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## Optimizing the analgesic effect of peripheral nerve blocks in the search for solutions to chosen shortcomings in regional anesthesia

## ABSTRACT

Regional anesthesia (RA) is currently seen as a technique of anesthesia that provides optimal postoperative analgesia. Its effectiveness and safety depend on the availability of adequately trained practitioners and the proper qualification of patients. RA is being implemented into the anesthetic practice in growing numbers of versatile surgical procedures, and its proven benefits over solitary general anesthesia have placed RA into postoperative standards of patient care. Respectable international and national anesthesia, as well as pain societies, are incorporating nerve blocks in their recommendations and guidelines as they become everyday tools for the practicing clinician.

The immense boom of regional anesthesia techniques is in part due to the introduction of ultrasound imaging into clinical practice which allows for the visualization of anatomical spaces, and nerves as well as aids in guidance of the needle trajectory and drug deposition. Ultrasound guidance has opened a vast array of novel or rediscovered regional blocks. In recent years, a new subset of ultrasound-guided RA techniques known as fascial plane blocks has evolved with the aim of injecting adequately large volumes of local anesthetics (LA) within fascial planes to block peripheral nerve branches found within the fascia or for the LA to spread along the body planes to reach paravertebral spaces. The increased number of possible nerve blocks and adjuvants in clinical practice allows for the personalization and optimization of anesthesia.

The effect of individual central or peripheral nerve blocks may limit a fast patient recovery to full activity and disrupt the course of convalescence, which goes against present perioperative recovery pathways. Such issues, in combination with the increasing complexity of RA techniques, lead to new challenges facing the anesthesia provider, including: introduction of motor-sparing peripheral nerve blocks, presence of rebound pain following the passage of the sensory block, optimal choice of the regional block technique, and safe use of RA in day-case surgery. To answer some of these debates, one must perform well designed randomized clinical trials to gain scientific ground before introducing changes to everyday clinical practice.

The common objective of this thesis was the search for the most optimal use of peripheral nerve blocks to overcome select shortcomings in three distinct surgical scenarios. The samples for the studies were chosen among patients undergoing surgery with predicted severe postoperative pain. The common interventions were modifications of peripheral nerve blocks that were compared to other RA modalities and in one study to a placebo. To assess the efficacy and safety of the regional blocks, the measured outcomes were assessments of postoperative pain control such as perioperative opioid consumption, opioid-related side effects, pain levels assessed by standardized scores, and time to first analgesic request.

In the first published manuscript (VI.1), we reported a randomized trial conducted in two university-affiliated tertiary care hospitals on a total of 101 adult patients scheduled for cadaveric renal transplantation. Study participants were allocated to either receive a Quadratus Lumborum Block type 2 (QLB) posterior to the quadratus lumborum muscle or a Transversus Abdominis Plane Block (TAPB) as part of the standardized anesthesia and care pathway. The study's main goal was to assess whether a unilateral QLB would be superior in reducing postoperative cumulative 24-hour opioid consumption when compared with a unilateral TAPB as the potential sensory coverage of the QLB is wider and may include alleviation of visceral pain. The study showed a statistically significant reduction in fentanyl use in the postoperative period, but no clinically significant benefits in pain intensity scores, incidence of opioid side effects or patient satisfaction levels.

In the second publication (VI.2), a total of 52 patients undergoing primary total knee arthroplasty (TKA) under spinal anesthesia were randomized into two groups. In the first group, participants received an additional 100 micrograms of intrathecal morphine (ITM) as part of standard spinal anesthesia, whereas in the second group, directly following a spinal block, they received a single shot distal femoral triangle block of the femoral nerve (SSFNB). The study aimed to compare the analgesic effect of these interventions with a special focus on possible opioid-related side effects. Our trial demonstrated equipotent analgesia and pain scores of both interventions, but with a statistically higher incidence of opioid-related side effects in the ITM group such as pruritus, nausea, and 2 patients in the ITM group required administration of naloxone due to respiratory depression, thus making ITM a suboptimal choice for day-case TKA.

In the third published randomized controlled trial (VI.3), we focused on intramuscular tramadol as an adjuvant for popliteal sciatic nerve block in patients undergoing paingenerating intramedullary calcaneal fracture fixation. The primary hypothesis was, that a 100 milligram of tramadol administered intramuscularly at the time of a popliteal block would extend the analgesic effect at least by 1.5 times covering night hours and protecting against severe rebound pain. The study results did not show a clinically meaningful sensory block extension or an opioid-sparing effect of tramadol for calcaneal fracture fixation.

In summary, the choice of the most suitable and optimal RA technique is still debated and requires further research. The three papers included in this dissertation help broaden our knowledge of the potential possibilities and effects of using different RA techniques in the chosen surgical procedures.