Study Protocol

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Title

Surgical treatment of proximal femoral fractures under peripheral regional anesthesia. A prospective pilot study.

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Study protocol (Summary)

Title

Surgical treatment of proximal femoral fractures under peripheral regional anesthesia. A prospective pilot study.

Introduction

Older multimorbid patients with hip fractures are a growing patient population due to demographic developments in western industrial nations. Hospital mortality increases with anesthesia risk and ranges from less than 1% (ASA (American Society of Anesthesiologists) Physical Status 1) to 50% (ASA PP 5). This presents the team with a number of challenges when patients are at high risk of anesthesia (ASA PP 3-4, associated hospital mortality 5-20%).

Surgical treatment can be performed under general or spinal anesthesia. Additional peripheral nerve blocks contribute to perioperative pain therapy.

The aim of the study is to demonstrate that the surgical treatment of proximal femoral fractures is possible using a peripheral regional anesthesia procedure.

Both spinal and general anesthesia can contribute to side effects such as postoperative delirium or circulatory instability. We postulate that these side effects occur less frequently when the procedure is performed under peripheral regional anesthesia.

We perform a double injection technique (dual-guidance concept: ultrasound and nerve stimulation). The first injection targets the sacral plexus under the piriformis muscle.

A second injection targets the lumbar plexus: psoas-compartment-block (segments L2-L4) and transmuscular quadratus-lumborum block (segments Th12-L1).

Study design

single-center, prospective

Study goal

anesthetic quality

Health economic goals

We expect the study results to improve the safety of multimorbid elderly patients undergoing hip fracture surgery.

Interventions

Intervention A	20ml ropivacaine 0.375% (parasacral sciatic nerve block)
Intervention B	20ml ropivacaine 0.375% (psoas-compartment block)
Intervention C	20ml ropivacaine 0.375% (transmuscular quadratus-lumborum block)
Intervention D	Supplemental analgesic (sufentanil) and/or sedative (propofol) medication

Patient population

Adult men and women undergoing surgical treatment of proximal femoral fractures.

Study center

HELIOS Medical Center Schwerin, Germany

Schedule

12-18 months

1. Introduction

Both general and spinal anaesthesia are established anaesthesia procedures for the surgical treatment of proximal femoral fractures. Additional peripheral nerve blockades are performed with the aim of perioperative analgesia.

2. Primary and secondary outcome parameters

With the present prospective study design, we examine whether the surgical treatment of proximal femoral fractures exclusively under peripheral regional anesthesia (blockade of the lumbosacral plexus) is a reliable anesthesia procedure.
The main objective is to determine the frequency of necessary supplementation by analgesics/sedatives (criterion 1) or the conversion rate (criterion 2) to general anaesthesia (infra- or supraglottic airway). Side effects (e.g. delirium and pneumonia rates), hospital length of stay and hospital mortality are recorded.

3. Study design

This is a single-center prospective study.

4. Schedule

The estimated recruitment schedule is approximately 12-18 months.

5. Patient population

5.1. Inclusion criteria

The following inclusion criteria must be met :

- Surgical treatment of proximal femoral fractures
- Age over 18 years
- Written informed consent

5.2. Exclusion criteria

Patients who meet one or more of the following criteria may not be included in the trial:

- local and systemic signs of inflammation
- known allergy to used local anaesthetics
- Participation in other studies

- Obesity from grade 2 (BMI>35)
- periprosthetic fractures- known persistent drug, drug or alcohol abuse

5.3. Co-morbidities

Preexisting co-morbidities are documented in the patient record.

5.4. Co-medication

All medications that are given in addition to the study medication are considered concomitant and are documented in the patient record (especially medications that have an inhibitory effect on the coagulation system).

6. Study protocol

6.1. Recruitment

The patients are recruited in the context of anesthesiological preparation. Patients who have confirmed their participation in the exam by written informed consent will first be clinically evaluated. If the patient meets all inclusion and no exclusion criteria, the patient is enrolled in the study.

6.2. Allocation of the study medication

After admission to the study, each patient receives a patient number, which is noted on the Case Report Form (CRF).

6.3. Monitoring and preoperative preparation

Patients are initially treated in the context of normal preoperative preparation. This includes the installation of a peripheral-venous access with connection of 1000ml balanced electrolyte solution. After connection of an oxygen nasal probe (2 l/min oxygen) and administration of 5-10 µg Sufentanil the patients are placed on the non-fractured side.

The following parameters are monitored until complete postoperative recovery:

- Blood pressure (NIBP) discontinuous
- ECG continuous
- SaO2 continuous

The parameters are documented in the anesthesia protocol. The minimum/maximum blood pressure and the need for circulatory drugs are recorded in the Patient Documentation Form.

6.4. Interventions

The ultrasound-guided regional anesthesia is performed by two experienced anesthetists. We use a Sonosite (EDGE) ultrasound device with convex transducer (C60 2-5MHz) and a Pajunk 21G-100mm Sonoplex needle in in-plane technique. At the same time, the needle position is confirmed by nerve stimulation (dual guidance concept). For this purpose we use a Stimuplex HNS12 from Braun, Melsungen, Germany (frequency 2Hz, pulse width 0.1ms, stimulation limit <1mA).
Double injection technique with three (1a-c) target structures. (Resulting Anaesthesia level Th12-S3)

Intervention 1a	20ml Ropivacaine 0.375%. Parasacral ischiadicus block (18) Segments L4-S3
Intervention 1b	20ml Ropivacaine 0.375% Psoas compartment block (16) Segments L2-L4
Intervention 1c	20ml Ropivacaine 0.375% transmuscular quadratus-lumborum block (20) Segments T12-L1

6.5. Follow-up

Patients are initially cared for in the postoperative anesthesia care-unit (PACU). Depending on the clinical condition of the patients, further care is provided either at the normal ward or on an intensive care unit. For all study patients, a daily clinical visit is made until discharge.

6.7. Health economic assessment

Peripheral regional anesthesia expands the spectrum of possible anesthesia procedures for proximal femoral fractures. The procedure can contribute to the reduction of perioperative complications, especially in cases where there is a high risk of anesthesia.

7. Adverse events

7.1. Adverse events due to the local anesthetic

Allergic reaction

Allergic reactions are very rare in amide-type topical anesthetics and are mostly due to the methylparaben preservative contained in larger packs (e.g., 50ml bottles).

Local toxicity

There are no major studies on local-toxic effects of prilocaine or ropivacaine. Possible would be a disturbance of the periaxonal milieu or the nervous blood supply (compartment effect of the local anesthetic depot). Neurological complications occurred after hyperbaric lidocaine was continuously administered intrathecally with 7.5% glucose. Similar observations were not made for peripheral nerve blocks.

Systemic toxicity

Systemic toxicity occurs at high plasma levels by intravascular injection or absolute or relative overdose with rapid resorption of the local anesthetic from the site of action.

The cerebral tendency to seizure is increased by the local anesthetic effect on inhibitory cortical centers. With or without preconvulsive warning signs (numbness of the tongue and perioral, metal taste, slurred speech, ear blades, blurred vision, restlessness), generalized convulsions occur. With rising plasma levels, coma and respiratory paralysis can occur.

Inhibition of intracellular ATP production and blockade of sodium channels (vasal, cardiac, sympathetic) results in hypotension and variable cardiac arrhythmias (bradycardia to asystole, ventricular arrhythmias to ventricular fibrillation).

7.2. Adverse events due to the peripheral nerve block

Nerve lesions may be due to needle trauma (vascular or nerve lesion) or as a result of improper positioning on the operating table. In addition, side effects may occur as a result of the stress situation: vagally mediated bradycardias (syncope) or anxiety episodes with hypertonic and/or tachycardic circulatory conditions.

7.3. Evaluation of adverse events

Ropivacaine is a drug approved for peripheral nerve blocks that we use within the maximum permitted dose and indication. All occurring complications are documented and the likelihood of the causal relationship with the regional anesthesia procedure is stated. Since this is a standard regional anaesthesia procedure, it can not be expected that previously unknown complications will occur.

7.4. Information to the ethics committee

In accordance with the GCP Regulation, any severe adverse event (SAE) or unexpected (SUSAR) adverse event occurring during the trial that could affect the safety of the subjects or the conduct of the trial will be reported to the relevant local ethics committee. The report is issued by the principal investigator.

Non-serious adverse events are documented in the Patient Documentation Sheet (CRF)

8. Dropout of patients

The non-intervention-related reasons for a drop-out include in particular the withdrawal of the patient's consent and the subsequent disclosure of exclusion criteria (e.g. participation in another clinical trial).

Drop-outs caused by the study intervention are e.g. severe cardiovascular complications (cardiac arrest, shock, threatening arrhythmias) due to the systemic toxicity of the local anaesthetic.

If necessary, regional anesthesia is supplemented by the administration of analgesics and sedatives or general anesthesia is performed. The time and dose of the narcotics are documented and the procedure is performed as planned without the patient being excluded from the study.

9. Statistical Analysis

The statistical test methods are described in the statistical analysis plan.

10. Data management

The investigator is responsible for the correct and complete entry of patient data into the case report form (CRF). A patient number (see 6.2.) is assigned to each patient on the CFR. The CRF is kept for 15 years. Any publication of data is anonymous.
The patient will be informed by the investigator about the valid privacy policy. The patient will receive a copy of the privacy policy signed by the patient with place and date. The original is deposited in the study file.

11. Ethical, legal and administrative aspects

The investigator ensures that the test is performed in accordance with existing laws and regulations (ICH and GCP Guidelines, AMG). The study protocol and patient information are submitted to the Ethics Committee of the University of Rostock.
Before starting the study, each patient must give written consent to the investigator, having previously been fully informed in an understandable manner about the nature, significance and scope of the clinical trial. The content of this information is documented on the consent form. The patient will be given a copy of the signed consent form. The original is deposited in the study file.

12. Publication

The aim is to publish the results of the study in a scientific journal.

13. Sponsorship and conflict of interest

The investigators declare no conflicts of interest.

14. Amendments

Any change to the study protocol will be substantiated and documented. The changes are considered part of the study protocol.

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16. Responsibilities

Ronald Seidel, MD	Principal investigator
Eduard Barbakow, MD	Investigator

17. Attachements

Attachement 1	Informed Consent Form
Attachement 2	Case Report Form