

HIRSLANDEN
ANAESTHESIA
SYMPOSIUM
2024



HIRSLANDEN
ANAESTHESIA SYMPOSIUM

Managing Rebound Pain in Regional Anaesthesia

*Pr P. Lavand'homme
Anesthesiology Department
Acute Postoperative and Transitional Pain Service*



Cliniques universitaires
SAINT-LUC
UCL BRUXELLES





HIRSLANDEN
ANAESTHESIA SYMPOSIUM

No conflict of interest
to declare



Status quo of pain-related patient-reported outcomes and perioperative pain management in 10,415 patients from 10 countries: Analysis of registry data

Eur J Pain 2022

Approximately half of patients reported worst pain intensities $\geq 7/10$ NRS and about a quarter spent over half of the first day after surgery in severe pain. Up to a third of patients reported that pain interfered considerably with activities in and out of bed and with their emotional well-being. Side-effects, such as nausea and drowsiness,

- What about the patients who have received a loco-regional anesthesia technique? (spinal anesthesia, plexus block)
- Most of these patients are ambulatory patients

Rebound Pain concerns a distinct population of patients

Loewenstein et al, AAHS 2022

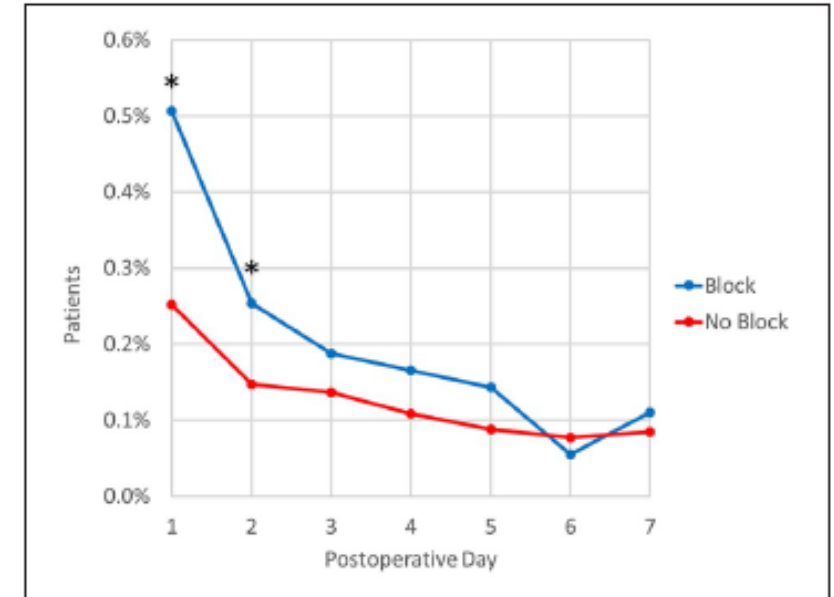
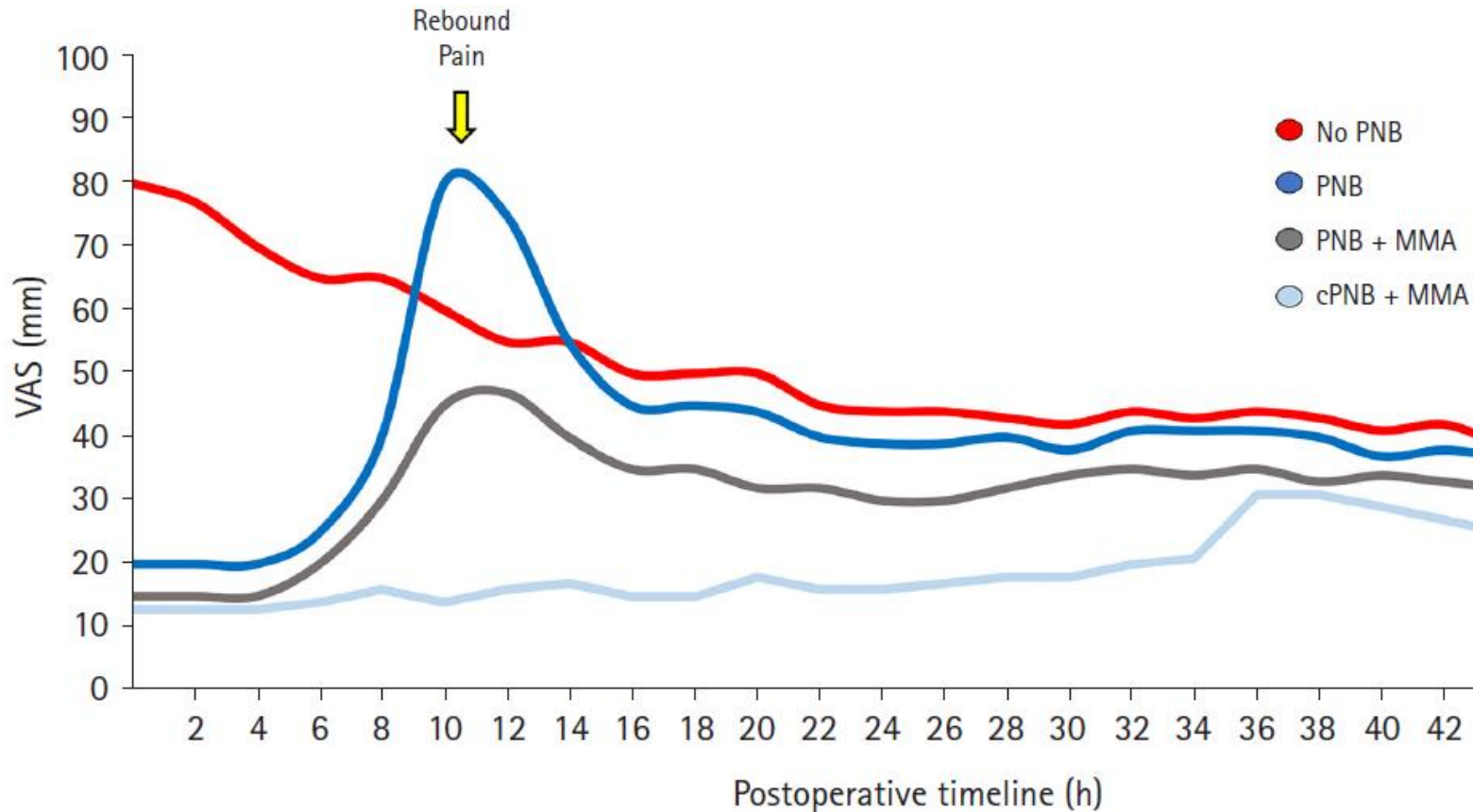


Figure 1. Daily emergency department visits after any upper extremity procedure.
*Statistically significant.

Munoz-Leyva et al, KJA 2020

Rebound pain: distinct pain phenomenon or non entity? Hamilton D. BJA 2021

Rebound pain: Undesired, yet unexplored

Bhatia & Metta, J Anaesthesiol Clin Pharmacol 2022

reversal in pain levels may be related to the phenomenon of “rebound pain,” a poorly described entity that is commonly defined as a dramatic increase in pain once single-injection regional anesthesia has dissipated [18, 20]. Different regions of the body have been shown to experience rebound pain after regional anesthesia at different times, modulated by increasing the length of analgesic efficacy

Rebound Pain

- Is **disproportionated** to the degree of noxious stimulus secondary to surgical incision and to the pain score patient would have had in the absence of a PNB despite the administration of usual multimodal analgesia

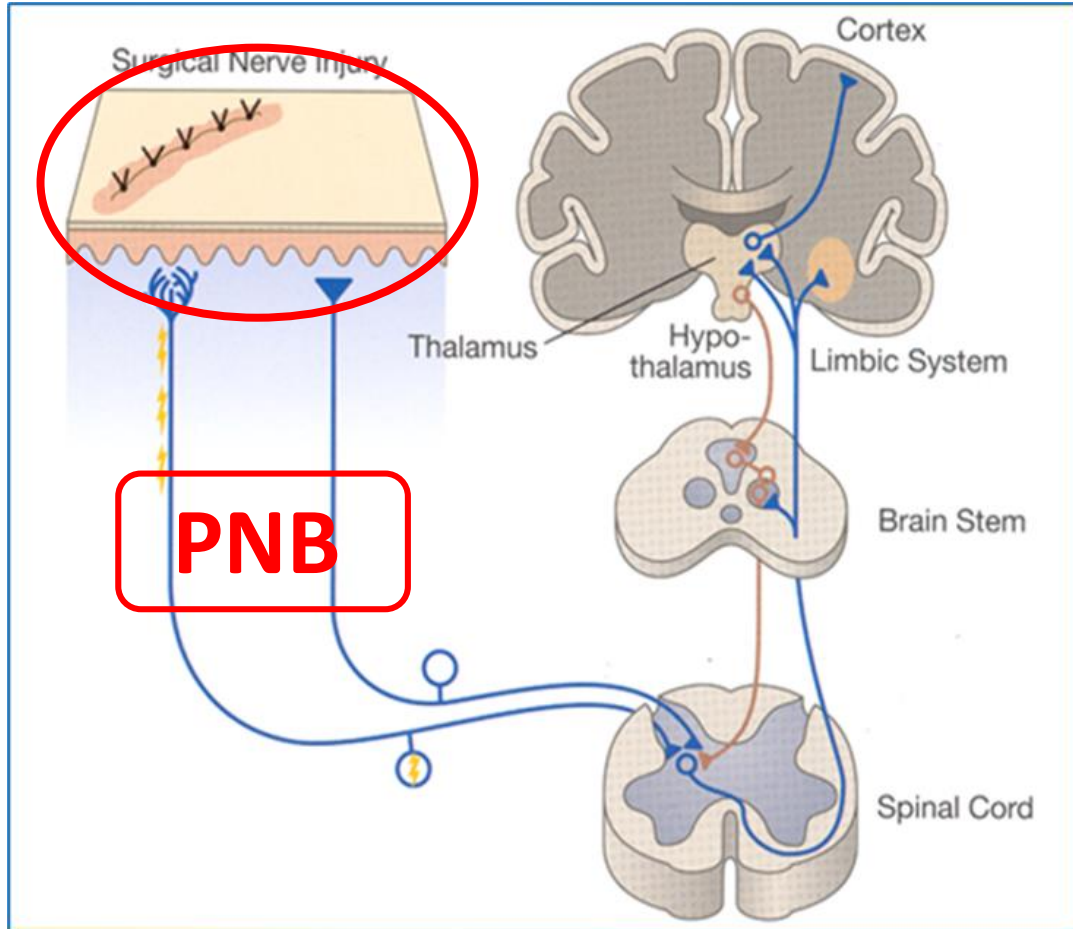
- NRS \geq 7/10
- Within the first 12-24h after PNB initiation; duration 3-6 h

- Considered as a « complication of RA » associated to
 - patient's dissatisfaction (Hade et al, Anaesth Intensive Care 2021)
 - Unplanned health care resources utilisation (Galos et al, CORR 2016; Loewenstein et al, AAHS 2022)
 - Persistent pain?

Incidence reported: up to 40 %! Sometimes higher!

(Barry et al, BJA 2021; Hade et al, Anaesth Intens Care 2021; Holmberg et al, Anaesthesia 2020; Touil et al, BJA 2022)

Mechanisms of Rebound Pain

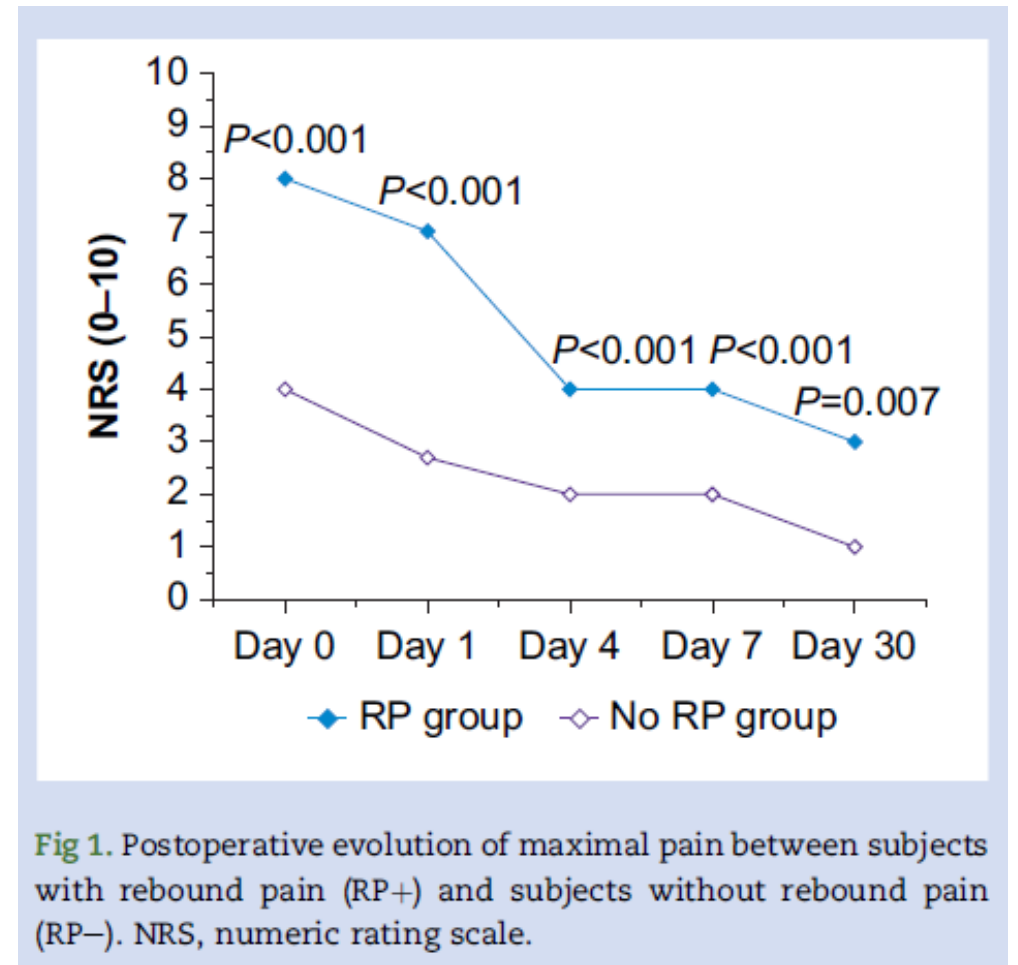


- Peripheral nerve block facilitates acute inflammatory responses induced by the surgical incision in mice (Yamada et al, RAPM 2016)
 - Local infiltration macrophages and neutrophils
 - Increased local release TNF, PGE2...
- Central mechanisms promote increased postoperative pain
 - Central sensitization
 - Emotional reaction (catastrophization)

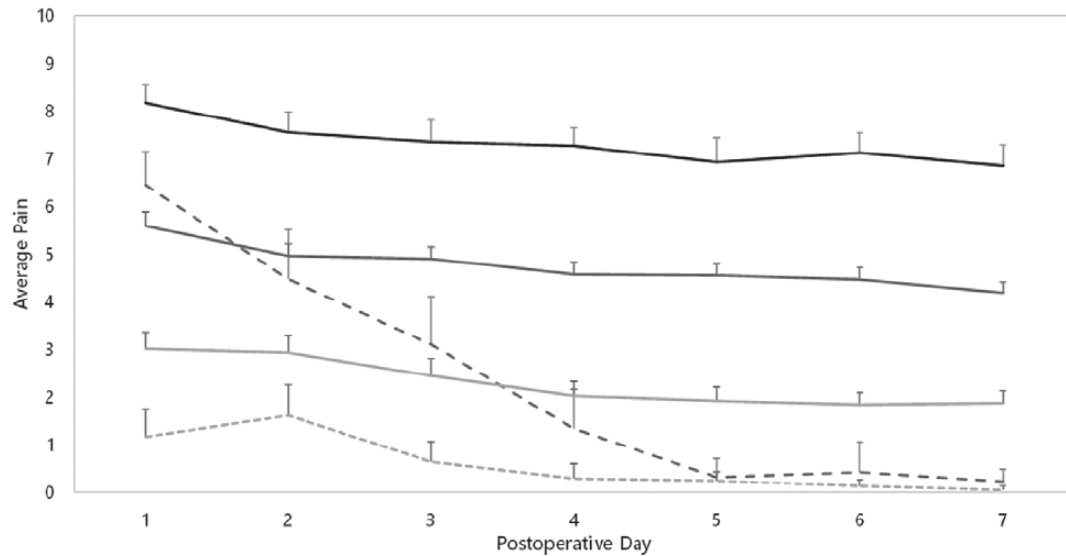
Risk factors

- Younger age
- Female sex
- Bone surgery (>< soft tissues)
- Catastrophization
- Severe preoperative pain (at mobilisation)

- *association of RP with higher perioperative pain trajectory – association with chronic pain??*



Patient and procedural determinants of postoperative pain trajectories: importance to have personalised medicine



Group-based pain trajectories for first 7 days after surgery. Error bars indicate 95% CIs.

Vasilopoulos et al,
Anesthesiology 2021

Conclusions: There are multiple distinct acute postoperative pain intensity trajectories, with 63% of patients reporting stable and sustained high or moderate-to-high pain over the first 7 days after surgery. These postoperative pain trajectories were predominantly defined by patient factors and not surgical factors.

RP prevention (1): Education

- Postoperative pain management still a problem
(particularly in ambulatory patients)
- Target high risk patients → Education
 - To explain RP could occur when PNB dissipates
 - To ensure patients will receive AND will use correctly the prescribed multimodal postoperative analgesic treatment



RP prevention (2): specific strategy using PNB continuous infusion

- *To smooth PNB dissipation and to allow more time for the inflammatory reaction to vanish*
- *Use of continuous femoral block reduces RP intensity in ACL surgery: 33h additional nerve block duration necessary to reduce RP score (by 1 unit) (Williams et al, RAPM 2007)*
- *ISB in rotator cuff repair surgery with continuous infusion for 48h in some patients (Salviz et al, Anesth Analg 2013)*

% patients with NRS > 7/10

	Day 1	Day 2	Day 3	Day 7
Continuous ISB (n=20)	15	10	20	5
Single Shot ISB (n=23)	78	35	22	13
General Anesthesia (n=20)	40	35	25	21

Liposomal bupivacaine?

- Adductor canal block for total knee arthroplasty: LB 10 mL with bupivacaine 0,25% 10 mL versus 20 mL bupivacaine 0,5%
- No difference

(Quaye et al, Arthroplasty 2024)

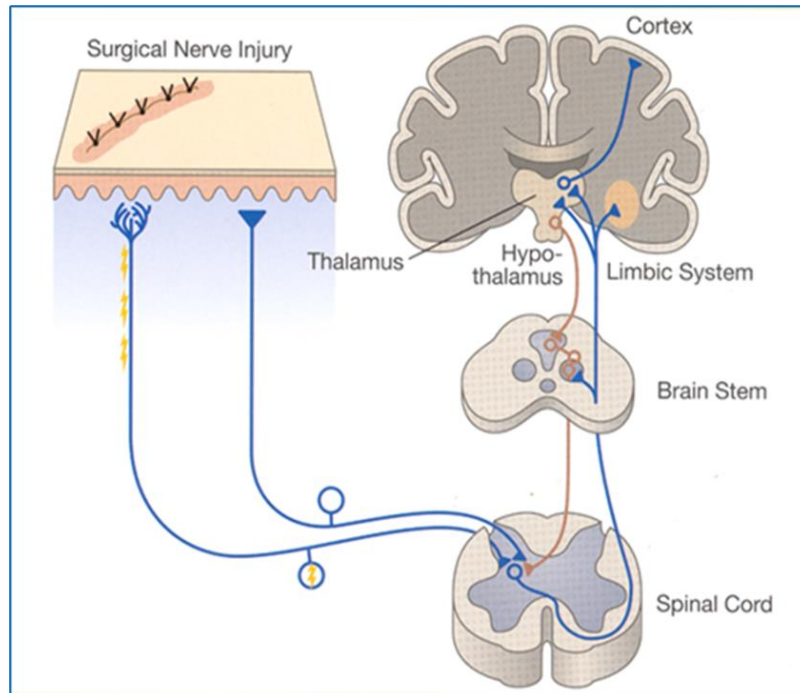
Variable ^a	Bupivacaine type used in adductor canal block (treatment arm)		P-value
	Liposomal	Conventional	
Pain scores over time			
PACU			
N	40	40	
Average pain score	0 [0–3.1]	0 [0–2.0]	0.94 ^b
Maximum pain score	0 [0–6.5]	0 [0–4.0]	0.94 ^b
POD-0			
N	40	40	
Average pain score	3.2 [2.5–4.4]	3.9 [2.6–4.8]	0.36 ^b
Maximum pain score	6 [5–7]	7 [5.1–8]	0.25 ^b
POD-1			
N	36	35	
Average pain score	4.5 [3.0–5.7]	5 [3.6–6.0]	0.43 ^b
Maximum pain score	6.7 [4–7]	7 [5–7.5]	0.61 ^b
POD-2			
N	34	34	
Average pain score	4 [1.9–5.8]	4.2 [3.0–5.6]	0.54 ^b
Maximum pain score	4.5 [2–7]	5.5 [4–7]	0.27 ^b

RP prevention (3): specific strategies using drugs

Intraoperative IV Ketamine (BJA 2022)

Evaluation of intraoperative ketamine on the prevention of severe rebound pain upon cessation of peripheral nerve block: a prospective randomised, double-blind, placebo-controlled study

Nassim Touil^{1,*}, Athanasia Pavlopoulou¹, Olivier Barbier², Xavier Libouton² and Patricia Lavand'homme¹

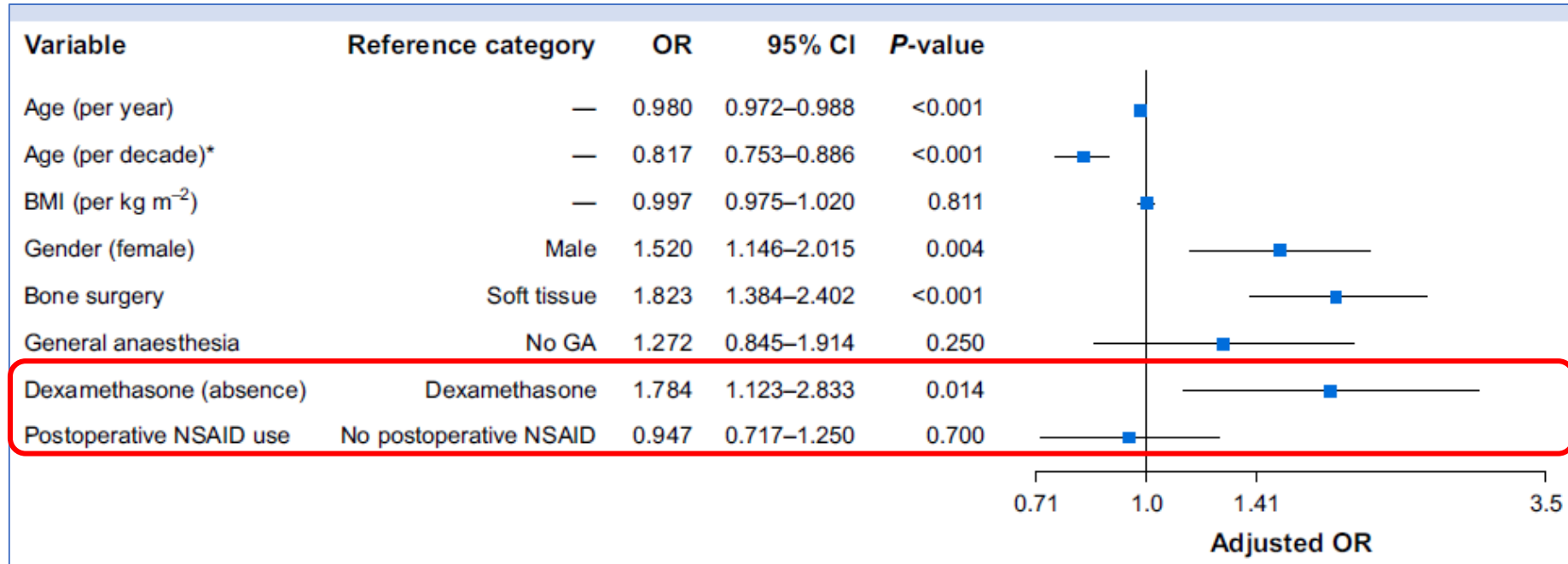


- No benefit of IV Ketamine at antihyperalgesic dose 0,3mg/kg vs placebo: 33% vs 47% (p=0,438)
- Even in patients with positive Temporal Summation and positive Central Sensitisation Index (CSI questionnaire)
- Similar findings in
 - retrospective study of Barry et al (BJA 2021)
 - Prospective study of Zhu et al (Clin Ther 2020) using 40 mg KET IV

RP prevention (3): specific strategies using drugs

Interooperative Dexamethasone: Intravenous DEXA

- Retrospective study (N=972) (Barry et al, BJA 2021)
- DEXA 4-20 mg IV



- Retrospective study (N=173) (Touil et al, J Clin Med 2023)
- DEXA 4-10 mg IV (anti-emetic dose) No clear DEXA dose dependent effect
- 23% RP vs 47% RP in placebo group (p=0,002)

Analgesic effect of intravenous dexamethasone after volar plate surgery for distal radius fracture with brachial plexus block anaesthesia: a prospective, double-blind randomised clinical trial*

Holmberg et al, Anaesthesia 2020

	DEXA IV 16 mg (n = 23)	Placebo (n = 24)	P value
Rebound pain (NRS > 7)	2 (9%)	12 (50%)	0,002
Severe pain (NRS 4 – 7)	16 (70%)	22 (92%)	0,072
Block duration (h)	21,5 (13 – 24)	12,7 (7 – 27)	< 0,001
Pain at 12 months	8 (38%)	13 (54%)	0,186

- At 6 months and 1 year, patients with chronic pain at the surgery site report higher pain intensity in the placebo group vs DEXA group

The Effects of Intravenous Dexamethasone on Rebound Pain After Nerve Block in Patients with Ankle Fracture: A Randomized Controlled Trial

Gao et al, J Pain Res 2022

- DEXA 10 mg IV (n=65) versus placebo (n=65)
- Adductor canal block + popliteal sciatic block combined to GA
- At day 1: ↓ systemic pro-inflammatory cytokines (TNF- α , IL-6, IL-1 β) in IV dexa group

	Group C	Group IV	P-value
Incidence of rebound pain, n (%)	28 (44%)	10 (15%)	<0.001 ^a
Median onset of rebound pain since nerve block resolution, min*	12 (5–30)	30 (12–67)	0.101 ^b
Mean duration of rebound pain, hours*	3.3±1.1	3.6±1.1	0.627 ^c
Duration of sensor block, hours	16 (14–18)	24 (22.5–27.5)	<0.001 ^b

The effects of dexamethasone added to ilioinguinal/iliohypogastric nerve (IIN/IHN) block on rebound pain in inguinal hernia surgery: a randomized controlled trial

- Ilio-inguinal and Ilio-hypogastric block +/- IV dexamethasone 5 mg

	Dexamethasone (<i>n</i> = 30)	Control (<i>n</i> = 30)	<i>P</i> values
Incidence of rebound pain (rest)			0.001
No	28.00 (93.33%)	17.00 (56.67%)	
Yes	2.00 (6.67%)	13.00 (43.33%)	
Incidence of rebound pain (motion)			< 0.001
No	28.00 (93.33%)	15.00 (50.00%)	
Yes	2.00 (6.67%)	15.00 (50.00%)	
Rebound pain time (rest)	12.00 ± 0.0	10.15 ± 2.08	0.25
Rebound pain time (motion)	12.00 ± 0.0	10.40 ± 2.03	0.30

Perineural DEXA (3,3 to 8 mg) also reduces RP Benefit/risk ratio?

**Dexamethasone added to levobupivacaine
prolongs the duration of interscalene brachial
plexus block and decreases rebound pain after
arthroscopic rotator cuff repair**

Morita et al, J Shoulder
Elbow Surg 2020

The effect of perineural dexamethasone on
rebound pain after ropivacaine single-
injection nerve block: a randomized
controlled trial

DEXA 8 mg vs placebo
Fang et al, BMC
Anesthesiol 2021

Other PNB adjuvants like α 2-adrenergic agonists:

- Clonidine: does not seem to prevent RP
- Dexmedetomidine: no study available

Intravenous Versus Perineural Dexamethasone for Reducing Rebound Pain After Interscalene Brachial Plexus Block: A Randomized Controlled Trial

Lee et al, J Korean Med Sci 2023

Dexamethasone dose = 5 mg

Variables	Perineural group (n = 36)	Intravenous group (n = 35)	P value
Incidence of rebound pain	16 (44.4)	7 (20.0)	0.028
Difference in the pain scores between before and after ISB resolution, NRS	4.9 ± 2.1	4.0 ± 1.7	0.043
Time to the first analgesic request, hours	19.9 (17.2–23.1)	15.1 (13.7–15.9)	< 0.001

Among patients experiencing rebound pain

	Perineural group (n = 16)	Intravenous group (n = 7)	P value
Rebound pain score, NRS	7.3 ± 0.6	7.1 ± 0.4	0.424
Onset of rebound pain			
Since performing ISB, hr	18.6 (17.2–19.3)	14.7 (14.2–16.5)	< 0.001
Since ISB resolution, min	13.0 (2.3–77.8)	82.0 (31.0–110.0)	0.135
Duration of rebound pain, hours	3.1 ± 1.2	3.4 ± 0.4	0.339
Time to the first analgesic request, hours	17.2 (16.8–18.8)	13.9 (12.8–15.5)	0.001

Conclusion



HIRSLANDEN
ANAESTHESIA SYMPOSIUM

Rebound pain after PNB is not a rare phenomenon (incidence up to 40%)

→ Could be considered as a complication of RA

Mechanisms still remain poorly understood

Risk factors have been pointed

→ Importance to **target high risk patients (education)**

Intraoperative **preventive strategies** should be considered

→ Best preventive treatment today: **intravenous DEXAMETHASONE** (ideal dose?)
perineural dexamethasone (toxicity?)