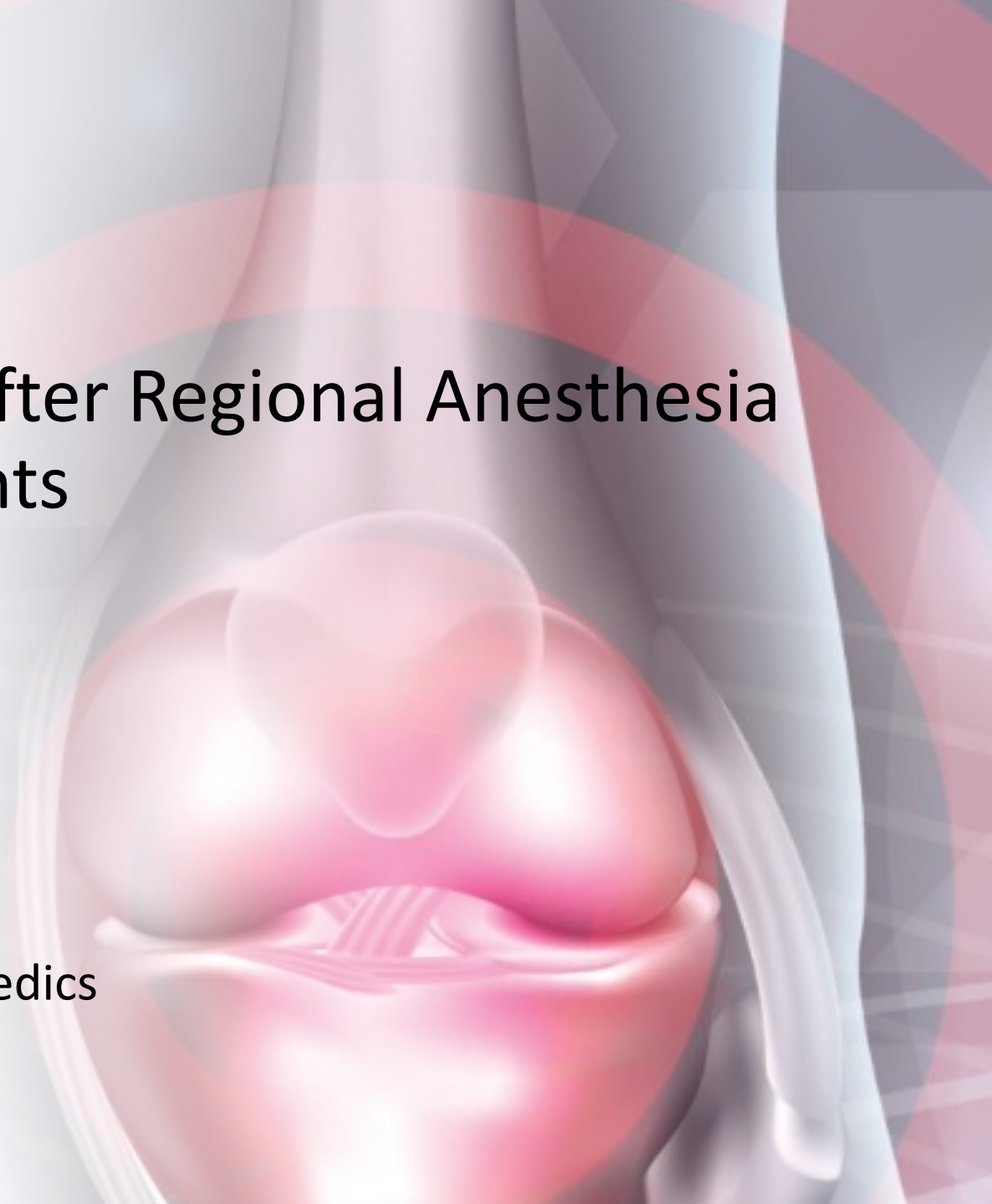
Ropivacaine Pharmacokinetics after Regional Anesthesia in Total Knee Arthroplasty Patients



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Analgesia approaches in Total Knee Arthroplasty
or
Anaesthetists vs Surgeons

	Femoral nerve block	**Local infiltration analgesia**
Early ambulation	✗	✓
Pain control	✓	✓
Induction time	✗	✓
Ease	✗	✓
Material costs	✗	✓
Risk of LAST	?	?
Dose	Weight based	Uniform

Local anaesthetic systemic toxicity
Rare?

1.8 per 1000 in peripheral nerve blocks

0.7 per 1000 in local infiltration analgesia

Mörwald EE, Zubizarreta N, Cozowicz C, Poeran J, Memtsoudis SG. Incidence of Local Anesthetic Systemic Toxicity in Orthopedic Patients Receiving Peripheral Nerve Blocks. Reg Anesth Pain Med. 2017 Jul/Aug;42(4):442-445.

Mitchell K, Cai E, Miller B*, et al* Local anesthetic systemic toxicity from local infiltration anesthesia in total joint arthroplasty: a single center retrospective study *Regional Anesthesia & Pain Medicine* Published Online First: 24 August 2023

How dangerous is the site of injection?

Classic

- Intravenous
- Intercostal
- Epidural/ caudal
- Peripheral nerve blocks
- Subcutaneous/infiltration

Gitman M, Barrington MJ. Local Anesthetic Systemic Toxicity: A Review of Recent Case Reports and Registries. Reg Anesth Pain Med. 2018 Feb;43(2):124-130

How dangerous is the site of injection?

Classic	**Modern**
Intravenous	Penile
Intercostal	Local tissue infiltration 17%
Epidural/ caudal	Epidural/caudal
Peripheral nerve blocks	Peripheral nerve blocks 8.5%
Subcutaneous/infiltration	TAP block

Gitman M, Barrington MJ. Local Anesthetic Systemic Toxicity: A Review of Recent Case Reports and Registries. Reg Anesth Pain Med. 2018 Feb;43(2):124-130

Prevention of Local Anesthetic Toxicity

Use	Calculate	Monitor
a less toxic local anesthetic	safe doses	for toxicity
ROPIVACAINE	WEIGHT BASED CALCULATIONS	MONITOR FOR PRODROMAL SYMPTOMS

Prevention of Local Anesthetic Toxicity

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ROPIVACAINE	WEIGHT BASED CALCULATIONS	MONITOR FOR PRODROMAL SYMPTOMS
ACCOUNTS FOR 21% OF LAST	NO RELATION BETWEEN WEIGHT AND PLASMA CONCENTRATIONS	25% HAVE ONLY CVS TOXICITY

	Conc.		Volume	Dose
	mg/mL	(%)	mL	mg
SURGICAL ANESTHESIA				
Lumbar Epidural	5	(0.5%)	15 to 30	75 to 150
Administration				113 to 188
Surgery				150 to 200
Lumbar Epidural				100 to 150
Administration	7.5	(0.75%)	15 to 20	113 to 150
Cesarean Section				
Thoracic Epidural	5	(0.5%)	5 to 15	25 to 75
Administration	7.5	(0.75%)	5 to 15	38 to 113
Surgery				
Major Nerve Block[†]	5	(0.5%)	35 to 50	175 to 250
(e.g., brachial plexus block)	7.5	(0.75%)	10 to 40	75 to 300
Field Block	5	(0.5%)	1 to 40	5 to 200
(e.g., minor nerve blocks and infiltration)				

300 mg or 3 mg/kg

Safety Reports on High-Dose Ropivacaine

300 mg

A randomized study comparing plasma concentration of ropivacaine after local infiltration analgesia and femoral block in primary total knee arthroplasty

Fatin Affas, Carl-Olav Stiller ✉, Eva-Britt Nygårds, Niclas Stephanson, Per Wretenberg and Christina Olofsson

800 mg

Population pharmacokinetics of ropivacaine used for local infiltration anaesthesia during primary total unilateral and simultaneous bilateral knee arthroplasty

Kirill Gromov † ✉ • Stanislas Grassin-Delyle † • Nicolai B. Foss • ... Anders Troelsen • Saik Urien † • Henrik Husted † • Show all authors • Show footnotes

400 mg

Pharmacokinetics of 400 mg ropivacaine after periarticular local infiltration analgesia for total knee arthroplasty

M. G. E. Fenten[1,2], S. M. K. Bakker[1], D. J. Touw[3], B. J. F. van den Bemt[4,5,6], G. J. Scheffer[2], P. J. C. Heesterbeek[7] and R. Stienstra[1]

Systemic Ropivacaine Concentrations Following Local Infiltration Analgesia and Femoral Nerve Block in Older Patients Undergoing Total Knee Arthroplasty

Kazune S, Nurka I, Zolmanis M, Paulausks A, Bandere D

Local and Regional Anesthesia 2023, 16:143-151

Published Date: **15 September 2023**

a pragmatic observational pharmacokinetic trial in ASA II-III patients

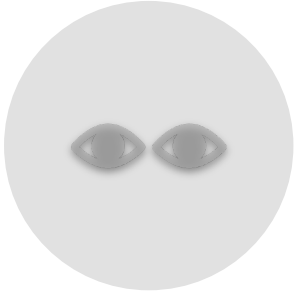
Using 225 mg bolus dose of ropivacaine for three blocks: femoral nerve block, local infiltration analgesia with and without adrenaline

to characterize total blood levels of ropivacaine with venous draws and construct a pharmacokinetic model

Questions

Is the fixed 225 mg dose safe (C_{max})?

Best block (C_{max}, exposure)?



How long do you need to monitor the patient (T_{max})?

What factors influence plasma ropivacaine levels (type of block, weight, age)?

Surgery performed under spinal anesthesia (15 mg plain bupivacaine, 3 mL, 5 mg/mL)

Midazolam administered for sedation if requested

Standard procedure with cemented posterior stabilized prosthesis and medial parapatellar approach

Tourniquet used; no wound drains left post-operation

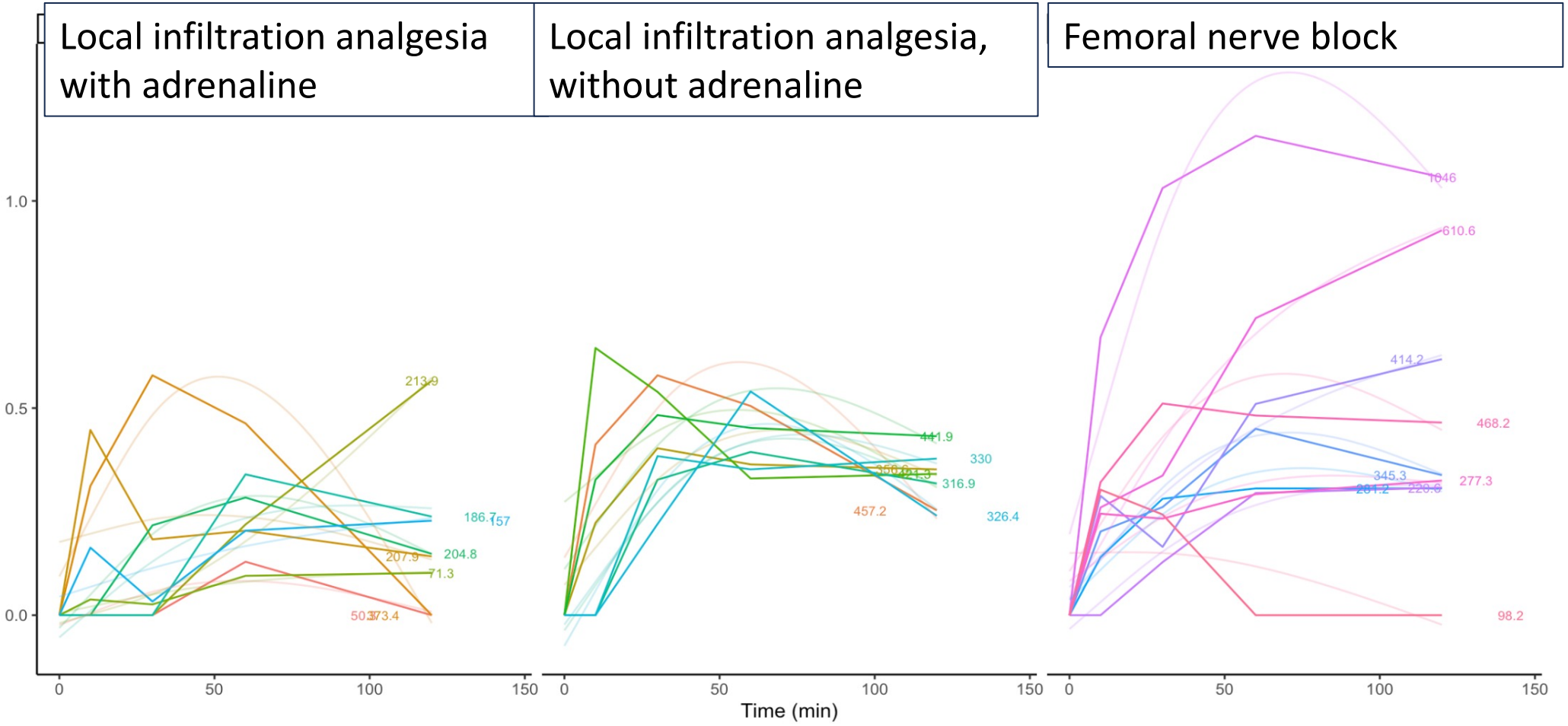
For Femoral Nerve Block Group:	**30 mL of 7.5 mg /mL ropivacaine (225 mg total dose)** End of injection marked as time zero (T0)
For Local Infiltration Analgesia Groups:	Sequential injections: 20 mL subcutaneously, 50 mL into posterior capsule, 80 mL around collateral ligaments **Group A received 225 mg ropivacaine (0.15%; 150 mL) with adrenaline 5 µg/ mL** **Group B received 225 mg ropivacaine (0.15%; 150 mL)** Tourniquet deflation marked as time zero (T0)

Patient demographics

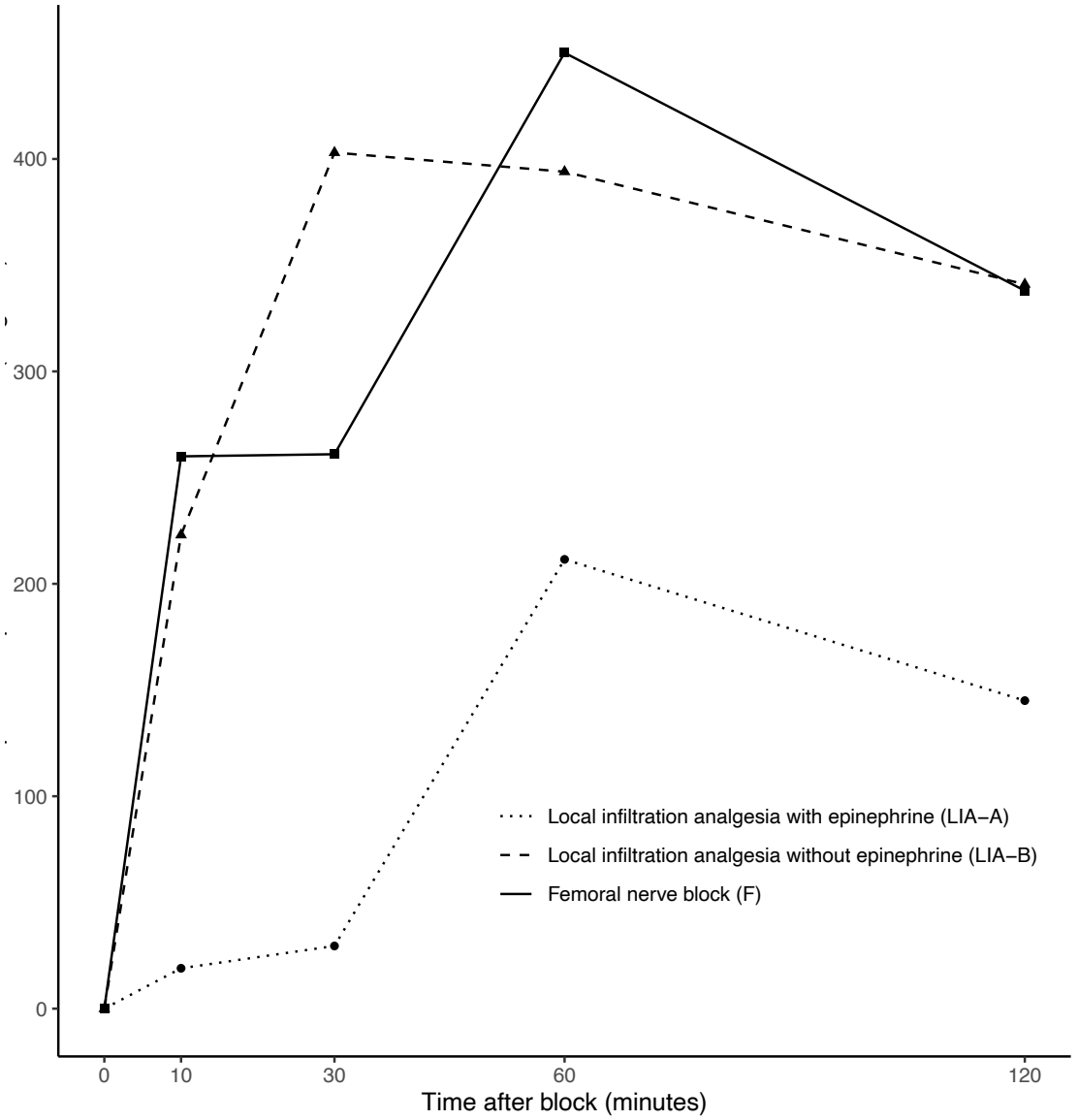
	Infiltration Analgesia with Epinephrine (N = 8)	Infiltration Analgesia Without Epinephrine (N = 7)	Femoral Nerve Block (N = 9)	Total (N = 24)	p value
Age (years)	76 (7.1)	73.4 (4.5)	76.4 (5.5)	75.4 (5.7)	0.56
Female (n (%))	6 (75.0%)	7 (100.0%)	8 (88.9%)	21 (87.5%)	0.34
Weight (kg)	82.9 (17.5)	88.6 (14.4)	79.2 (14.9)	83.2 (15.5)	0.51
Height (m)	1.7 (0.1)	1.6 (0.1)	1.6 (1.6, 1.7)	1.6 (0.1)	0.14
BMI (kg/m^2)	30.1 (6.6)	35.1 (4.9)	30.3 (4.4)	31.6 (5.6)	0.16

Individual patient plasma concentrations

Threshold plasma ropivacaine concentration for toxicity is 2.2 mcg/mL



There was a significant difference in plasma ropivacaine concentrations between groups at 30, 60 and 120 minutes with group LIA-A having significantly lower concentrations than either group LIA-B (p = 0.01) or group F (p = 0.002).



The mean individual peak plasma concentrations of total ropivacaine in groups LIA-A, LIA-B and FNB were 0.334 (95% CI 0.181–0.488), 0.490 (95% CI 0.395–0.584) and 0.545 (95% CI 0.309–0.782) µg mL $^{-1}$ (p = 0.16).

The mean time to reach the maximum plasma concentration (t_{max}) was **36** minutes (95% CI 20–52) for group LIA-B, which was significantly shorter compared to **73** minutes (95% CI 37–108) for group LIA-A and **78** minutes (95% CI 45–111) for group FNB (p = 0.03)

Patient characteristics

Age showed a moderate positive correlation:

- Peak plasma concentration of ropivacaine (R = 0.37, p = 0.08)
- Time taken to reach peak concentration (R = 0.33, p = 0.12)

No correlation with weight

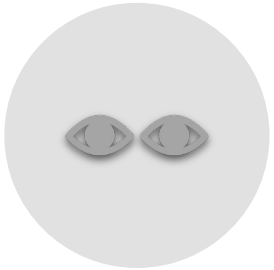
Conclusions

Is the fixed 225 mg dose safe (C_{max})?

YES

Best block (C_{max}, absorption within 120 minutes)?

Local infiltration analgesia with adrenaline



How long do you need to monitor the patient (T_{max})?

AT LEAST 75 minutes after tourniquet release

What factors influence plasma ropivacaine levels (type of block, weight, age)?

Patients over 75 need dose reduction