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PERIOPERATIVE ANALGESIC STRATEGIES FOR LONG BONE FRACTURES. IS THERE A NEED FOR A STANDARDIZED PROTOCOL? A SCOPING REVIEW

M.S. MOLDOVAN[1,2] A. MIRONESCU[1]

Abstract: *Acute perioperative pain that accompanies limb fractures and exceeds the threshold of tolerability has a high risk of becoming chronic. There are many controversies regarding current pain management options, like opioids and nonsteroidal anti-inflammatory drugs. This study aimed to comprehensively search the literature for ways to achieve perioperative analgesia in patients with long bone fractures. This research was a scoping review that included a systematic search of randomized controlled trials and observational studies in three international databases: MEDLINE, Scopus, and Web of Science. Ten thousand nine hundred forty-three articles were found and screened. After applying the inclusion and exclusion criteria, 77 articles were included in the final descriptive analysis. Peripheral nerve blocks play a significant role in perioperative multimodal analgesia; of the articles described in this review, 46.75% revolved around regional anesthesia. Other findings of pharmacologic agents that are of benefit in improving pain scores in surgically treated long bone fractures and need future research are Gabapentinoids, Magnesium sulphate, Vitamin C, Esmolol, and low-dose Ketamine.*

Key words**:** *Limb fractures, analgesia, peripheral nerve blocks, perioperative, pain scores*

1. Introduction

It is known that orthopedic procedures are associated with a higher incidence of postoperative pain than non-orthopedic procedures [1]. Moreover, internal fixation of limb fractures is known to be painful on the first postoperative day, with a mean Numeric Rating Scale (NRS) score higher than 4.5 [2]. If NRS is a scale where a score of four out of ten is associated with moderate pain, and the patient requires rescue analgesia, we can consider that four out of ten is the limit of

[1] Faculty of Medicine, *Transilvania* University of Braşov
[2] Brasov County Clinical Emergency Hospital
*Corresponding author: mara.tantau.mt@gmail.com

tolerability. Quantifying pain intensity, giving medication to the patient for analgesia, and optimizing functional status are fundamental elements of pain management [3]. There are many complications of inefficiently treated acute pain, such as thrombosis, immune suppression, a slowing in wound healing, hemodynamic changes, acute coronary syndromes, dysfunction in bowel movements, and dysfunction of the respiratory system [4]. Even though different classes of analgesics administered via different routes are usually used to treat postoperative pain, the standard-of-care analgesic to treat acute fracture-related pain is opioid-based, opioids which are known to have other effects such as nausea and vomiting, prolonged sedation, and impeding recovery after surgery [1], [5]. Nonsteroidal anti-inflammatory drugs are also very controversial, as some published studies report that they inhibit bone healing [6].

It is known that regional anesthesia is associated with better postoperative analgesia in comparison with general anesthesia, facilitating earlier return of motion with better motor power [7].

Studies have demonstrated the superiority of multimodal analgesia in relieving pain [8].

The goal was to review literature for randomized controlled trials and observational studies examining various perioperative pain management strategies for limb fractures, to determine which are most effective in alleviating pain, and to investigate the necessity of a standardized opioid-sparing pain management protocol suitable for the opioid-naïve general population.

2. Materials and Methods

Because of the very diverse ways of managing initial pain of the fractured bones and then the subsequent pain that follows the surgical treatment of the limb fractures, a scoping review was chosen to comprehensively assess the best strategies for maintaining perioperative limb fracture analgesia.

In conducting this scoping review, we followed the Arksey and O'Malley framework and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) [9, 10].

Three databases (MEDLINE, Scopus, and Web of Science) were searched from their inception until April 21, 2025. The following terms and Boolean operators were adapted for each database: (Fractures OR "musculoskeletal injury" OR "musculoskeletal trauma" OR "orthopedic injury" OR "orthopedic trauma") AND ("pain management" OR analgesia) AND (perioperative OR postoperative OR preoperative OR intraoperative OR preemptive OR surgery).

Inclusion criteria were randomized controlled trials and observational studies in English about perioperative pain management in adult patients with limb fractures (shaft and distal part of long bones). The included articles rigorously examined the efficacy of the analgetic techniques with pain scores recorded at different time intervals perioperatively.

Exclusion criteria were: studies in which patients had proximal long bone fractures (to avoid the shoulder and hip joint region), animal studies, fractures in pathologic bone (metastasis, fragility fractures, osteoporosis), other musculoskeletal injuries (luxation,

dislocation, ligament and tendons injuries, soft tissue injuries), articles on chronic pain (complex regional pain syndrome, chronic postsurgical pain) and in which pain was assessed after discharge, articles about the rehabilitation process, studies on specific populations (geriatric, opioid use disorder, dementia, diabetic, obese, pediatric etc.).

Articles about analgesic strategies for closed reductions in the ED or analgesia for positioning before spinal anesthesia were not included.

Other articles, such as case reports, case series, study protocols, conference presentations, reviews, systematic reviews, meta-analyses, letters to the editor, and notes, were also excluded from the study.

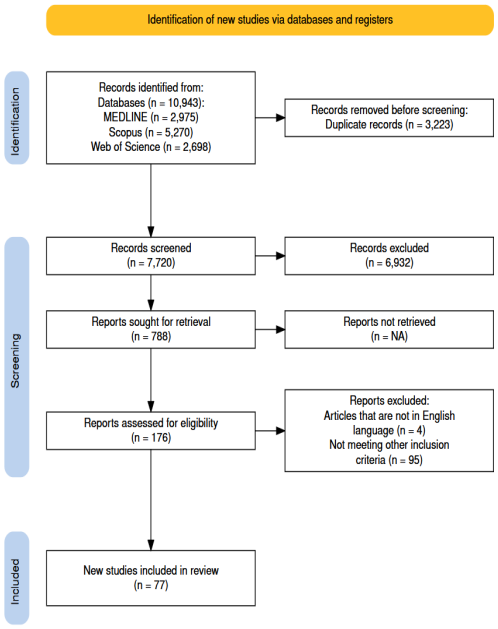

Fig. 1. *PRISMA flow diagram*

3. Results and Discussion

We screened 7,720 articles by title (Figure 1). Seven hundred eighty-eight articles passed this screening, and their abstracts were retrieved and reviewed. We further eliminated 612 articles that did not meet the inclusion criteria. One hundred seventy-six articles were read in full, and then we eliminated another 99 articles that did not meet the inclusion criteria from our study.

The final analysis included 77 articles.

The six appendices at the end of the article give brief information about the articles included in this study: the interventions, the control (if used), and the intervention's benefit in improving pain scores. The pain assessment tools used and the time interval of assessment were carefully documented.

In Figure 2, the distribution of articles according to the type of fracture studied can be observed.

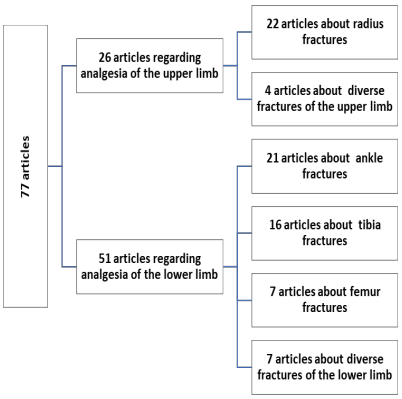

Fig. 2. *Types of fractures studied*

3.1. Lower limb

3.1.1. Tibia fractures

For tibial fracture perioperative analgesia, sixteen articles were found, with pain being controlled via regional anesthesia [11-15], intravenous and oral routes of administration [4, 5], [16-21] peri-fracture administered analgesia [22] and physical therapy and melotherapy [23, 24].

Five studies regarding lower limb fractures found that preemptive gabapentinoid administration improved pain scores [11], [14], [16,17], [21]. One study found that a single dose of 600 mg Gabapentin administered one hour before surgery significantly decreased pain scores six hours after surgery, more than Oxycodone and Diclofenac [5]. Another study found that preemptive administration of 300 mg of Gabapentin had similar efficacy to 1g of intravenously administered Paracetamol [19].

Gabapentinoids are anticonvulsants that act through central and peripheral mechanisms, have antihyperalgesic action, and prevent the release of many pain-related neurotransmitters [17], [19], [21].

Another promising finding was that administration of Ketorolac significantly decreased pain scores more than opioid-based analgesia at 24h after surgery [16] .

In a study of 82 patients, intraoperative administration of a continuous infusion of Esmolol was found to be effective in reducing postoperative pain, opioid consumption, and prolonging the duration of analgesia [20]. It was the only article in our orthopedic population to study the analgesic effect of this short-acting beta-blocker. Perioperative administration of beta-blockers not only decreases the input of the central nervous system, but some animal studies showed that it reduces the cortical neuronal excitatory responses in the cingulate cortex [20].

Concerning peripheral nerve blocks as an anesthesia technique, the postoperative pain scores are lower when compared with general anesthesia [11], spinal [13] and epidural anesthesia [25].

Interestingly, there were two studies about intrathecal administration of Magnesium sulfate in addition to bupivacaine with benefits regarding postoperative pain scores, total analgesic requirements for 24 hours post-surgery, and prolongation of the sensory block [15], [26].

A study published in 2019 [27] on patients with tibia, fibula, and distal femur fractures who received Nitroglycerin in addition to Fentanyl showed that experienced pain levels were lower in that group of patients. Even though it is not recommended in hemodynamically unstable patients, Nitroglycerin has an analgesic effect induced by the nitric oxide release mechanism [27].

Two articles studied the effect of music as adjuvant therapy on 90 patients. According to these studies, listening to music can significantly reduce pain intensity after surgery [23], [28].

Physical therapy was not left out; a study published in 2018 showed that foot massage significantly reduced pain at 30 minutes and 2 hours after intervention [24].

3.1.2. Femur fractures

Only seven articles found studied exclusively femur shaft fractures [29-35].

To start with local anesthetic administration practices, an article dating from 1982 on 25 patients concluded that femoral nerve block helps reduce pain, with the mention that complete pain relief

can be achieved when the fracture is located in the middle third of the femoral shaft [35].

Although it is not about the population included in this study, it is worth mentioning that a single-shot femoral nerve block is a preoperative recommendation for hip fracture patients, as it results from the PROSPECT (procedure-specific postoperative pain management) guideline published in 2024 [36].

In two articles [30, 32] the effect of perineurally administered Dexmedetomidine via a femoral nerve block was found to be of benefit in terms of increasing the duration of postoperative analgesia and reducing intraoperative and postoperative opioid consumption.

At last, a randomized controlled study on 82 patients showed that an intraoperative post-fixation hematoma injection with Ropivacaine can significantly reduce postoperative pain scores [29].

As for intravenously administered analgesia, two articles were of interest [31, 34] . Low-dose Ketamine infusion (0.1 and 0.05 mg/kg/h) combined with a continuous infusion of Remifentanil significantly reduced postoperative pain scores. The explication is that low-dose Ketamine (at less than 10% of the anesthetic dose) can directly reduce and prevent opioid induced hyperalgesia and acute tolerance [34].

In a study on 135 patients [31] a multimodal regimen consisting of intravenous Acetaminophen, Diclofenac, Morphine, and oral Pregabalin administered 30 minutes preoperatively significantly reduced the need for peridural administered analgesia after surgery.

3.1.3. Ankle fractures

We documented 21 research articles on ankle fractures. Of these, nine involved peripheral nerve blocks [1, 37-44]. An observational study [39] of 96 patients with ankle fractures concluded that preoperative or postoperative administration of peripheral nerve blocks is associated with significantly lower Visual Analog Scale (VAS) pain scores and lower narcotic usage postoperatively when compared to no peripheral nerve block administration. A favorable conclusion came from a study that showed better recovery at 24 hours when using peripheral nerve blocks as opposed to intravenous analgesia only [45]. One study showed a modest decrease in opioid consumption when peripheral nerve blocks are used in patients with distal tibia and ankle fractures [46]. Another study showed that when compared with spinal anesthesia, anesthesia provided by peripheral nerve blocks provides a superior postoperative pain profile [40]. Timing of the block is also essential, as preoperative blocking of the popliteal sciatic nerve and saphenous nerve is associated with lower pain scores than the same procedure being done postoperatively [1]. Also, rebound pain must be considered when planning a multimodal analgesic plan, as a study published in 2012 showed that after a popliteal nerve block, rebound pain was observed between 8 and 24 hours postoperatively [44]. In resolving this problem, another study concluded that a continuous infusion popliteal sciatic nerve block significantly reduces rebound pain and the need for oral opioid analgesia when compared to a single-shot block [42]. A recent study on 57 patients

showed similar results, but for a continuous adductor canal block [37]. Based on the VAS pain scores in one study, postoperative pain peaks at 24 hours after surgery, which coincides with the maximal use of pain control medications. This is caused by a rebound pain as the effects of PNB diminish [47].

In one study, Dexamethasone, as an adjuvant to local anesthetics in sciatic and femoral nerve blocks, lowers pain scores more than Ketorolac via patient-controlled analgesia (PCA) [38]. Also, a study on 95 patients showed that peripheral nerve blockade in association with Ketorolac patient-controlled analgesia is superior in terms of postoperative pain control to peripheral nerve block with no PCA [41].

Regarding intravenously administered analgesics, studies of Ketorolac [48-50] showed a reduction in pain intensity on the first postoperative day. A study comparing analgesia obtained from the combination of Naproxen and Pregabalin to Naproxen alone showed similar efficacy between the groups [51]. As for the effect of the COX2 selective inhibitor Parecoxib, a study on 40 patients showed no better results in controlling pain than placebo [52].

Acetaminophen is not to be forgotten as part of multimodal analgesia, being effective in reducing pain scores when compared to placebo [53].

Administration of Vitamin C was found to reduce pain in the second week postoperatively, as it limits the tissue injury and acts as a neuroprotective and neuro-modulating agent [54].

The effect of surgical site injections is also studied, with four articles reporting mixed results[55-58].

When compared with a Placebo, one study found that Liposomal Bupivacaine significantly decreased pain scores [58], while another study concluded that even though local infiltration of Ropivacaine, Epinephrine, and Morphine significantly reduced pain scores, the results were below the minimal clinically significant difference [57].

In a cohort of 89 patients, local infiltration analgesia with 0.5% Ropivacaine into the dermis and subcutaneous tissue surrounding the incision proved to be more efficient in reducing pain scores than patient-controlled analgesia with Morphine [56].

In terms of pain management, the infusion of local anesthetic combined with adrenaline (WALLANT technique) into the syndesmosis space, subcutaneously, and in the hematoma at the fracture site was inferior to preemptive popliteal fossa nerve block [55].

Physical methods of alleviating pain by applying cold were also studied in one study, which showed a similar effect between evaporative coolants and ice packs [59].

3.2. Upper limb

3.2.1 Radial fractures

For the upper limb, articles about analgesia in surgically treated radial fractures were the most numerous.

Twelve of the twenty-two studies were about peripheral nerve blocks [8, 60-71], while three were about local infiltration analgesia [72-74].

A study on patients with fractures of the radius, the ulna, and both bones of the forearm compared the effect of Dexmedetomidine or Clonidine added to Levobupivacaine in axillary brachial plexus block, and the conclusion was that

Dexmedetomidine is superior to Clonidine in terms of duration of analgesia [75].

Other studies about adjuvants to peripheral nerve blocks that showed improvement in postoperative pain scores are also using dexmedetomidine [63] and the combination of Fentanyl-Lidocaine [71].

For surgically treated radius fractures, peripheral nerve blocks significantly lower postoperative pain scores, even in a study where, at the end of the surgery, the patient received local anesthetic wound infiltration with Levobupivacaine [64], [67, 68]. Interestingly, in another study on 59 patients, nerves blocked distally assured the same level of pain control compared with surgical site infiltration, when using the same local anesthetic regimen [61].

When comparing the efficacy of different local anesthetics used perineurally, a significant reduction in pain scores is reported when using liposomal bupivacaine and not plain bupivacaine[60]. When comparing peripheral nerve blocks with Levobupivacaine and Ropivacaine, the results for achieving better postoperative analgesia favor Levobupivacaine. At the same time, Ropivacaine is preferred for faster recovery of motor function [65]. Another study obtained better results with the improvement of postoperative pain scores when using the short-acting local anesthetic Mepivacaine in comparison with Ropivacaine when practicing supraclavicular brachial plexus block; it seems that patients who received Supraclavicular block with Ropivacaine had worse pain progression after the block resolved [66].

The timing of the nerve block is also essential in blocks of the upper limb; a study published in 2017 [70] showed that infraclavicular brachial plexus block practiced preoperatively significantly reduces pain scores and results in lower analgesic consumption compared with a postoperative placed block.

When comparing single with continuous brachial plexus block, a study concluded that continuous block is effective in controlling rebound pain at postoperative hours 9 and 12 [62].

Four studies reported results about some intravenously administered medication[76-79], and two articles explored adjuvant analgesia techniques [80, 81].

A study that compared intravenous with perineural administration of Magnesium concluded that magnesium is more effective in reducing pain scores in the early postoperative period as an additive to ropivacaine in supraclavicular brachial plexus block [76].

Another study on 56 patients with radius fractures found that a 6-day Methylprednisolone taper significantly improves pain relief and reduces opioid consumption in the early postoperative period [77].

3.2.2. Humeral shaft fractures

Studies about analgesia in humeral shaft fractures were scarce. In this study, only two articles about humerus fractures that respected the inclusion criteria were found and included in our descriptive analysis [82, 83].

At last, a study was found about intravenous regional anesthesia with 0.5% Lidocaine and Atracurium in patients with fractures of the phalanges and metacarpal bones, and the conclusion was that the combination results in a significant reduction of pain during surgery and the

postoperative period when compared with Lidocaine only [84].

In the end, pain evaluation in all these studies is an essential topic of discussion. It is known that there is high variability in evaluating pain in different studies [2]. There are different pain-assessing tools and timelines, and the moment of measuring pain (at rest, with movement, etc.) is variable.

It is important to note that pain assessment is challenging since pain is a subjective experience. Hence, it is essential to assess perceived pain with subjective scores. The purpose is to determine whether pain is tolerable, whether action is needed to increase analgesia, or whether the analgesic given is adequate.

In our study, pain scores were evaluated in most studies (57.14%) via the Visual Analog Scale score.

4. Future Directions and Recommendations

In our opinion, a more standardized approach is necessary to manage perioperative limb fracture pain better. It is essential to consider the benefit of analgesia via peripheral nerve blocks, but take the necessary precautions to prevent the appearance of rebound pain. The goal is not to abolish pain altogether but to maintain it under the patient's threshold of tolerability to enhance the recovery after surgery. There is a need for larger-scale randomized studies so that a perioperative pain management plan can be documented for this population, a strategy that can manage the pain intensity under the tolerability threshold, and thus lessen the need for rescue analgesia such as opioids.

5. Conclusion

Pain management in long bone fractures of the limbs is complex, with multiple ways of achieving analgesia that are still being studied and need more research. Drugs like Gabapentinoids, Magnesium sulphate, Vitamin C, Esmolol, and low-dose Ketamine have improved pain scores in some studies, but more research is needed on bigger cohorts. There is a need for multimodal analgesia, meaning different pharmacologically active drugs administered in various ways to maintain pain under the tolerability threshold. Peripheral nerve blocks are essential in obtaining low postoperative pain scores, but intravenous and oral analgesics are critical to preventing rebound pain.

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Appendix 1. Tibia Fractures

Nr. Crt.	Author, year	Type of study	No	ASA grade	Intervention	Control	Pain assessment tool	Benefits of the intervention regarding pain scores
1.	Hess-Arcelay et al., 2024 [16]	RCT	96	Not Specified (NS)	Oral acetaminophen and intravenous ketorolac	Opioid based	VAS (12,24,36, 48h after surgery)	Significant decrease in pain scores at 24h after surgery in the intervention group
2.	Abrishami et al., 2024 [5]	RCT	111	NS	Oxycodone/ Gabapentin/ Diclofenac	NS	VAS (2, 4, 6, 12, and 24 hours after surgery)	Gabapentin significantly decreased pain scores more than Oxycodone and Diclofenac at 6h after surgery
3.	Zhang et al., 2022 [12]	Retrospective observational	177	I-II	- Ultrasound-guided nerve block (sciatic, popliteal, and femoral nerve block) combined with general anesthesia	General anesthesia only/ Spinal-epidural anesthesia with nerve block/ Spinal-epidural anesthesia only	VAS (12, 24, 26h after surgery)	Significantly higher pain scores in the intervention group
4.	Kellam et al., 2022 [22]	RCT	28	NS	Perifracture deep (Morphine, Clonidine, Ketorolac) and superficial (Morphine/epinephrine) multimodal analgesia via gel foam sponges.	Placebo	VAS (immediately post-surgery, 4, 8, 12, 16, 20, and 24 h)	Significantly decreased pain scores at 4, 8, and 12 hours post-surgery in the intervention group
5	Zhao et al., 2022 [11]	RCT	128	I-II	Ultrasound-guided nerve block anesthesia using GELOGIQ E9 color Doppler ultrasound diagnosis system with ropivacaine for femoral and sciatic nerve block after induction of general anesthesia	Conventional general anesthesia	VAS at 6, 12, 24 h post-surgery.	The ultrasound-guided group had significantly lower post-surgical pain scores at 6, 12, and 24 hours after surgery.

Nr. Crt.	Author, year	Type of study	No	ASA grade	Intervention	Control	Pain assessment tool	Benefits of the intervention regarding pain scores
6.	Ferraz et al., 2021 [23]	RCT	70	NS	Listening to music for 30 minutes (15 minutes before and 15 minutes during the dressing change)	intravenous sodium dipyrone, intravenous tramadol hydrochloride and intravenous ketoprofen	NRS Before and after the patient put on headphones	Patients in the intervention group presented significantly lower pain scores.
7.	Shokri et al., 2020 [13]	RCT	107	I-II	SOFT block: femoral, obturator and sciatic nerve block with Bupivacaine	Spinal anaesthesia with bupivacaine	VAS (1, 3, 6, 12, 18, 24 hours post-surgery)	Pain scores were significantly lower in the SOFT group at 3, 6, and 12 hours after surgery.
8.	Eraghi et al., 2019 [17]	RCT	50	NS	Clonidine one hour before and after surgery/ Pregabalin administered one hour before and one hour after surgery.	NS	VAS (6, 12, 24 hours post-surgery)	At 6 h after surgery, pain scores were significantly lower in the pregabalin group than in the clonidine group, but Clonidine showed a statistically significant analgesic effect compared to pregabalin overall.
9.	Cooke et al., 2019 [14]	RCT	42	NS	Continuous infusion femoral nerve block (bupivacaine) placed before induction of general anesthesia; used in addition to IV morphine PCA pump and breakthrough medications.	-IV morphine PCA pump -breakthrough IV dilaudid, morphine, fentanyl, PO oxycodone, acetaminophen as needed and an intraoperative dose of Toradol as needed.	VAS (4, 8, 12, 24, 36, 48, and 72 hours after surgery)	No benefit, no significant difference in pain scores
10.	Pasyar et al., 2018 [24]	RCT	66	NS	Foot massage 20 hours post-surgery, performed for 10 minutes (5 minutes per leg), using sweet almond oil, including feet, legs, heels, and toes, and routine care.	The control group received routine care without the foot massage intervention.	NRS Before intervention, 30 minutes and 2 hours after intervention	Foot massage significantly reduced pain at both time intervals

Nr. Crt.	Author, year	Type of study	No	ASA grade	Intervention	Control	Pain assessment tool	Benefits of the intervention regarding pain scores
11.	Akhondzadeh et al., 2018 [4]	RCT	48	I-II	Intravenous lidocaine: bolus followed by continuous infusion terminated at the end of surgery.	Placebo	VAS (1, 2, 4, 12, 16, 20, and 24 hours after surgery)	Significantly reduced post-surgical pain scores in the intervention group
12.	Olapour et al., 2017 [18]	RCT	70	I-II	Intravenous magnesium sulfate infused starting 1 hour after sensori-motor blockade/ Intravenous sufentanil infused starting 1 hour after sensorimotor blockade.	NS	VAS (0, 1, 4, 8, 16, and 24 hours after the end of anesthesia)	Sufentanil was more effective than magnesium sulfate in reducing post-surgical pain and delaying the need for additional narcotics.
13.	Khalili et al., 2017 [19]	RCT	96	I-II	Oral gabapentin half an hour before surgery/ Intravenous paracetamol half an hour before surgery.	Placebo	VAS (2, 4, and 6 hours after operation)	Significant reduction in pain scores in both the gabapentin and paracetamol groups.
14.	Mokaram et al., 2016 [15]	RCT	210	I-II	Group N: neostigmine added to bupivacaine and fentanyl/ Group M: magnesium sulfate added to bupivacaine and fentanyl	Group F: received bupivacaine and fentanyl as intrathecal drugs for spinal anesthesia	NRS (During surgery: every 20 minutes and 6 and 12 hours after surgery)	The addition of magnesium sulfate to intrathecal bupivacaine-fentanyl significantly reduced post-surgical pain scores.
15.	Haghighi et al., 2015 [20]	RCT	82	I-II	Esmolol: Loading dose before anesthesia induction, followed by a maintenance dose until the closure of the incision.	Placebo	VAS (Entering the recovery unit, 3 and 6 hours after surgery)	Intravenous intraoperative esmolol is effective in reducing post-surgical pain.
16.	Panah Khahi et al., 2011 [21]	RCT	64	I-II	Gabapentin administered two hours before surgery	Placebo	VAS (2,12,24h after surgery)	Gabapentin significantly decreases post-surgical pain two hours after surgery.

APPENDIX 2*. Articles that studied analgesia in groups of different types of fractures of the lower limb*

Nr. Crt.	Authors	Study type	Type of fracture	No	Intervention	Control	Pain assessment	Benefit of the intervention
1.	Samra et al., 2024 [25]	RCT	Tibia and fibula	92	Dual ultrasound and nerve stimulator-guided lumbar plexus-sciatic nerve block (DUNLuPS)	Epidural anaesthesia	NRS (At admission to PACU, at 6, 12, 24 h post-surgery)	Post-surgical pain management was better with DUNLuPS.
2.	Adharsh et al., 2024 [3]	RCT	Tibial and femoral shaft	60	Pregabalin 2 hours before surgery	Placebo	VAS (at 6, 12, 24, 48 hours after surgery)	Pre-operative pregabalin significantly reduced post-surgery pain scores compared to a placebo
3.	Lantieri et al., 2023 [46]	Observational retrospective cohort study	Distal tibia and ankle fractures, including pilon fractures	723	Single-shot peripheral nerve blocks targeting the sciatic and saphenous nerves.	Patients who did not receive peripheral nerve blocks	VAS (DAY 1, 2 and 3 post surgery)	Patients who received peripheral nerve blocks showed modest reductions in opioid use and pain scores on postoperative day 1.
4.	Kwamboka et al., 2023 [28]	RCT	Tibia and fibula fractures	20	Music played for 20 minutes at a self-preferred volume level, administered once on day-3 after surgery to the intervention group	Conventional pain management therapy without music	VAS before intervention (0 minutes) and 25 minutes after conventional therapy.	- Music therapy significantly reduced pain levels in the intervention group compared to the control group
5.	Rahimzadeh et al., 2019 [27]	RCT	Tibia, fibula, and distal femur fracture	75	- Group B: Fentanyl 10 mc/kg + Nitroglycerin 500 mc, Group C: Fentanyl 10 mc/kg + Nitroglycerin 1000 mc.	Fentanyl 10mc/kg + Placebo	VAS (prior to putting the pain pump and at 4, 8, 12, 24, 48 hours post-surgery)	Patients receiving a higher dose of nitroglycerin experienced lower pain levels.
6.	Elkassabany et al.,	Prospective cohort	Tibia and ankle	93	Administration of popliteal and	Patients received only	Revised American Pain Society	Patients receiving regional

Nr. Crt.	Authors	Study type	Type of fracture	No	Intervention	Control	Pain assessment	Benefit of the intervention
	2015 [45]	study			saphenous nerve blocks	systemic analgesia	Patient Outcome Questionnaire 24h after surgery	anesthesia demonstrated better quality of recovery at 24 hours.
7.	Khalili et al., 2011 [26]	RCT	Tibia and/or fibula	79	MgSO4 plus isobaric bupivacaine administered intrathecally once as part of spinal anesthesia.	Isobaric bupivacaine combined with normal saline intrathecally	Verbal rating scale 5 minutes before injection, after the start of surgery, and every 15 minutes until surgery was completed.	- The addition of MgSO4 to bupivacaine without opioids resulted in prolonged sensory block duration and reduced post-surgery analgesic consumption without additional side effects.

APPENDIX 3. ***Femur fractures***

No.	Authors	Type of study	No	ASA status	Intervention	Control	Pain assessment	Benefits of intervention
1	Yue et al., 2023 [29]	RCT	82	NS	Post-surgery hematoma injection with ropivacaine	Standard multimodal pain regimen	VAS 0,8,16,24 h post-surgery	Reduced post-surgery pain score in the interven-tion group
2	Vinod et al., 2022 [30]	RCT	70	I-II	Ultrasound-guided femoral nerve block with Bupivacaine + Dexmedetomidine and Subarachnoid block with heavy Bupivacaine	Ultrasound-guided FNB with Bupivacaine + Normal Saline and Subarachnoid block with heavy Bupivacaine	NRS (Before and after the block, post-surgery every 2 hours until 24 hours)	The addition of Dexmedetomidine significantly increased the duration of post-surgery analgesia compared to FNB alone.
3	Makkar et al., 2019 [31]	RCT	135	I-II	Intravenous acetaminophen, diclofenac, morphine, and oral pregabalin were administered 30 minutes pre-operatively. -	The control group received intravenous saline and a placebo in the preoperative period.	VAS (Immediately upon shifting to recovery, then at 30 min, 1, 2, 4, 8, 12, 24, and 48 h)	Preemptive multimodal analgesic regimen significantly reduced the number of patient-controlled Epidural Analgesia boluses required post-surgery.
4	Memary et al., 2017 [32]	RCT	62	I-II	Dexmedetomidine is administered via a femoral nerve block	Did not receive femoral nerve block	VAS (Immediately post-surgery, and at 6, 12, and 24 hours after surgery)	Perineural administration of dexmedetomidine significantly reduced intraoperative and post-surgery narcotic consumption.
5	Pan et al, 2016 [33]	RCT	314	NS	Intravenous morphine titration: 3-mg increments every 5 minutes until VAS ≤ 3	Intravenous ibuprofen: 800 mg once after hospitalization when VAS > 7	VAS every 5 minutes after the first injection	Intravenous morphine titration provided a faster and greater reduction in pain scores compared to intravenous ibuprofen within the first hour.
6	Deng et al., 2009 [34]	RCT	200	NS	Ketamine: - Group A initial dose, then 0.1 mg/kg/h for 24 hours/ Group B initial dose, then 0.05	Group D, which received an equivalent volume of normal saline	VAS (every 4 hours for 24 hours)	VAS scores in groups A and B were significantly lower than in groups C and D

No.	Authors	Type of study	No	ASA status	Intervention	Control	Pain assessment	Benefits of intervention
					mg/kg/h for 24 hours/ Group C initial dose, then 0.01 mg/kg/h for 24 hours	only.		
7	Tondare et al., 1982 [35]	RCT	25	NS	Femoral nerve block using Labat's technique with lidocaine hydrochloride 1% and adrenaline	NS	Subjective and objective assessment of the movement of the fracture site, rotation of, and traction on the injured limb before and after giving the nerve block.	Femoral nerve block was useful for transportation and immobilization of patients with the fractured femur shaft

APPENDIX 4*. Ankle fractures*

Nr crt	Author	Type of study	N	ASA	Intervention	Control	Pain assessment	Benefits of intervention
1	Park et al., 2025 [37]	RCT	57	NS	Continuous sciatic nerve block and continuous adductor canal block (cACB)	Continuous sciatic nerve block and single-injection adductor canal block (sACB),	VRS (4, 8, 12, 24, 48, and 72 hours after surgery)	cACB provided significantly better post-surgery pain control than sACB at 12, 24, 48, and 72 hours after surgery.
2	Choi et al., 2024 [51]	RCT	70	NS	Naproxen with pregabalin (Group B), administered 2 hours before surgery and then every 12 hours for 14 days	Naproxen (Group A) administered 2 hours before surgery and then every 12 hours for 14 days	VAS (6,12,24,48,72h after surgery)	The study found comparable pain reduction between Group A and Group B
3	Lee et al., 2023 [38]	RCT	60	NS	Group B: sciatic and femoral nerve blocks with ropivacaine combined with dexamethasone disodium phosphate, epinephrine	Group A: Patient-controlled analgesia with ketorolac initiated approximately 10 hours after peripheral nerve block (PNB) induction with ropivacaine.	VAS (6, 12, 18, 24, 32, 40, 48, and 60 hours after PNB)	Pain scores were significantly lower in the group receiving peripheral nerve blocks with ropivacaine combined with dexamethasone and epinephrine compared to the group receiving PCA.
4	Samineni et al., 2022 [39]	Observational retrospective cohort study	96	NS	Popliteal sciatic nerve blocks administered either preoperatively, within 30 minutes before surgery or post-surgery, within 30 minutes of entering the PACU	No peripheral nerve block	VAS (at 0, 8, 16, 24 hours after surgery)	PNBs are associated with significantly lower VAS pain scores and lower total narcotic usage during the post-surgery period.
5	Caglar et al., 2022 [55]	Prospective, non-randomized	40	NS	WALANT technique: Mixture of lidocaine, epinephrine, and NaHCO3. Administered in three steps: haematoma block,	Peripheral nerve block technique: Mixture of bupivacaine and lidocaine in a 1:1 ratio, approximately 30 minutes before	VAS (- Intrasurgically: Every 10 minutes Post-surgically: Every hour for 5 hours)	The peripheral nerve block technique was more successful in pain management for unimalleolar fractures, with lower mean intrasurgical and

Nr crt	Author	Type of study	N	ASA	Intervention	Control	Pain assessment	Benefits of intervention
					subcutaneously, and at the fracture site.	surgery.		postsurgical VAS scores.
6	Sort et al., 2021 [40]	RCT	160	NS	Ultrasound-guided popliteal sciatic and saphenous blocks with ropivacaine.	Spinal Anaesthesia with hyperbaric bupivacaine	NRS from administration of anesthesia until 27 hours post-anesthesia	Peripheral nerve block anaesthe-sia provided a superior post-surgery pain profile com-pared to spinal anaesthesia.
7	Angthong et al., 2021 [52]	RCT	40	NS	Parecoxib before surgery and then every 12 h for the initial 48 h post-surgery	Placebo	Verbal Numerical Rating Score for pain intensity, Verbal Numerical Rating Percentage for pain relief 0, 4, 12, 24, and 48 hours after surgery	The perioperative administration of parecoxib did not significantly improve post-surgery pain control or reduce opioid requirements compared to placebo.
8.	McDonald et al., 2020 [50]	RCT	106	NS	Intravenous ketorolac intra-operatively and every 6 hours. Perioperative regional anesthesia (popliteal and saphenous nerve blocks)	Administration of opioids alone without ketorolac and peripheral nerve block	VAS POD 1-7	Ketorolac reduced pain, particularly on the first day after surgery, and had mixed effects on other post-surgery days.
9.	Li et al., 2020 [56]	Retrospective observational cohort study	89	NS	Local infiltration analgesia with ropivacaine injected into the dermis and subcutaneous tissue surrounding the incision.	Intravenous patient-controlled analgesia with morphine	VAS (Every eight hours from 8 hours to 48 hours after surgery)	Local infiltration analgesia significantly reduces early post-surgery pain
10	Lee et al., 2020 [41]	RCT	95	NS	Peripheral nerve block (PNB) for all participants; Patient-controlled analgesia (PCA) with ketorolac	PNB with no PCA	VAS (6, 12, 18, 24-, 36-, 48-, and 72-hours post-surgery)	There was a significant difference in VAS pain scores at 24 hours post-surgery between the treatment and control groups.

Nr crt	Author	Type of study	N	ASA	Intervention	Control	Pain assessment	Benefits of intervention
11	Alexander et al., 2020 [1]	Retrospective cohort observational study	302	NS	Preoperative popliteal sciatic nerve block with Ropivacaine/ Preoperative adductor canal block with Ropivacaine/ Post-surgery popliteal sciatic and adductor canal blocks	No block	NRS (Preoperatively, upon arrival to the PACU, and upon discharge from the PACU)	Patients receiving preoperative nerve blocks had significantly lower pain scores than those receiving post-surgery blocks or no blocks.
12	Park et al., 2019 [59]	RCT	63	NS	Evaporative coolants: Re-soaked compression bandage with spray coolant every 2 hours for 12 hours a day over 5 days.	Ice packs: Applied for 10 minutes, followed by a 10-minute rest period, repeated every 2 hours for 12 hours a day over 5 days.	VAS post-operative day 1-5	Evaporative coolants exhibited comparable efficacy to ice packs in reducing preoperative edema and pain in patients with ankle fractures.
13	Jain et al., 2019 [54]	RCT	60	NS	Vitamin C for 6 weeks/ Diclofenac sodium twice a day for 5 days, with additional use as needed	Placebo	VAS (Week 1, 2, 6, 3 months)	Vitamin C supplementation improved VAS scores at the second- and sixth-week follow-ups.
14	Hanacock et al., 2019 [57]	RCT	100	NS	Ropivacaine, Epinephrine, Morphine and Saline solution.	No intervention	VAS every 4h for the first 48h post-surgery	Intervention significantly reduced immediate in-hospital pain scores, but below the minimal clinically important difference
15	Davidovitch et al., 2017 [58]	RCT	84	NS	Liposomal bupivacaine and bupivacaine injecttion administered intraoperatively and injected into periosteal, peritendinous, surrounding muscles, and subcutaneous tissue	Placebo	VAS (4, 24, 48, 72 hours, and 336 hours (14 days))	Pain scores were significantly lower in the interventional group versus control at each time point assessed.

Nr crt	Author	Type of study	N	ASA	Intervention	Control	Pain assessment	Benefits of intervention
16	Ding et al., 2015 [42]	RCT	50	NS	Continuous infusion popliteal sciatic nerve block through an On Q pump (On Q group)	Single-shot popliteal sciatic nerve block	Before discharge from PACU (VAS) - 8, 12, 24, 48, and 72 hours after surgery (NRS) - 2, 6, and 12 weeks after surgery (VAS and NRS)	Pain scores were significantly lower in the On Q group at 12 hours and 2 weeks post-surgery. - Continuous infusion significantly reduced "rebound pain" .
17	Lee et al., 2014 [43]	Prospective observational study	58	NS	Double block - femoral and sciatic nerve blocks	Sciatic nerve block alone	VAS during operation, immediately after surgery, 2 hours post-surgery, 1 day post-surgery, 2 days post-surgery	The double block offers good post-surgery pain control for patients with hindfoot and ankle disease.
18	Goldstein et al., 2012 [44]	RCT	51	I-III	Popliteal block, Saphenous block. Narcotic pain medication post-surgery: intravenous Morphine via PCA pump.	The control group consists of patients who received general anesthesia without any regional anesthesia	VAS 2, 4, 8-, 12-, 24-, and 48-hours post-surgery	Popliteal blocks provided superior pain control compared to general anesthesia alone for up to eight hours post-surgery.
19	Ortiz et al., 2010 [48]	RCT	60	NS	Ketorolac orally twice daily/ Etoricoxib twice daily/ Diclofenac twice daily	NS	VAS 0, 2, 4, 8, 12, and 24 hours	All three treatments showed similar efficacy in pain reduction.
20	Norman et al., 2001 [49]	RCT	54	I-II	Intravenous ketorolac administered before tourniquet inflation	Intravenous ketorolac administered after tourniquet inflation.	VAS Preoperatively and post-surgery at 2, 4, 6, 8, 10, 12, and 24 hours after tourniquet inflation	Intravenous ketorolac has preemptive analgesic effects when administered before tourniquet inflation in ankle fracture surgery.
21	Schug et al., 1998 [53]	RCT	61	I-II	Oral acetaminophen. Morphine via PCA 72 hours or until PCA discontinuation	Placebo as an adjuvant to morphine by patient-controlled analgesia (PCA) post-surgery.	NRS Daily assessment for 72 hours or until PCA discontinuation	Patients receiving acetaminophen had lower pain scores on Day 1 compared to those receiving a placebo.

APPENDIX 5. ***Radius fracture***

Nr crt	Author	Type of study	N (i/c)	ASA	Intervention	Control	Pain assessment	Benefit of intervention
1.	Ramegowda et al., 2024 [76]	RCT	50	I-II	Ropivacaine perineurally + magnesium sulfate in 100 ml isotonic saline IV /Ropivacaine perineurally + magnesium sulfate perineurally	-	VAS 0, 4, 8, 12, 24 post-surgery	Pain scores were significantly lower in the perineurally administered Magnesium group
2.	Chan et al., 2024 [60]	RCT	80	I-III	Plain bupivacaine + liposomal bupivacaine	Plain bupivacaine	NRS - post-surgery day 0: 4, 8, and 12 hours after surgery. - Post-surgery day 1: 8:30 am, 12:00 noon, and 4:00 pm. - post-surgery days 2 to 7: Once a day	The addition of liposomal bupivacaine to standard bupivacaine in the supraclavicular brachial plexus block significantly reduced post-surgery pain scores at rest in the first 48 hours after surgery.
3.	Sciard et al., 2023 [61]	RCT	59	NS	median and radial nerves block with ropivacaine at the end of the surgery	Surgical site injection with the same drug regimen		both techniques gave comparable level of pain control during the first 48 hours after surgery
4.	Lee et al., 2023 [62]	RCT	66	NS	Single Infra-clavicular brachial plexus block for all groups/ IV PCA group: Fentanyl citrate IV PCA with doses based on body/ Continuous block group: Continuous infraclavicular BPB with ropivacaine.	BPB only group	VAS 4, 6, 9-, 12-, 24-, and 48-hours post-surgery, as well as two weeks after the operation	Continuous infraclavicular BPB did not reduce total opioid consumption compared to BPB only but was effective in controlling rebound pain at 9 and 12 hours after surgery
5	Ahmed et al., 2022 [63]	RCT	40	I-II	Dexmedetomidine: 1ug/kg (Group-B only)	Group-A received only Bupivacaine	VAS Immediately after recovery post-extubation and at the first demand of rescue analgesia	The visual analogue scores for pain were comparable immediately post-extubation but significantly lower in the Dexmedetomidine group at the time of first rescue

Nr crt	Author	Type of study	N (i/c)	ASA	Intervention	Control	Pain assessment	Benefit of intervention
								analgesia.
6.	Zangrilli et al., 2022 [8]	RCT	43	NS	Preop.: Supraclavicular brachial plexus block+ Pregabalin+ celecoxib+ Acetaminophen Post-surgery day 1-3: Pregabalin and Celecoxib daily, Acetaminophen every 6 hours, Oxycodone every 4-6 hours PRN breakthrough pain POD 4 until 6 weeks: Acetaminophen every 6 hours PRN pain Oxycodone every 4-6 hours PRN breakthrough pain	Preop.: upper extremity block Post-surgery: Acetaminophen as needed and Oxycodone q4-6 hours PRN break through pain	Vas preoperatively and post-surgery on post-surgery day 1 and 3, and at weeks 1, 2, and 6.	A multimodal pain control regimen used for patients undergoing elective outpatient wrist fracture surgery showed similar pain control compared to conventional methods. A rebound narcotic requirement was noted after the multimodal protocol was discontinued.
7.	Nho et al., 2022 [64]	RCT	72	I-II	Ultrasound-guided axillary block with ropivacaine, lidocaine and dexamethasone	General anesthesia	VAS scores at 2, 4, 6, 12, and 24 h after surgery	BPB resulted in lower pain scores at all time points up to 24 hours post-surgery.
8.	Gottschalk et al., 2022 [77]	RCT	56	NS	Intravenous dexamethasone at the time of surgery and oral methylprednisolone taper.	Received intravenous dexamethasone at the time of surgery.	VAS recorded three times a day (morning, afternoon, and evening) for the first 7 days post-surgery.	Methylprednisolone significantly improved pain relief and reduced opioid consumption
9.	Shahid et al., 2021 [65]	RCT	56	I-II	Group R: Ropivacaine administered under ultrasound guidance/ Group L: Levobupivacaine administered under ultrasound guidance. -	-	VAS scores were recorded every 5 minutes for the first 30 minutes after block administration, and then every hour until the score reached 4.	Levobupivacaine had a faster onset of sensory and motor blocks compared to ropivacaine. - Levobupivacaine provided a longer duration of analgesia compared to ropivacaine.
10.	Sellbrant et al., 2021 [66]	RCT	90	I-III	Supraclavicular block with	General anesthesia	NRS before surgery, 2, 24,	The mepivacaine group had

Nr crt	Author	Type of study	N (i/c)	ASA	Intervention	Control	Pain assessment	Benefit of intervention
					mepivacaine/ Supraclavicular block with ropivacaine		48, 72 hours after surgery, and at block resolution	significantly lower post-surgery pain scores and opioid consumption compared to the ropivacaine group.
11	Wong et al., 2020 [67]	RCT	52	I-III	Infraclavicular nerve block with local anesthetic solution lignocaine with 1:200,000 adrenaline and ropivacaine. Sedation with propofol infusion during surgery Post-surgery: Regular oral paracetamol every 6 h for 3 days or until discharge	General anesthesia plus local anesthetic wound infiltration with levibupivacaine	NRS upon arrival to PACU, 1 hour, 2 hours, 24 hours, 48 hours, and at 3 and 6 months after surgery	Regional anesthesia significantly reduced post-surgery pain scores at rest and with movement compared to general anesthesia.
12	Moradkhani et al., 2020 [78]	RCT	64	I-II	Propofol and Ketamine administered as a bolus, with additional doses given as needed until complete immobility was achieved. – Sufentanil administered as needed.	Received only propofol	VAS at the time of block and every 5 minutes during surgery until the end of the operation.	The combination of ketamine and propofol did not significantly differ from propofol alone in terms of pain, nausea, vomiting, hallucinations, and patient satisfaction.
13	Jung et al., 2020 [72]	RCT	101	NS	Surgical-site multimodal drug injection with ropivacaine, morphine sulphate, ceftezole, and normal saline solution, admin-istered to periosteal area and pronator quadratus muscle, and to subcutane-ous area and skin.	Patients who did not receive a local multimodal drug injection	VAS 1 hour before surgery and at 4, 8, 24, and 48 hours after surgery.	Patients who received a surgical-site multimodal analgesic injection after palmar plating for distal radius fractures had no clinically important reduction in pain scores.
14	Johnson et al., 2020 [68]		80		PNB	GA		Patients in the nerve block only group showed a statistically significant decrease in pain at discharge

Nr crt	Author	Type of study	N (i/c)	ASA	Intervention	Control	Pain assessment	Benefit of intervention
15	Akhondzadeh et al., 2019 [71]	RCT	60	I-II	- Group F: lidocaine 1% and fentanyl - Group K: lidocaine 1% and ketamine	-	VAS at 15 minutes, 30 minutes, 1, 2, 3, 4, 5, 6, 9, 12 and 24 hours after the block	Fentanyl-lidocaine resulted in significantly lower pain intensity and opioid consumption compared to ketamine-lidocaine.
16	Ganta et al., 2018 [69]	RCT	50	NS	Continuous infusion through an OnQ pump: 0.2% ropivacaine for 48 hours (OnQ group).	Single-shot infraclavicular block: 20mL of 2% lidocaine with 1:200,000 epinephrine plus 20mL of 0.5% bupivacaine with 1:300,000 epinephrine (SSB group).	VAS 8, 12-, 24-, 48-, and 72-hours post-surgery	- The OnQ pump did not provide statistically improved post-surgery pain control compared to a single nerve block for distal radius fractures.
17	Holmberg et al., 2017 [70]	RCT	52	I-II	Preoperative Ultrasound-guided infraclavicular brachial plexus block with ropivacaine 0.75%	Post-surgery block	NRS 30 min, 1 h, 2 h, 4 h, 8 h, and 24 h after surgery.	The preoperative block significantly reduced pain scores and resulted in lower analgesic consumption at one-week post-surgery.
18	Alter et al., 2017 [73]	RCT	41	NS	Liposomal Bupivacaine (Exparel) before incision.	Plain bupivacaine	NRS POD 0-5	Exparel resulted in significantly lower pain levels and fewer opioid pills consumed on the day of surgery compared to Marcaine.
19	Nazari et al., 2017 [80]	RCT	82	NS	Inhaled aromatherapy with pure essential oil of lemon: 2 drops per non-absorbent cloth pinned to the collar for 30 minutes; dose based on 1 drop per 20 kg body weight; applied before surgery and at 8- and 16-hours post-surgery.	Received routine care services	VAS before surgery and at 8 and 16 hours after surgery	Inhaled aromatherapy reduced pain in patients undergoing orthopedic surgery for distal radius fractures. - The recovery rate was higher in the treatment group compared to the control group, indicating a faster recovery from pain.

Nr crt	Author	Type of study	N (i/c)	ASA	Intervention	Control	Pain assessment	Benefit of intervention
20	Lee et al., 2015 [81]	RCT	36	NS	- TENS: 50 Hz, 15 min/day, continuously for 5 days	Sham TENS group, where the method was identical to that of the real TENS group but no electrical stimulus was applied.	VAS Before TENS (pre-TENS period) and 5 minutes after completion of TENS (post-TENS period) - Frequency: Every day for 5 days after surgical treatment	The VAS scores did not differ significantly between real and sham TENS groups before treatment, but were lower in the real TENS group post-treatment. - TENS reduced post-surgery pain in the immediate post-treatment period.
21	Chung et al., 2010 [74]	RCT	44	NS	Perifracture site injections with a local anesthetic mixture consisting of ropivacaine, morphine, and epinephrine	Intravenous PCA alone after axillary nerve block	VAS 4 hours, 8 hours, 24 hours, and 48 hours after surgery	Perifracture site injections did not provide additional pain control benefits.
22	Abbasivash et al., 2009 [79]	RCT	46	I-II	IVRA with 200 µg NTG and lidocaine diluted in saline.	lidocaine diluted with saline	VAS Before tourniquet deflation - At 5, 10, 15, 20, 25, and 30 minutes after tourniquet deflation - At 30 minutes and 2, 4-, 6-, 12-, and 24-hours post-surgery	The addition of NTG to lidocaine in IVRA improved the onset and duration of sensory and motor blocks, enhancing anesthesia quality. - NTG reduced tourniquet pain and decreased the need for intraoperative and post-surgery analgesics.

APPENDIX 6. *Upper limb*

Nr crt	Author, year	Type of fracture	Type of study	N	Intervention	Control	Pain assessment	Benefit of intervention
1	Kumar et al., 2021 [75]	Fractures of the radius, fractures of the ulna, and both bone fractures of the forearm	RCT	80	Ultrasound-guided axillary brachial plexus block with Levobupivacaine and Dexmedetomidine.	Ultrasound-guided axillary brachial plexus block with Levobupivacaine and Clonidine.	VAS every 30 minutes	Dexmedetomidine provided a longer duration of sensory and motor blocks than Clonidine.
2	Kumar et al., 2014 [82]	Fractured shaft of humerus - Fractures of radius and ulna	RCT	30	Pre-operative stellate ganglion block with lidocaine under ultrasound guidance at the C7 vertebra level. General anesthesia	Received 3 ml of 0.9% saline during ultrasound-guided stellate ganglion block. General anesthesia	VAS 0, 2, 4, 6, 8, 12, and 24 hours after surgery	There were significant differences in pain visual analogue scale scores at rest between the lidocaine and saline groups at certain time points.
3	Bedi et al., 2017 [83]	Lower end of humerus	RCT	93	Clonidine added to 0.5% bupivacaine for brachial plexus block/ Clonidine administered intravenously.	Bupivacaine with 2 ml of NS in the block and 10 ml of NS intravenously as placebo.	VAS at 1, 6, 12, and 24 hours after the procedure.	Addition of clonidine to bupivacaine in brachial plexus blocks results in longer post-surgery pain relief compared to bupivacaine alone.
4.	Elhakim et al., 1994 [84]	Fractures of the phalanges and metacarpal bones of the hand	RCT	40	IVRA -lidocaine with 2 mg atracurium (given to one group of patients)	Received lidocaine	VAS during surgery, immediately after tourniquet deflation, 5 minutes after deflation, 15 minutes after deflation	There was a significant decrease in pain during surgery and after surgery in the intervention group.