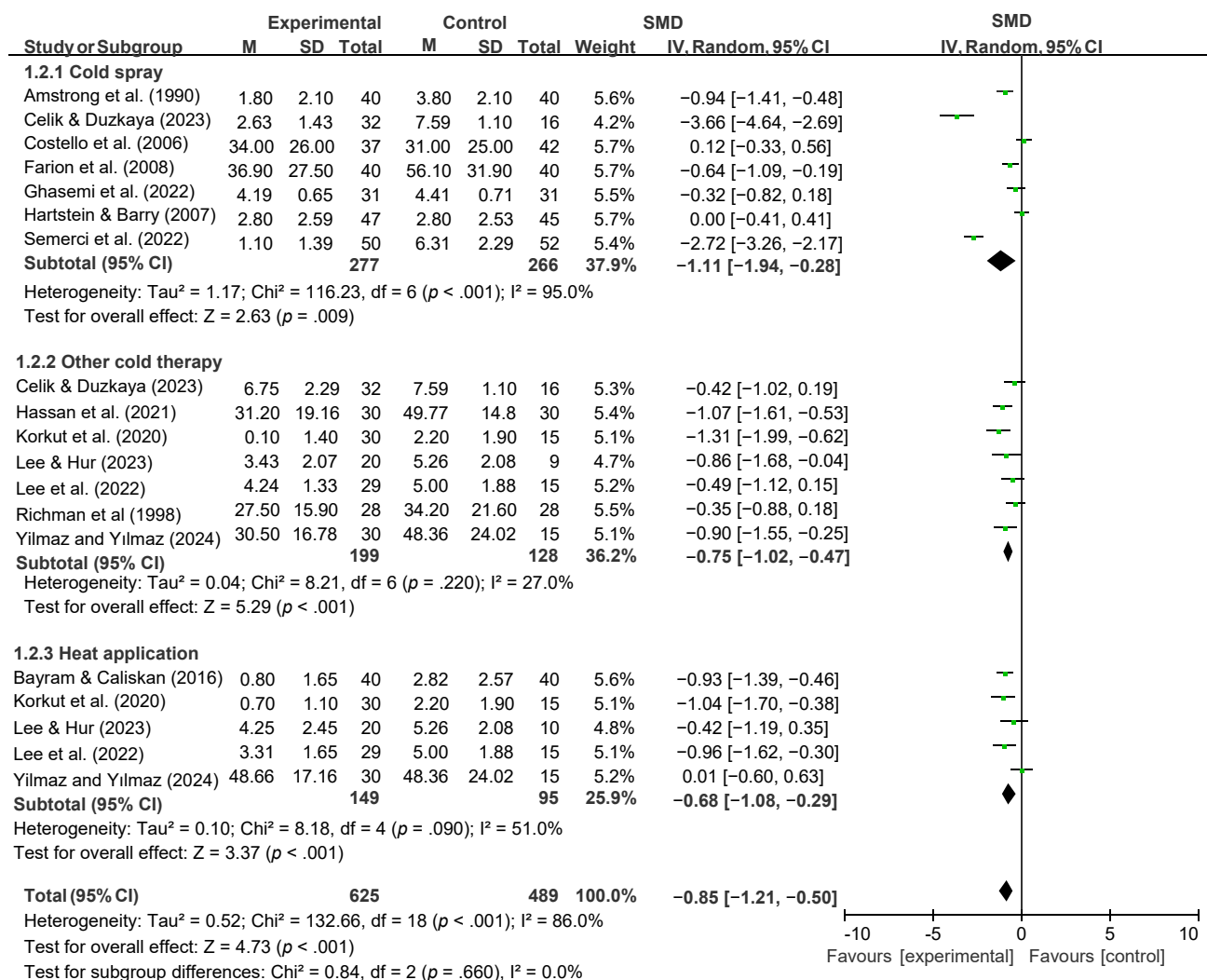
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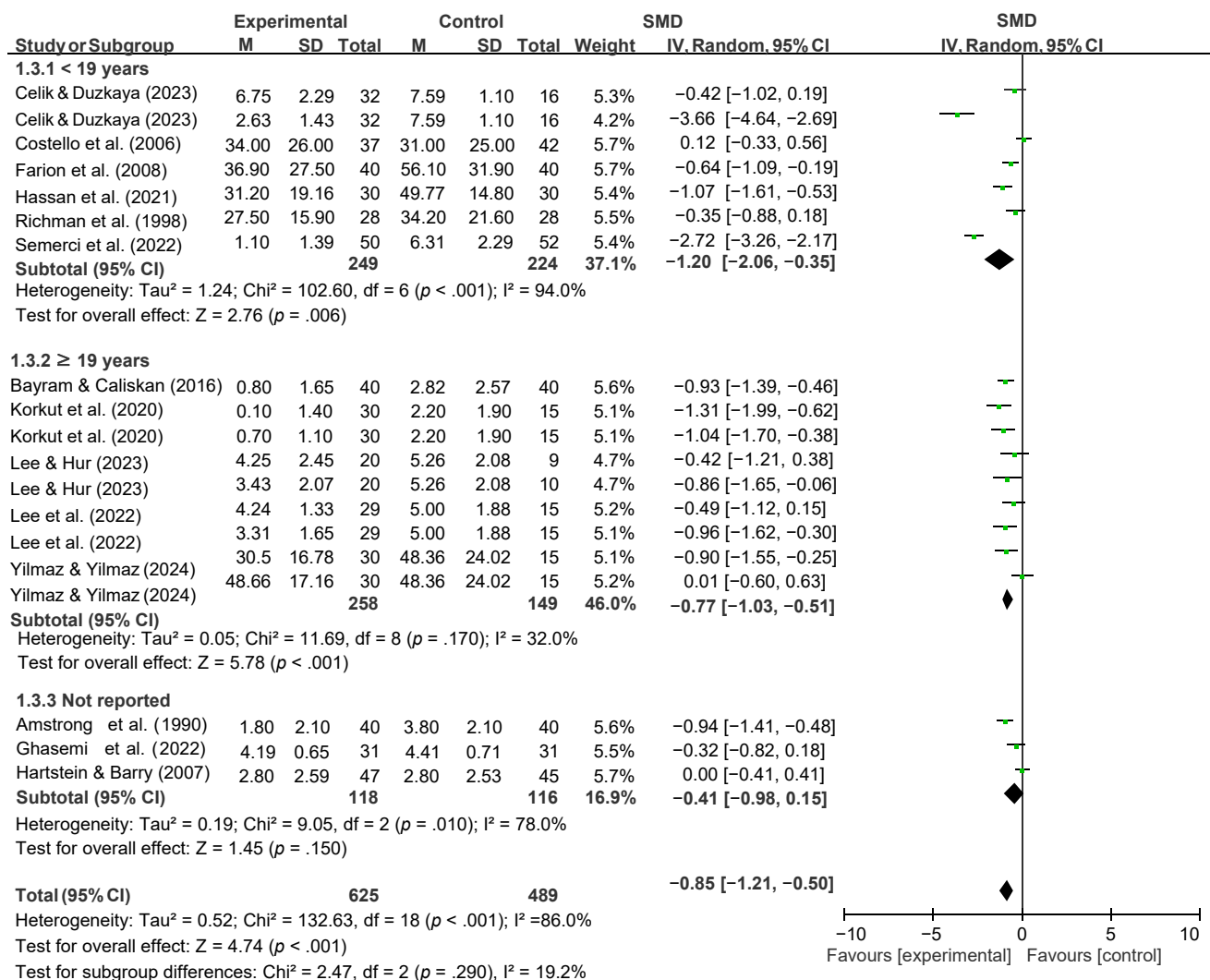
Appendix 3. Comparison of pain management methods.

M = Mean; SD = Standard deviation; IV = Inverse variance; CI = Confidence interval; SMD = Standardized mean difference.



Appendix 4. Effectiveness of intervention based on age.

M = Mean; SD = Standard deviation; IV = Inverse variance; CI = Confidence interval; SMD = Standardized mean difference.



Appendix 5. Publication bias.

SE=Standard error; SMD=Standardized mean difference.

