

ORIGINAL RESEARCH

PERIOPERATIVE MEDICINE

Effect of cold marble application for vascular access in obese patients: a randomized controlled trial

Erkan Bayram ¹, Müslüm Çiçek ²

Authors' affiliations:

1. Erkan Bayram, Assistant Professor, Department of Anesthesiology and Reanimation, Istinye University Medical Park, Gaziosmanpaşa Hospital, Istanbul, Türkiye; Email: drekanbayram@gmail.com; {ORCID:0000-0002-8527-8321}
2. Müslüm Çiçek, Professor, Department of Anesthesiology and Reanimation, Istinye University Medical Park, Gaziosmanpaşa Hospital, Istanbul, Türkiye; Email: muslum.cicek@isu.edu.tr; {ORCID:0000-0001-9187-8342}

Correspondence: Dr. Erkan Bayram, Email: drekanbayram@gmail.com

ABSTRACT

Background: Peripheral intravenous (IV) cannulation in obese patients is often more painful and may trigger a stronger autonomic response because of difficult venous access and higher sympathetic tone. Cervical cold stimulation is a simple, non-pharmacological maneuver that may enhance vagal activity and modulate pain perception. This study aimed to determine whether brief bilateral cold marble application to the lateral neck can reduce cannulation pain and blunt hemodynamic changes in obese patients.

Methods: In this prospective, randomized, controlled trial, 180 obese adults scheduled for elective surgery were enrolled; 169 patients were included in the final analysis. Patients were randomized into three groups: no intervention (Control), bilateral room-temperature marble application (RTM), or bilateral cold marble application at 4°C (CM). The marble was applied over the lateral cervical region for 30 seconds immediately before IV cannulation. Cannulation was performed by a blinded anesthesiologist using a 22-gauge catheter. The primary outcome was cannulation pain assessed by a 10-cm numeric rating scale (NRS). Secondary outcomes were changes in heart rate (HR) and blood pressure.

Results: Baseline demographic and hemodynamic variables were similar among groups. Cannulation pain showed a significant between-group difference ($P < 0.001$): mean NRS was 4.9 ± 1.8 in the Control group, 4.3 ± 1.7 in the RTM group, and 3.5 ± 1.6 in the CM group, indicating the greatest analgesic effect with cold application. The proportion of patients reporting mild pain (NRS ≤ 3) was highest in the CM group. HR response also differed: HR increased after cannulation in the Control ($+2.4 \pm 4.2$ bpm) and RTM ($+2.7 \pm 4.4$ bpm) groups, whereas it slightly decreased in the CM group (-1.1 ± 3.8 bpm), consistent with attenuation of the autonomic response. Blood pressure changes were small and clinically insignificant in all groups. No adverse events related to the intervention were observed.

Conclusion: A 30-second bilateral cold marble application to the lateral cervical region is an easy, inexpensive, and safe technique that reduces IV cannulation pain and blunts the heart rate response in obese patients. This maneuver can be readily integrated into routine practice, particularly in bariatric and anxious populations, to improve procedural comfort.

Abbreviations: CM: cold marble, IV: intravenous, bpm: beats per minute, NRS: Numerical Rating Scale. RTM: room-temperature marble application,

Keywords: Autonomic response; Cold Temperature; Obesity; Venipuncture; Pain Management; Vagus Nerve

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1. INTRODUCTION

Obesity has become one of the most important health problems of our time.¹ Its prevalence is steadily increasing all over the world, and this trend brings along many metabolic, cardiovascular, and respiratory disorders.² Because of these comorbidities, obese patients are admitted to hospitals more frequently and undergo a wide variety of diagnostic and therapeutic procedures. Almost all of these procedures require reliable venous access, which makes intravenous cannulation a routine but essential part of daily clinical practice.³

However, establishing peripheral intravenous (IV) access in obese patients is far from simple. The thickened subcutaneous tissue and altered vascular anatomy cause veins to become deeper and less visible, making cannulation technically difficult.⁴ This often leads to multiple attempts, prolonged procedure times, and greater patient discomfort.⁵ In addition, the increased sympathetic activity and impaired autonomic regulation frequently seen in obese individuals contribute to hemodynamic fluctuations, higher anxiety, and a lower pain threshold.⁶ Taken together, even a simple IV cannulation may become a stressful, painful, and complication-prone procedure in this group of patients.

Several non-pharmacological methods have been tested to improve patient comfort and facilitate vascular access. Among them, the Valsalva maneuver and transcutaneous auricular vagus nerve stimulation (taVNS) are the best known.⁷⁻⁹ Although effective, both approaches have important limitations, as they either require active patient participation or depend on special devices. Cold application to the cervical region, on the other hand, is a much simpler and cheaper technique. By stimulating vagal fibers and baroreceptors, localized cold exposure has the potential to reduce pain perception and modulate autonomic responses at the same time.¹⁰

Studies performed in non-obese populations have shown that cold stimulation can reduce pain during vascular access.¹¹ Yet, to date, there is no clear evidence regarding its effectiveness in obese patients, who actually represent the group most likely to benefit. The higher incidence of difficult intravenous access, increased procedural anxiety, and vulnerability to complications make this issue particularly relevant.¹²

For this reason, the present study was designed to evaluate the analgesic and autonomic effects of cold marble application to the lateral cervical region during intravenous cannulation in obese patients. We hypothesized that this brief and non-pharmacological intervention would lower pain scores and attenuate autonomic stress compared with control and sham

conditions. However, there is limited evidence regarding whether cervical cold application can modulate both pain perception and autonomic activity, particularly in obese patients.

2. METHODOLOGY

This prospective, randomized, controlled trial was conducted between May 2025 and August 2025 at the Department of Anesthesiology and Reanimation, Istinie University Medical Park Gaziosmanpaşa Hospital, Istanbul, Turkey. The study protocol was approved by the Institutional Review Board of Istinie University (Approval No: 2025/03), and written informed consent was obtained from all participants prior to enrollment. The trial adhered to the principles of the Declaration of Helsinki.

A total of 180 adult patients scheduled for elective surgery under general anesthesia were assessed for eligibility. Inclusion criteria were: age between 18 and 65 years, body mass index (BMI) ≥ 35 kg/m², American Society of Anesthesiologists (ASA) physical status II–III, and absence of known peripheral vascular disease, uncontrolled hypertension, arrhythmias, or autonomic dysfunction.

Patients with coagulation abnormalities, previous neck surgery, significant carotid artery disease, local infection, chronic analgesic use, psychiatric illness, or refusal to participate were excluded.

Only patients who achieved successful intravenous cannulation at the first attempt were included in the analysis. Patients requiring multiple attempts were excluded to avoid potential confounding effects.

Patients were randomized into three groups using a computer-generated randomization sequence in a 1:1:1 ratio. Group assignments were placed in sealed, opaque envelopes prepared by a statistician not involved in data collection to ensure allocation concealment. Both the anesthesiologist performing cannulation and the investigator recording outcomes were blinded to group allocation, ensuring an unbiased assessment, while patients were aware of the marble application but not of the temperature hypothesis.

Group C: Control group (no intervention)

Group RM: Room-temperature marble group

Group CM: Cold marble group

Due to the nature of the intervention, patients were aware of the marble application but were not informed about the temperature hypothesis. They were told that the study was designed to examine the effects of “different physical stimulation techniques” on cannulation-related

discomfort. A dedicated nurse, who was not involved in data collection or cannulation, prepared and applied the marbles. The investigator responsible for recording Numeric Rating Scale (NRS) pain scores and hemodynamic parameters was blinded to group allocation.

Importantly, the anesthesiologist performing intravenous cannulation was also blinded to group assignment, ensuring procedural consistency and minimizing potential bias.

Patients were positioned supine, and the lateral cervical region over the carotid sinus at the level of the thyroid cartilage was identified bilaterally. The marble was applied bilateral cervical region for 30 seconds.

In Group CM, a marble cooled to 4 °C in a medical refrigerator was applied to the skin for 30 seconds immediately prior to intravenous cannulation.

In Group RM, a marble stored at room temperature (~22 °C) was similarly applied for 30 seconds.

In Group C, no intervention was applied.

Marble temperatures were verified using an infrared thermometer before each application. A standardized, polished marble sphere (diameter: 2 cm, weight: approximately 10 g) was used for all applications. Each marble was disinfected and stored in sterile conditions prior to use. For standardization, a new marble was used for every patient, retrieved from the refrigerator immediately before use.

Peripheral intravenous cannulation was performed in the dorsum of the hand using a 22-Gauge intravenous catheter (Introcan Safety®, B. Braun, Germany). All cannulations were performed by a single experienced anesthesiologist (>5 years of practice) in obese patients. Only first-attempt successful cannulations were included in the analysis to ensure procedural consistency. The anesthesiologist performing the cannulation and the investigator recording NRS and hemodynamic data were both blinded to group allocation, ensuring unbiased assessment.

Patients were aware of the marble application but were not informed about the temperature hypothesis. Accordingly, the trial followed an operator- and assessor-blind design, while participants remained partially blinded to the intervention. Only first-attempt cannulations were analyzed; patients requiring more than one attempt were excluded.

The primary outcome was pain during intravenous cannulation, measured using a 10-cm Numeric Rating Scale (NRS), marked 0 = no pain to 10 = the worst imaginable pain. The NRS score was assessed by the

blinded investigator immediately (<1 minute) after successful cannulation.

Secondary outcomes included: Heart rate (HR) and mean arterial pressure (MAP) were measured at three time points: baseline (before intervention), immediately after marble application (or 30s wait in controls), and immediately after cannulation. All hemodynamic parameters were continuously monitored using a standard multiparameter monitor (Infinity Delta®, Dräger, Germany), and values were recorded manually at the predefined time points.

Sample Size Calculation

Based on pilot data from 15 patients (NRS difference 2.1 ± 1.5 , Cohen's $d = 0.45$), a power analysis was conducted using G*Power v3.1. To achieve 80% power at an alpha level of 0.05, the minimum required sample size was 56 patients per group. To compensate for potential dropouts, 60 patients per group were included, resulting in a total sample size of 180 patients.

Statistical Analysis

All statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Shapiro–Wilk test and expressed as mean \pm standard deviation (SD) or median [interquartile range, IQR], as appropriate. Categorical variables were summarized as frequencies and percentages.

Within-group comparisons of heart rate (baseline vs post-cannulation) were made using paired t-tests with Bonferroni correction. Between-group differences in heart rate change (Δ HR) were analyzed with one-way ANOVA followed by Bonferroni post-hoc tests. Pain scores (NRS) were compared among the three groups using the Kruskal–Wallis test with Dunn–Bonferroni adjustment.

Pain intensity categories were defined as mild (NRS 1–3), moderate (NRS 4–6), and severe (NRS 7–10). Categorical comparisons among groups were performed using the Chi-square or Fisher's exact test, as appropriate. Correlation between pain scores and heart rate change was evaluated using Spearman's rank correlation coefficient.

A P-value of < 0.05 was considered statistically significant.

3. RESULTS

A total of 180 patients scheduled for elective bariatric surgery under general anesthesia were initially enrolled and randomized equally into three groups (Control [C],

Variable	Group C	Group RM	Group CM	P-value
Age (y)	45.3 ± 8.4	46.1 ± 9.2	44.6 ± 8.7	0.72
BMI (kg/m ²)	38.2 ± 1.3	36.9 ± 1.4	37.1 ± 1.5	0.65
SBP (mmHg)	126 ± 8	127 ± 7	125 ± 9	0.58
DBP (mmHg)	78 ± 6	79 ± 7	77 ± 6	0.66
HR (bpm)	77 ± 8	78 ± 9	79 ± 8	0.71
ASA II/III (n, %)	40 / 20 (67/33%)	41 / 19 (68/32%)	39 / 21 (65/35%)	0.93

Data are presented as mean ± SD or number (%). One-way ANOVA or Kruskal–Wallis tests were used as appropriate. Categorical variables were compared using the Chi-square test. P < 0.05 was considered statistically significant.

Groups	NRS (Mean ± SD)	Mild (1–3)	Moderate (4–6)	Severe (7–10)	P-value
Group C	4.9 ± 1.8	18 (32.7)	23 (41.8)	14 (25.5)	< 0.001 *
Group RM	4.3 ± 1.7	33 (57.9)	17 (29.8)	7 (12.3)	
Group CM	3.5 ± 1.6	32 (56.1)	19 (33.33)	6 (10.52)	

**Kruskal–Wallis test followed by Dunn–Bonferroni post-hoc comparisons. Pain intensity was classified as mild (NRS 1–3), moderate (NRS 4–6), and severe (NRS 7–10). Data are presented as number (%) or mean ± SD. Between-group comparisons were performed using the Kruskal–Wallis test with Dunn–Bonferroni adjustment. P < 0.05 was considered statistically significant.*

Groups	ΔHR (beats / min)	P-value (Overall)	Post-hoc Comparisons (P)
Group C	+2.4 ± 4.2	< 0.001 *	C vs CM < 0.001; C vs RM 0.68; RM vs CM 0.002
Group RM	+2.7 ± 4.4		
Group CM	−1.1 ± 3.8		

**One-way ANOVA followed by Bonferroni-corrected pairwise comparisons. ΔHR = (Heart rate immediately after cannulation) – (Baseline heart rate). Data are expressed as mean ± SD. Positive values indicate an increase in HR relative to baseline. P < 0.05 considered statistically significant.*

Room-temperature Marble [RM], and Cold Marble [CM]; 60 patients each). However, 11 patients were excluded from the final analysis for the following reasons: five due to unsuccessful first-attempt intravenous cannulation, three because of withdrawal of consent prior to intervention, and three owing to protocol deviations or incomplete data collection (Figure 1). Consequently, 169 patients were included in the final analysis (C = 55, RM = 57, CM = 57). All analyzed patients underwent successful first-attempt cannulation performed by the same experienced anesthesiologist. Baseline demographic and hemodynamic parameters were comparable across the three groups, with no

significant differences in age, BMI, ASA physical status, or baseline hemodynamic values (P > 0.05) (Table 1). The mean age of participants was approximately 45 years, and all patients were candidates for bariatric surgery with a BMI ≥ 35 kg/m². Baseline systolic blood pressure, diastolic blood pressure, and heart rate were evenly distributed, confirming appropriate randomization.

Pain intensity during intravenous cannulation showed a significant difference among the groups (P < 0.001) (Table 2). In the cold marble (CM) group, mild pain (NRS 1–3) was reported by 56% of patients, moderate pain (NRS 4–6) by 33%, and severe pain (NRS 7–10) by 10%. In the room-temperature marble (RM) group, 58%

Parameter	Group C	Group RM	Group CM	P-value
Baseline SBP (mmHg)	126 ± 9	127 ± 8	125 ± 9	0.68
Post-application SBP (mmHg)	125 ± 9	124 ± 9	123 ± 9	0.47
Post-IV SBP (mmHg)	125 ± 9	124 ± 8	122 ± 8	0.41
Baseline MAP (mmHg)	94 ± 7	95 ± 8	93 ± 7	0.63
Post-IV MAP (mmHg)	93 ± 7	92 ± 8	91 ± 8	0.55

Data are expressed as mean ± SD. Within-group changes were analyzed using paired t-tests with Bonferroni correction. Between-group comparisons used one-way ANOVA. P < 0.05 was considered statistically significant.

of patients reported mild pain, 30% moderate pain, and 12% severe pain. In contrast, the control group exhibited a higher incidence of moderate-to-severe pain, with 33% mild, 42% moderate, and 25% severe pain. The mean NRS scores were 4.9 ± 1.8 in the control group, 4.3 ± 1.7 in the RM group, and 3.5 ± 1.6 in the CM group ($P < 0.001$). These findings indicate that cervical cold stimulation significantly reduced pain intensity compared with both the control and room-temperature conditions.

Heart rate changes (Δ HR) during cannulation also differed significantly among groups ($P < 0.001$) (Table 3). The mean Δ HR was $+2.4 \pm 4.2$ bpm in the control group, $+2.7 \pm 4.4$ bpm in the room-temperature group, and -1.1 ± 3.8 bpm in the cold marble group. Post-hoc analyses revealed significant pairwise differences between the CM group and both other groups (Bonferroni-adjusted $P < 0.01$), whereas no difference was found between the control and room-temperature groups. In the CM group, heart rate decreased immediately after the application of cold marble and remained below baseline after cannulation, indicating a sustained parasympathetic response and a reduction in sympathetic activation. The mean HR in the CM group decreased from 79 ± 8 bpm at baseline to 76 ± 8 bpm after cold application and remained 78 ± 9 bpm after cannulation.

Systolic and mean arterial pressures showed minimal, non-significant changes from baseline to post-cannulation in all groups, with slightly greater reductions observed in the CM group (Table 4). The average systolic blood pressure in the CM group decreased by approximately 3 mmHg after cold application, whereas changes in the other groups were negligible. Mean arterial pressure values followed a similar trend. No significant within-group changes or between-group differences were detected for blood pressure parameters ($P > 0.05$). Respiratory rate and peripheral oxygen saturation (SpO_2) remained stable across all measurements, with no between-group differences ($P > 0.05$).

A moderate negative correlation was observed between pain intensity and Δ HR ($P = -0.35$, $P < 0.001$), suggesting that patients who experienced greater pain also exhibited a stronger autonomic response, while the attenuation of HR in the CM group was consistent with reduced pain perception. No adverse events related to vagal stimulation—such as bradycardia, syncope, or hypotension—were observed in any patient during the study.

Overall, cold marble application resulted in a significant reduction in pain perception and autonomic reactivity during intravenous cannulation in obese patients. Baseline characteristics and hemodynamic parameters were comparable across groups, supporting that the observed effects were directly attributable to the intervention rather than patient variability.

4. DISCUSSION

This randomized clinical study shows that briefly applying a cold marble to the side of the neck during intravenous cannulation can lessen pain and influence autonomic responses in obese patients. The finding is important because these patients often have both difficult venous access and an exaggerated physiological reaction to stress.

The mechanism behind this effect seems to involve more than one pathway. According to the Gate Control Theory, stimulation of large-diameter A-beta fibers blocks pain signals carried by slower C-fibers at the spinal level, which reduces pain perception.^{13,14} Cooling in the neck area also activates vagal afferents and carotid baroreceptors, increasing parasympathetic tone and lowering sympathetic drive. Together these effects may explain the slower heart rate and greater autonomic stability we observed. The response resembles the diving reflex, where facial or cervical cooling slows the heart through vagal activation.^{15,16} In contrast to carotid sinus massage, however, the cold marble achieves a similar autonomic balance without causing excessive vagal stimulation or discomfort. Our results align with

emerging evidence that gentle somatosensory stimuli can modulate parasympathetic tone.

Obesity is known to increase sympathetic tone and reduce vagal control, which leads to higher resting heart rate and blood pressure fluctuations during stress.^{6,17} The fall in heart rate in the cold marble (CM) group suggests that cervical cooling temporarily restores this imbalance by easing sympathetic activity. This may help obese patients tolerate procedures better, providing a simple and safe way to stabilize their hemodynamic response.

A smaller but noticeable effect was also seen in the room-temperature marble (RM) group. Even without cooling, gentle tactile stimulation in the neck region seemed to calm patients slightly. Touch itself can have a reassuring and distracting influence, and the feeling that something helpful is being done may reduce anxiety.¹⁸ Higher preprocedural anxiety is known to heighten pain sensitivity and increase postoperative analgesic use, while simple calming contact can have the opposite effect.^{19,20} It is possible that the mild improvement in the RM group came not from physiological changes but from this psychological reassurance. The idea supports the biopsychosocial view of pain, where both physical and emotional factors shape the patient's experience.

Our results are in line with the work of Adıgüzel et al., who also showed that cooling the lateral neck lowers both pain scores and heart rate during venous access.¹⁰ Their study confirmed that local cold stimulation can trigger both analgesic and autonomic effects. By extending these findings to obese individuals, our research adds to the understanding of how such a simple method can benefit patients with increased sympathetic reactivity.

Our findings are consistent with non-pharmacological methods activating vagal or baroreceptor pathways, supporting the idea that gentle peripheral stimulation can modulate autonomic tone through central mechanisms. Compared with other non-pharmacological techniques like the Valsalva maneuver or transcutaneous auricular vagus nerve stimulation (taVNS), the cold marble method is much easier to use. It requires no cooperation from the patient, no equipment, and no special training. This makes it suitable for use in emergency departments, bariatric clinics, and oncology units, where anxiety and technical challenges often coexist.

5. LIMITATIONS

Our study has several limitations. First, it was conducted at a single center with a moderate number of participants, which may limit generalizability. Second, we did not record advanced autonomic markers such as heart-rate variability or baroreflex sensitivity, so the physiological mechanism can only be inferred. In addition,

preprocedural anxiety levels were not measured, which could represent a confounding factor since anxiety strongly affects pain perception. Finally, excluding patients after randomization—such as those with unsuccessful first-attempt cannulation or protocol deviations—may introduce attrition bias and has the potential to affect the internal validity of the study. Future studies combining anxiety scales with objective autonomic data would help to clarify how emotional and physiological responses interact.

6. CONCLUSION

In conclusion, short-term cooling of the lateral neck with a simple marble offers an inexpensive, safe, and practical way to reduce pain and sympathetic stress during venous access in obese patients. Beyond the physiological explanation, the results remind us that small, thoughtful interventions and a sense of reassurance can make routine procedures more comfortable and humane.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Conflict of interest

All authors declare that there was no conflict of interest.

9. Funding

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors' contribution

EB: Concept, conducted the study, manuscript writing

MC: Concept, manuscript writing

11. REFERENCES

1. World Health Organization. Obesity and overweight: fact sheet. Geneva: World Health Organization; 2025 May 7 [cited 2025 Jan 20]. Available from: <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>
2. Blüher M. Obesity: global epidemiology and pathogenesis. *Nat Rev Endocrinol.* 2019;15(5):288–98. DOI: 10.1038/s41574-019-0176-8
3. Armenteros-Yeguas V, Gárate-Echenique L, Tomás-López MA, Cristóbal-Domínguez E, Moreno-de Gusmão B, Miranda-Serrano E, et al. Prevalence of difficult venous access and associated risk factors in highly complex hospitalised patients.

- J Clin Nurs. 2017;26(23–24):4267–75. DOI: 10.1111/jocn.13750
4. Latos M, Szymczak A, Solecki M. Intravenous access in patients with morbid obesity. *Pielęgniarstwo Chirurgiczne i Angiologiczne*. 2024;18(2):71–4. DOI: 10.5114/pcia.2024.141479
 5. Malik A, Dewald O, Gallien J, Favot M, Kasten A, Reed B, et al. Outcomes of ultrasound-guided peripheral intravenous catheters placed in the emergency department and factors associated with survival. *Open Access Emerg Med*. 2023;15:177–87. DOI: 10.2147/OAEM.S405692
 6. Grassi G, Drager LF. Sympathetic overactivity, hypertension and cardiovascular disease: state of the art. *Curr Med Res Opin*. 2024;40(suppl 1):5–13. DOI: 10.1080/03007995.2024.2305248
 7. Alan N, Khorshid L. Evaluation of efficacy of Valsalva maneuver during peripheral intravenous cannulation on pain. *Pain Manag Nurs*. 2022;23(2):220–4. DOI: 10.1016/j.pmn.2021.01.013
 8. Sanchez-Perez JA, Gazi AH, Rahman FN, Seith A, Saks G, Sundararaj S, et al. Transcutaneous auricular vagus nerve stimulation and median nerve stimulation reduce acute stress in young healthy adults: a single-blind sham-controlled crossover study. *Front Neurosci*. 2023;17:1213982. DOI: 10.3389/fnins.2023.1213982
 9. Zhang Y, Luo Y, Wu Q, Han M, Wang H, Kang F. Effect of transcutaneous auricular vagus nerve stimulation on conditioned pain modulation in trigeminal neuralgia patients. *Pain Ther*. 2024;13(6):1529–40. DOI: 10.1007/s40122-024-00654-x
 10. Canikli Adıgüzel S, Akyurt D, Ültan Özgen G, Bahadır Altun H, Çakır A, Süren M, et al. The effect of cold application to the lateral neck area on peripheral vascular access pain: a randomised controlled study. *J Clin Med*. 2023;12(19):6273. DOI: 10.3390/jcm12196273
 11. Yılmaz E, Yılmaz D. The effect of three different nonpharmacological methods on cannulation success during peripheral intravenous catheter placement in the emergency unit: a randomized controlled trial. *BMC Anesthesiol*. 2024;24:362. DOI: 10.1186/s12871-024-02723-2
 12. Ng M, Mark LKF, Fatimah L. Management of difficult intravenous access: a qualitative review. *World J Emerg Med*. 2022;13(6):467–78. DOI: 10.5847/wjem.j.1920-8642.2022.104
 13. Fernandes EC, Pechincha C, Luz LL, Kokai E, Szucs P, Safronov BV. Primary afferent-driven presynaptic inhibition of C-fiber inputs to spinal lamina I neurons. *Prog Neurobiol*. 2020;188:101786. DOI: 10.1016/j.pneurobio.2020.101786
 14. Ropero Peláez FJ, Taniguchi S. The gate theory of pain revisited: modeling different pain conditions with a parsimonious neurocomputational model. *Neural Plast*. 2016;2016:4131395. DOI: 10.1155/2016/4131395
 15. Ackermann SP, Raab M, Backschat S, Smith DJC, Javelle F, Laborde S. The diving response and cardiac vagal activity: a systematic review and meta-analysis. *Psychophysiology*. 2023;60(3):e14183. DOI: 10.1111/psyp.14183
 16. Jungmann M, Vencatachellum S, Van Ryckeghem D, Vögele C. Effects of cold stimulation on cardiac-vagal activation in healthy participants: randomized controlled trial. *JMIR Form Res*. 2018;2(2):e10257. DOI: 10.2196/10257
 17. Tomar A, Ahluwalia H, Isser HS, et al. Analysis of ventricular repolarization parameters and heart rate variability in obesity: a comparative study. *Sci Rep*. 2024;14:25855. DOI: 10.1038/s41598-024-76580-x
 18. Packheiser J, Hartmann H, Fredriksen K, Gazzola V, Keysers C, Michon F. A systematic review and multivariate meta-analysis of the physical and mental health benefits of touch interventions. *Nat Hum Behav*. 2024;8(6):1088–1107. DOI: 10.1038/s41562-024-01841-8
 19. Carpenter LL, Kronenberg EF, Tirrell E, Kokdere F, Beck QM, Temereanca S, et al. Mechanical affective touch therapy for anxiety disorders: feasibility, clinical outcomes, and electroencephalography biomarkers from an open-label trial. *Front Psychiatry*. 2022;13:877574. DOI: 10.3389/fpsy.2022.877574
 20. Bayram E, Dolğun İ. Does preoperative waiting time influence anxiety and analgesic demand? A prospective observational study. *Ir J Med Sci*. 2025;Advance online publication. DOI: 10.1007/s11845-025-04102-3