Educational and Clinical Aspects of Peripheral Nerve Blockade

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Chapter 1

General introduction

Historical technical developments in peripheral nerve blockades

During the times of progress in medicine, the discoveries of new techniques and pharmacological developments of the vibrant 19th century, it was Sir Francis Rynd who performed the first documented nerve block with morphine in 1845.[1] Alexander Wood followed this example with better equipment, consisting of a syringe and a needle, to inject morphine close to the nerve in 1855. In the same period, cocaine, derived from the leaves of Erythroxylon coca, was introduced into clinical practice for its systemic effects.[2] Karl Koller, a Viennese ophthalmologist, searched for agents with local insensibility capacities for eye surgery, and by chance he found the ideal agent. A small sample of cocaine, given by his friend Freud, numbed his tongue. Experiments with cocaine followed successfully, after which Koller instilled cocaine to the eye of patients for local anesthesia prior to eye surgery. The preliminary results of Koller's clinical trial with cocaine were presented during a meeting of ophthalmologists in Heidelberg (1884). In the same year William S. Halsted, a surgeon in New York, experimented with cocaine after reading Koller's report and performed the first axillary nerve block by injecting cocaine under direct vision near the nerves. Later, other local anesthetics were developed, because of the addictive and toxic side effects of cocaine. Hirshel (1911) and Kuhlenkampff (1928) refined the techniques to a percutaneous axillary block of the brachial plexus.[3] These pioneers gave rise to the development of a plethora of unprecedented approaches and new nerve block techniques, often associated with incomplete anesthesia and unexpected failures or complications.

In contrast to general anesthesia, the use of peripheral nerve blocks in regional anesthesia became less popular due to the moderate success rates. The site of needle insertion was defined upon the basis of external anatomical landmarks, and eliciting paresthesia of the nerve with the needle subsequently localized the nerve. Although Perthes had already described the technique of electrical nerve stimulation in 1912, it took half a century before an electrical stimulator suitable for clinical application in localizing a nerve was available.[4] Using this method, corresponding motor contractions are elicited by electrical stimulation when the needle is advanced into the vicinity of the nerve or neural plexus. The current of the

nerve stimulator should be reduced to the threshold at which minimal motor responses are still observed. The quantity of the threshold would be proportional to the distance between the needle tip and the nerve according to the law of Coulomb. A minimum of 0.3-0.5 mA was advised as a safe and effective threshold. Standard needles were soon replaced by specially designed needles with an isolated shaft and blunt tip. This method was believed to contribute to patient safety by reducing the risk of nerve damage, which, however, has never been proved.

Although the axillary block was the most commonly used technique for anesthesia of the upper limb, even with guidance by an electrical nerve stimulator the success rates were still around 80-90%.[5,6] On basis of anatomical studies, incomplete anesthetic blocks were attributed to uneven spread of local anesthetics as a consequence of variable presence of interneural fascial septa.[7,8] In 2002, a percutaneous variant of the invasive nerve stimulation technique was developed. This technique was used for pre-locating the nerves by indenting the skin with an electrical stimulation pen to elicit accompanying motor and sensory responses.[9] The stimulation pen was believed to assist in determining the optimal puncture site for superficial nerve blocks. After evaluation of the value of the electrical stimulation pen in a volunteer study this technique proved to be unreliable.

At the same time, high resolution ultrasonography was introduced that almost revolutionized the field of regional anesthesia. Now pre-location of the nerve was possible by direct visualization of the nerve using ultrasound imaging. The first study of ultrasound-guided supraclavicular nerve block of the brachial plexus was published by Kapral in 1994.[10] Earlier, Ting and Sivagnanaratham reported the use of ultrasonography just to identify the axillary artery for surrounding it with local anesthetics as a new kind of nerve block technique of the brachial plexus.[11] From this time on use of ultrasound guided peripheral nerve blocks accelerated rapidly. Ongoing technological advancements in ultrasound equipment such as higher frequency and high resolution, together with other technical innovations in software made the performance of ultrasound-guided nerve blocks increasingly more accessible. Many advantages of ultrasonography-guidance have been found, such as shortened performance and onset time, improved quality of the block, and the ability to reduce the minimum effective volume of local anesthetic required.[12-15] Possibly, reduction of volumes of local anesthetics ends in adverse shortening of the duration of action. Ultrasound might support in optimizing patient's position for applying a specific peripheral nerve block. Adjusting the arm position prior to the performance of an axillary brachial plexus block could change ultrasonic visibility and locations of nerves.

However, the value of nerve stimulation remains evident, and this technique is often used in combination with ultrasound to identify the nerves with more safety and reliability. Nerve stimulation provides functional information to the inexperienced user of ultrasonography in addition to the ultrasonography images of the targeted nerves.

Education

The training of peripheral nerve blocks has always been a point of discussion, and has been a shortcoming in many educational programms.[16-18] Up to now, no academic center in the Netherlands has a residency program containing a well-defined curriculum for ultrasound-guided regional anesthesia. Inadequate exposure to these techniques during training results in a lack of confidence and competence. Current training methods are still based on 'trial and error', which implies acquiring skills through practice in patients under supervision. This process conflicts with ambitions of providing consistently high levels of patient safety and comfort.

The introduction of high-resolution ultrasound to regional anesthesia asks for new skills that must be trained by the anesthesiologist. Anesthesiologists have never used before real-time imaging techniques or ultrasound. For example, the use of ultrasound reveals the immense importance of a thorough knowledge of anatomy. In addition to classical systematic anatomy a more topographic anatomy is required and knowledge of sono-anatomy, which means that the appearance of different tissues on an ultrasound image has to be identified for interpreting the internal anatomical structures. The mastering of new skills requires appropriate training strategies that include the use of ultrasound equipment, handling of the ultrasound probe, identification of sono-anatomy and improved hand-eye coordination to enable advancement of the needle tip to close proximity of the target nerve whilst avoiding surrounding vital structures. There is a growing interest in new training methods, such as simulation training systems for the tuition of unknown techniques to novices. Current learning methods involving 'trial and error' techniques in patients are increasingly regarded as unethical. Therefore, the need for sufficient suitable simulation facilities increases.

Clinical developments

Since the 1990's, renewed interests in the clinical application of peripheral nerve blockades have accompanied technical developments. Peripheral nerve blockades were no longer considered as an alternative intraoperative anesthesia technique, but

were increasingly used for improved postoperative analgesia by continuous infusion of local anesthetics instead of single injections. The first provisional catheter technique for continuous administration of local anesthetics was performed by Ansbro long time ago (1946).[19] This unstable construction, consisting of a blunt needle to a rubber tube and a piece of cork with adhesive stripping for fixation, was not worth following. Years later the technique was adjusted by percutaneous insertion of an intravenous catheter adjacent to the plexus.[20] Later on, special nerve catheter sets for continuous infusion were developed by pharmaceutical and medical companies and became widely available.
Continuous nerve block techniques offer more site specific pain therapy with fewer side effects and fewer serious complications compared to systemic opioids and epidural analgesia in the management of postoperative pain for patients undergoing surgery of their limbs.[21, 22] Still, general anesthesia followed by postoperative intravenous opioid patient-controlled-analgesia is more widely accepted by surgeons, anesthesiologists and patients and is less dependent on specific technical skills. However, patients suffer from more side effects such as nausea, vomiting, headache, dizziness and fatigue, resulting in prolonged recovery times and significant discomfort. Epidural anesthesia offers excellent postoperative analgesia, but its use is becoming increasingly restricted, mainly due to safety concerns regarding perioperative anticoagulation and the risk of serious neuraxial complications.[23, 24] In addition, the potential side effects of epidural analgesia such as bilateral motor blockade, bradycardia, hypotension and urinary retention might limit postoperative convalescence and mobilization. A faster recovery and improved pain control with fewer side effects after regional anesthesia compared to systemic and epidural analgesia can be of great advantage in the well-being of patients, especially in the elderly. Thus, the anesthetic management of patients requiring major orthopedic surgery favors a peripheral nerve block as main part of a multimodal postoperative analgesia package.
Another reason of growing interest of peripheral nerve blocks is in the field of chronic pain. Persistent surgical pain is recognized as a major health problem.[25] Unrelieved severe postoperative pain is one of the most important predictors for the development of chronic surgical pain.[26] The prevalence of persistent knee pain following total knee arthroplasty has been reported to occur from 5% to as many as 44% of patients.[27] Use of regional anesthesia for postoperative pain relief may reduce the risk of chronic surgical pain. In this context, more attention is paid for use of peripheral nerve blocks in treatment of severe pain following total knee arthroplasty.

An additional reason for interest in peripheral nerve blocks is related to health economics. In recent years there has been an extensive search for the best methods of postoperative analgesia management for reaching a discharge condition of the patient much faster. Savings in hospital stay are urgently needed in the light of cost explosion in health care inflicted by advances in medical technology and demographic changes of an aging population. Notably, the increasingly large number of older patients undergoing total knee replacement asks for increased use of methods supporting an accelerated recovery.[28-31] Hence, peripheral nerve blocks play an important role in the postoperative pain management and functional outcome of patients undergoing total knee arthroplasty and are one of the fundamental elements of a successful pathway for shortened hospital stay in the respective patient population.

Aims of this thesis

The aim of this thesis was to elucidate important clinical and educational aspects of peripheral nerve blockades, especially ultrasound-guided regional anesthesia (UGRA).

The following questions were answered in the course of this investigation:

– How to learn a new technique? What methods are available to learn ultrasound-guided regional anesthesia? (Chapter 2). The standard technique of learning manual skills in anesthesia has been ‘learning by doing’. The literature was reviewed and future directions in education in UGRA and research in education in UGRA outlined. The following chapter discusses an example to improve education by technical aids.

– Does a tutorial help to improve the training of ultrasound-guided regional anesthesia for novices in the identification of sono-anatomy? (Chapter 3) Here the value of an onboard tutorial for self-education of trainees in UGRA was evaluated. The tutorial improved the identification of sono-anatomy, however the effect was small and many more training tools than a tutorial are needed to learn UGRA. Probably, transcutaneous nerve stimulation is a potential tool for the trainee to identify superficial nerves that cannot be recognized from the sono-anatomical image. Therefore, in the following study the correlation of sono-anatomy and stimulation-thresholds of transcutaneous nerve stimulation were investigated.

– Does the level of nerve stimulation correlate with the distance between the stimulation electrode and the nerve stimulated as measured by ultrasound? (Chapter 4) Unfortunately, there was no correlation of the depth and position of the nerves seen by ultrasound and the observed excitability and thresholds of transcutaneous electrical stimulation. Another aspect of regional anesthesia has been the best positioning of the patient for a specific block. Thus, for an axillary plexus block the patient has traditionally been positioned on his back with shoulder and elbow 90 degree flexed. Therefore, we investigated systematically in volunteers whether this traditional positioning is actually also for UGRA the best position to visualize the plexus with ultrasound.

– Does traditional patient positioning used for landmark techniques also guarantee the best nerve visibility when using ultrasound? (Chapter 5) Overall the positioning had no great effect on nerve visibility in the axilla. Especially, the visibility of the radial nerve, which is most difficult to identify being often hidden behind the axillary artery, could not be improved. The visibility of two other nerves could be improved by positioning. However, their visibility is usually not a problem during UGRA of the axillary brachial plexus. UGRA enables to reduce volumes of local anesthetics for peripheral nerve blocks. In the next step we evaluated the effect of a reduced volume of local anesthetics on the duration of its action.

– What is the effect of reduced volumes of local anesthetics on the duration of sensory and motor block in ultrasound guided axillary brachial plexus block (Chapter 6). Reduction of volume of local anesthetics restricted the duration of sensory and motor block of individual nerves significantly and time to first request of postoperative analgesia was also significantly reduced. After investigating the education of UGRA and technical aspects, in the last two chapters improvement in postoperative pain therapy, length of hospital stay and long-term pain and functional outcome were investigated.

– Does effective perioperative pain management provided by peripheral nerve blockades in patients undergoing total knee arthroplasty (TKA) shorten hospital stay? (Chapter 7) To what extent is peripheral nerve blocking of the leg needed in patients undergoing TKA? Although the quality of pain therapy was significantly different it did not influence the length of hospital stay

– Does improved postoperative pain therapy result in improved long-term

functional outcome and less chronic postsurgical pain? (Chapter 8). No significant differences could be demonstrated in functional outcomes and pain scores after one year, whereas significant differences were found in immediate postoperative pain scores among different types of peripheral nerve blocks for TKA. Mode of postoperative analgesia management affects functional outcome in the first period following total knee replacement. Some analgesia techniques and medications have beneficial effects on functional outcome after TKA.

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Chapter 2

Time to stop 'learning by doing' in regional anesthesia

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Submitted

Summary Statement

The literature on education and learning of ultrasound-guided regional anesthesia (UGRA) is reviewed. Models, phantoms, cadavers and simulators are useful tools educating UGRA, but more research is needed to avoid learning while doing blocks in patients.

Abstract

Background

The American Society of Regional Anesthesia and Pain Medicine (ASRA) and the European Society of Regional Anaesthesia and Pain Therapy (ESRA) Joint Committee has given recommendations on education and learning of ultrasound guided regional anesthesia (UGRA). A survey in the Netherlands revealed that there are no structured curricula for training UGRA for residents or attendants in any teaching hospital. A minority of centers offers some kind of education in UGRA, but the teaching material varies tremendously in content, extent and techniques employed.

Methods

We did a systematic review of the literature on education in UGRA. The results were structured according to the ESRA/ASRA recommendations on the 4 steps of UGRA education.

Results

Although the quality of most studies is moderate to weak, there are quite a few findings that are interesting. Single teaching sessions with electronic tutorials and e-learning modules can increase comprehension of ultrasound technique and sonoanatomy, although the effects are small. Sophisticated medium- to long-term teaching programs using measurable parameters to control learning progress generally displayed better results, pushing the trainees to the asymptotic part of the learning curve. These manual skills can be developed without touching a patient, thereby avoiding 'learning by doing'.

Conclusions

There is urgent need for further research comparing different educational techniques, for the development of true high-fidelity simulators and testing their efficiency. Education programs should be tailored to the individual needs of a trainee. Furthermore, the effects of improved training programs on patient safety and quality of care have to be investigated.

Chapter 2

Time to stop 'learning by doing' in regional anesthesia

Introduction

In the recent years, new techniques have been introduced into clinical routine anesthesia practice, including widespread use of ultrasound. This new technique is used during placement of central venous lines with convincing evidence for improved patient safety,[1] placement of arterial and peripheral venous lines, trauma admission to the emergency room, cardiac care as well as in invasive acute and chronic pain treatment. All these indications for ultrasound need special training. Ultrasound guided regional anesthesia (UGRA) is a challenging, complex skill and requires competence, which is far different from standard techniques in anesthesiology.

Some data suggest that the use of ultrasound for regional anesthesia contributes to patient safety, although this has not been proven.[2] Technical developments in UGRA itself, like new linear transducers with a higher frequency range and smaller footprints, portable machines with an improved software package for better target visualization, and needles with a modified surface to change the beam reflection cannot guarantee for improved patient safety. Therefore, the question 'Can ultrasound increase the safety of regional anesthesia procedures?' should be rephrased into 'how can we teach UGRA in order to increase patient safety?'.

There is a growing awareness and general believe that teaching methods like 'see one, do one, teach one' and 'training on the job' impair patient safety and quality of care, since it may increase the risk of complications and injury.[3] Learning by doing without substantial experience from previous lectures, hands-on and simulation training sessions has some other drawbacks like dependence on case mix and capacity, increase of procedure time, a higher risk of unsuccessful blocks, more procedure-related pain and patient discomfort, and misuse of ultrasound equipment resulting in technical damage of the machine or ultrasound transducer. However, present-day anesthesiologists became professionals by 'see one, do on' teaching methods. For obvious reasons we have to leave the old ways and discover new learning methods enabling to achieve an expert-derived level of performance in UGRA before starting in clinical practice.

Methods

Literature Search

To ascertain what is known about education and training methods to improve proficiency in UGRA, a literature search was conducted to English written journals in the database PUBMED until January 2013. The following combined medical subject headings were used: [Ultrasonography] AND [Education] OR [Teaching] AND [Anesthesia, Conduction]. After excluding reviews, letters, comments, editorials and unrelated articles 31 abstracts were captured of which 22 original articles contributed to learning of UGRA. Main criterion for the selection was: 'would the information of the article help to achieve a better quality of education of UGRA?' Two authors, JTW and MFS checked reference lists of the selected articles independently and found 5 additional articles of interest that were not captured in our search. A flow diagram of the search is shown in Figure1. Quality according to the GRADE guidelines (from the Grading of Recommendations Development and Evaluation working group) and study design of the selected publications varied widely: only 3 randomized controlled trials were found, but many observational studies, some surveys and reports. Selected publications were reviewed and categorized according to didactic components for UGRA.[4, 5]

Classification of the 27 selected publications in respect to education of UGRA was performed in 6 sections:

1. Understanding device operations
2. Image optimization
3. Image interpretation
4. Visualization of needle insertion and injection
5. Miscellaneous or general issues
6. How much education is necessary

1. Understanding device operations

Only one observational prospective study reported a pre-training quiz of 32 tested components of a portable ultrasound machine, where 10 trainees described 23% components correctly and 18% correctly described function of each component.[6] Thereafter, a presentation was shown to demonstrate the dials of settings and functions. Probably, trainees learned what was lacking in their knowledge. Unfortunately, a post-training quiz was not conducted, withholding the results of the presentation. Besides, it remains unclear whether knowledge of physics and artefacts of ultrasound were also tested.

Flowdiagram

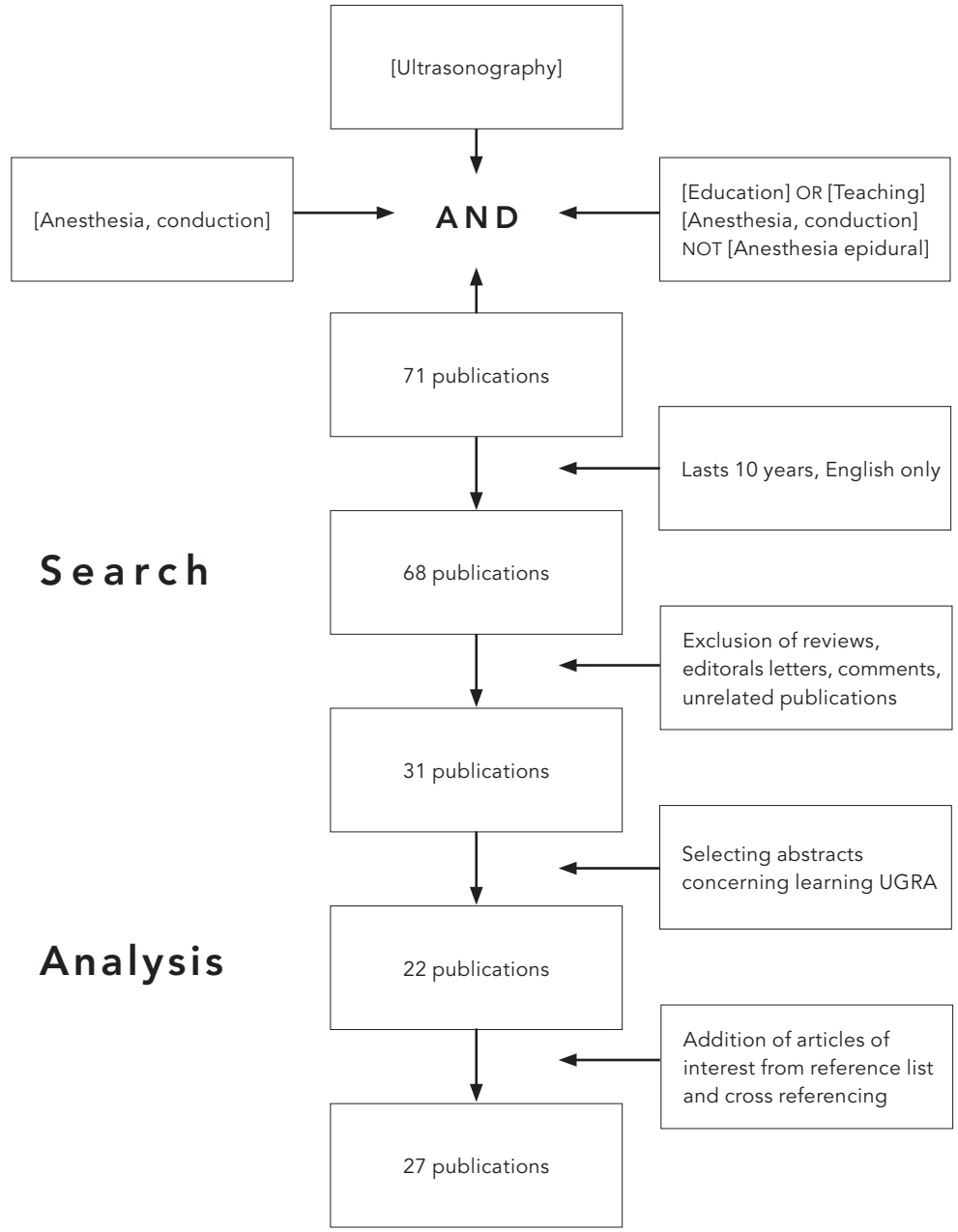

Figure 1 Flow diagram of literature search in PubMed until January 2013

Although knowledge of the machines used is of uttermost importance, there are no e-learning modules or standardized test to verify adequate skill to handle an ultrasound machine. This is surprising, since adequate introduction into any medical device is mandatory in many countries.

2. Image optimization

Correct device settings and efficient transducer movements are fundamental to image optimization. It was well shown that the unintentional probe movement is one of the most frequently (26,9%) committed errors.[6] Automated movement analysis systems have shown that during the increase of dexterity the frequency and amplitude of movements and thus time required are reduced. Chin et al. objectively investigated hand movements during scanning and needling phase of residents, fellows in UGRA and experienced anesthesiologists(consultants).[7] Time and amplitude of movements were significantly shorter in the consultant group compared to residents, while number of movements per minute was similar. In fellows, the time required to perform a supraclavicular block at the end of their fellowship was significant reduced compared to the start of the program. The validated automated movement analysis system used in this study seems an ideal tool to judge on the value of education techniques and paradigms. Thus, validated automated movement analysis systems should be used as auto-feedback for the trainees and to monitor the progress in motor learning for image optimization next to guidance of an experienced mentor.

3. Image interpretation

For identifying target structures and avoiding significant damage, knowledge of sono-anatomy is of great importance during performance of UGRA. Most trainees need to refresh anatomy and have to be introduced into sono-anatomy. In a randomized controlled study in UGRA novices (n=35) Wegener et al. evaluated the value of an on-site electronic tutorial. The number of correct identification of 27 anatomical structures related to the brachial plexus improved significantly from 50% to 62% when using an on-site tutorial on the ultrasound machine.[8] Four weeks of training in UGRA significantly improved the number of correct identification of anatomical structures (mean 9.9 vs. 14.1) in an observational study.[9] During scans for ultrasound guided pediatric ilioinguinal blocks, 6 novices reliably identified bony landmarks after 7 scans while reliable identification of the ilioinguinal and iliohypogastric nerves occurred after 18 scans.[10] Another option for beginners to identify the correct nerves non-invasively might be parallel use

of ultrasound and percutaneous nerve stimulation. Unfortunately, the correlation between localization by percutaneous nerve stimulation and the ultrasound picture is rather poor.[11]
In conclusion, electronic tutorials can improve understanding of sono-anatomy to some degree, but especially difficult anatomical structures require feedback by an experienced teacher.

4. Visualization of needle insertion and injection

Niazi et al. showed in a randomized controlled trial that an hour simulation training on a low fidelity simulation model for needling and proper hand eye coordination, in addition to a conventional training, success rates of residents improved significantly from 51.3% to 64%.[12] Prolonging simulation training from one to two hours improved accuracy and shortened time to reach a target in a low fidelity simulation experiment.[13] Whether providing more variability by simulation training on high fidelity models could further improve success rate is unknown. However, Tsui described both the usefulness and the obstacles of human cadavers for training UGRA: advantages of learning the sonographic anatomy and becoming aware of the vicinity of vital structures, but on the other hand the rigidity resulting in poor positioning and imaging, the lack of pulsating arteries as internal landmarks, not enabling the confirmation of Doppler and the inability of using nerve stimulation.[14]
The number of supervised attempts that are needed for competence in ultrasound needle visualization in a cadaver model was investigated by Barrington et al.[15] Fifteen trainees performed 30 simulated sciatic nerve blocks in a bovine model, which were supervised and videotaped. After each procedure the supervisor provided feedback in response to ten predefined quality compromising behaviors. Videotapes of each procedure were analyzed by only one blinded observer assessing needle visualization and transducer steadiness on the basis of a predefined scoring system. Learning curves were constructed for each trainee and categorized into proficient, not proficient and undetermined. A wide variability in individual learning curves was found and an estimation of 28 supervised attempts was calculated for a success rate of 90%. The three most common quality compromising behaviors that provided feedback were poor transducer handling, malpositioning of the target nerve on screen and advancement of the needle while not visualized. Similarly, De Oliveira constructed mathematical learning models to extract learning curves for basic skills in UGRA.[16] Thirty trainees performed 25 attempts compromising one experiment for needle visualization and a second experiment for injecting saline

around a target structure without any feedback. Experiments were recorded on videotapes and reviewed independently by two blinded observers, rating the performances according to predefined image quality scores. Any discrepancies were re-evaluated by the observers together. Only 30% of the trainees attained proficiency advancing the needle in-plane and only 11% of the trainees managed to deposit saline around a target. It was calculated that the trainees would require 37 attempts for a visible advancement of a needle in-plane and 109 attempts for learning adequate deposition of the local anesthetic. Noteworthy, training experiments were performed without any feedback, which is called 'discovery learning' or 'learning by doing'. This learning method is less efficient at all, because it consumes much more time for practicing and needs much more repetition.[17] Feedback on completion of a task is one of the essences of supervising and stimulates proficiency of trainees.

Previously, Sites et al. evaluated learning curves in 10 inexperienced residents, each performing 6 simulations of an ultrasound guided block.[6] The greatest improvements were made after the first and second simulation. The accuracy score increased by 36% and 59%, respectively, compared to the first simulation. Furthermore the time required was reduced in the second and third simulation by 38% and 48%, respectively, also compared to the first. The most common mistake was advancement of the needle without visualization. The same group characterized the learning behavior of 6 residents performing 520 nerve blocks.[18] All blocks were videotaped and reviewed on quantitative and qualitative behaviors by two independent experts. 398 errors were found, divided in 7 quality-compromising behaviors. Again, most common quality compromising behavior was needle advancements without visualization followed by unintentional transducer movements. In this study Sites found some new elements of procedural competence like recognition of maldistribution. In contrast, McCartney et al. demonstrated a very high accuracy of recognizing spread of local anesthetics in trainees.[19] Similarly, Cheung et al. observed mistakes of 26 trainees using a high-fidelity simulator: maintaining visualization of the needle, aligning the needle with the transducer and angling the needle were the most common mistakes.[20] All studies evaluating learning curves in UGRA demonstrated a large interindividual variability.[10-17] Probably, individual baseline skills of complex and fine motor control and visuospatial awareness determine the progress of proficiency in UGRA. Visuospatial awareness is the mental process that involves visual and spatial awareness. E.g. visuospatial awareness is needed in UGRA to work from a visual 2-dimensional ultrasound image to 3-dimensional needle advancement in direction of a target. How can we identify

trainees with low capacity and even more important: can we improve baseline skills for low capacity trainees?

Smith et al. evaluated predictors of ultrasound-guided procedural performance in 40 trainees of UGRA.[21] They measured motor and visuospatial skills by Block Design Test, which is a validated subtest of the Wechsler Adult Intelligence scale III. This test was strongly correlated with the performance success of a simulated ultrasound-guided nerve block. Furthermore, subjects who commonly practiced dexterous activity, like piano playing or video games, performed significantly faster in ultrasound skill assessment. In contrast, psychomotor performance in a couple of validated tests did not correlate with performance in ultrasound-guided skill assessment. Thus, it will be interesting to investigate whether specific training of visuospatial skills can improve performance of UGRA.

A Virtual Reality (VR) based environment has been described that will adapt to the skill level of the trainee and assess their progress providing the outcome to trainers. In this way, measuring quantity and quality of errors, providing prompt feedback and individualized training could be realized. However, such simulators have to be validated.[22] There have been proposals what an ideal high-fidelity simulator should be capable of.[23]

Thus, the development of high-fidelity simulators with automated prompt feedback will be an important direction of future research. Until then, training in UGRA should be done in cadavers and phantoms under the guidance of an experience teacher.

5. Miscellaneous or general issues

In order to assess technical skills of UGRA Cheung et al. proposed an assessment tool, containing a list of 22 items from which each item should be rated as not, poorly or well performed.[24] The list starts with positioning of the patient and ends at recognition of correct spread of the local anesthetic. In addition, for non-technical skills of UGRA a Global Rating Scale of 9 categories was developed applying a 5-point Likert scale score. However, this approach has neither been evaluated nor validated.

For beginners in UGRA outside a teaching hospital, a large gap between following courses with hands-on workshops and the start of UGRA in daily practice has to be overcome. In a small survey the level of comfort of trainees (n=12) and their intention to perform UGRA in their daily clinical practice were tremendously increased after a web-based simulator training.[25] However, the motivation was halved again after one further month. Sufficient training opportunities afterwards was found to be one of the most important determinants of getting experienced

in UGRA followed by the presence of high-quality supervisors.[26] Training should be repeated on a regular base when UGRA is not performed frequently. A very high initial success rate of 97.3% was found when 22 trainees performed 222 supervised ultrasound guided and nerve stimulated interscalene blocks during a 4-week block rotation. A sound training program proceeded, but its impact on the success rate was not studied and an objective assessment of proficiency was lacking.[9]

Moore et al. reported the improvement in UGRA-associated skills and proficiency using a dual integrated teaching program with simulators and real time feedback in 9 pediatric anesthesia fellows.[27] Using a validated simulation and real feedback model for the assessment, technical and cognitive skills of UGRA increased from 56.7% and 52.5% in baseline to 78.9% and 79.2% after one year respectively. Whether skills would have been less without or would have been improved even more with a more intensive teaching program was not studied. Number of cases in daily practice per trainee was not mentioned and caseloads were not included in the assessment. Recently, Rosenberg et al. described 3 well developed high fidelity simulation models with pulsating arteries for most common blocks: upper extremity, femoral and sciatic popliteal.[28] Until now its value for training is unknown, while the costs of these models will be high. Also Smith et al. described a magnificent learner-centered training model that requires self directed knowledge and skill development, based on what is learned rather than on what is taught.[29] Internet-based e-learning modules and several internet pages like the recently established ESRA Academy among others offer a range of opportunities to expand the knowledge on sono-anatomy, provide manuals of ultrasound machines and show block performance. However, the efficiency and efficacy of all these tools on successful block rate and procedure-related complications have not been evaluated until today.

In conclusion, the attention on all levels of learning should focus more on what is learned than on what is taught.

6. How much education is necessary?

Determining caseloads requirement is of great importance for training of residents and inexperienced anesthesiologists. Traditionally, caseloads have been determined for peripheral nerve block to establish a specified level of proficiency in the training curriculum of an anesthesiologist. Thus, patients were exposed to doctors suboptimal in proficiency and safety of the procedure. Fortunately, most studies investigating dexterity and learning curves in UGRA

are done in cadavers or phantoms.[13,14,18,19,25] However, not all simulation training could improve performance immediately.[18] Furthermore, the slopes of the learning curves in sono-anatomy recognition seem to vary tremendously between different blocks. Performance of 18 scans was sufficient for a reliable identification of the ilioinguinal and iliohypogastric nerve,[10] whereas none of 18 anesthesiologists achieved competence in the sono-anatomy of the lumbar spine after 20 supervised scanning trials.[30] Regarding performance of blocks Luyet et al. demonstrated that novices in UGRA reached the plateau of the learning curve after just 13 blocks,[31] whereas Sultan et al. observed that anesthesiologists required more than 100 axillary plexus blocks for having a significantly better technique than those with an experience of 50-80 blocks.[32] To achieve competence in performing a simulated sciatic nerve block novices required 28 blocks.[15] This tremendous variation in attempts required to achieve competence is most likely due to the different variables taken as measurement of ultrasound skills. While Luyet et al. defined a surgical block as success, Sultan et al. evaluated the technique on a 63-point task-specific scale.[31,32] Thus, for UGRA there are no generally predefined required 'case load' numbers for a novice to gain sufficient experience to safely and efficiently perform an ultrasound guided block. Therefore, it will be of imminent importance that skills in UGRA will be identified, which are testable, clinically relevant and valid. These skills have to be acquired before trainees perform their first block in patients. However, in a survey of ASRA members practicing UGRA more than 80% had no experience with cadaver or animal training and the greatest amount of time in training of UGRA was allocated to 'self taught'.[33]

In conclusion, the attention should switch from caseload requirement for learning a technique to finding testable indicators of sufficient skills on every level of learning.

What is recommended?

The American Society of Regional Anesthesia and Pain Medicine (ASRA) and the European Society of Regional Anaesthesia and Pain Therapy (ESRA) Joint Committee published recommendations for education and training in UGRA in 2009[4] and 2010[5] and recently completed these recommendations for ultrasound-guided procedures in pain therapy.[34] The committees summarized the 10 common tasks used when performing an ultrasound-guided nerve block (see Table 1) and described the core competencies and skill sets associated with UGRA. They also showed both a training practice pathway for postgraduate anesthesiologists and a residency-based training pathway to present adequate

ideas for each training level. Furthermore, they announced the review on a periodic basis and the publication of updates and modifications to these recommendations when appropriate.

Recommendations of the ASRA/ESRA Joint Committee in the Netherlands

We also evaluated the implementation of the recommendations of the ASRA/ESRA Joint Committee by telephone interviews with all educational institutions for Anesthesiology in the Netherlands.
To date, the recommendations have not been adopted or integrated in any curriculum of the residency program. In addition, preliminary attempts for an Introduction program of UGRA in the curriculum are lacking in the Netherlands up to now, while regional anesthesia is a mandatory part of the curriculum. Three of the eight Dutch training programs offer an institutional education in UGRA for residents, differing in time, frequency and content. These programs largely depend on the commitment of a few interested experts and mainly on the interest of the individual resident.

Training ultrasound in other medical specialties and training models

A literature search was conducted to training models for ultrasound in other medical specialties in order to determine what kind of models from other specialties we can adopt for UGRA. Results of this search are shown in table 2. Surgeons described significantly improved skill performance after simulation and proficiency based surgical education of residents.44 The use of simulation models to assist with the teaching and learning of laparoscopic operation skills offers advantages of learning in an safe environment that promotes problem solving, questioning and transformational learning. Objective assessments of performances is an important instrument for allowing evaluation of level and progress of learning. Translating these technical possibilities of stimulation models into the field of UGRA would be an advantage for all learners.

List of 10 tasks that are helpful in performing an ultrasound-guided nerve block

1. Visualize key landmark structures including blood vessels muscles, fascia, and bone.
2. Identify the nerves or plexus on short-axis imaging.
3. Confirm normal anatomy and recognize anatomic variation(s).
4. Plan for a needle approach that avoids unnecessary tissue trauma.
5. Maintain an aseptic technique with respect to the ultrasound equipment.
6. Follow the needle under real-time visualization as it advances toward the target.
7. Consider a secondary confirmation technique, such as nerve stimulation.
8. When the needle tip is presumed to be in the correct position, inject a small volume of a test solution. If solution is not visualized during this test injection, presume that the needle tip is intravascular or out of the imaging plane.
9. Make necessary needle adjustments if an undesired pattern of local anesthetic spread is visualized. The visualization of local anesthetic should occur through the entirety of the injection to avoid an intravascular injection.
10. Maintain traditional safety guidelines including the presence of resuscitation equipment, frequent aspiration, intravascular test dosing, standard monitoring, patient response, and assessment of injection characteristics

Table 1 List of ten common tasks used for performing UGRA, formulated by jointed committees of ASRA

Training model	Purposes	Results	Speciality (author)
Computer based simulation with 3-dimensional heart model	Diagnosing abnormal fetus	Spatial orientation skills	Obstetrics (Lee)[35]
Simple Gelatin mold for needle insertion, track and tip visualization	Ultrasound guided amniocentesis	Reducing threats to patient safety and operator confidence	Obstetrics (Smith) [36]
VR-patient model *	Ultrasound examination in pelvic pathology	Probe movement and visualization of pelvic pathology	Gynaecology (Heer)[37]
Plastic spine in water and cadaver specimen model	Diagnosing spinal stenosis during spine surgery	Reliable detection of spinal stenosis	Neurosurgery (Fritz)[38]
Living animal model	Laparoscopic ultrasonography in detecting liver colorectal metastases.	High accuracy rate of detecting	Surgery (Restrepo)[39]
Life like model: Plexiglas tube and porcine colon with plastic bags	Endorectal ultrasonography for diagnosing and treating anorectal pathology	Acquired technical skills for diagnosing and interventional procedures	Enteral Endoscopy (Bussen)[40]
Synthetic arm skin filled with a mix of gelatin and fiber.	Ultrasound guided vein cannulation	Faster vascular access	Emergency Medicine (Blaivas) [41]
Living animal: anesthetized pigs with intra thoracic or intraabdominal fluid	Diagnosing intraabdominal and intrathoracic bleeding in trauma patients	Decrease of error rate from 17 to 5% after tenth examination	Traumatology (Abu-Zidan)[42]

Table 2 An overview of simulation training models outside the field of UGRA, stating the learning objectives and outcome. * VR: virtual reality.

Conclusion

Learning by doing impairs patient safety and quality of care. Understanding of the ultrasound device should be standardized and testable, which might easily be included in an e-learning module. Correct device operation will be the first requirement of image optimization. Handling of the probe can be trained by giving feedback on the frequency and amplitude of movements. Possibly, such automated dexterity feedback may guide training more effectively than just looking for an optimal picture. Also image interpretation can be enhanced by electronic tutorials for novices. However, for in depths learning especially of difficult or deep anatomical structures an experienced trainer will be indispensable. The most common mistake of needle insertion is advancement of the needle without visualization. Furthermore, correct deposition of fluid around a target structure is a very difficult for a beginner. These tasks can easily be learned in cadaver or phantom, but direct feedback is required to accomplish fast learning. Since these are only visuospatial and motor task, it might be possible implement automatic feedback learning in a high-fidelity simulator. For the time being, experienced teachers giving frequent feedback are inevitable in guiding needle insertion and local anesthetic deposition. The evaluation of skills on every level of learning and the curriculum should not be standardized for all trainees, but individualized to each trainee, because inter-individual learning curves can vary tremendously. Similarly, because of these varying slopes of learning curves, no fixed numbers can be given to acquire proficiency in a certain technique. Thus accomplishment of a technique must be evaluated by skill testing and by number of blocks performed. A lot of UGRA learning can already be done and evaluated with e-learning, examining models, training visuospatial and motor skills in cadavers, phantoms and simulators. However, a lot of research is needed validating these training techniques and adequately defining and testing UGRA skills.

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Chapter 3

Value of an electronic tutorial for image interpretation in ultrasound-guided regional anesthesia

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Abstract

Background and Objectives

Use of ultrasound guided regional anesthesia (UGRA) requires considerable training. An embedded electronic tutorial as an element of an ultrasound machine may help to identify sono-anatomy for novices. Therefore, we investigated whether an electronic tutorial could improve accuracy or speed of performance in identifying anatomical structures.

Methods

35 novices in UGRA participated in a workshop on brachial plexus sono-anatomy. Following a lecture, training in handling of ultrasound machines and hand-eye-coordination, participants were randomized to group (S) using a standard ultrasound machine and group (T) using the same type of machine with an onboard electronic tutorial. Each participant had to identify 27 anatomical structures from the brachial plexus in a volunteer. A correct identified structure scored 1 point. An experienced observer noted scores and time required. Scores ± SD(%) and times ± SD(s) were compared between groups by analyses of independent samples T-test and ANOVA. Influence of anesthesia experience was determined by multivariate analyses.

Results

Group T scored significant higher (16.8 ± 3.6 (62%) vs. 13.4 ± 4.4 (50%), p=0.018), whereas time required was longer (1053 ± 244s vs. 740 ± 244s, p=0.001). Multivariate analysis revealed that experience had no influence on scores or time required. Examination of structures took more time in the beginning than at the end in group T.

Conclusions

An electronic tutorial can help novices in UGRA to identify anatomical structures. A significant increase in correct identifications was gained at the expense of significantly longer time required for this process. Increased time required may partly be related to unfamiliarity with the tutorial.

Chapter 3

Value of an electronic tutorial for image interpretation in ultrasound-guided regional anesthesia

Introduction

Performance of UGRA requires specialized skills and an extensive training.[1] Essential to a safe and effective practice of UGRA is a detailed knowledge of anatomy for reliable identification of anatomical structures on sonographic images.[2] Training novices in UGRA generally starts with teaching device operations, scanning techniques and image optimization. In a second step, the identification of sono-anatomy is tought.[3-10] Learning sono-anatomy is a challenging and demanding process that can deter many novices from starting UGRA in daily practice.[11-12]

Also teaching sono-anatomy is time-consuming for trainers, because it requires a 1:1 teaching situation as well as a 'volunteer model'. To support and facilitate this phase of learning, manufacturers have introduced embedded electronic tutorials as an element of ultrasound machines. The tutorial investigated here (MyLabOne, Esaote®, Genova, Italy) contains 'how to do' aids to speed the onset and improve the quality of peripheral nerve blocks. A photo displays the anatomical landmarks where the plexus/nerve should be approached. A second frame gives a schematic picture of the anatomy. A third window gives an example of the topographic sono-anatomy with description of the most relevant structures. Furthermore, instead of the text describing the sono-anatomy, a frame displaying the real-time anatomy of the actual patient (or volunteer) can be activated on the same screen. A typical screen shot of the ultrasound machine and tutorial is given in figure 1. Although this tutorial was written by a very experienced teacher in UGRA, the value of such a tutorial has never been validated or tested before. Moreover, it has to be determined whether the tutorial accelerates the learning curve. We hypothesized that an electronic tutorial increases the number of correctly identified anatomical structures of the brachial plexus by physicians inexperienced in the technique. Secondary aim was to determine the time required to identify anatomical structures with and without the tutorial.

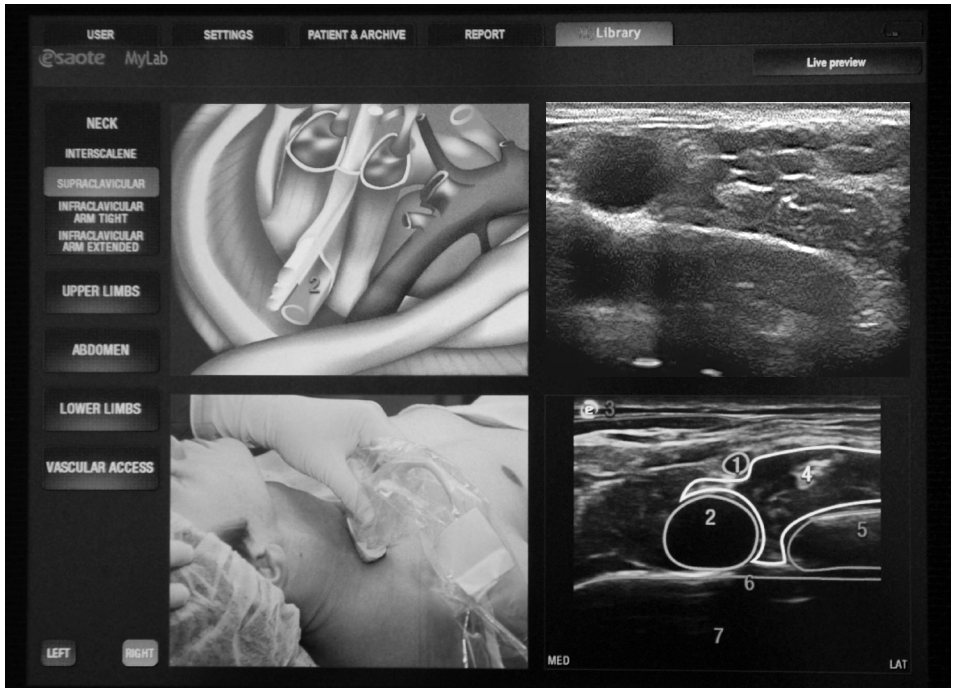

Figure 1 Example of the electronic tutorial for the supraclavicular block on the display of the ultrasound machine. When the block/anatomical location of the brachial plexus is chosen (here supraclavicular plexus), the following pictures are displayed: 1. Lower left, a photograph of the landmarks and the location and orientation of the probe. 2. Upper left, a schematic anatomical picture of the brachial plexus supraclavicularly. 3. Lower right, a typical ultrasound picture of the region with a delineation of relevant anatomical structures. 4. The legend of the ultrasound picture and a short description on how to perform the block. This frame can be switched back and forth to the real-time picture of the brachial plexus.

Table of structures

	start		end			
Time	hh : mm : ss		hh : mm : ss		score	max
Interscalene plexus	: :		: :			7
Carotid artery	: :		: :			
Internal jugular vein	: :		: :			
Vagus nerve	: :		: :			
Sternocleidomastoid muscle	: :		: :			
Anterior scalene muscle	: :		: :			
Middel scalene muscle	: :		: :			
Nerve roots (C5, 6, 7, 8)	: :		: :			
Supraclavicular plexus	: :		: :			5
Subclavian artery	: :		: :			
First rib	: :		: :			
Pleura	: :		: :			
Plexus	: :		: :			
Dorsal scapular artery	: :		: :			
Infraclavicular plexus	: :		: :			7
Pectoral muscles	: :		: :			
Subclavian artery	: :		: :			
Subclavian vein	: :		: :			
Pleura	: :		: :			
Lateral cord	: :		: :			
Medial cord	: :		: :			
Posterior cord	: :		: :			
Axillary plexus	: :		: :			8
Axillary artery	: :		: :			
Coracobrachialis muscle	: :		: :			
Biceps muscle	: :		: :			
Triceps muscle	: :		: :			
Musculocutaneous nerve	: :		: :			
Median nerve	: :		: :			
Ulnar nerve	: :		: :			
Radial nerve	: :		: :			
Total score (max = 27)						27

Table 1 Table of structures associated with the interscalene, supraclavicular, infraclavicular and axillary sites of the brachial plexus for recording time and scores.

Methods

This randomized controlled study was conducted at the Academic Medical Center Amsterdam, Netherlands. The institutional Medical Ethics Committee gave a waiver for this investigation because the Medical Research Involving Human Subject Act (WMO) does not apply to the comparison of skill in ultrasound identification of predefined anatomical structures acquired with or without use of tutorial. Eligible participants were novices (residents and anesthesiologists) with little to no experience in UGRA. Participants signed up for an institutional free basic ultrasound course on UGRA of the upper limb. After enrolment for the course, written informed consent was obtained. Exclusion criteria for participation in the study were experience in UGRA (> 30 ultrasound-guided blocks in total), missing the introduction lecture or unwillingness to participate. Data of participants were collected on gender, years of general experience in anesthesia, estimated number of peripheral nerve blocks performed with a nerve stimulator and with ultrasound. The study took place during 4 institutional basic hands-on ultrasound courses for 8 to 9 participants from January to April 2011. We arranged eight volunteers (two for each session) to serve as sono-anatomy models. The course started with a 90 minutes lecture on physics of ultrasound, anatomy and sono-anatomy of the brachial plexus. The lecture was highly standardized and especially the anatomical structures later to be identified at four levels (interscalene, supraclavicular, infraclavicular, axillary) of the brachial plexus were explained in detail. After the lecture, participants were trained in handling of ultrasound machines ('knobology') and practiced hand-eye coordination on a phantom for 45 minutes.
The tutorial investigated here (MyLabOne, Esaote®, Genoa, Italy) contains 'how to do' aids for most frequently performed peripheral nerve blocks. A photo displays the anatomical landmarks where the plexus/nerve should be approached. A second frame gives a schematic picture of the anatomy. A third window gives an example of the topographic sono-anatomy with description of the most relevant structures. Furthermore, instead of the text describing the sono-anatomy, a frame displaying the real-time anatomy of the actual patient (or volunteer) can be activated on the same screen. A typical screen shot of the ultrasound machine and tutorial is given in Figure 1. Then participants were randomized by means of sealed opaque envelopes into group S using a standard ultrasound machine and group T using the same type of ultrasound machine with an onboard electronic tutorial (Fig. 1). Each participant had to identify 27 anatomical structures (see Table 1) at 4 predefined levels of the brachial plexus in a live volunteer model using the standard ultrasound machine (group S) or the same machine with a tutorial (group T). Scanning and identification was performed in a fixed sequence of levels: first interscalene, second supraclavicular, third infraclavicular and finally axillary in both groups. An UGRA-experienced observer noted the correct identifications and time required after explaining the standard or tutorial ultrasound machine, respectively. Time allowed for identification of a given structure was limited to a maximum of 2 minutes. The observer helped with questions of the participants regarding the ultrasound machine. In order to avoid influences of differences in individual sono-anatomy between different models, we switched the models between group S and group T halfway during each course.

For each anatomical structure correctly identified, one point was given, resulting in a maximum score of 27 points (i.e.100%) for each participant. Furthermore, time required for identification of each anatomical structure was noted, while time measured in group T included use of the tutorial. Groups were compared with regards to scores ± SD (%) and time ± SD (s) required at each anatomical structure, at each location and at the whole examination.
The primary aim of the study was to detect a difference in scores of correctly identified anatomical structures. Power analysis revealed that to detect a 10% difference in percentage of correctly identified structures with a power of 80% and an alpha of 0.05 a group size of n=17 was needed assuming a standard deviation of 10%. Values are expressed as mean ± SD. Scores and required time were compared between groups by using independent samples T-test and analysis of variance (ANOVA), respectively. Influence of experience in anesthesiology in general (years, staff, resident) and in regional anesthesia (numbers of patients) and gender on scores and required time was determined by multivariate analysis. P-values < 0.05 were considered statistically significant.

Demographic data

Group	S (n= 18)	T (n=17)
M / F	8 / 9	8 / 10
Staff/Resident	8 / 9	8 / 10
Experience (yrs)	5.0 (0-20.0)	5.0 (1.0-17.0)
Neurostimulation (nrs)	50 (0-250)	35 (0-400)
Ultrasound (nrs)	2 (0-30)	3 (0-25)

Table 2 Variables of demographic data are presented as median (range) or as number (discrete variables).

CONSORT Flow diagram

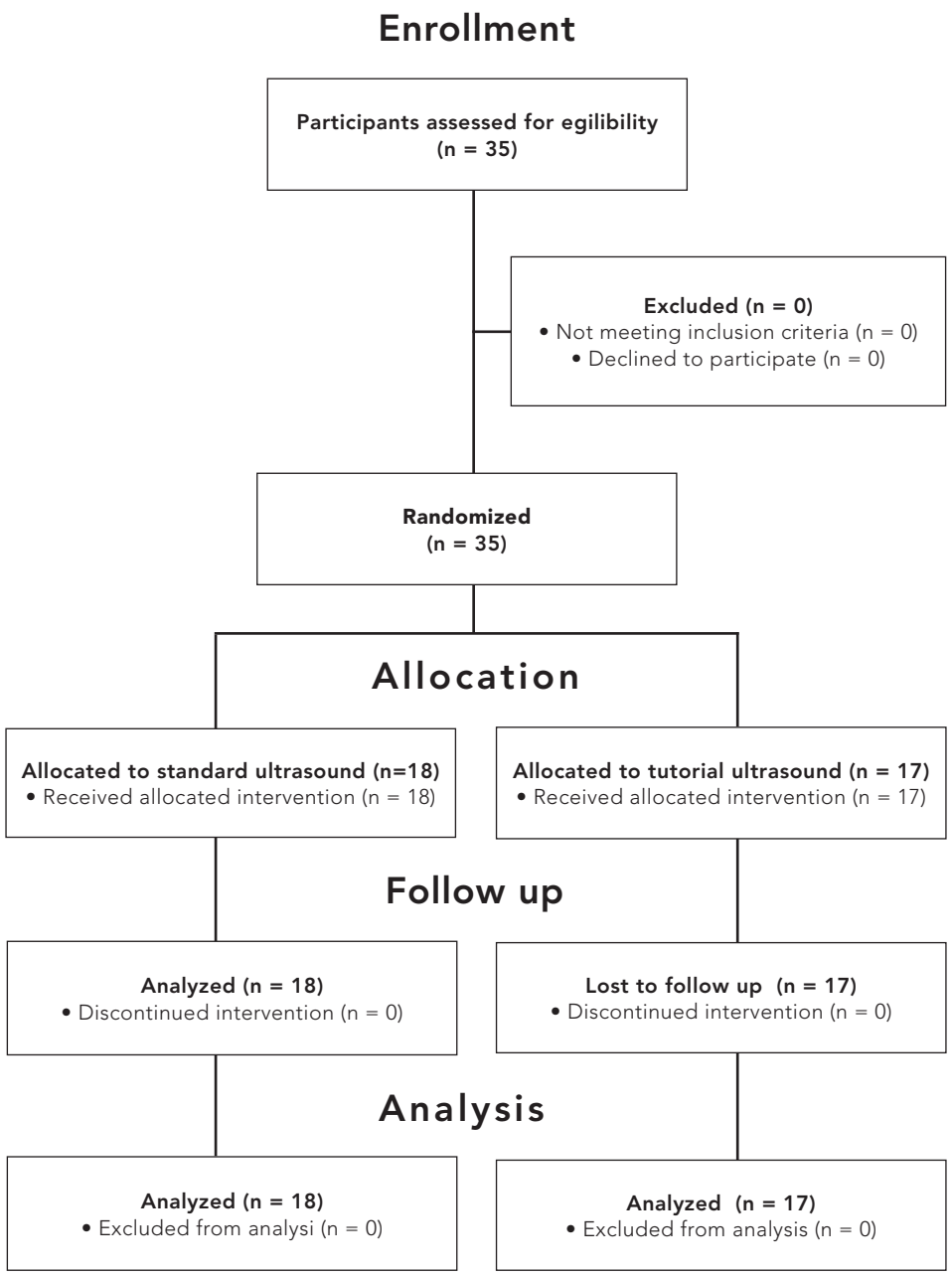

Figure 2 CONSORT Flow diagram

Correct identification of anatomical structures

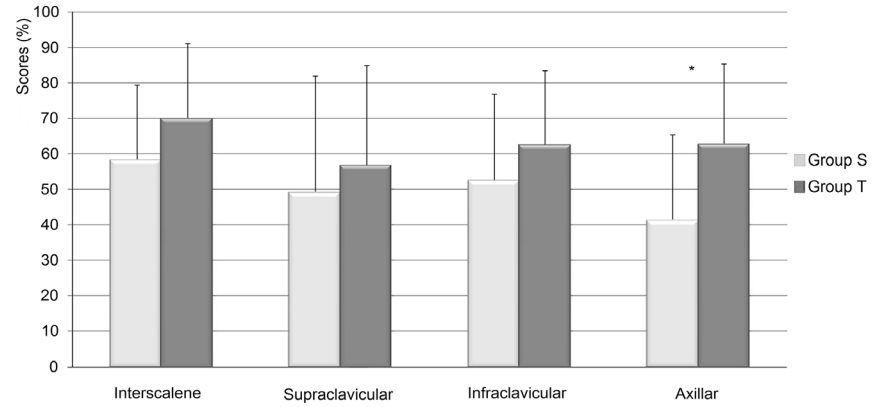

Figure 3 Subgroup analyzes of scores of correct identification of anatomical structures spread over four locations are delineated as percentages. Scores tended to be better in group T, but this was only significant at the axillary region at the end of the examination. Data are displayed as mean (SD) and were analyzed using independent samples T-test and ANOVA. * = $p < 0.05$

Required time for identification

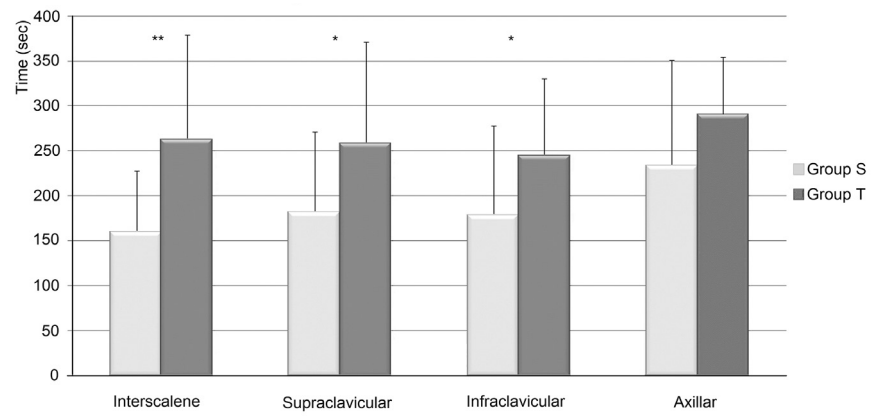

Figure 4 Times required for identification of anatomical structures of the brachial plexus at 4 sites are displayed. The scanning proceeded according to a fixed order, starting at the interscalene and ending at the axillary site. Significant differences in time were demonstrated between groups at the interscalene, supraclavicular, and infraclavicular sites, whereas no significant difference was found at the axillary region. Data are displayed as mean (SD) and were analyzed using independent-samples t test and ANOVA. *$p < 0.05$, **$p < 0.01$.

Results

A total of 35 volunteers with minimal experience in UGRA, but varying experience in anesthesia from first year residents to consultants with more than a decade experience in anesthesia, participated. A flow chart describing randomization and possible drop-out is displayed in figure 2. No participant was excluded after randomization, 18 participants were randomized to group S and 17 to group T. Characteristics of group S (n=18) and T (n=17) like gender ratio, staff to resident ratio, years of experience, number of performed blocks with nerve stimulation, and number of ultrasound guided blocks before study inclusion were comparable (table 2).

Group T scored higher in identifying anatomical structures (16.8 ±3.6 vs. 13.4 ± 4.4, p=0.018) compared to group S of totally 27 structures. Thus, with the aid of the tutorial the score increased from 50% to 62% of correct identifications. A subgroup analysis at the different sites of the brachial plexus (interscalene, supraclavicular, infraclavicular and axillary) revealed a significant improvement in identification only at the axillary site (fig. 3).

Mean time required for scanning and identifying of all anatomical structures linked to the brachial plexus was significantly longer in group T (1053±244s) compared to group S (740 ±244s), p=0.001). Identification took significant longer especially at the interscalene site in group T, but no significant difference was found at the axillary site (figure 3). Differences in time required for scanning and identification decreased gradually between group S and T during the progress of assessment of the brachial plexus.

Multivariate analyses revealed that experience in anesthesia generally or in regional anesthesia with nerve stimulation guided blocks specifically did not influence total scores (general experience p=0.50, nerve stimulation guided experience p=0.70) or time required (general experience p=0.51, nerve stimulation guided experience p=0.40. Even some minimal experience in UGRA did not influence total scores (p= 0.59) or time required to identify structures (p=0.93) compared to participants without any experience. Similarily, no difference was found between residents and staff or between men and women. Moreover, which live model was used for scanning and identification did not affect scores (p=0.47) or time (p=0.28).

However, availability of a tutorial on the ultrasound machine was the only influencing factor on total score (p=0.036) or time required (p=0.001) as determined by multivariate analysis.

Discussion

During scanning of the brachial plexus novices identified 62% of anatomical structures correctly with the aid of an electronic tutorial, while the control group scored only 50%. At the axillary site identification was even 21% better with the use of the tutorial. Subgroup analysis of the different anatomical structures revealed that the score improved over time with the electronic tutorial, while the time needed to identify structures with the tutorial decreased over time. No other factor (anatomy of the model, experience of the anesthesiologist, gender) influenced score or time. Interestingly, being resident or staff did not influence the scores or time, although electronic skills and chronological experience between residents and staff may vary widely.

After a 90-minute basic course of sono-anatomy of the brachial plexus, group S failed to identify half of the basic anatomical structures. In contrast, the electronic tutorial accelerated the learning curve of UGRA, although more than one third of the basic anatomical structures were still not recognized in group T. At the axillary site (the last scanned region of the exam) identification in group T was significant better then in groups S compared to the other scanned sites. It is unclear whether utilization of the tutorial increased by its extended use. Settings of the ultrasound machine were optimized with help of an expert observer to exclude impaired identification due to poor handling of the ultrasound machine. The benefit of a basic training of 90 minutes to identify anatomical structures with ultrasound was disappointing, as is supported by previous publications showing slow learning curves for anesthesiologists in ultrasound assessment.[13]

The increased time required in group T is at least partly related to the unfamiliarity of the students with the electronic tutorial. The difference between groups in required time decreased from the first (interscalene) to the last anatomical region (axillary) scanned (fig. 3). Thus, for the last part of the investigation (axilla) there was no difference in time requirement detectable between groups. Results may have been improved, if usage of the onboard tutorial would have been more familiar.

The American Society of Regional Anesthesia (ASRA) and European Society of Regional Anesthesia (ESRA) recommend a skillset for proficiency in UGRA divided into four major categories: (1) understanding device operations, (2) image optimization, (3) image interpretation, and (4) visualization of needle insertion and injection of the local anesthetic solution.[14] In the present study the focus lied on the third skillset of image interpretation, thus the correct and

timely identification of basic anatomical structures. The list of anatomical structures tested contained all the structures from the recommended skillset for image interpretation.[14] Thus, the tested structures are agreed to be important for the practice of UGRA.

Recognition of anatomical structures on a sonogram starts with finding of specific patterns and landmarks, which should be consistent with corresponding cross-sectional anatomy. Application of simple sonographic anatomical patterns can provide a strategy to correctly locate nerves when performing ultrasound-guided cervical and brachial plexus anesthesia.[15] This complex visual recognition process should be trained repeatedly by putting cross-section anatomy images, simplified drawings and defined ultrasound images together.[1] Repetitive training sessions are essential to reinforce learning and acquire procedural skills, as part of a deliberate practice model.[16] When expertise in pattern recognition progresses, small anatomical variations will not confuse the novices.[17] We considered participants as inexperienced up to 30 UGRA procedures. It is still unknown how many procedures are needed to achieve any competence in UGRA. However we demonstrated that little experience of less than 30 UGRA procedures did not improve identification of structures or time required.

Eight different models took part in this investigation leading to a wide range of anatomical variations, finally allowing representative results. These models were equally distributed between groups avoiding a possible bias of different models for a given group. Furthermore, multivariate analysis reconfirmed that the differences in scores of correct identification between groups were not associated with different models. Interestingly, other variables like general or specific experiences in regional anesthesia of the participants did not influence the learning curve. This observation is in line with a recent study investigating the learning curves between novices in UGRA with no earlier RA experience and novices in UGRA with considerable experience in nerve stimulator guided RA.[18] As in our study, there were no significant differences in learning curves found. However, results of the multivariate analysis must be interpreted with extreme caution due to small n-values.

The advantage of the tutorial became more obvious at the end of the observation period, showing that time requirement differences disappeared over time. Thus, it may be reasonable to assume that an introduction to the tutorial might have increased its advantages. However, that might have given the tutorial group some extra teaching which would have been difficult to control. In order to avoid the bias of given the tutorial group extra training we did not give such an extra teaching session. Likely, the acceleration of learning in UGRA with the support of an electronic tutorial would have had been even greater if the novice should have known how to apply it.

In conclusion, an electronic tutorial improved correct identification of anatomical structures by 12% at the expense of a 42% increase in time required for the examination. This increased time requirement may be related to unfamiliarity with the tutorial. However, the just 12% absolute improvement in structure recognition and overall low scores demonstrate that UGRA cannot be learned in a few hours workshop.

Acknowledgements

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Chapter 4

Comparison of percutaneous electrical nerve stimulation and ultrasound imaging for nerve localization

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British Journal of Anaesthesia.2011 Jan;106(1):119-23

Abstract

Background and Objectives

Percutaneous nerve stimulation (PNS) is a non-invasive technique to localize superficial nerves before performing peripheral nerve blocks, but its precision has never been evaluated by high-resolution ultrasound. This study compared stimulating points at the skin with the position of nerve structures determined by ultrasound. Correlations between distances and percutaneous stimulation thresholds were determined.

Methods

PNS was performed in 20 healthy volunteers systematically with a stimulating pen at the neck after attaching a transparent film with 49 (7×7) perforations. Stimulation thresholds were measured and impedance was controlled. Thereafter, an independent observer measured the depth (D) of the most superficial nerve structure with ultrasound. Distances between stimulating points and the most superficial nerve structure (S) were measured. Correlations between associated stimulating thresholds and distances D and S were calculated.

Results

The stimulating point with the lowest current was identical to the point closest to the nerve in only 10% of measurements. Median S was 12.6 (3.4-32.0) mm and D 7.6 (0.3-28.6) mm. Distances did not correlate with percutaneous stimulation thresholds.

Conclusion

PNS with a stimulating pen is not a reliable technique for nerve localization in the brachial plexus as verified by high-resolution ultrasound.

Chapter 4

Comparison of percutaneous electrical nerve stimulation and ultrasound imaging for nerve localization

Introduction

Electrical nerve stimulation has been the gold standard for nerve localization during peripheral nerve blockade before high-resolution ultrasound became available. In contrast to invasive nerve stimulation using a needle, a non-invasive technique has been described to localise superficial nerves percutaneously[1-5] at considerably lower costs than high-resolution ultrasonography.[6-10]
In 2007 a commercial devise was launched to percutaneously identify nerves to depths up to 3 cm (Stimuplex® Pen, B. Medical Inc. Bethlehem, PA). Identification of the brachial plexus with this stimulating pen was reported to be rapid and non-painful.[11] In theory, the function is based on the relationship between electrode-to-nerve distance and current thresholds.[12] Since electrical impedance in biological tissues varies,[13 14] this relationship is not always linear.[15] Primary aim of the present study was to assess the value of percutaneous nerve stimulation (PNS) for superficial nerve localisation compared to ultrasound. Therefore, we investigated whether points on the skin with the lowest current corresponded to locations where the nerve is most superficial to the skin. Secondary aim was to define the correlation between minimal current for PNS and the nerve to skin distance measured with ultrasound.

Methods

In this prospective observational study, 20 volunteers underwent PNS and subsequently ultrasound examination of the neck. After Institutional Medical Ethical Committee approval, written informed consent was obtained from all subjects. Inclusion criteria were age above 18 years and American Society of Anesthesiologists (ASA) classification I or II. Additional exclusion criteria were infection at the site of investigation, known allergy to adhesive transparent film or ultrasound gel, [16] implanted pacemaker or cardio defibrillator (ICD), neurologic deficit of the arm, known peripheral neuropathy, pregnancy or lactation period. Demographic data like gender, age, size and weight, left or right-handed from each volunteer were collected.

Percutaneous nerve stimulation study

The volunteers were positioned supine with the head turned maximally to the left side. A standardized perforated and transparent film (Tegaderm ®, 3M,

Maplewood, MN) was attached to the skin on the right side of the neck parallel to the clavicle to cover the skin at the interscalene grove. Beforehand the transparent film was prepared with 49 perforations (3 mm Ø) in a square pattern (7 rows of 7 perforations) of 7 mm distances between the centres of the perforations (i.e. 4 mm distance between the edges of the perforations) and red coloured for easy recognition of the perforations (Fig. 1a). A neutral electrode (3M Red Dot; 3M, Maplewood, MN) was connected to the positive lead of a nerve stimulator (Stimuplex® HSN12, B.Braun, Melsungen, Germany) and placed on the opposite shoulder.
The stimulating pen was applied at each perforation while intending the metal ball of the pen completely into the skin without lateral displacement (Fig. 1b). In order to lower skin conductance gel was applied to the tip of the pen. A rectangular constant current stimulus with a pulse width of 1 ms and a frequency of 2 Hz was generated by the nerve stimulator. The electrical current (0-5 mA) was increased gradually until muscle twitches were elicited. Paresthesias and local twitches of muscles (mostly platysma) directly at the stimulating pen were not regarded as positive stimulation. Stimulation of trapezius muscle and diaphragm were regarded as inadequate motor responses. Minimal threshold (mA) and resistance (kΩ) for evoked motor response and type of activated muscle (group) were noted for each stimulated point.

Ultrasound examination

Following PNS, the brachial plexus (at the level of the neck) was examined by a second independent observer, blinded to the results of the stimulating pen examination. The plexus was first identified with a 13-6 MHz linear ultrasound probe (HFL 38 x & Turbo M, Sonosite Inc., Bothell, WA). Thereafter, the probe was applied to each of the 7 rows at the transparent film in a standardized manner. In order not to compress tissues, the probe was attached perpendicular to the skin with the least possible pressure (Fig. 1c). At each row ultrasound images were saved for off line analysis. The most superficial nerve structure was identified on the ultrasound image. Any vital structure like arteries or venes between the skin and the most superficial nerve structure was determined.

Calculations and data analysis

All perforations were represented on the ultrasound images by means of projecting a maze. The perforations where motor responses could be provoked were identified on the ultrasound image.
Following distances were measured (Fig. 2):

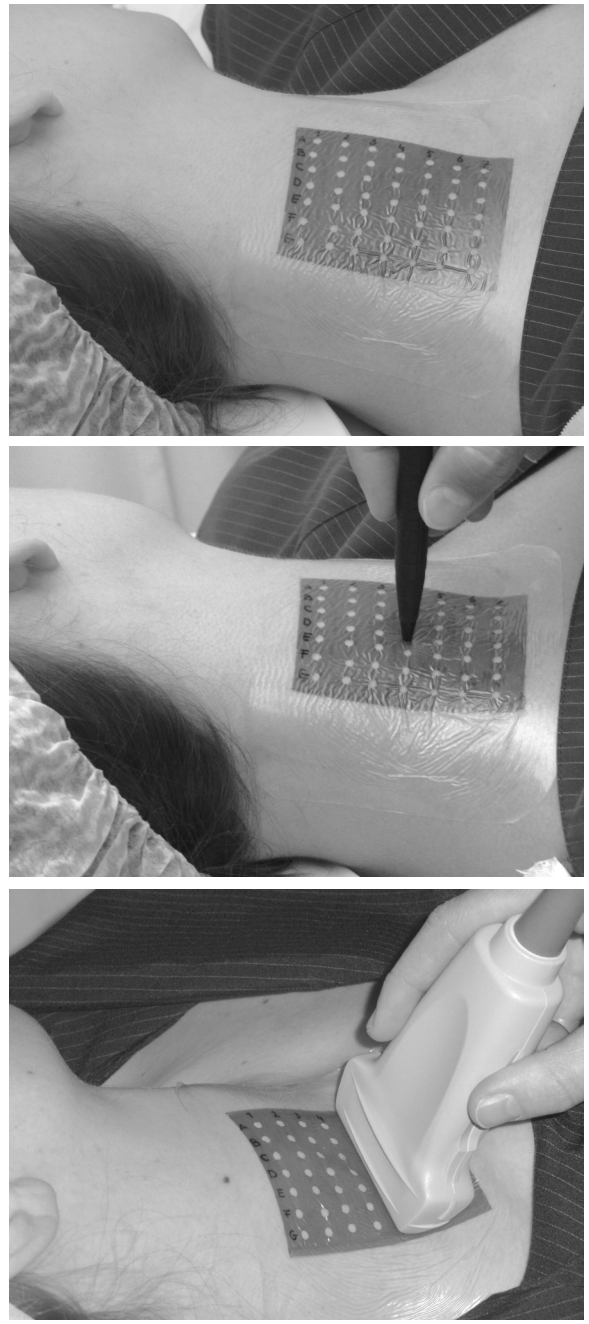

Figure 1

a. Perforated transparent film covering the skin at the interscalene groove.

b. The stimulating pen applied to the perforations at the skin.

c. The probe is placed at one of the seven rows for ultrasound examination.

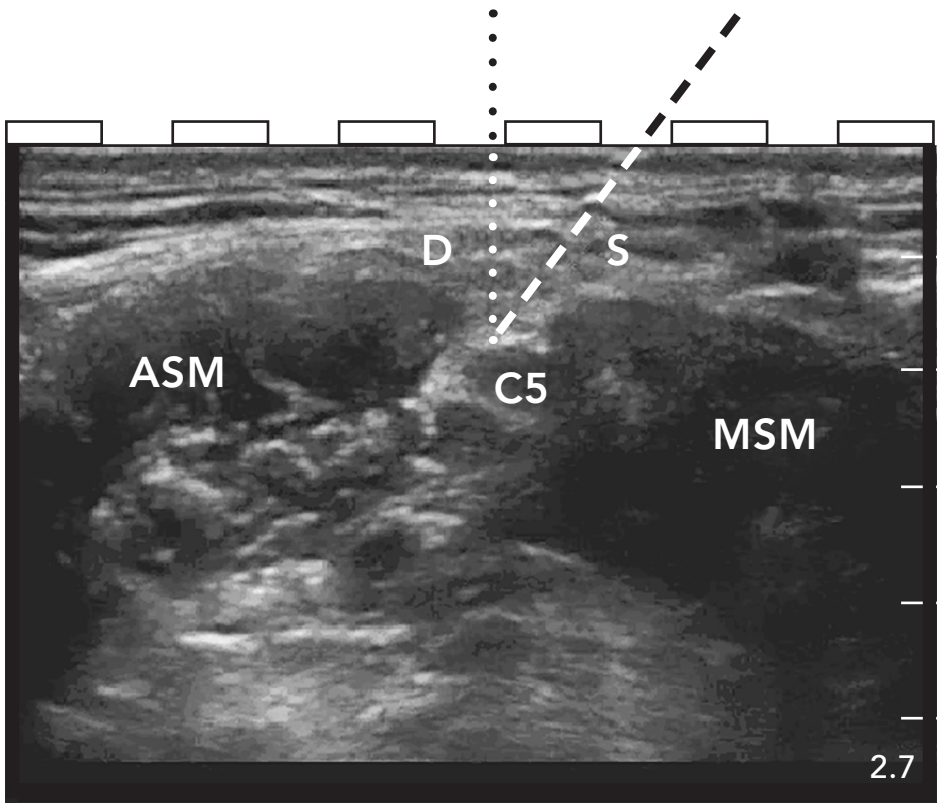

Figure 2 Schematic picture of ultrasound scan and transparent film with the perforations for the stimulating points. ASM, anterior scalene muscle; MSM, medial scalene muscle. D (dotted line) is the depth of root C5, which is the most superficial nerve structure. S (dashed line) is the shortest distance between the stimulating point in the perforated film and root C5.

– Shortest distance between center of stimulating pen and the most superficial border of the nerve structure (S).
– Depth of the most superficial nerve structure (D) (shortest distance between skin and the most superficial border of the nerve structure).
Finally, distances S and D were correlated separately with the associated percutaneous current thresholds at the perforations where a motor response could be provoked. All these correlations were recalculated and controlled for measured skin conductance.

Statistics

Data are presented as median (range). Correlations were analyzed without assuming normal distribution of data, thus non-parametrically. Spearmans rank-sum-correlation test was used and subsequently controlled for the measured skin conductance. *P*-values smaller than 0.05 were considered statistically significant.

Demographic data

Gender	**male/female**	**12/8**
Age Years	34.5	(29-65)
Bodylength	M 1.78	(1.62-1.91)
Bodyweight	Kg 75.0	(58-105)
BodyMassIndex	kg/m2 24.4	(20.3-28.8)
Handedness	right/left	17/3

Table 1 Demographics of the volunteers (n = 20) presented in median (range)

Results

Twenty volunteers participated in this study. Demographic data are presented in table 1.

Of the total 980 points (20 volunteers x 49 stimulation points in the adhesive film) tested with PNS, at 181 points an adequate muscle twitch of the arm was obtained (deltoid muscle at 74 points, biceps muscle at 5 points, triceps muscle at 3 points, supination or/and flexion of forearm at 57 points, movements of hand or/and fingers at 50 points). At 8 points stimulations of more than one muscle group were observed. Responses defined as inadequate were observed at 297 points (trapezius muscle at 273 points and diaphragm contractions at 24 points). No responses were observed at 483 points. Local platysma contractions were elicited at 138 points and they were combined with other responses at 119 points. *Per* volunteer a median of 5 (0-41) motor responses were elicited. In four subjects no motor response could be provoked at all. In three subjects isolated or combined diaphragm contractions were observed during stimulation.

At those points inducing an adequate motor response the median minimal electrical current was 3.25 mA (1.0-5.0). Median resistance was 8.5 kΩ (2.1-21.1) at all stimulated points.

After visualizing the brachial plexus with ultrasound at each row containing 7 perforations each, we determined the responses at the closest related perforations to the site at the skin most superficial to the nerve structure. 140 ultrasound images (20 volunteers x 7 images) were examined. Only in 10.0% the point at the skin with the lowest current was identical to the point closest to the most superficial nerve structure.

Median distances S and D from the points with the lowest current to the plexus (as visualized with ultrasound) were 12.6 mm (3.4-32.0) and 7.6 mm (0.3-28.6) respectively.

Typical examples of three different subjects comparing the distance S (stimulating point at the skin to most superficial nerve structure) and the minimal current (mA) eliciting an adequate motor response are shown in figure 3.

No positive correlation could be demonstrated between the minimal current at the positive response points and distance S (Fig. 4) or D (Fig. 5).

Using ultrasound, the dorsal scapular artery was identified superficial to the brachial plexus in the supraclavicular region in 3 volunteers. Nevertheless, a positive motor response was elicited in two persons at this location.

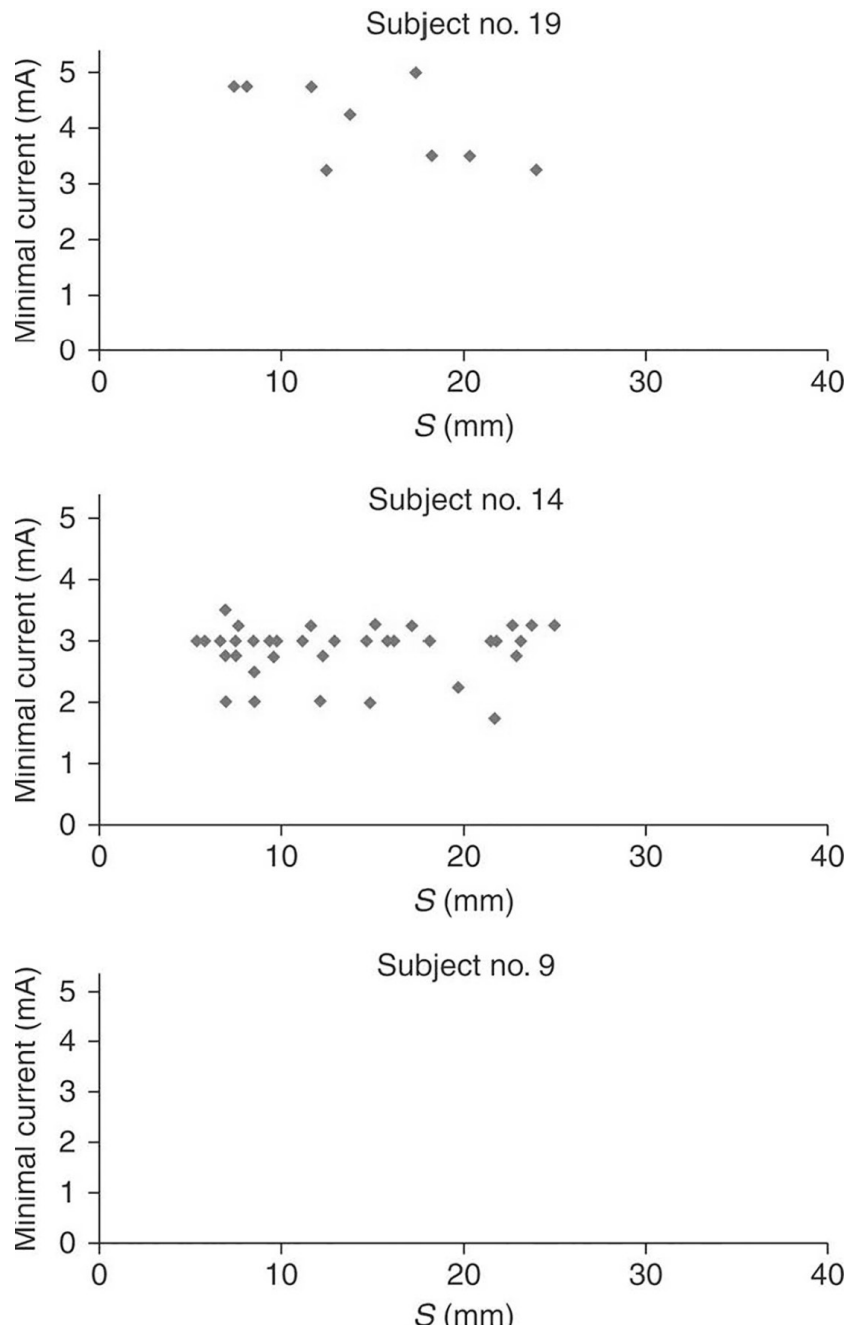

Figure 3 Three representative examples of correlation between the shortest distance S from the points with a motor response and the plexus (x-axis) and the minimal stimulation current at this point (y-axis). No motor responses were detected in subject 9.

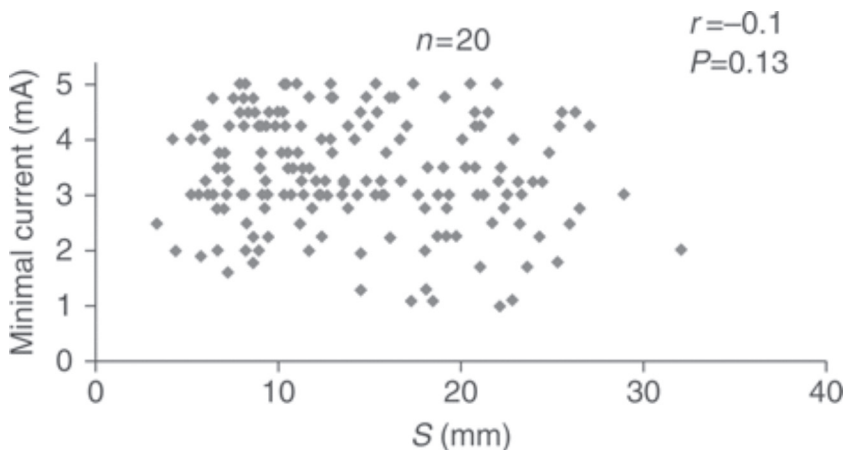

Figure 4 Shortest distances (S) between the motor response point to the plexus (x-axis) and minimal stimulating currents (y-axis).

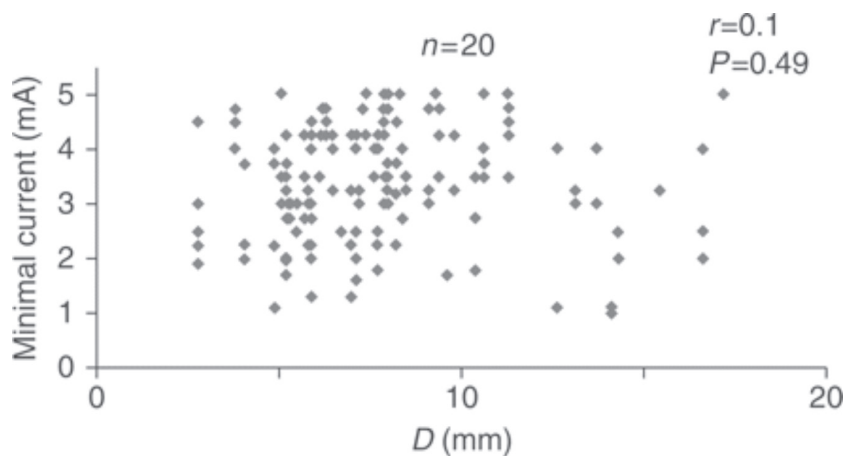

Figure 5 Depth of the most superficial nerve structures (D) (x-axis) and minimal currents (y-axis).

Discussion

Only a low percentage of the points localized with the stimulating pen at the skin of the interscalene and supraclavicular area corresponded to the points where the plexus was most superficial to the skin according to ultrasound visualization. Most of the points localised with the stimulating pen and ultrasound differed and was on average 1.3 cm apart. Distances between the stimulating pen and the most superficial nerve structure (distance S) or the depth (distance D) of the nerve structure did not correlate with the stimulating current thresholds. Occasionally the dorsal scapular artery was located between the skin and a nerve structure while a motor response was provoked by the stimulating pen directly above the artery.

PNS with a stimulating pen is used as a new non-invasive method to localise the optimal point on the skin for needle insertion during peripheral nerve blockade. Touching the skin with a stimulating pen at the anatomical landmarks of the neck can help to locate the brachial plexus.[1-4] The Stimuplex® Pen was launched by B. Braun in 2007 as a non-invasive device for locating superficial peripheral nerves. Unfortunately, the published data to evaluate its value are sparse. There is just one feasibility pilot study, which has only been published in abstract form.[11] Studies comparing this tool with ultrasound are lacking.

Capdevilla et al.[5] used percutaneous electrode guidance with a needle tip for prelocating the median, radial and ulnar nerve and measured the required depth for a nerve block after needle insertion in patients. All three nerves could be stimulated percutaneously in 85.5% of patients. The graphics suggested a positive relationship between the depth of the needle and the minimal percutaneous stimulating current required to provoke a motor response. Differences in the results to our study can be explained by the use of a stimulating needle for measuring depth of the nerve. Tissue may be dislocated while penetrating with an atraumatic needle. Thus, measuring distances between skin and nerve with a stimulating needle is less reliable. Furthermore, the correlation varied over a wide range and unfortunately correlation coefficients and p-values were not mentioned. Another reason for the differences in correlation to this study could be differences in electrical tissue characteristics in the neck and the axilla. In the present study we used ultrasound to measure and calculate the distances from the stimulating pen at the skin to the most superficial nerve structure.

The principle of PNS is based on the relationship between the intensity of the electrical current delivered and the distance between the stimulating pen and the

stimulated nerve. The current is believed to vary with the inverse of the square of the distance. Thus, a much larger stimulating current will be required as the pen moves away from the nerve according to Coulomb's law: $E = K (Qr^{-2})$ where E is the current intensity at a distance r from the electrical source, K is a constant dependent on the electrical properties of the medium through which the current is transmitted and Q is the minimal stimulating current of the electrical source.[12] The problem with this model is that the electrical properties of different human tissues vary considerably in specific electrical resistance (i.e. blood 150 Ωcm, skeletal muscle transverse 675 Ωcm, fat tissue about 2kΩcm and dry skin above 100 kΩcm). [17 18] Therefore, in men the relationship of conductivity and distance in inhomogeneous tissues cannot be linear.

More recent data comparing minimal stimulation current and distance between the needle tip and the nerve in patients using high-resolution ultrasound suggest that the correlation distance-current is not consistent.[19] In this study the stimulation threshold outside and inside the nerve trunk was the same in some patients. Stimulation thresholds greater then 0.2 mA could not rule out intraneural placement in 64% of patients. Clearly, these data were gathered by using hypodermic insulated needles after penetration of the skin in the proximity of nerve where the tissue resistance is supposedly more homogenous.

Another reason for not demonstrating any correlation between the distance and the stimulating thresholds might have been lack of indentation of the skin with the stimulating pen. Usually the skin is impressed considerably with the stimulating pen when clinically trying to identify nerves percutaneously. For methodological reasons this was not done in our study in order to avoid displacement of anatomical structures when using percutaneous electrical stimulation compared with ultrasound. Besides, there is no reason to believe that varying impression of the skin should change the correlation between depth and stimulation current since tissue resistance will still be variable. Tilting of the ultrasound probe could have influenced measured distances at the images. Since we placed the probe perpendicular to the skin with minimal pressure we reduced possible inaccuracies to a minimum.

Furthermore, anatomical structures like blood vessels could have interrupted the current to the nerve structure. Blood vessels like the dorsal scapular artery [20] running through the plexus were found only at 3 of 140 ultrasound images. However, above these arteries a motor response was elicited. This is a potentially hazardous situation when the stimulating pen would have been used as a needle guiding technique.

Finally, we compared ultrasound with PNS for localisation of the brachial plexus. A pure stochastic correlation of stimulus intensity and distance to the nerve structure is in striking contrast to the theory of nerve stimulation and may raise important questions regarding technique and theory of nerve stimulation. In Conclusion, compared to ultrasound, PNS is not a reliable technique for identifying the brachial plexus at the neck. Furthermore, ultrasound can give much more information about anatomical variations that might be missed just using a nerve stimulation technique.

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Chapter 5

Influence of arm position on ultrasound visibility of the axillary plexus

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Submitted

Abstract

Background and Objectives:

Contemporary axillary brachial plexus block is performed by separate injections targeting the radial, median, ulnar, and musculocutaneous nerve. These nerves are arranged around the axillary artery, making ultrasound visualization sometimes challenging. In particular the radial nerve can be difficult to see being frequently localized behind the artery. The primary aim of this study was to investigate which arm position optimizes the visibility of the radial nerve. Secondary aims were the visibility and position of the other axillary nerves during varying arm positions.

Methods

Following ethical committee approval, one anesthesiologist performed bilateral ultrasound examinations of the axillary plexus on 20 volunteers. Each arm was placed in different positions (shoulder (S) 90° or 180°, elbow (E) 0° or 90°) and scans were performed as far proximal as possible in the axilla, and additionally 5 cm distally to this point (proximal (P) vs. distal (D), respectively), resulting in eight different scans stored for off-line analysis. Two blinded anesthesiologists assessed visibility scores, distances and angles of the nerves relative to the artery.

Results

No significant differences between arm positions were found in the visibility score of radial ($p=0.359$) and musculocutaneous nerves ($p=0.073$). Visibility of the median nerve was improved in positions S90°/E0°/D and S180°/E0°/P ($p=0.02$). The ulnar nerve was more visible in position S180°/E 0°/P and D ($p=0.007$). The greatest distance between artery and radial nerve was 7.4±4.7mm at an angle of 120±14° in position S180°/E 0°/D.

Conclusions

The visibility of the radial nerve could not be significantly improved by varying the position of the arm. S180°/E0° provided the best overall visibility and accessibility of nerves.

Chapter 5

Influence of arm position on ultrasound visibility of the axillary plexus

Introduction

During the last decade, the use of high-definition ultrasound has renewed the interest in peripheral regional anesthesia.[1] Surprisingly, although ultrasound is used to directly target nerves and plexus, extremities are still most often positioned as if performing landmark-oriented approaches. These positions were generally based on dissectional anatomical studies. For example, the brachial plexus in the axillary region is approached with the extremity positioned as described by Winnie.[2] However, because of the mobility of the shoulder, the brachial plexus at the axillary level is particularly susceptible to rearrangement of its structures according to position.

Axillary brachial plexus block is one of the most commonly used methods of regional anesthesia.[3] Separate blockade of the four main constituent nerves (radial, median, ulnar, musculocutaneous) significantly increases success rate.[4] These nerves are arranged around the axillary artery within a neurovascular sheath. The position of the nerves inside the sheath is not fixed and allows a certain extent of movement. Furthermore, fibers are to a variable degree, exchanged between individual nerves.[5] Anatomy in the axillary fossa is variable,[6] which may render axillary block by single nerve blockade more difficult. Moreover, at the level of intersection of pectoralis major and biceps humeri muscle, where the axillary block is usually performed, only the radial, median, and ulnar nerve are consistently found within the common neurovascular sheath. The musculocutaneous nerve usually separates more proximally, and is usually found between the biceps and coracobrachialis muscles.[7, 8] Due to its anatomic position behind the axillary artery, the radial nerve is the most difficult to visualize when using ultrasound.[9]

Determining the optimal position of the arm for visualization of the radial nerve during the performance of the axillary brachial plexus block might render ultrasound guided axillary blocks even more efficient and safe. Thus, we investigated the influence of arm positioning on the sono-anatomy of the axilla and the visibility of the nerves most proximal in the axilla and 5 cm distally to this point. The primary objective of the study was to assess the ultrasound visibility of the radial nerve at two levels in four different arm positions. Secondary objectives were visibility, position and distance of all four nerves to the brachial artery and the skin.

Methods

This prospective observational study was conducted at the Department of Anesthesiology of the Academic Medical Centre (AMC) Amsterdam in November 2012.

Volunteers

Following Local Ethical Committee approval and registration in the national trial register (NL42116.018.12), 20 volunteers were recruited by placing an advertisement on the Department's bulletin board. Inclusion criterion was age > 18 years. Exclusion criteria were: refusal of ultrasound examination, restriction in shoulder movement, local infection, Body Mass Index ≥ 30 kg/m2 to avoid poor visibility due to obesity. After obtaining written and informed consent from each volunteer, demographic data such as gender, age, size and bodyweight as well as handedness were collected.

Ultrasound Examinations

All examinations were performed by one anesthesiologist (V.F.) experienced in regional anesthesia, using one ultrasound machine (M-Turbo; Sonosite; Bothell, WA, USA) with a linear multifrequency probe 13-6 MHz (HFL38X; Sonosite; Bothell, WA, USA). After a short introduction and explanation of the procedure, volunteers were placed supine for a bilateral ultrasound examination of the axillary region. Depth and gain were optimized for each volunteer and 'resolution mode' was selected on the ultrasound machine. To avoid shifting of the nerves during scanning, minimal probe pressure was exerted on the skin with only light compression of veins. Each arm was placed in four different positions:

1. Shoulder 90°/elbow 90°(=S90/E90)
2. Shoulder 90°/elbow 0°(=S90/E0)
3. Shoulder 180°/elbow 90°(=S180/E90)
4. Shoulder 180°/elbow 0°(=S180/E0)

In these four positions scans were performed at two levels: Proximal level (=P): at the intersection between the lower border of the pectoralis major muscle and the biceps brachii muscle (marked as proximal). Distal level (=D): Five centimetres distally from the first level (marked as distal). In all positions the forearm was kept in a neutral position midway between pronation and supination. Thus, eight different scans of each axilla were performed, results are shown in Table 1.
During each scan a 4 second-long video clip was captured, saved and encrypted for subsequent retrospective blinded viewing and assessment.

Image assessments and measurements

After completion of all examinations, video clips were assessed independently by two blinded assessors (M.F.S., J.T.W.), experienced in regional anesthesia. In each clip radial, median, ulnar and musculocutaneous nerves were assessed on visibility using a six-point visibility scale:

0 = no nerve identified,
1 = nerve identified with a high probability,
2 = nerve identified, but most of it not visible,
3 = nerve identified, more than 50% of its borders can be precisely distinguished from surrounding structures,
4 = nerve completely visible, but fascicles poorly defined,
5 = nerve completely visible and multiple fascicles identifiable.

Any discrepancy in visibility scores was discussed afterwards and clips were reviewed in order to find a consensus for the score.
Distances from each nerve to the skin and to the artery and angles from each nerve to the artery were measured. The shortest distances from nerves to skin and to the artery were measured in millimetres. The centers of the artery and each nerve were reference points for angle measurement (degrees). In cases where the nerve was not visible on the clip, distances and angles were not recorded. All data obtained were entered in a computer spreadsheet (SPSS, Chicago, IL, USA) for statistical analysis. Mean measurements of distances and angles from the nerves to the artery were geometrically visualized.

Statistical Analysis

Power analysis had revealed that to detect a clinical meaningful increase of visibility of the radial nerve of 30%, assuming a standard deviation of 20% with a power of 80 and an alpha of $p < 0.001$ (compensated for 6 comparisons), a group size of n=18 would be required. Assuming a 10% dropout, we included 20 volunteers.
Volunteer demographics are expressed in mean ± SD or median and range, where appropriate. Visibility scores of the radial, median, ulnar and musculocutaneous nerve, distances to the axillary artery, distances to the skin and angle with respect to artery are represented in mean ± SD in each of the eight scan positions. One way repeated measures analysis of variance was used to compare visibility scores in different scan positions and validated by Mauchly's sphericity test to reduce the likelihood of type I errors. Therefore visibility scores were taken at interval level. Post hoc tests were used to test for the multiple comparisons where appropriate. A value of $p < 0.05$ was considered to be statistically significant. Statistics were calculated with use of SPSS 20.0 for Windows (SPSS, Chicago, IL, USA).

Eight positions for scanning the axillary plexus

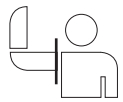
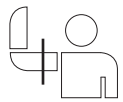
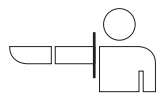
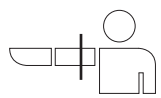
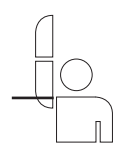
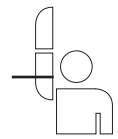
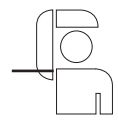
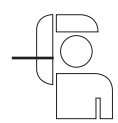
Position	Abbreviation	Picure	Colour
Shoulder 90⁰ abduction Elbow 90⁰ flexion Proximal scan	S90/E90/P		
Shoulder 90⁰ abduction Elbow 90⁰ flexion Distal scan	S90/E90/D		
Shoulder 90⁰ abduction Elbow 0⁰ flexion Proximal scan	S90/E0/P		
Shoulder 90⁰ abduction Elbow 0⁰ flexion Distal scan	S90/E0/D		
Shoulder 180⁰ abduction Elbow 0⁰ flexion Proximal scan	S180/E0/P		
Shoulder 180⁰ abduction Elbow 0⁰ flexion Distal scan	S180/E0/D		
Shoulder180⁰ abduction Elbow 90⁰ flexion Proximal scan	S180/E90/P		
Shoulder 180⁰ abduction Elbow 90⁰ flexion Distal scan	S180/E90/D		

Table 1 Eight positions for scanning the axillary plexus. Description of the positions, abbreviations and pictures. Last column represents corresponding colours, used in the results.

Results

Participant flow

Twenty volunteers were recruited in November 2012. All volunteers signed written informed consent without any drop-out. None of the volunteers experienced any harm or discomfort during the examinations. Demographic data of the volunteers are presented in Table 2.

Visibility Scores

For analysis of visibility scores, 320 video clips were captured from 40 axillary regions of twenty volunteers in 8 different scan positions. Mean ± SD visibility score in eight different scan positions are shown in Figure 1. We failed to identify the radial nerve in 10% of the clips (visibility score = 0) in scan position S180°/E90°/D, in 12.5% of cases in scan position S180°/E0°/P and in 22.5% in scan positions S90°/E90°/P, S90°/E0°/P and S90°/E0°/D. No significant differences in visibility score of the radial (p=0.359) and musculocutaneous nerve (p= 0.073) were found among the eight scan positions, whereas significant differences were found in visibility of the median (p= 0.02) and ulnar nerve (p=0.007). Post hoc testing demonstrated significantly improved visibility of median nerve in scan positions S90°/E0°/D and S180°/E0°/P compared to the 'classical' position of S90°/E90°/P (Fig 1b). Visibility of the ulnar nerve was significantly better in positions S180o compared to S90o (except S180o/E90°/D) (Fig. 1c).

Demographic data

Sex (male,female), n	10/10
Age, y	35±8
Body length, cm	180±9
Body weight, kg	71±12
BMI, kg/m2	22.0±2.1
Handedness (right/left), n	20/0

Table 2 Volunteer characterics. Continuous variables are presented as means±SDs; categorical variables are presented as counts.

Orientation of the nerves to the artery and the skin in different positions

Mean positions of the nerves in relation to the artery in the eight different scan positions with the artery as reference points are geometrically demonstrated in a transverse view in Figure 2.

Radial nerve

Significantly greater distances between the radial nerve and the artery were found in shoulder positions of 180°, whereas smallest distance was found in position shoulder 90°, elbow 90° or 0°, distal ($p<0.001$). Smallest distance to the skin of 6.9 mm (2.6) was found in a position shoulder 180°, elbow 0°, proximal, and greatest distance was 13.2 mm (3.5), found in a position shoulder 90°, elbow 90°, distal ($p<0.001$).

Median nerve

No significant differences in distance from the median nerve to the artery were found, ranging from 9.9±5.9 mm to 15.0±12.9 mm in different scan positions. However, significant differences were found in distances to the skin ($p<0.001$) with the smallest distance of 3.0±1.4 mm in position shoulder 90°, elbow 0°, proximal and a greatest distance of 5.4±2.1 mm in position shoulder 90°, elbow 90°, distal.

Ulnar nerve

No significant differences in distance from the ulnar nerve to the artery were found at different scan positions, ranging from 2.7±4.0 mm to 4.3±3.9mm, whereas distance to the skin was greatest in position shoulder 90°; elbow 0°; distal (5.3±1.8mm) and smallest in position shoulder 180°; elbow 90°; proximal. ($p<0.001$)

Musculocutaneous nerve

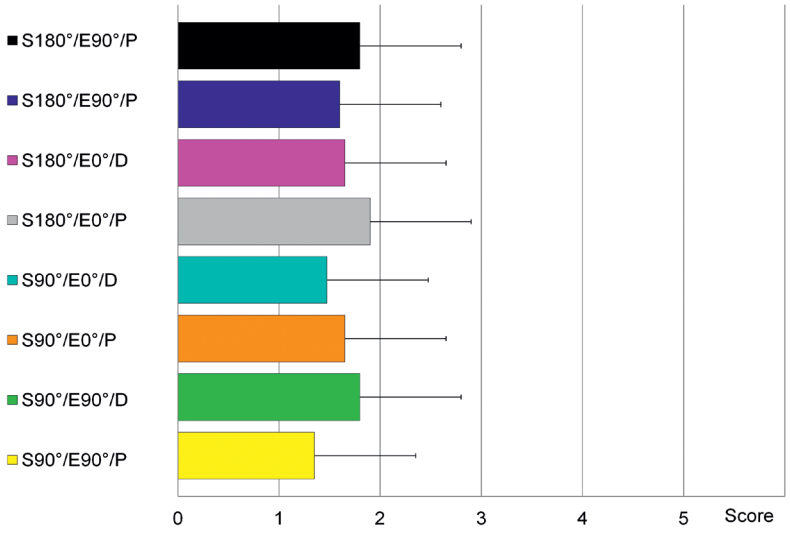
Distance to the artery was greatest in position shoulder 90°, elbow 90°, distal (13.9±5.4mm) and smallest in position shoulder 180°, elbow 0°, proximal (9.0±4.4mm, $p<0.001$). Distance to the skin was greatest in position shoulder 180°, elbow 90°, distal (12.6±4.2 mm) and smallest in position shoulder 90°, elbow 90°, proximal (9.8±3.4 mm) and in position shoulder 90°, elbow 0°, proximal (9.8±3.2 mm, $p<0.001$).

Discussion

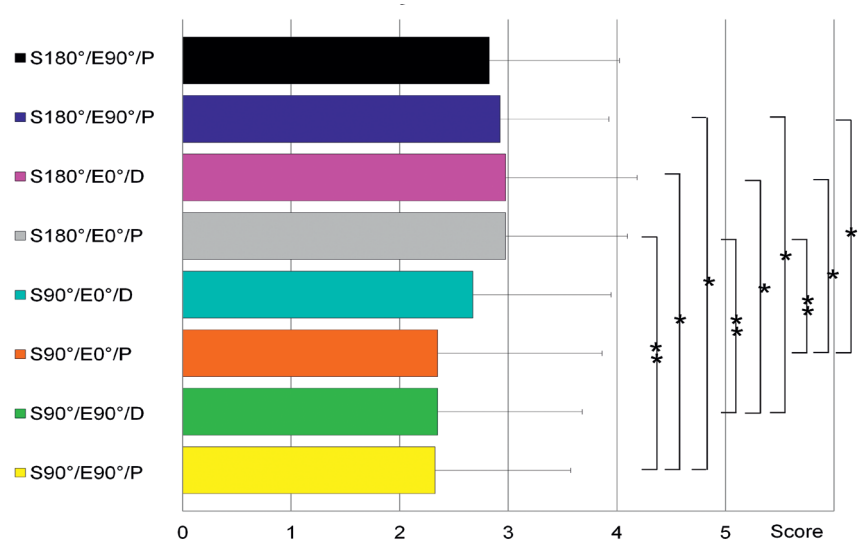
Visibility of the radial nerve was not affected by changing the position of the shoulder, elbow or the scan level in the axilla. However, within subjects, analysis demonstrated a significantly improved visibility of the median nerve when scanning in position shoulder 180°; elbow 0°; proximal or the position shoulder 90°; elbow 0°; distal. In addition, a significantly improved visibility of the ulnar nerve was found when the shoulder was positioned in 180° except when the elbow was flexed, while scanning at the distal level in the axilla. The arm position providing optimal visibility of all four nerves simultaneously is shoulder 180°; elbow 0°; proximal.

Remarkably, there was a wide variation in distance and angle from the radial nerve to the artery (Fig. 2a), while the varying positions of the arm and scan levels did not influence the visibility of the nerve. This may be due to the fact that the radial nerve is often obscured behind the axillary artery by dorsal enhancement and lateral shadowing artifacts. In contrast, despite being consistently located anterior to the artery, the visibility of the median and ulnar nerve changed significantly with differing arm positions. Median and ulnar nerve were consistently in front of the artery, but their visibility changed significantly in different positions. In the position shoulder 90°; elbow 0°; proximal; the radial nerve is most often vertically located under the artery, making invisibility of the radial nerve very likely due to acoustic enhancement of the artery (Fig. 2a). The distance from the radial nerve to the artery was greatest when the shoulder was abducted 180° and the scan performed distal in the axilla, theoretically reducing the risk of a deterioration in visibility as a result of artifacts induced by the artery.[10] However, this scan position did not improve the visibility of the radial nerve. Aside from the influence of the artery, there are several other possible causes of poor to moderate visibility of the radial nerve. The radial nerve does not travel parallel to the artery and the skin, but after passing superficial to the latissimus dorsi tendon and teres major muscles in the axilla, it runs diagonally in the fascial plane of the long and median head of the triceps, and spirals oblique across the posterior surface of the humerus.[11] Thus scanning of the brachial plexus and artery in the short axis at the level of the axillary artery is not perpendicular to the axis of the radial nerve, resulting in poor reflection and visualization. Moreover, muscular branches to the heads of the triceps arise from the radial nerve at the level of the axilla and proximal humerus in highly variable numbers and levels, resulting in individual

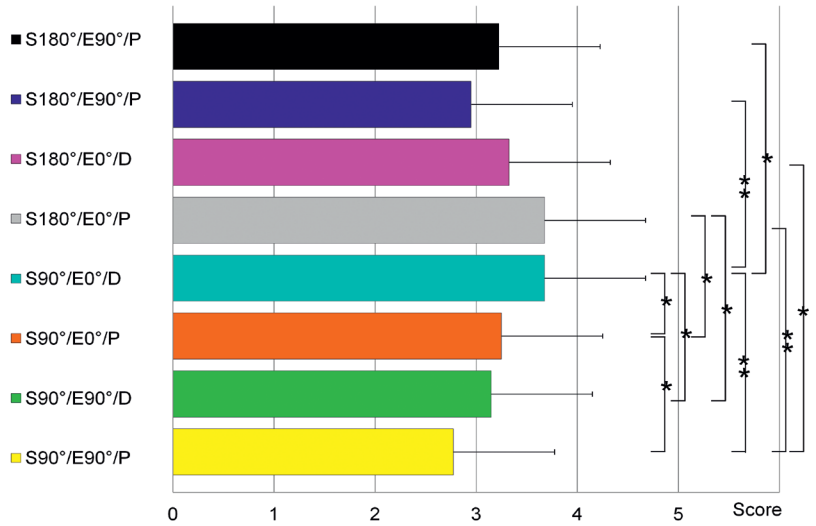
Visibility Radial Nerve



Visibility Ulnar Nerve



Visibility Median Nerve



Visibility Musculocutaneus Nerve

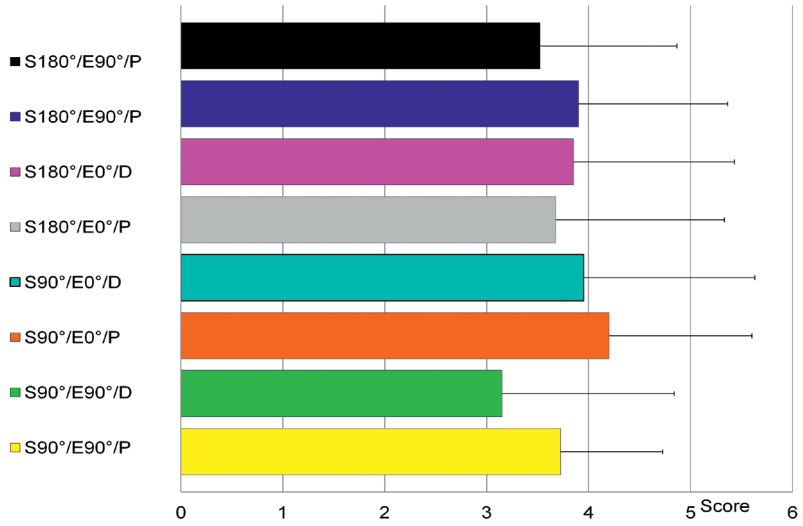
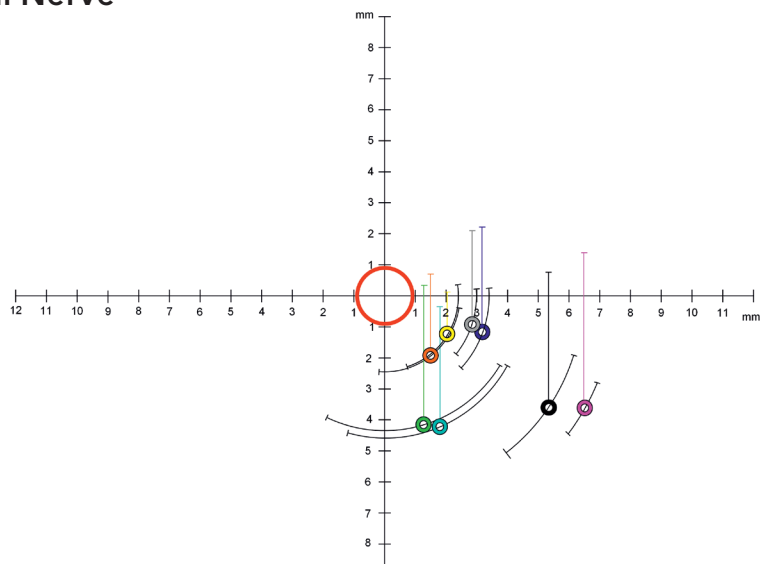
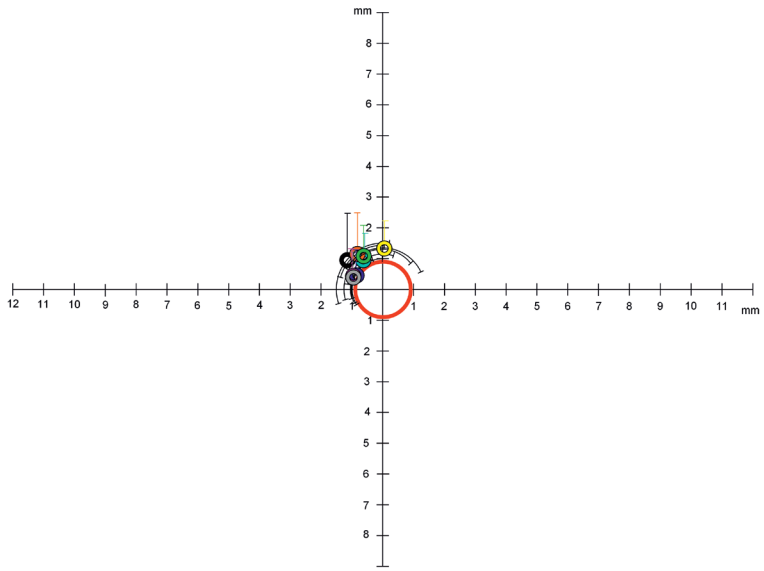


Figure 1 Visibility scores of the radial nerve (A), median nerve (B), ulnar nerve (C) and musculocutaneus nerve (D) in eight different positions, represented in corresponding color (see table 1). Visibility Score is 0-5, where score 0 represents 'nerve not visible' and score 5 represents 'nerve completely visible'. * $p<0.05$, ** $p<0.005$

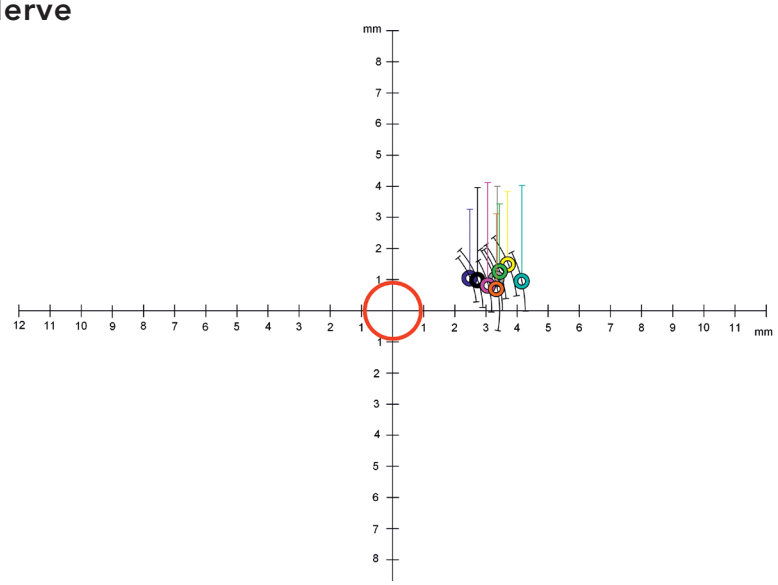
Radial Nerve



Median Nerve



Ulnar Nerve



Musc. Cut. Nerve

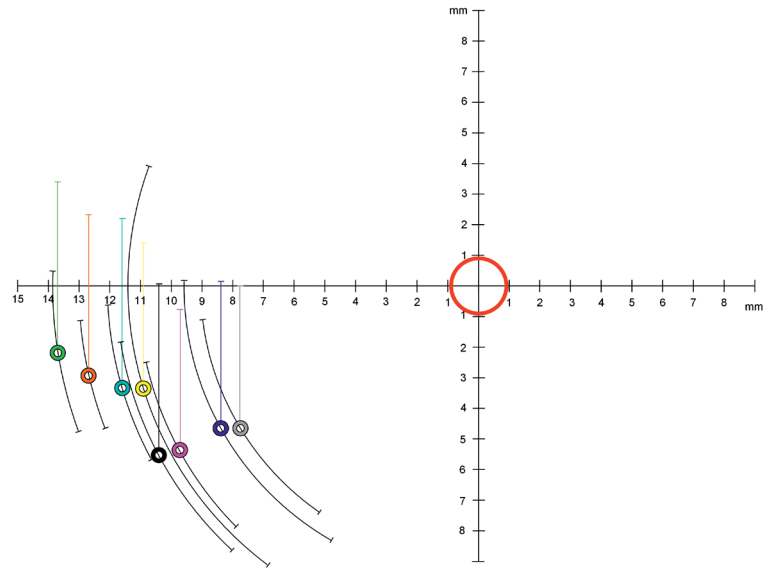


Figure 2 Geometric presentation of the distances (mm) and angles (degrees) of the radial nerve (A), median nerve (B), ulnar nerve (C) and musculocutaneus nerve (D) in relation to the brachial artery in eight different positions, represented in corresponding color (table 1).Lines represent SD of mean distance and curves represent SD of mean angle to the brachial artery. Brachial artery is the reference point on the X- and Y- axis.

differences in visibility scores.[12] In a similar study of the sciatic nerve undertaken in the popliteal fossa, visualization of the division of the sciatic nerve into the tibial nerve and common peroneal nerve was difficult because of differences in angulation, direction, depth and internal architecture of nerve tissue.[13]

Our results are partly in agreement with findings obtained by Wong et al., who found it impossible to visualize the radial nerve in two of 48 patients. In contrast to our current study, the latter examination was not performed in standardized views, and radial nerve identification was verified by nerve stimulation.[14]

The percentage of between 10 and 22.5 % of the video-clips wherein the radial nerve was not identifiable seems high, however, for methodological reasons the scans were very standardized and very little movement was allowed to identify the nerve. Thus, it is not surprising that the rate of identification is lower than when free scanning is possible. One may argue that nerve identification just by looking at short clips is fallible. Thus, transcutaneous identification might be an option in volunteers, but this has been shown in earlier studies to be almost of no value in locating the nerves where they are superficially located.[15] Although the visibility score of the radial nerve does not change significantly between the different arm positions, it is most superficial to skin and most distant to the artery at position shoulder 180°; elbow 0°; proximal. An additional benefit in this same position is the high visibility score of the median and ulnar nerve.

In addition, the location of the musculocutaneus nerve varied widely in differing arm positions, without affecting nerve visibility. Therefore, although this position (shoulder 180°; elbow 0°; proximal) does not increase the visibility of the radial nerve significantly, it seems to be the most advantageous for the integral visibility and location of all nerves.

Movement of the shoulder to 180° extends the coracobrachial muscle, and straightening the elbow extends the biceps muscles whilst shifting and decreasing the cross-section of the muscle layers. This is one of the reasons why in this arm position the nerves are most superficial to the skin and in the case of the median and ulnar nerve most visible.

Limitations

Before using this new position of the shoulder as a standard positioning in clinical practice a few things must be considered. The scans taken were short and the probe was only marginally moved in order to have a high degree of standardization. In clinical practice the probe is variably moved according to the individual anatomy. Nevertheless, we could identify a position that results in the most superficial nerve depth, and leads to the highest visibility of two of the nerves. Furthermore, the volunteers were younger and leaner than the average patient population. Furthermore, some (older) patients might not able to abduct their shoulders to 180°. As the radial nerve does not run parallel to the artery it would have been interesting to study the degree of tilting that is required for an improved visibility of the radial nerve in the arm position where the radial nerve is most far away from the artery. Nevertheless, in clinical daily practice it is worth attempting to position the patient arm to shoulder 180°; elbow 0°; proximal to optimize the visibility of the median and ulnar nerve.

We used a 6-point scale for the nerve visibility score, while a four step scale was used in the study of Wong and in a study about the visualization of the sciatic nerve.[14, 16] However, there is no standardized or validated scale for ultrasonic nerve visibility. In our opinion we could classify the visibility more precisely by defining each score in detail in advance. Other studies have been performed to determine a recommended patient position on the basis of nerve to skin distances measured with ultrasound for an infraclavicular block.[17, 18] In a study by Bigeleisen et al., success rate, performance- and onset time were measured in patients undergoing a supraclavicular block. We did not determine these variables since our study was performed in volunteers to explore a recommended position for the axillary brachial plexus block in order to increase visibility of the often ‘problematic’ radial nerve. Although we could not identify a position that enhanced the visibility of the radial nerve, we did identify a position that increased the visibility of median and ulnar nerve, and exposed most nerves to a more superficial position more distant from the artery. It remains to be determined whether selecting for an arm position with good overall visibility will also translate into a clinically appreciable benefit, such as shorter time to block, or a higher block success rate.

In conclusion, we recommend an arm position with the shoulder in 180° abduction, elbow 0° and a proximal scan level for ultrasound guided axillary brachial plexus block in order to allow the best visibility, especially of the ulnar and median nerve.

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Chapter 6

Effect of local anesthetic volume (15 vs 40 ml) **on the duration of ultrasound-guided single shot axillary brachial plexus block** A prospective randomized, observer-blinded trial

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Abstract

Background and Objectives

One of the advantages of ultrasound-guided peripheral nerve block is that visualization of local anesthetic spread allows for a reduction in dose. However, little is known about the effect of dose reduction on sensory and motor block duration. The purpose of the present study was to compare the duration of sensory and motor axillary brachial plexus block (ABPB) with 15 or 40 mL mepivacaine 1.5%.

Methods

Thirty patients were randomly allocated to receive ultrasound-guided ABPB with either 15 (group 15 mL, n = 15) or 40 mL (group 40 mL, n = 15) mepivacaine 1.5%. Onset, efficacy, and duration of sensory and motor block were compared.

Results

Two patients in group 15 mL needed an additional rescue block before surgery and were excluded from subsequent analysis. The overall median duration of sensory and motor block was significantly shorter in group 15 mL (225 [148-265] min vs 271 [210-401] min and 217 [144-250] min vs 269 [210 - 401] min, respectively; $p < 0.01$). Duration of sensory and motor block of individual nerves was significantly shorter in group 15 mL (20%-40% reduction for sensory and 18%-37% for motor block). Time to first request of postoperative analgesia was also significantly reduced in group 15 mL (163 [SD, 39] vs 235 [SD, 59] min, respectively, $p < 0.05$). There were no differences in the other block characteristics.

Conclusion

In ABPB with mepivacaine 1.5%, reducing the dose from 40 mL to 15 mL (62.5%) shortens the overall duration of sensory and motor block by approximately 17% to 19%, reduces sensory and motor block duration of individual nerves by 18% to 40%, and decreases the time to first request of postoperative analgesia by approximately 30%.

Chapter 6

Effect of local anesthetic volume (15 vs 40 ml) on the duration of ultrasound-guided single shot axillary brachial plexus block A prospective randomized, observer-blinded trial

Introduction

Peripheral nerve block as an anesthetic technique plays an important role in modern regional anesthesia. The most important prerequisites for the use of peripheral regional anesthesia in daily clinical practice are success rate and safety. Ultrasound guidance shortens block performance time, reduces the number of needle insertions, and shortens the block onset time.[1] Recent publications illustrate that the volume of local anesthetic can be significantly reduced with the use of ultrasound.[2–10]
Axillary brachial plexus block (ABPB) is widely used to provide anesthesia for surgery of the forearm, wrist, and hand. The procedure is relatively safe, and complications are uncommon.[11] Before the introduction of ultrasound, volumes of 40 mL or more were commonly used.[12] Recent research has focused on reducing the volume necessary to establish adequate ABPB. Volumes of 5 mL per nerve[13] or even as low as 1 mL lidocaine 2% per nerve[6] have been reported to achieve successful ABPB. However, the effect of dose reduction on block duration remains unknown.
The purpose of the present study was to evaluate the effect of the volume of mepivacaine 1.5% on the duration of sensory and motor block in ultrasound-guided ABPB.

Materials and Methods

Patients

This prospective single-blinded, randomized study was approved by the Institutional Review Board Nijmegen and registered at http://www.trialregister.nl (NTR2371) before participant enrolment. Patients scheduled for a single-shot ABPB for hand, wrist, or forearm surgery were assessed for eligibility during the preoperative screening visit. Patients were informed about the study verbally and in writing, and written informed consent was obtained from all patients. The study was conducted at the Sint Maartenskliniek, Nijmegen, The Netherlands, between July 2010 and March 2011 in accordance with the Declaration of Helsinki and later revisions thereof, as well as ICH guidelines for Good Clinical Practice.
Eligible participants were adults 18 years or older with American Society of Anesthesiologists physical health classification I-III and a body weight greater than 50 kg. Exclusion criteria included contraindications for regional anesthesia (infection at the injection site, coagulopathy), known hypersensitivity to amide-type local anesthetics, known history of peripheral neuropathy, and known history of hepatic or renal insufficiency.

Anesthetic Procedure

All patients received paracetamol 1000 mg orally 3 times daily and meloxicam 15 mg orally once daily, starting on the morning of surgery. Additional postoperative pain treatment was provided upon patient request and consisted of oxycodone 10 mg orally 4 to 6 times daily.

Using a computer-generated sequence of random numbers and a sealed envelope technique, 30 patients were randomly allocated to receive ultrasound-guided ABPB with either 15 (group15 mL, n = 15) or 40 mL (group 40 mL, n = 15) mepivacaine 1.5%. After establishing intravenous access and routine monitoring (electrocardiogram, non-invasive blood pressure, and peripheral oxygen saturation), ABPB was performed under ultrasound guidance (L12-5 linear probe connected to Philips HD11 XE; Philips, Eindhoven, The Netherlands) using a short-axis, in-plane technique. Blocks were performed under aseptic conditions using chlorhexidine skin preparation and sterile ultrasound probe covers (Flexasoft; Medicocare, Numansdorp, The Netherlands).

A 100-mm, 22-gauge, insulated, short-bevel needle (Stimuplex; B. Braun, Melsungen, Germany) was inserted laterally in the axilla. The needle was connected to a nerve stimulator (Stimuplex HNS 11; B. Braun) that was set to deliver 100 Nc (0.1 millisecond, 1 mA), only to facilitate identification of the individual nerves. After identifying the musculocutaneous, median, ulnar, and radial nerves, each nerve was blocked with either 10 mL (40 mL group) or 3 to 4 mL (15 mL group) mepivacaine 1.5%.

Time was designated t = 0 upon conclusion of the block procedure.

Clinical Assessments

In the first 30 min after injection of the local anesthetic solution, a blinded observer assessed the onset of sensory and motor block every 5 min. Sensory block of the medial antebrachial cutaneous, musculocutaneous, radial, median, and ulnar nerves was assessed by pinprick at specific sites (Table 1).

Sensory block was scored on a 3-point scale as 0 = absent, 1 = partial, and 2 = complete.

At the same intervals, motor block of the musculocutaneous, radial, median, and ulnar nerves was assessed (Table 1) on a similar 3-point scale (0 = no, 1 = partial, and 2 = complete motor block). A complete overall sensory block was defined as a total score of 10; complete overall motor block was defined as a total score of 8. In case of insufficient analgesia at the surgical site at t = 30 min, an additional rescue block was placed in the block room, and the patient was excluded from further analysis.

Surgery was performed under regional anesthesia. In the case of patient discomfort or upon patient request, sedation was provided with propofol (25-60 µg/kg per minute) and remifentanil (0.01-0.05 µg/kg per minute). If sedation was insufficient for patient discomfort, patients were converted to general anesthesia.

Upon arrival at the recovery room, offset of sensory and motor block was assessed by a blinded observer every 15 min in the same manner as preoperatively until full recovery. The primary outcome parameter was overall duration of sensory block. Overall duration of sensory block was defined as the time from t = 0 until the first postoperative measurement where total sensory score had returned to 0. Overall duration of motor block was defined similarly. Duration of sensory and motor block of individual nerves was defined as the time from t = 0 until the first postoperative measurement where the sensory and motor score for the individual nerve was 0. Secondary outcome parameters included overall duration of motor block, duration of sensory and motor block of individual nerves, block onset time, block efficacy, and time to first request for additional postoperative pain treatment (TTFR). Block onset time was defined as the time from t = 0 until the time sensory, respectively, motor score was maximal. Block efficacy during surgery was assessed as successful (no intraoperative sedation necessary), partially successful (intraoperative sedation necessary), or unsuccessful (conversion to general anesthesia). Time to first request for additional postoperative pain treatment was defined as the time interval from t = 0 until the time the first request for postoperative analgesia was made.

Sample Size and Statistical Analysis

The sample size calculation was based on the overall duration of sensory block. Robaux et al[14] found a sensory duration of ABPB (with 40 mL mepivacaine 1.5%) of 183 (SD, 43) min. Based on these data, the sample size required to have a 90% probability of detecting a decrease in duration of 60 min (level of significance 0.05) was 12 patients per group using an unpaired t test. Compensating for dropout, we chose to include 15 patients per group.

Analysis was per protocol. Data were analyzed using the GraphPad InStat v. 3.10 package (GraphPad Software Inc, San Diego, California). The Kolmogorov-Smirnov test was used for normality testing. Continuous, normally distributed data are presented as mean (SD), and non-normally distributed data as median (range). Statistical comparison between the groups was based on the Student t test for normally distributed data, and the Mann-Whitney U test for nonparametric comparisons. For comparisons within groups, normally distributed data were compared using the 1-way analysis of variance, and non-

normally distributed data using the Kruskal-Wallis test. Post hoc comparisons were made using Tukey-Kramer or Dunn multiple comparisons test as appropriate. Categorical data were compared using Fisher exact test. In the case where a parameter was normally one group and non-normally in the other group, the data are presented as median (range), and a nonparametric test as used for statistical comparison. All tests were 2-sided, and $p < 0.05$ was considered statistically significant.

Results

Thirty patients were included, 15 in each group. A flowchart of patients enrolled in this study is presented in Figure 1. In group 15 mL, 2 patients needed a rescue block before surgery because of incomplete block in the surgical area, compared with 0 patients in group 40 mL. These 2 patients were excluded from subsequent analysis. There were no significant differences in patient demographics between the 2 groups (Table 2). On 7 time points postoperatively, we were unable to obtain a measurement of sensory and motor blocks in 6 patients because of temporary patient unavailability. In 5 patients, these missing data did not affect the outcome parameters because sensory and motor blocks were still present at the next measurement. In 1 patient (group 40 mL), we missed 2 consecutive measurements during which both sensory and motor blocks had completely resolved. In this patient, we took the first time point following the missing data to calculate overall block duration; replacing this time point with the first time point where we were unable to obtain a measurement (30 min earlier) revealed that this did not significantly affect the results.

Block Characteristics

Thirty minutes after block placement, 7 of 13 patients in group 15 mL had a complete sensory block (maximum score of 10) versus 9 of 15 patients in group 40 mL (not statistically significant [NS]). Onset of complete sensory block was 21 (SD, 5)min in group 15 mL (n = 7) and 22 (SD, 6) min in group 40 mL(n = 9) (NS). After 30 min, motor block was complete (maximum score of 8) in 8 of 13 patients in group 15 mL versus 11 of 15 patients in group 40 mL (NS). Onset of complete motor block was 22 (SD, 8) min and 23 (SD, 7) min in group 15 mL (n = 8) and group 40 mL (n = 11), respectively (NS). There were no significant differences between the groups in the onset times of sensory/motor block of individual nerves. Data on sensory and motor block scores of individual nerves are shown in Table 3.

The median overall duration of sensory block in group 40 mL was 271 (range, 210-401) min versus 225 (range, 148-265) min in group 15 mL ($p < 0.001$). The median overall duration of motor block was 269 (range, 210-401) min in group 40 mL versus 217 (range, 144-250) min in group 15 mL ($p < 0.001$)

Overall duration was largely determined by the duration of sensory and motor block of the ulnar nerve. In 10 of 13 patients in group 15 mL and 10 of 15 patients in group 40 mL, the ulnar nerve was among the last to recover. Within each group, there were no significant differences in the duration of sensory and motor block between the individual nerves. Between groups, the duration of both sensory and motor blocks for each individual nerve was significantly longer in group 40 mL. Data on overall and individual block characteristics are summarized in Table 4 and Figures 2-4.

Twelve patients, 6 in each group, requested additional postoperative analgesia. Time to first request for additional postoperative pain treatment was significantly shorter in group 15 mL (163 [SD, 39] min) as compared with group 40 mL (235 [SD, 59] min) (P < 0.05). Twenty-five patients underwent surgery without need for additional sedation. Three patients, 2 in group 15 mL and 1 patient in group 40 mL, needed sedation because of patient discomfort. None of the patients required conversion to general anesthesia.

Sensory and Motor Testing

Nerve	Sensory test Site	Motor Test
Medial antebrachial cutaneous forearm	-	Medial side
Musculocutaneous	Lateral side forearm	Elbow flexion
Radial	Dorsum of hand	Wrist extension
Median	Ventral top of middle finger	Thumb opposition
Ulnar	Hypothenar eminence	Finger abduction

Table 1 Sensory and Motor Testing

Discussion

In the present investigation, a local anesthetic volume reduction of 60% resulted in an approximately 17% shorter overall sensory and 19% motor block duration and a reduction in TTFR of approximately 30%. Because overall duration is determined by the last nerve to recover, this parameter may underestimate the effect of a reduction in dose. Indeed, we found that the reduction in duration for individual nerves was larger, varying from 20% to 40% for sensory block and from 18% to 37% for motor block. The ulnar nerve was least affected by the reduction in dose; the 2 nerves most strongly affected were the medial antebrachial cutaneous and musculocutaneous nerves.

Duration of peripheral nerve block depends on several factors, such as the choice of local anesthetic, the site of injection, and the presence of adjuncts, for example, clonidine or epinephrine. Some studies in children indicate that the use of ultrasound guidance itself provides a longer duration of sensory blockade compared with nerve stimulation without ultrasound.[15,16] The dose of local anesthetic administered when performing peripheral nerve block is determined by volume and concentration; the manner in which these parameters affect duration is controversial. In a study aimed to determine the minimum effective anesthetic volume for blocking the median and ulnar nerve with mepivacaine 1.5%, Ponrouch et al.[17] found that the use of ultrasound as compared with nerve stimulation reduced the effective anesthetic volume by 50%. They also found a significant correlation between the volume of local anesthetic and the duration of sensory blockade, the correlation being higher with lower volumes. Similar findings were reported in a volunteer study designed to determine the ED99 volume of mepivacaine 1.5% for sciatic nerve block, showing a proportional relation between volume of local anesthetic per millimetre squared cross-sectional nerve area and duration of sensory block.[18] In a study comparing low-volume (16 mL) ultrasound-guided ankle block with a conventional higher-volume (30 mL) landmark technique using ropivacaine 0.5%, Fredrickson et al.[19] found that average postoperative pain was marginally higher in the low-

Consort flowchart

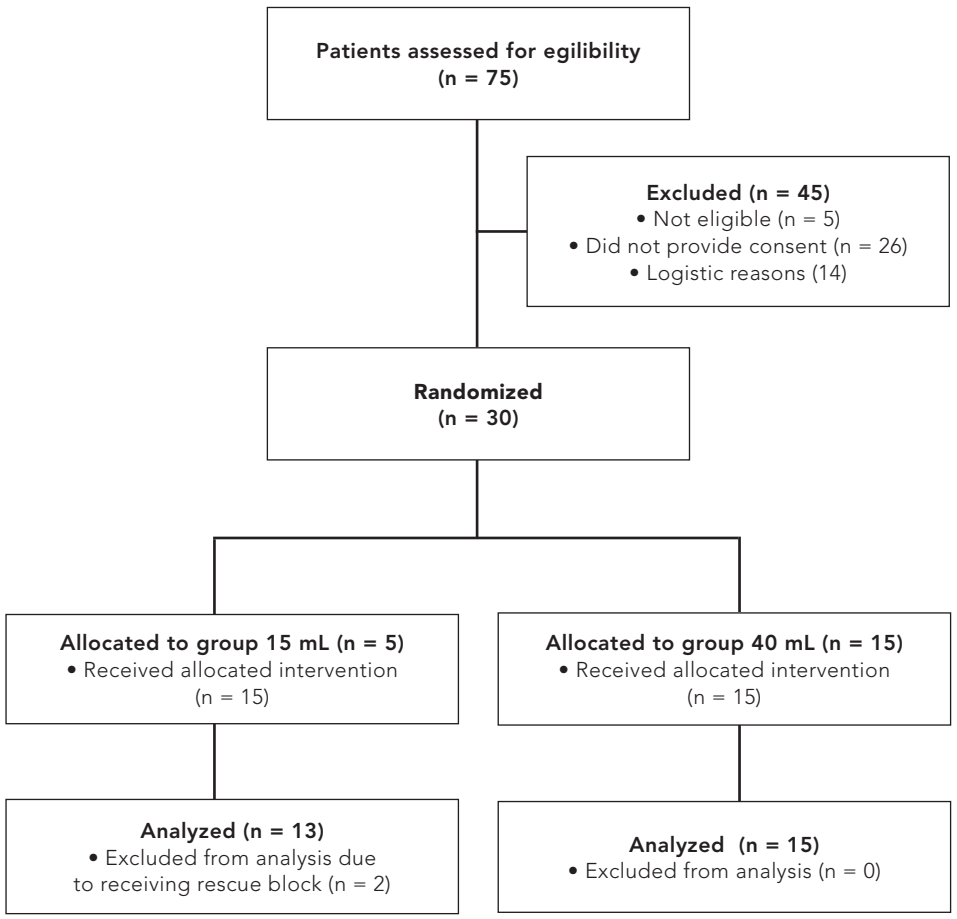

Figure 1 Flowchart of patients enrolled in the study.

Baseline Characteristics

	Group 15mL (n = 13)	Group 40mL (n = 15)
Sex, no. male/no. female	5/8	4/11
Age, y	53 (16)	55 (9)
Height, cm	171 (9)	173 (8)
Weight, kg	76 (13)	78 (14)
Body mass index, kg/m2	25.8 (3.7)	25.8 (2.8)
Duration of surgery, min	23.2 (15.6)	21.5 (10.7)

Table 2

Group 15 mL: axillary brachial plexus block with 15 mL mepivacaine 1.5%.

Group 40 mL: axillary brachial plexus block with 40 mL mepivacaine 1.5%.

Values are numbers or mean (SD).

volume group. Although the authors did not measure block duration or the time to first request of postoperative analgesia directly, the results suggest a shorter duration of sensory block associated with the low-volume group. On the other hand, Serradell et al.[20] compared the number of complete sensory blocks for different volumes (20, 28, 36 mL) of mepivacaine 1% in axillary block and found no differences in success rate, onset time, and duration of analgesia among the 3 groups. The results of the latter study suggest that 200 mg mepivacaine in a volume of 20 mL provides adequate axillary block and that increasing the volume/dose of mepivacaine to 280 or 360 mg does not result in a higher success rate or a longer duration of analgesia. Duration of analgesia reported by Serradell et al.[20] was 231 (SD, 45) min in their group receiving axillary block with 200 mg mepivacaine in 20 mL. Interestingly, the TTFR in our group 40 mL (600 mg mepivacaine) was similar (235 [SD, 59] min), whereas the TTFR in our group 15 mL (225 mg mepivacaine) was considerably shorter. Although differences in methodology preclude making direct comparisons, these observations may indicate that the reduction in block duration seen in our study is caused by the reduction in volume from 40 mL to 15 mL rather than the reduction in dose from 600 mg to 225 mg. However, further study is required to substantiate this. The data from our study are in accordance with the studies reporting a correlation between volume of local anesthetic and duration of peripheral nerve block.

The possibility of reducing the volume (and dose) of local anesthetic with ultrasound-guided peripheral nerve block is an obvious advantage from a safety perspective. Short- to intermediate-acting local anesthetics, such as mepivacaine, are used for surgeries where postoperative pain is expected to be

Block Scores of Individual Nerves

Nerve	Group 15mL (n = 13)			Group 40mL (n = 15)		
	Score 2	Score 1	Score 0	Score 2	Score 1	Score 0
Med. Anteb. Cut. sens.	11	2	-	14	1	-
Musculocutaneous sens.	12	1	-	12	3	-
Musculocutaneous mot.	9	4	-	13	2	-
Radial sens.	10	3	-	12	3	-
Radial mot.	11	2	-	11	4	-
Median sens.	11	2	-	14	1	-
Median mot.	11	2	-	15	-	-
Ulnar sens.	11	2	-	15	-	-
Ulnar mot	11	2	-	14	1	-

Tabel 3 Block Scores of Individual Nerves at 30 min. Groups as defined in Table 2. Values are numbers. Med. Anteb. Cut. indicates medial antebrachial cutaneous nerve; sens,,sensory block score; mot, motor block score.

Sensory and Motor Block Duration

	Group 15mL (n = 13)	Group 40mL (n = 15)	P	Difference * %
Overall sensory block duration	225 (148-265))	271 (210-401)	<0.001	17
Overall motor block duration	217 (144-250)	269 (210-401)	<0.001	19
Med. anteb. cut. Nerve				
Sensory block, min	157 (98-235)	262 (191-301)	<0.0001	40
Musculocutaneous nerve				
Sensory block, min	154 (68-235)	247 (151-296)	<0.01	38
Motor block, min	160 (114-233)	254 (150-311)	<0.0001	37
Radial nerve				
Sensory block, min	173 (103-235)	235 (177-401)	<0.001	26
Motor block, min	190 (114-225)	262 (150-351)	<0.001	27
Median nerve				
Sensory block, min	184 (133-265)	241 (192-349)	<0.001	24
Motor block, min	173 (129-235)	245 (207-301)	<0.001	29
Ulnar nerve				
Sensory block, min	202 (148-250)	252 (210-351)	<0.001	20
Motor block, min	210 (144-250)	256 (210-401)	<0.001	18

Tabel 4 Sensory and Motor Block Duration of Individual Nerves. Groups as defined in Table 2. Values are median (range). *Difference, difference between the medians of group 40 mL and group 15 mL as a percentage of the median value of group 40 mL. Med. anteb. cut. nerve indicates medial antebrachial cutaneous nerve.

moderate and/or short-lived. Block duration should cover surgery and the immediate period afterward, but prolonged analgesia postoperatively is not indispensable, and a reduction in block duration caused by reduced volume has little clinical relevance if surgery can be concluded before the block starts to wear off. Whether the pharmacodynamic findings regarding volume of mepivacaine equally apply for other local anesthetics, such as ropivacaine or levobupivacaine, remains to be determined. In situations where a long-acting local anesthetic is preferred, a shorter duration of sensory block may be an unfavourable trade off when the intention is to obtain long-lasting postoperative analgesia. In those circumstances, the advantage of a dose reduction must be balanced against the possibility of a shorter duration of postoperative analgesia. In cases where prolonged postoperative analgesia is desirable, the use of a Perineural catheter technique should be considered. Determining the lowest volume without decreasing duration of sensory block requires further study.

A limitation of our study is that we did not determine whether intraneural spread was present; although we tried to avoid intraneural injection, we cannot exclude the possibility that this may have occurred with individual nerves, which may have prolonged block duration.

In conclusion, reducing the volume of mepivacaine 1.5% for ABPB from 40 mL to 15 mL resulted in a reduction of overall block duration of approximately 17% to 19%, a reduction of block duration in individual nerves ranging from 18% to 40%, and a reduction in TTFR of approximately 30%.

Duration of overall sensory (A)

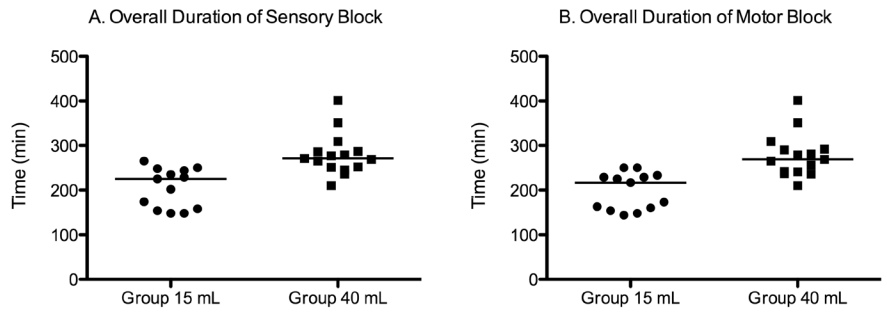

Figure 2 Dots are individual data horizontal bars represent median values.

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Duration of sensory block

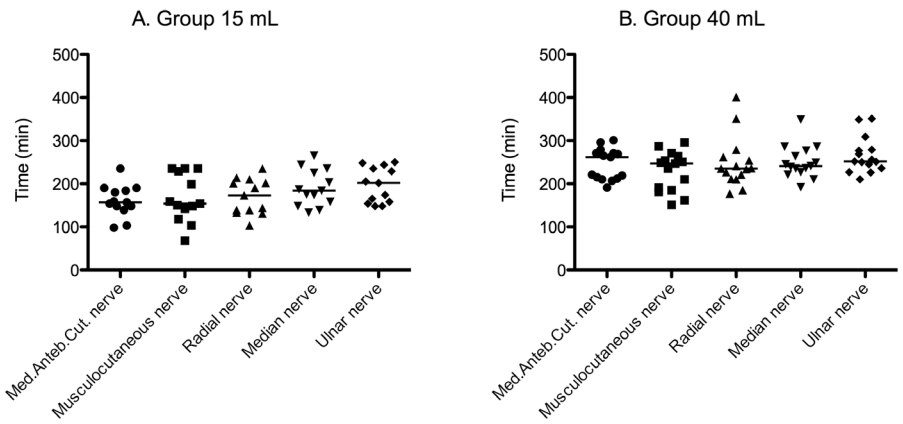

Figure 3 Duration of sensory block of individual nerves in group 15 mL (A) and group 40 mL (B). Dots are individual data; horizontal bars represent median values. Med. anteb. cut. indicates medial antebrachial cutaneous nerve.

Duration of motor block

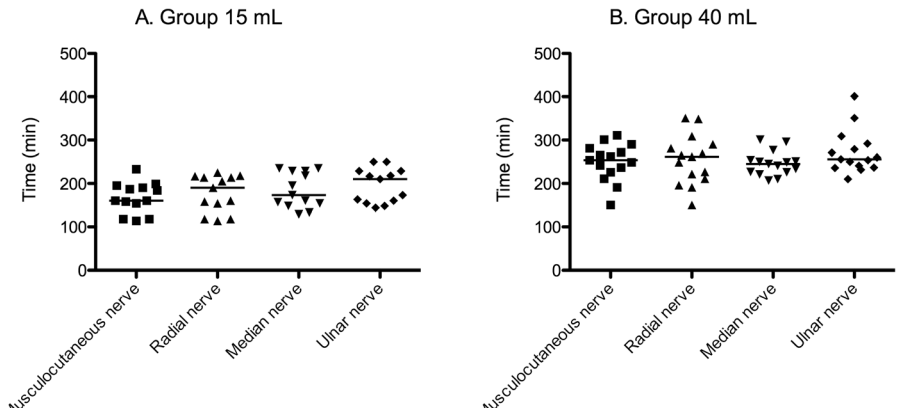

Figure 4 Duration of motor block of individual nerves in group 15 mL (A) and group 40 mL (B). Dots are individual data; horizontal bars represent median values.

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Chapter 7

Value of single-injection or continuous sciatic nerve block in addition to a continuous femoral nerve block in patients undergoing total knee arthroplasty

A prospective, randomized controlled trial

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Abstract

Background and Objectives

Continuous femoral nerve block in patients undergoing total knee arthroplasty (TKA) improves and shortens postoperative rehabilitation. Primary aim of this study was to investigate whether the addition of sciatic nerve block to continuous femoral nerve block will shorten time-to-discharge readiness.

Methods

Ninety patients undergoing TKA were prospectively randomized to 1 of 3 groups: patient-controlled analgesia via femoral nerve catheter alone (F group) or combined with a single injection (Fs group) or continuous sciatic nerve block (FCS group) until the second postoperative day. Discharge readiness was defined as the ability to walk and climb stairs independently, average pain on a numerical rating scale at rest lower than 4, and no complications. In addition, knee function, pain, supplemental morphine requirement, local anesthetic consumption and postoperative nausea and vomiting (PONV) were evaluated.

Results

Median time-to-discharge readiness was similar: group F 4 (2-16) days, group Fs 4 (2-7) days and group FCS 4 (2-9) (P=0.631). No significant differences were found regarding knee function, local anesthetic consumption or PONV. During the day of surgery, pain was moderate to severe in group F, while group Fs and FCS experienced minimal pain (P<0.01). Patients in group F required significant more supplemental morphine on the day of surgery and the first postoperative day. Until the second postoperative day pain was significantly less in group FCS (P<0.01).

Conclusion

A single-injection or continuous sciatic nerve block in addition to a femoral nerve block did not influence time-to-discharge readiness. A single-injection sciatic nerve block can reduce severe pain on the day of the surgery, whereas a continuous sciatic nerve block reduces moderate pain during mobilization on the first 2 postoperative days.

Chapter 7

Value of single-injection or continuous sciatic nerve block in addition to a continuous femoral nerve block in patients undergoing total knee arthroplasty
A prospective, randomized controlled trial

Introduction

Total knee arthroplasty (TKA) reduces pain and improves function resulting in a higher quality of life for patients with knee osteoarthritis.[1] These patients can suffer from considerable postoperative pain, which is known to impair early intensive physical therapy and rehabilitation. Good postoperative pain control is probably the most important factor to accelerate knee rehabilitation.[2-4] Meanwhile, hospital stay after TKA has been shortened by introduction of clinical pathways including standardized pain therapy allowing accelerated mobilization: a good postoperative pain management should allow intensive physical therapy and early discharge. With patient-controlled intravenous (IV) opioids alone, moderate to severe pain can persist, especially during mobilization.[2,5,6] Continuous epidural analgesia as well as continuous peripheral nerve blocks provide improved analgesia and a significantly shortened rehabilitation time when compared to pure opioid therapy.[3] In a risk-benefit analysis peripheral nerve blocks offer more site specific analgesia with lower incidence of adverse effects compared to epidural analgesia.[7-9] For balancing adequate analgesia with limited quadriceps motor impairment, patient-controlled femoral nerve block can be used.[10] Although a recent meta-analysis could not find any advantage of a continuous femoral nerve block in comparison to a single injection,[11] in most institutions it is considered standard for TKA.[12] However, continuous femoral nerve block might lead to insufficient pain relief in the posterior region of the operated knee.[13,14] Yet, the discussion continues whether a supplemental sciatic nerve block plus analgesia via a femoral nerve catheter is beneficial in these patients.[14-17] Pham et al.[18] demonstrated better pain relief at rest and decreased morphine consumption when combining continuous femoral and sciatic nerve blockade. Unfortunately, in this study, data from patients with continuous and single-injection sciatic block were not analyzed separately. Morin et al.[19] reported improved analgesia in patients undergoing TKA with combined continuous femoral and sciatic nerve block for a median of 3 days but also reported more problems while performing active exercises and more insecure walking in patients with an additional sciatic nerve block. Therefore, we shortened the time of nerve blocks in order to not interfere with early ambulation. Finally, a recent meta-analysis concluded that further studies are needed to evaluate the value of adding sciatic nerve block to femoral nerve block in patients undergoing TKA.[11]
We hypothesize that addition of sciatic nerve block (single-injection or continuously) to a patient-controlled femoral nerve blockade will shorten time-to-discharge readiness, and improve postoperative knee mobilization and pain relief after TKA.

Methods

This trial was designed as a single center, prospective, randomized, controlled study. Approval of the study was obtained by the Medical Ethics Committee of the Academic Medical Centre of Amsterdam (07/321 MEC) and the study was registered in the national trial register (NTR2207). Progress of the study and adverse event rates were annually reviewed by the hospital ethics committee.

Study participants

All eligible patients scheduled for total knee replacement arthroplasty (TKA) in a clinical pathway were enrolled 1 week before knee operation. After provided with written and verbal information, the subject's written informed consent was obtained on admission. Inclusion criteria consisted of age older than 18 years and American Society of Anesthesiologists (ASA) classification I to III. Exclusion criteria were infection near the insertion site of any catheter, coagulation disorders, allergy to local anesthetics, prior surgery near the site of nerve block, inability to use the patient-controlled analgesia device, pregnancy or lactation, known hepatic or renal insufficiency and preexisting neurologic deficit of the operated leg. Normal motor and sensory function of the operated leg was evaluated before randomization. The study period included the time from admission for TKA until hospital discharge.

Randomization

Eligible patients were randomized into 3 groups using opaque-sealed envelopes containing the treatment assignment. Thus, 90 patients were randomly allocated to 1 of 3 equally sized groups:
F: Patients receiving patient-controlled femoral nerve block only
Fs: Like group F combined with a single-injection sciatic nerve block
FCS: Like group F combined with a continuous sciatic nerve block

Preoperative knee function and pain assessment

Preoperative functional capacity of the knee was assessed by active range of motion, measuring knee flexion with a goniometer. Ratings were documented of preoperative knee pain on a numeric rating scale (NRS, range 0 - 10, 0 = no pain, 10 = most imaginable pain) during movement.

Nerve block techniques

After establishing venous access and standard hemodynamic monitoring

(electrocardiogram, pulse oximetry, noninvasive blood pressure measurement), peripheral nerve blocks were placed under aseptic conditions in the preoperative holding area by 1 of 3 anesthesiologists with extensive experience in ultrasound-guided nerve block procedures. All patients received a stimulation femoral nerve catheter (Stimucath continuous nerve block set with a 18-gauge Tuohy needle and 20-gauge catheter, Arrow International, Inc, Reading, Pa), inserted via an ultra-sound guided inguinal in-plane approach in supine position. The needle tip was positioned dorsomedial to the femoral nerve under ultrasound guidance (HFL 38 probe connected to Micromaxx, Sonosite Inc., Bothell, WA) and nerve stimulation (Stimuplex HSN12, B.Braun, Melsungen, Germany; pulse width, 0.1 ms; frequency, 2 Hz). The stimulating catheter was advanced or repositioned aiming for stimulation current < 0.6 mA. Ultrasound identification of the catheters was difficult in patients with a body mass index greater than 30 kg/m^2. The lowest current inducing muscle contractions via the catheter was registered. After negative aspiration, a loading dose of 20 mL levobupivacaine 0.375% was administered slowly in fractions of 5 mL.
For patients of group Fs and FCS, before placement of the femoral nerve catheter, a sciatic nerve block was established via a parasacral approach, as described by Mansour,[20] in lateral decubitus position with guidance of a nerve stimulator. In the Fs group, a stimulating needle (15 cm 20 G needle, Stimuplex A [B.Braun] was used, and in the FCS group, a stimulating needle with a catheter set was used (15 cm 18 G needle, 100-cm 20 G catheter, Contiplex Tuohy, [B.Braun]). After eliciting dorsal or plantar flexion of the foot with a current preferably below 0.6 mA, a loading dose of 20 mL levobupivacaine 0.375 % was injected intermittently after negative aspiration. In the FCS group, the catheter was inserted 5 cm beyond the needle tip. Nerve catheters were secured to the skin with a catheter stabilization device (Statlock, for winged catheters, Bard, Inc, Covington, Ga) and covered with a transparent dressing (Tegaderm; 3M, St. Paul, Minn).
Time needed for establishing the nerve block from first needle penetration to withdrawal of the needle (for single-injection blocks) and catheter fixation (for continuous techniques) was registered. All electrical stimulation thresholds were noted.
After injection of local anesthetics, sensory and motor block was examined based on a 3-point scale every 5 minutes during the first 45 minutes (Table 1).[21] Femoral sensory function was tested by pinprick 10 cm proximal of the patella and femoral nerve motor function by knee extension. Sciatic motor function was tested by foot plantar/dorsal extension and sensory function by pinprick sensation at the lateral calf and the dorsum of the foot.

During the surgery

Patients received lorazepam 1 mg 2 hours and acetaminophen 2 g 1 hour before surgery. 45 minutes after application of the initial bolus at the femoral nerve site, a continuous infusion of levobupivacaine 0.125% 10 ml/h was started via the femoral nerve catheter in all groups. In group FCS, a second continuous infusion of levobupivacaine 0.125% 10 ml/h was started via the sciatic catheter 45 min after catheter placement.

General anesthesia was induced with propofol target-controlled infusion set to 3 to 5 µg/ml and remifentanil 0.5 µg/kg per minute and maintained with 2 to 3 µg/ml and 0.1 to 0.25 µg/kg per minute, respectively. Infusion rates were adjusted as required, and patients were ventilated via a laryngeal mask. A pneumatic tourniquet was placed on the thigh before surgery and inflated to 300 mmHg during surgery. Total needs of propofol and remifentanil, duration of surgery and time of tourniquet were recorded

Postoperatively on Postanesthesia Care Unit

Postoperatively, the continuous femoral nerve infusion was changed to patient-controlled femoral nerve infusion (5-mL bolus, 30-minute lockout; basal rate 6 ml/h [Perfusor fm; B Braun]) in all groups. In the FCS group, the additional continuous sciatic infusion was maintained during the postoperative period (10 mL/h).

Supplemental morphine IV was administered for pain control if pain on a NRS was higher than 4. Consumption of morphine and NRS at 1, 2, and 3 hours postoperatively were noted. The extent of postoperative nausea and vomiting (PONV) were graded as none = 0, mild = 1 and severe = 2. Patients with PONV received ondansetron 4 mg IV and, when the symptoms persisted, additionally droperidol 0.625 mg IV was added.

Postoperatively on surgical ward

All patients received standardized postoperative analgesia with acetaminophen 1 g 4 times daily. In the absence of any contraindications, diclofenac 50 mg was added 3 times daily, combined with esomeprazol 20 mg once daily for gastric protection. Alternatively, tramadol was started 50 mg 3 times daily. An extra dose of tramadol (100 mg) was administrated before removal of nerve catheters. If NRS remained high despite these treatments, morphine was administered for pain relief as required. Perineural infusions were continued for 36 hours and catheters were removed on the morning of the second postoperative day (POD

CONSORT Flowdiagram

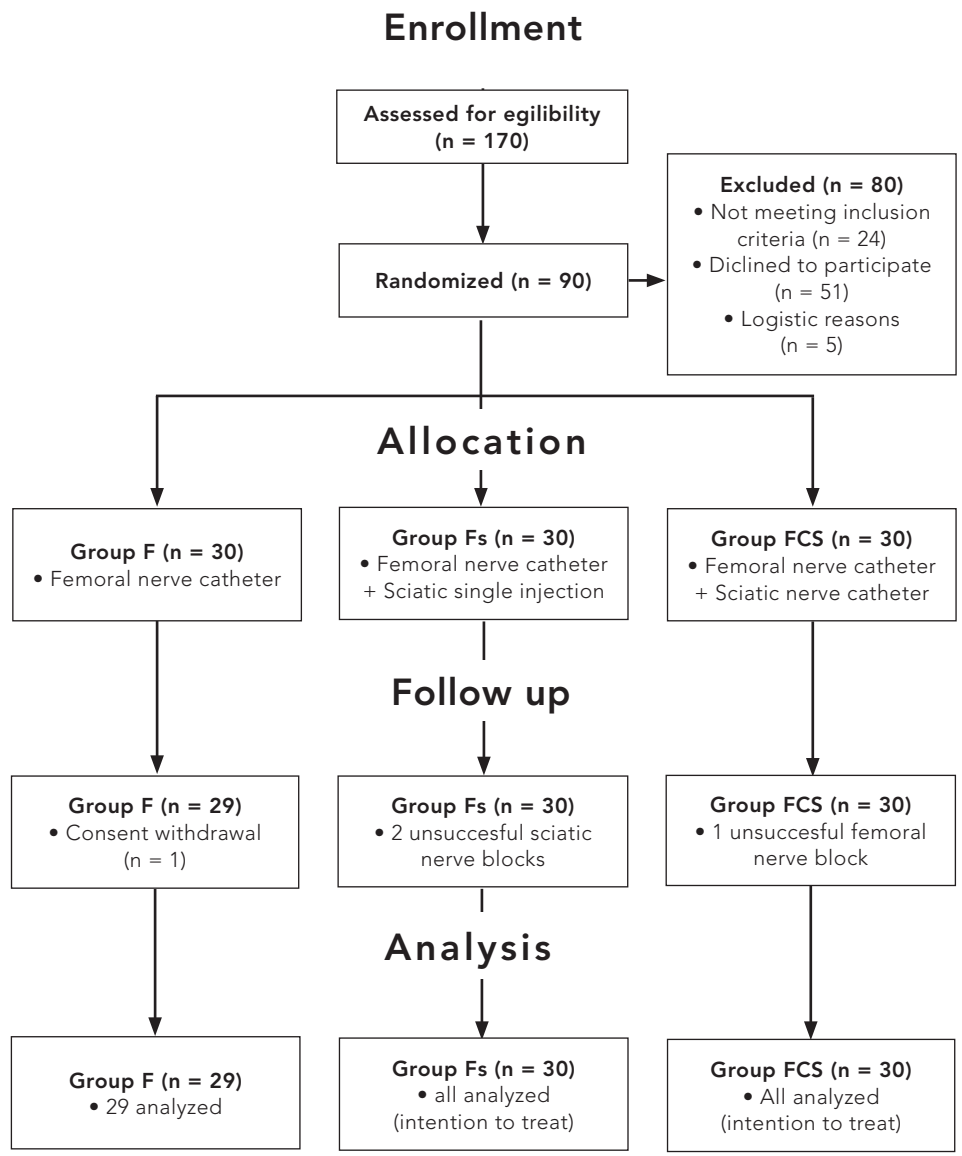


Figure 1 CONSORT diagram showing flow of patients for TKA through the study

2). Deep vein thrombosis prophylaxis was provided with fondaparinux 2.5 mg/0.5 mL subcutaneously daily, starting the evening on the day of surgery and continued for 4 weeks.
Physical therapy started on POD 1 until discharge. Functional capacity was assessed daily and recorded with the Medical Research Council scale for muscle strength of the quadriceps (MRC-Q) and active range of motion of the knee (AROM) with a goniometer by the physical therapist.

Readiness to discharge and functional outcome

The primary endpoint was time-to-readiness for discharge. Criteria were as follows:
1. Ability to walk 25 m or more with walking aids and to climb a flight of stairs. This endpoint was checked daily at 10 am and 2 pm by a physical therapist.
2. A pain score below 4 on a numeric rating scale as taken by nurses educated in pain measurement and therapy.
3. Absence of serious complication as examined by an orthopedic surgeon on a daily base.
These discharge criteria were checked daily by an investigator. Furthermore, short-term functional capacity was determined by MRC-Q and active flexion of the knee daily by a physical therapist. Duration of actual admission was also noted.
Secondary endpoints were pain scores measured on a NRS at rest and during movement, supplemental consumption of morphine, local anesthetic consumption and grade of PONV. These variables were noted daily at 8 am and 6 pm on the ward starting the day of operation until the third postoperative day. Patients were assessed daily by the surgeon for complications during admission, as well as six weeks postoperatively.

Scale of sensory and motor function

- **S1** normal sensation
- **S2** touch sensation, no pain
- **S3** no sensation
- **M1** full power
- **M2** decreased power
- **M3** no power

Table 1 Scale of sensory and motor function
Examination of sensory and motor block based on a 3 point scale and tested every 5 minutes during the first 45 minutes after femoral and sciatic nerve blocking.

Statistical Analysis

We considered a 25% reduction in discharge readiness to be clinically relevant (normal length of stay 4 days). On the basis of previous data, we assumed a standard deviation of 1 day. Sample size analysis indicated that a group size of 30 patients would allow showing a 25% difference between groups at a 90% power and at a 2-tailed alpha level of 0.05 (after bonferroni correction for multiple comparisons). Intention-to-treat analysis was conducted.
Comparisons between groups were made by Kruskal-Wallis test and, if significant, by unpaired 2-sided Mann-Whitney U-test. Dichotomous variables were compared on contingency table by Fisher exact test. A value of $p < 0.05$ was considered significant. The p-values of the primary end points (readiness to discharge) were corrected by Bonferroni-Holmes adjustment for multiple comparisons.

Demographic data

	Group F (n = 29)	Group Fs (n = 30)	Group FCS (n = 30)
Age	62 (50-79)	65 (43-81)	66(43-83)
Sex (M/F)	11/18	9/21	8/22
Height (cm)	174 (158-188)	171 (150-187)	173(159-188)
Weight (kg)	84 (72-116)	82 (62-125)	89 (68-118)
BMI (kg.m-2)	30.3 (23.2-39.7)	28.6 (21.0-48.8)	27.8 (22.1-39.6)
ASA I/II/III	13/ 13/ 3	13 / 17/ 2	9 /16 / 5
NRS preop	5.4 (3.0-7.5)	6.5 (2.0-10)	6.3(0-10)
AROM (degrees)	120 (70-130)	110 (60-135)	110 (80-135)

Table 2 Demographic data. Patient characteristics presented as median (range) or absolute number as appropriate. There were no significant demographic differences between the 3 groups ($p > 0.05$). ASA = American Society of Anesthesiologists status; NRS = pain score as numeric rating scale; AROM = active range of motion of the knee

Characteristics of block and surgical

Variables	Group F (n = 29)	Group Fs (n = 30)	Group FCS (n = 30)
Alfentanil (mcg)	500 (250-1000)	1000 (0-1750)	1000 (250-2000)
Propofol (mg)	0 (0-40)	0 (0-50)	0 (0-100)
Femoral catheter placing duration (min'sec")	5'56" (2'30" 21'00")	7'41"(2'20"-26'00")	6'40"(3'20"-24'12")
Femoral catheter threshold (mA)	0.44 (0.20-0.80)	0.40 (0.20-0.90)	0.35 (0.1-0.6)
Sciatic injection duration (min'sec")		3' 49"(1'10"-22'0")	
Sciatic threshold (mA)		0.38 (0.2-0.9)	
Sciatic catheter placing duration (min'sec")			4'46"(2'00"-15'15")
Sciatic catheter threshold (mA)			0.30 (0.1-0.60)
Length of surgery (min)	93 (51-150)	87 (53-178)	93 (69-134)
Tourniquet time (min)	88 (33-152)	75 (14-158)	69 (15-109)

Table 3

Data are given as median (range). There were no statistical significant differences between groups ($p > 0.05$).

Results

Patients were included between February 2008 and April 2010. A CONSORT flow diagram of eligible and participating patients is demonstrated in Figure 1. Four patients had a staged bilateral TKA. One patient (F group) withdrew consent after randomization and refused to give NRS scores or other data. Therefore, no data from this patient could be analyzed. Patients with primary failed blocks (1 femoral in group FCS, 2 sciatic blocks in group Fs) were included in an intention-to-treat analysis.
Demographic data and values for required sedation, block performance, and tourniquet as well as surgery duration are shown in Tables 2 and 3 per group. There were no significant demographic differences between the 3 groups. Three patients had no signs of nerve block within 40 minutes. The other 86 patients developed signs of motor and sensory block within 15 min, whereas complete block took up to 40 minutes. There were no significant differences between groups regarding onset times of blocks.

Readiness to Discharge and Functional Outcome

Median time-to-readiness to discharge was similar for all 3 groups: group F, 4.0 days (2.0-16.0 days), group Fs, 4.0 days (2.0-7.0 days) and group FCS 4.0 (2.0-9.0 days) (Figure 2). The actual median length of hospital stay was equal to the time-to-readiness to discharge and did not differ between groups: group F, 4 days (3-16 days), group Fs, 4 days (4-10 days), group FCS, 4 days (4-10 days).
Similarly, no significant differences were found in active knee flexion at the time-of-readiness to discharge: F group, 75 degrees [range, 55-90 degrees], Fs group 80 degrees [range,55-95 degrees] and in FCS group 80 degrees [range, 40-95 degrees] or in MRC-Q: F group, 3 [range, 3-4], Fs group 3 [range, 2-4] and FCS group 3 [range, 2-5]). Likewise, there were no significant differences in active flexion (Figure 3) or MRC-Q between all groups at POD 2, 3, and 4 or at discharge.

Postoperative pain and analgesic consumption

Patients in F group had significantly more postoperative pain at the day of TKA compared with those it the Fs and FCS groups (Figure 4). During the first postoperative hours in the postanesthesia care unit, patients of F group experienced moderate to severe pain with a median pain score of 7 (range, 0-10), whereas patients of Fs and FCS groups had a median pain score of 0 (range 0-10, $p < 0.01$). Patients in the F group needed 16 mg (range, 0-42 mg) morphine IV in contrast to the Fs (2 mg [range, 0-22]) and FCS groups (0 mg [range,0-12], $p < 0.01$; Table 4).

When patients still experienced pain scores higher than 4 after morphine 15 to 20 mg IV, supplemental medication like S-ketamine 5 to10 mg IV and clonidine 75 to 150 μg were administered (9 patients of group F, 1 patient of group Fs and 1 patient in group FCS, $p < 0.01$). Nevertheless, patients in the F group still had more pain at the end of the day (NRS POD 0, at 6 pm in group F, 4 [range, 0-7], Fs group, 0 [range, 0-8] and FCS group, 0 [range, 0-6]; $p < 0.01$). Until POD 2, pain at rest and during mobilization was significantly less in FCS group. However, pain during mobilization was moderate in F and Fs groups (median NRS ≤ 5; figure 4B) and mild at rest in all groups. Rescue medication with morphine was increased in the F group on POD 0 to 2 (Table 4). Incidence of postoperative nausea and vomiting was 6.7% without significant difference between groups.
No significant difference for delivered boluses of levobupivacaine 0.125% applied via the patient-controlled femoral nerve block was found between groups (Table 5).

Postoperative morphine consumption

Morphine (mg/24 h)	Group F (n = 29)	Group Fs (n = 30)	Group FCS (n = 30)	P value
POD 0	16(0-42) 27/29	2(0-22) 16/30	0(0-16) 11/30	0.000
POD 1	0(0-48) 5/29	0(0-5) 1/30	0(0-0) 0/30	0.006
POD 2	0(0-48) 7/29	0(0-8) 3/30	0(0-0) 0/30	0.011
POD 3	0(0-40) 3/29	0(0-13) 1/30	0(0-0) 0/30	0.149

Table 4 Postoperative morphine consumption. A significant difference was found between group F and both other groups on POD 0 & 1, but only between group F and group FCS on POD 2. After the day of operation (POD 1-3) median (range) morphine consumption was 0 mg for all groups. When morphine was given orally the equipotent dose was calculated (oral:iv; 3:1) and added to the total morphine requirement. The number of patients per group who required morphine is given below.

Complications

Twelve patients did not mobilize according to the schedule because of hematoma, swelling, or wound leakage (4 patients in the F group, 5 patients in the Fs group, 3 patients in the FCS group). One patient (F group) required surgical drainage on POD 3. The number of patients with delayed mobilization included 3 of totally 4 patients (3 patients in the Fs group and 1 patient in the FCS group), who had fallen down because of unaccompanied mobilization on POD 2.
After diagnosis of a full motor block of the foot in 11 patients of group FCS on POD 1, infusion of continuous sciatic nerve block was interrupted temporarily until motor function was restored and then infusion of levobupivacaine was continued at a lower infusion rate (6 ml/hr) and motor block did not reappear in any of these patients.

Active Range of Motion

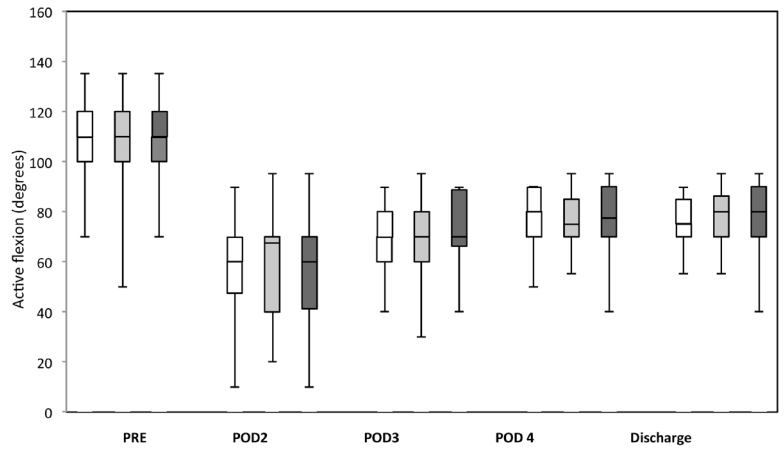


Figure 2 The range of motion of the different treatment groups over time. Box plots representing the degree of active knee flexion per group and per day. The white boxes represent the F group (only femoral catheter), light gray boxes represent the Fs group (femoral catheter and sciatic single injection), and dark gray boxes represent the FCS group (femoral and sciatic catheter). There were no significant differences between groups at any time.

Discussion

Addition of a single-injection or continuous sciatic nerve block to a continuous femoral nerve block for postoperative pain treatment after TKA did not improve time-to- discharge readiness or knee function in this randomized controlled trial. However, early postoperative pain relief was much better controlled at rest and during mobilization, whereas opioid requirements were reduced in patients with a sciatic nerve block. The group receiving a continuous sciatic catheter had significantly less pain during mobilization.

Patients with continuous femoral nerve block alone experienced severe postoperative pain on day of TKA, whereas the addition of a sciatic block provided complete pain relief. Thus, sciatic nerve block combined with a continuous femoral nerve block improved the quality of early postoperative analgesia significantly and also in a clinical relevant manner. The difference in median pain score between groups was 7 on a NRS from 0 to 10 and are in line with observational studies[22,23] and 2 other randomized trials.[24,25] The high pain scores in the F group are concerning and may be explained by the fact that our patients received only short-acting and ultra short-acting opioids before and during the surgery. However, the use of longer-acting opioids might be insufficient for those patients requiring up to 42 mg morphine and who still had moderate to severe pain scores during the early postoperative period. Even the addition of S-ketamine and clonidine as nonopioid rescue analgesics was needed frequently in the F group to achieve sufficient pain control.

One may argue that patient-controlled systemic analgesia would have reduced the maximum pain scores and might have been a better indicator for a good postoperative pain therapy. However, it is difficult to include an additional patient-controlled infusion pump and handling two patient-controlled systems in elderly patients shortly after a major operation under general anesthesia.

Because median pain scores at rest were 2.0 or lower in all groups from POD 1 on, we could not demonstrate any advantage of a sciatic nerve block for pain relief at rest from that time on. However, addition of a continuous sciatic nerve block controls pain significantly better during mobilization. Although the pain reduction is according to International Association for the Study of Pain (IAPS) definitions clinically relevant, the median pain scores during mobilization were moderate in patients receiving a femoral nerve block with or without single-injection sciatic nerve block.

Readiness to discharge was not affected when combining a sciatic nerve block to a continuous femoral nerve block in our study. While Ilfeld et al.[26,27] demonstrated in two multi-center studies a difference in time to reach discharge

Bolus dosis of levobupivacaine 0.125 % per group.

		Group F (n = 29)	Group Fs (n = 30)	Group FCS (n = 30)
POD 1	8 am	25 mg (0-119)	6 mg (0-163)	6 mg (0-144)
	6 pm	13 mg (0-94)	3 mg (0-106)	0 mg (0-75)
POD 2	8 am	6 mg (0-44)	0 mg (0-56)	0 mg (0-25)

Table 5

Levobupivacaine (mg/12 hours) delivered as bolus via patient-controlled femoral nerve block (basic infusion rate levobupivacaine 0.125% 6 ml/hr). There were no statistically significant differences between groups.

Readiness to Discharge

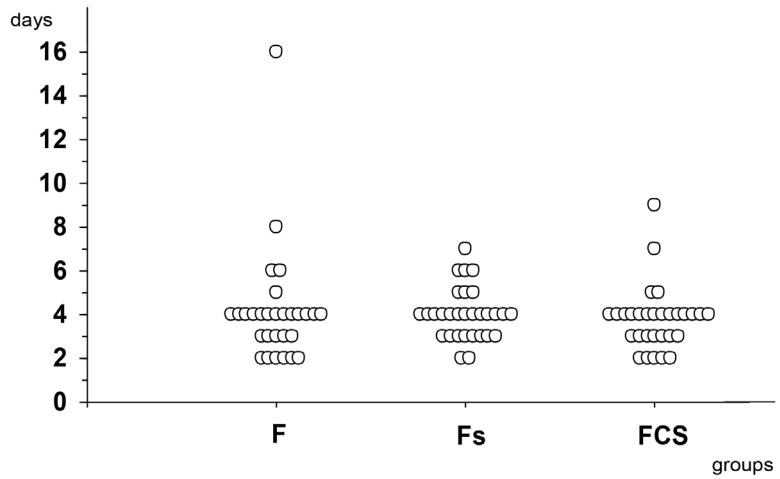
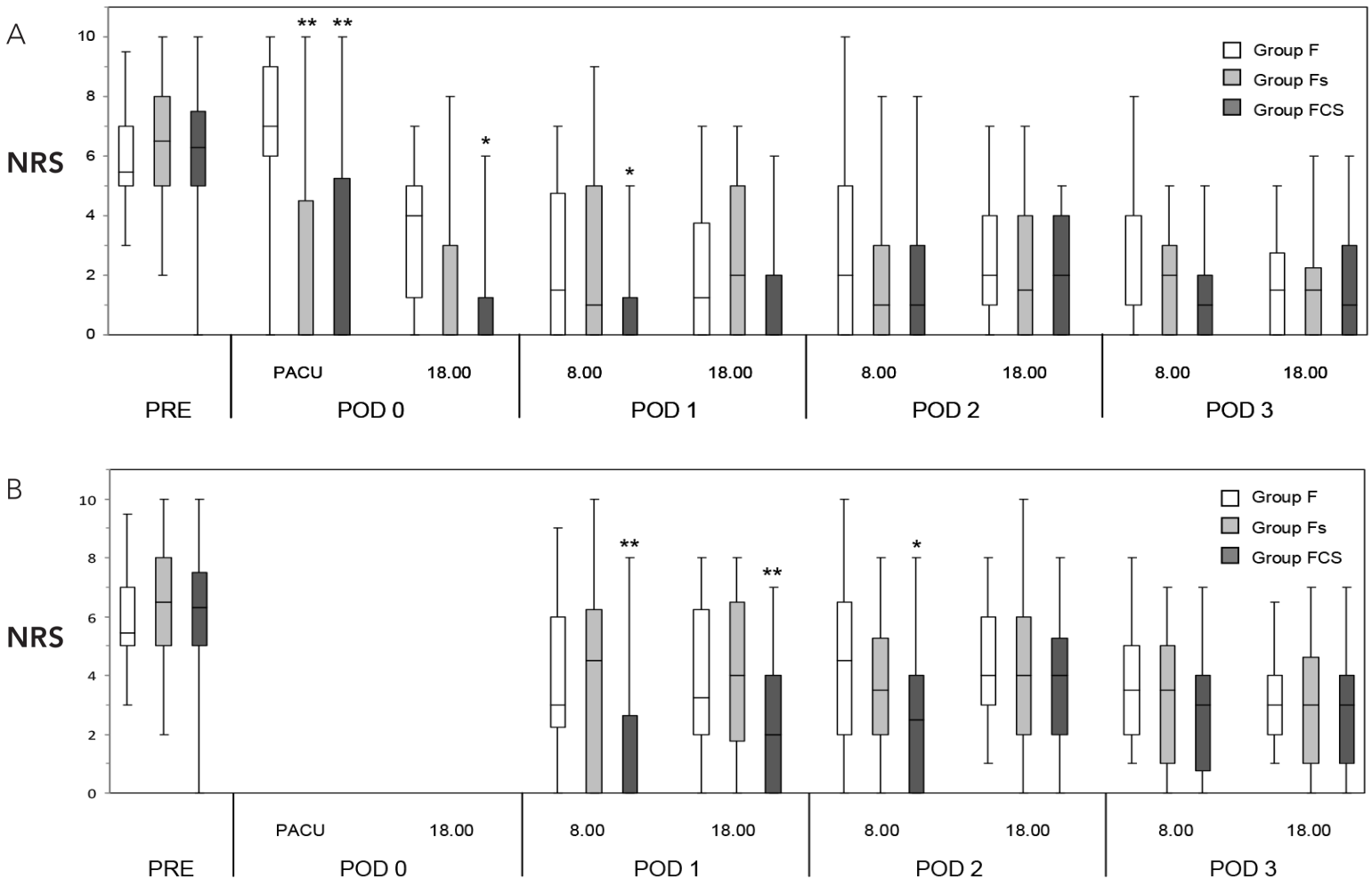


Figure 3 Time points when each of 89 patients reached discharge criteria for each treatment group. There were no statistical significant differences between groups (P=0.631).



Pain at rest (A) and during mobilisation (B)

Figure 4 Pain at rest (A) and during mobilization (B) over time per group. The white boxes represent the F group (only femoral catheter), light gray boxes represent the Fs group (femoral catheter and sciatic single injection), and dark gray boxes represent the FCS group (femoral and sciatic catheter). For each patient, POD 2 pain score measurements (NRS, numeric rating scale) are performed at 8:00 am (left) and 6:00 pm (right). All patients who received a sciatic block had significant lower pain scores at rest on POD 0 (postanesthesia care unit and 6:00 pm) ($p < 0.01$), whereas only the patients with a sciatic nerve catheter had significantly less pain on POD 1 ($p < 0.05$). Although the differences were clinically relevant on day 0 according to International Association for the Study of Pain (IASP) definition ([DELTA] NRS >2), they were not clinically relevant on day 1. The patients with a continuous sciatic nerve catheter had statistically significant pain reduction during mobilization on POD 1 and 2; however, postoperative pain during mobilization was always below preoperative values in all groups. *$p < 0.05$. **$p < 0.01$.

criteria when pain was better controlled with an extended continuous femoral nerve block over four days compared to a continuous femoral nerve block overnight addition of a sciatic nerve block did not have an effect on readiness to discharge in our study. However, because discharge criteria, patient population, clinical pathway, and systemic analgesic management were different between the cited study and the present investigation, it is difficult to draw conclusions from comparisons of these two studies.[26,27]

A sciatic nerve block, specially a continuous block, might impair motor function and thereby might have a negative effect on active knee movement, thereby delaying hospital discharge. Of the patients in the FCS group, 36.7% had a motor block on POD 1. Subsequently, the infusion was stopped and later restarted at a lower rate. Thus, none of the patients had a motor block on POD 2; furthermore, all regional anesthesia was stopped at 6 am on POD 2. No patient of any group reached discharge criteria on POD 1. Therefore, it is highly unlikely that the high incidence of motor block in group FCS had influenced the discharge criteria.

One may also argue that the addition of a sciatic nerve block requires more patient preparation time. Establishing of sciatic nerve block took, on average, less than 5 min, and therefore had little impact on the clinical pathway. However, in institutions with less experience in regional techniques, this time might be longer and more relevant.

In patients having considerable more pain (like those in the F group) one should expect an increased demand and delivery of levobupivacaine 0.125%. However, no differences were found between groups in total bolus dose via patient-controlled femoral block.

Worrisome are the four falls during mobilization at the beginning of the study period. Falls occurred in three patients of the Fs group and one patient of the FCS group on POD 2. In all cases our safety instructions for mobilization were violated. We repeated education to nurses and patients about nerve block induced motor weakness and risks of falling and observed no further falls thereafter. Our study is underpowered to draw conclusions on the influence of blocks on fall incidents. Previously, worries about the risk of falling when using a femoral block in patients undergoing TKA have been expressed.[28,29] The incidence of falls reported by these authors is lower than the incidence we determined, probably due to underreporting in these retrospective studies. Recently Ilfeld et al.[30] re-analyzed the risk of falling in their prospective randomized studies in patients undergoing TKA with or without continuous femoral nerve block. The authors observed significantly more fall incidents in the groups with continuous femoral nerve block, although none of the falls led to a change in treatment or delay of hospital discharge. Incidents of falls were moderately higher than the incidents we observed. As shown recently, effective fall prevention is much more than handle an information folder or to just advice the patient that he/she should not ambulate on his own.[31]

A limitation of the study is the missing blinding of patients.

In conclusion, combining sciatic nerve block to femoral nerve catheter did not influence readiness to discharge or short-term knee function. A single-injection sciatic nerve block can reduce severe pain on the day of operation, whereas a continuous sciatic nerve block reduces moderate pain during mobilization on the first 2 postoperative days. Therefore, improved pain therapy cannot simply be translated into reduced hospital stay and improved short-term rehabilitation.

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Chapter 8

Long-term pain and functional disability after total knee arthroplasty with and without single-injection or continuous sciatic nerve block in addition to continuous femoral nerve block: a prospective, 1-year follow-up of a randomized controlled trial

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Abstract

Background and Objectives

This is a follow-up to determine long-term outcomes after total knee arthroplasty (TKA) in patients enrolled in a previous randomized trial that found reduced postoperative pain after addition of sciatic nerve block to continuous femoral nerve block for TKA.

Methods

Physical function after TKA was evaluated at 3 and 12 months in patients (n = 89) receiving continuous femoral nerve block alone (group F), combined with a single-injection (group Fs) or continuous sciatic nerve block (group FCS) after TKA, until the second postoperative day. Physical function, stiffness, and pain were measured by using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Oxford Knee Score 12-item knee questionnaires, and visual analog scale at rest and during mobilization before TKA and 3 and 12 months afterward. Post hoc, a median split on poor functioning (WOMAC) was analyzed.

Results

Western Ontario and McMaster Universities Osteoarthritis Index, Oxford Knee Score 12-item knee, and visual analog scale scores improved significantly in all patients, without any differences among groups. Median (range) WOMAC at 3 months were in group F, 83 (20--97); group Fs, 72 (25-99); and group, FCS 76 (28-100) and at 12 months 87 (35-98), 77 (43-100), and 89 (35-100), respectively.

Conclusions

No differences were detected in the secondary outcomes we examined. Thus, improved postoperative outcome did not translate into improved functional outcome or long-term pain.

Chapter 8

Long-term pain and functional disability after total knee arthroplasty with and without single-injection or continuous sciatic nerve block in addition to continuous femoral nerve block: a prospective, 1-year follow-up of a randomized controlled trial

Introduction

Recently, we demonstrated significant reduction of postoperative pain and analgesic requirements after total knee arthroplasty (TKA), combining a sciatic nerve block (single injection or continuous infusion) with a continuous femoral nerve block in a randomized controlled trial.[1] However, despite improved pain therapy, no differences in short-term function and readiness to discharge could be demonstrated among the 3 study groups.
The same patients were followed up, as a secondary aim of the recently published investigation,[1] to determine whether an additional sciatic nerve block could improve long-term knee function and reduce pain. Thus, we examined functional outcome of the previous study groups at 3 and 12 months' follow-up and present the results in this report.
Preoperative poor knee function and severe pain may be important risk factors for developing chronic postoperative pain and impaired knee function after TKA.[2,3] Therefore, to generate a new hypothesis to guide future research, we analyzed post hoc whether patients with poor preoperative knee function may benefit, especially from a sciatic nerve block.

Methods

This is a follow-up of a previously performed single-center, prospective, randomized controlled study in patients for TKA, comparing a continuous femoral nerve block with or without a single or continuous sciatic nerve block. The follow-up was prospectively planned as a secondary aim of the randomized controlled trial, which was approved by the Medical Ethics Committee of the Academic Medical Center in Amsterdam (07/321 MEC) and registered, including this secondary aim, in the National Trial Register (NTR2207). Before surgery, patients provided written and verbal informed consent. Details of the study methods have been published previously in Regional Anesthesia and Pain Medicine.[1]

Study Intervention

Follow-up took place in 89 patients of the completed randomized controlled study. Patients were previously randomized and divided into 3 groups for TKA: patient-controlled analgesia via femoral nerve catheter alone (group F) or combined with a single-injection (group Fs) or continuous sciatic nerve block

(group FCS) until the second postoperative day. Patients with primary failed blocks (2 sciatic blocks in group Fs, 1 femoral in group FCS) were included in an intention-to-treat analysis. Postoperatively, all patients received standardized oral analgesics containing acetaminophen 1 g at 4 times daily and diclofenac 50 mg at 3 times daily, combined with esomeprazole 20 mg. Alternatively, tramadol was started 50 mg at 3 times daily. Oral analgesics were continued after discharge if necessary. Physical therapy was started within a predefined program twice daily on postoperative day 1 and continued after discharge twice weekly for the first 6 weeks.

Outcome measurement

Knee function was evaluated through 2 self-reporting validated questionnaires: the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire and the Oxford Knee Score (OKS) 12-item knee questionnaire. The WOMAC evaluates quality of life in the dimensions of pain (5 items), stiffness (2 items), and function (17 items).[4] A validated version for the Dutch language was used with a 5-point Likert scale from 0 to 4 for each question.[5] Raw values were summed and standardized (0–100) for each dimension and for WOMAC totally, where a higher score represents better function and less pain. Western Ontario and McMaster Universities Osteoarthritis Index is recommended in the Osteoarthritis International Research Society's guidelines for clinical trials.[6] Oxford Knee Score questionnaire is a disease- and site-specific questionnaire specifically developed for knee arthroplasty patients.[7] The OKS questionnaire contains 12 items that assess pain and physical disability. Each item is rated from 1 (least difficulty/severity) to 5 (most difficulty/severity). A Dutch-validated version was used with a 5-point Likert scale for each question, leading to a total score that ranged from a best functional score of 12 to the worst functional outcome of 60, with higher scores representing more severe knee problems.[8] Using both questionnaires for outcome measurements will give a complete view of leg and knee function. Baseline-written WOMAC, OKS, and visual analog scale (VAS) scores were collected preoperatively. Preoperative VAS was measured at rest only, because there was no standardized mobilization during physiotherapy. At 3 and 12 months after TKA, patients were invited by mail to complete written WOMAC and OKS questionnaires and VAS, at rest and during mobilization. To reduce loss of follow-up, patients were requested by telephone to return completed questionnaires after a waiting period of 2 weeks.

This follow-up is an analysis of the prospectively defined secondary aim of a randomized controlled trial, which was powered for accelerated discharge readiness. Therefore, this analysis of a secondary aim is subject to type II error; that is, an existent difference might not be detected because of small sample size. Intention-to-treat analysis was used. Comparisons among groups were made using Kruskal-Wallis test and unpaired 2-sided Mann-Whitney U test. Dichotomous variables were compared on contingency table using Fisher exact test. $P < 0.05$ was considered significant. The p-values of the main end points (WOMAC and OKS) were corrected using Bonferroni-Holmes adjustment for multiple comparisons among groups. The different dimensions of the WOMAC and VAS values were also analyzed (WOMAC pain, WOMAC stiffness, WOMAC function, and VAS, at rest and during mobilization).

Because poor preoperative function and severe preoperative pain may be associated with poor postoperative functional outcome and pain,[2,3] we decided to separately reanalyze patients with poor preoperative function. A post hoc median-split analysis, based on the preoperative functional score (median baseline WOMAC), was applied to test the hypothesis that only patients with severe disabilities and severe pain preoperatively (baseline WOMAC < median baseline WOMAC) might benefit from an improved postoperative pain management. Median baseline WOMAC of all patients could be calculated only after completing inclusion of all patients. Thus, only the preoperatively severely disabled patients were analyzed per group. Naturally, the severely disabled were not evenly distributed among groups. Outcome data of the preoperative severely disabled patients (baseline WOMAC < median baseline WOMAC) were reanalyzed for all 3 groups. The variables tested were improvements in WOMAC score or subscore (WOMAC pain, WOMAC stiffness, WOMAC function), OKS, and pain, at rest and during mobilization from preoperatively to 3 or 12 months, respectively. $P < 0.05$ was considered statistically significant. This was done in the light of possible hypothesis generation for future studies and not to delineate any conclusion from a post hoc analysis.

Results

Patients were included between February 2008 and April 2010 during the previously performed randomized controlled trial. After collection of all data, the follow-up was completed in May 2011.

A CONSORT flow diagram of eligible and participating patients in the follow-up is demonstrated in Figure 1. Patients with primary failed blocks (1 femoral in group FCS, 2 sciatic blocks in group Fs) were included in an intention-to-treat analysis. Patients were excluded from analysis if data of both follow-up periods (3 and 12 months) were missing (3 patients in group F [10%] and 1 patient in group FCS [3%]). One patient (group Fs) did not complete baseline questionnaires before randomization, which we considered a protocol violation. Characteristics and preoperative baseline scores of WOMAC, OKS, and VAS of all patients; those lost to follow-up; and those remaining are shown in Table 1.[9]

WOMAC improved remarkably in all patients after TKA at the middle- and long-term period (>100%), but no statistically significant differences were found among groups at 3 months (P = 0.75) and 12 months (P = 0.68) (Fig. 2); neither did the separate dimensions WOMAC function, WOMAC stiffness, and WOMAC pain show statistically significant differences among groups at 3 and 12 months, nor did the OKS questionnaire (Table 2). Likewise, when pain was measured by VAS at rest and during mobilization, no statistically significant differences among groups were observed at 3 and 12 months (Figs. 3A, B). Patients lost to follow-up did not change the baseline patient characteristics systematically. Preoperative level of functioning was not equally distributed among groups, because median baseline WOMAC was better in group F (50) compared with group Fs (34) and group FCS (34), although the difference was not statistically significant (P = 0.09).

We analyzed patients with a moderate to poor preoperative knee function by categorizing patients with a preoperative WOMAC as equal to or less than the median preoperative WOMAC of all patients (WOMAC <=36.7). Meeting this condition, WOMAC stiffness was found to be statistically significantly worse after 3 (P = 0.01) and 12 months (P = 0.02) in patients of group F compared with groups Fs and FCS (Fig. 4). Also, a statistically significant higher pain score (VAS) during mobilization was found after 3 months in group F (7.5 [3.6–8.5]compared with the other groups (Fs, 3.5 [0.0–7.1]; FCS, 3.0 [0.0–9.5]), with p = 0.023, whereas no statistically significant differences could be found after 12 months (p = 0.43). No statistically significant differences could be demonstrated in the other scores or subscores.

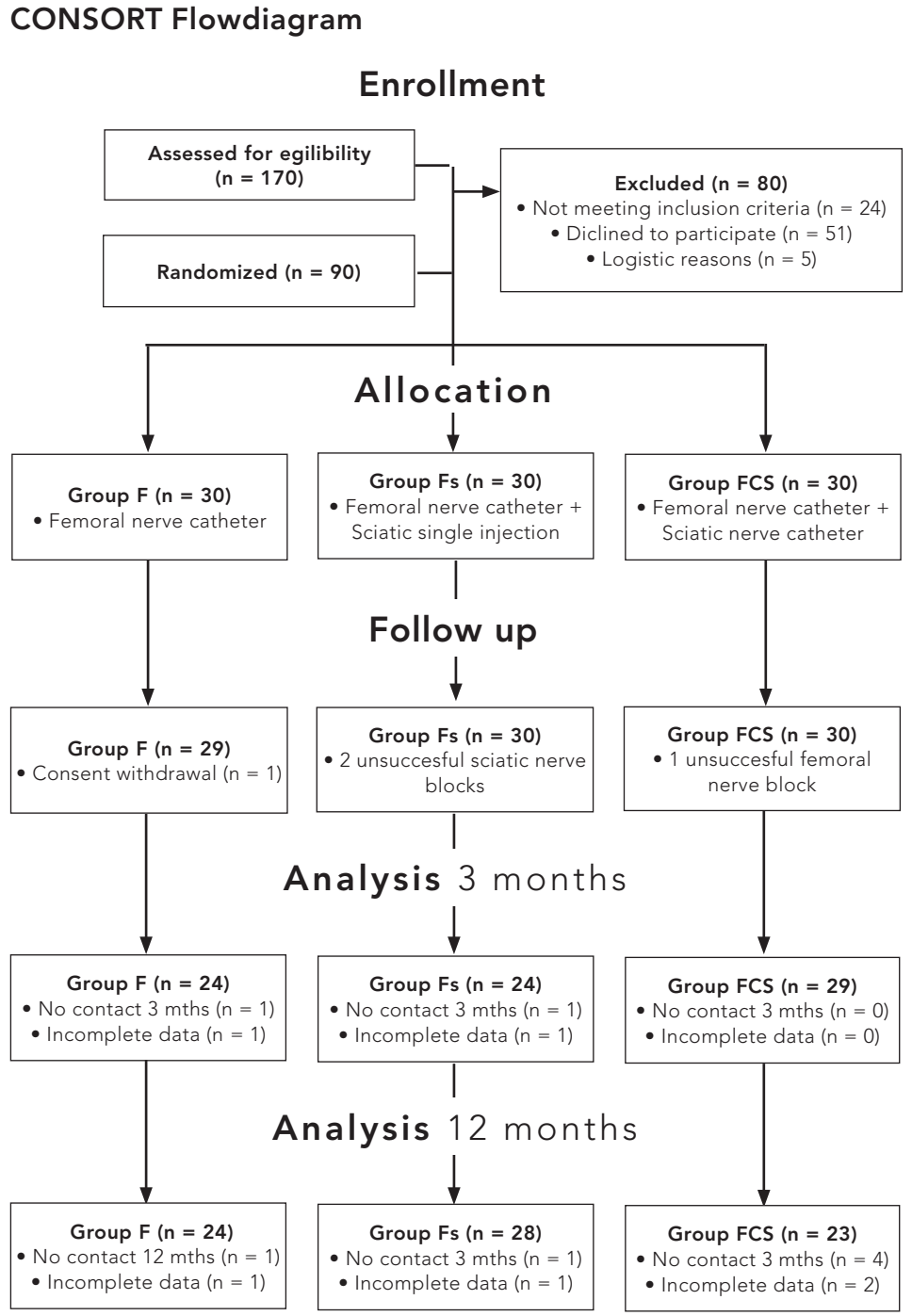

Figure 1 CONSORT diagram showing flow of patients after TKA through the follow up study.

Discussion

Knee function improved greatly in all patients after TKA. No midterm or long-term effect of the addition of a sciatic nerve block (single injection or continuous) for patients undergoing TKA was found in physical function, knee stiffness, pain at rest, or during mobilization at 3 and 12 months postoperatively. Post hoc subgroup analysis revealed that patients with poor preoperative knee function experienced less knee stiffness and pain during mobilization at the midterm and long term after addition of a sciatic nerve block for TKA. However, because groups and specially subgroups of poor preoperative functioning were small, it is entirely unclear whether this is a chance coincidence or a beneficial effect of the sciatic nerve block.

Ilfeld et al [10] similarly found no long-term effect on knee function (WOMAC) after extended postoperative femoral perineural infusion for 4 days after TKA. Likewise, 2 other studies failed to show statistically significant differences in recovery of knee function after 3 months in patients with a continuous femoral nerve block compared with a single injection.[11,12] However, Carli et al. [13] demonstrated a better functional recovery at 6 weeks in patients with a femoral nerve block compared with local infiltration analgesia techniques. Whether an improved functional outcome could have been demonstrated at 3 or 12 months as well has not been studied. Persistent moderate to severe pain during mobilization 1 month after TKA has been reported in 68% patients when a local infiltration analgesia technique was used. On the other hand, regional analgesic techniques (epidural and femoral) facilitated early rehabilitation in patients undergoing major knee surgery when compared with patient-controlled analgesia with morphine.[14–16]

Thus generally, regional anesthesia techniques have repeatedly been shown to improve acute postoperative pain management and shorten hospital stay and short-term rehabilitation, but no improvement in pain and knee function has been shown after more than 6 weeks postoperatively.

Apparently, there are other important factors that affect the rehabilitation of knee function, pain, and quality of life after TKA. Both surgical and patient-related factors may influence recovery and outcome.[17,18]

Postoperative knee function after TKA primarily depends on preoperative condition.[18–24] Because patients undergoing TKA have end-stage knee osteoarthritis, most patients suffer from long-standing pain and impaired physical functioning preoperatively. Patients with high preoperative pain levels,

combined with low pain thresholds, have a higher risk for persistent pain after total knee replacement, which is interpreted as central sensitization.[25] Furthermore, joint replacements in patients with severe preoperative pain and poor physical function are associated with worse postoperative outcomes.[26] Thus, pain treatment for TKA should be focused on reducing existing preoperative chronic pain and may be initiated before TKA. Therefore, we analyzed post hoc the category of patients with moderate to poor preoperative functioning (WOMAC <=36.7).

Study Limitations

The scores reported here (WOMAC, OKS, VAS) were secondary aims for the original study and obviously have no statistical strength of primary outcomes. The study was powered for discharge readiness and the long-term functional outcome and pain were only a secondary aim. However, post hoc power analysis revealed that the follow-up had 90% power ([alpha] < 0.05) to detect a 0.75 ratio in rank sums; that is, it was equally powered for 1 of the long-term outcome parameters, as for the primary aim. Furthermore, squeezed distribution of preoperative functional scores between groups (WOMAC score; Table 1) may have influenced the results. Moreover, one might argue that up to 20% missing data points in some groups might have biased the results. However, even at time points where only 3% of data were missing, no significant differences could be detected. The statistically significant improvement in self-reported knee stiffness and pain, recorded during mobilization at 3 and 12 months in patients with poor preoperative knee function when a sciatic never block was added for TKA (subgroups Fs and FCS), should be interpreted with extreme caution. Although it sounds plausible, the reported improvement is subject to considerable error for several reasons. The post hoc median-split analysis divided the groups unevenly, and thus very small numbers were analyzed, leading to high risk of a type I error. Furthermore, only a few subscores displayed significant improvement, but none of the overall scores changed significantly. For example, only pain scores during mobilization at 3 months were improved, not at 12 months. In addition, although a number of parameters were tested at 2 time points, no adjustment for multiple comparisons was performed. The post hoc results can be used to generate hypothesis but cannot be interpreted and definitely should not influence current clinical management.

In conclusion, in patients undergoing TKA, improved short-term postoperative analgesia by means of sciatic nerve block, combined with a continuous femoral

nerve block, does not translate into improved long-term knee or leg function, stiffness, or pain level, at rest or during mobilization.

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Chapter 9

Summary

General conclusion

Summary

Chapter 1

Peripheral nerve blocks became an essential part of regional anesthesia and have a growing interest. Previous and present developments for performance of peripheral nerve block techniques are described. High frequency ultrasonography for guidance of peripheral nerve blocks was the latest important invention. Ultrasonography enables to visualize target nerves, adjacent vital structures, needle advancement and the spread of local anesthetics during its administration. However, this technique requires totally new skills and proficiency of the anesthesiologist.
Ultrasound guidance gave rise to more frequent and wider clinical application of peripheral nerve blocks. Large groups of patients may benefit from peripheral nerve blocks for postoperative pain control after surgery of their limbs. Patients undergoing total knee arthroplasty experience improved postoperative pain control and mobilization with peripheral nerve blocks.

Chapter 2

Education and learning of ultrasound-guided regional anesthesia is reviewed according to the recommendations of the European and American Society for Regional Anesthesia in 4 steps. Models, phantoms, cadavers and simulators are helpful tools for educating ultrasound guided regional anesthesia. Generally, teaching programs using objective measures to control the learning progress improve the results. Still, there is an urgent need for further research to compare different educational techniques, to develop true high-fidelity simulators and to test their efficiency. Education programs should be tailored to the individual needs of a trainee. More importantly, the effects of improved training programs on quality of care should be investigated.

Chapter 3

Identifying sono-anatomy is an important part of the learning process when starting ultrasound guided regional anesthesia.
An embedded electronic tutorial as an element of an ultrasound machine may help to identify sono-anatomy for novices. Therefore, we investigated in a randomized controlled study whether an embedded electronic tutorial could improve accuracy or speed of performance in identifying anatomical structures. Novices in ultrasound guided regional anesthesia participated in a workshop on brachial plexus sono-anatomy. Following a lecture and training in handling of

ultrasound machines and hand-eye coordination, participants were randomized in either a group using a standard ultrasound machine, or a group using the same type of machine with an onboard electronic tutorial. A significant increase in correct identifications was achieved with help of the tutorial at the expense of significantly longer time required for this process. Increased time required may partly be related to unfamiliarity with the tutorial.

Chapter 4

Several years ago a percutaneous electrical nerve stimulation pen was introduced for non-invasively localizing superficial nerves .This technique would facilitate the performance of a nerve block. The function of the pen was based on the theoretical linear relationship between current thresholds and electrode-to-nerve distance. However, the current to distance relationship is rarely linear because of varying electrical impedance in biological tissues. The reliability of a percutaneous electrical nerve stimulation pen was never studied. Therefore we measured stimulation thresholds and impedances of the brachial plexus with the pen systematically at 49 locations of the skin at the interscalene groove of volunteers. We compared the stimulation thresholds and impedances of the pen to the distances at the same locations from skin to plexus, measured with ultrasound. Only in 10% of the locations a relationship was found between stimulation thresholds and distances. Thus, use of the percutaneous electrical nerve stimulation pen cannot be recommended.

Chapter 5

When performing an ultrasound guided axillary brachial plexus block visibility of the radial nerve, often hidden behind the axillary artery, can be challenging in the traditional arm position of shoulder and elbow bent at 90°. Therefore we studied the influence of arm positioning on visualization of the brachial plexus at the axilla in volunteers. Visibility of the nerves and distances to the artery were determined in eight different arm and scan positions and analyzed on captured video clips by two blinded observers. Visibility of the radial nerve did not improve in different arm positions. However, the distance between the radial nerve and the artery was significantly greater and the visibility of the median and ulnar nerves significantly improved in a position of shoulder 180° and elbow straight. Arm position of shoulder 180° and elbow straight provided the best overall visibility and accessibility of nerves.
Different causes of poor visibility of the radial nerve are discussed. Whether the same results will be find in older or obese patients is still unknown, but adaption

of the traditional arm position may facilitate the performance of an ultrasound guided axillary brachial plexus block.

Chapter 6

One of the advantages of ultrasound- guided peripheral nerve blocks regarding safety is the visualization of the spread of local anesthetics, allowing a dose reduction. Recently, research has been focused on reducing local anesthetics to a minimum effective volume for establishing an adequate peripheral nerve block when using ultrasound. However, effects of reduced volumes on block duration are unknown. Therefore, we assessed the duration of action of an ultrasound-guided single shot axillary brachial plexus block after a 60% reduction of mepivacaine 1.5% (15 vs 40 ml) in a prospective randomized, observer-blinded trial. The overall duration of sensory and motor block was significantly reduced by 17% and 19% respectively, whereas time to first request of postoperative analgesia was shortened by 30%. Reduction in block duration for individual nerves was larger, varying from 20% to 40% for sensory block and from 18% to 37% for motor block.
The advantages of dose reductions should be balanced against the shortened block duration. Still, effects of dose reduction in long acting local anesthetics has to be determined.

Chapter 7

Patients undergoing total knee arthroplasty can suffer from severe postoperative pain, which is known to impair early intensive physical therapy and rehabilitation. A continuous femoral nerve block during the first postoperative days improves postoperative pain control and rehabilitation. However, pain relief might be insufficient in the posterior region of the knee that is innervated by the sciatic nerve. Therefore we investigated whether the addition of a sciatic nerve block (single-injection or continuously) to a continuous femoral nerve block shortens time to discharge readiness and improves early postoperative knee function in a randomized controlled trial. Secondary, we assessed postoperative pain scores at rest and during mobilization and determined postoperative opioid consumption. This trial revealed that a single-injection or continuous sciatic nerve block in addition to a femoral nerve block did not influence time to discharge readiness or rehabilitation of knee function. Though, a single injection sciatic nerve block reduced severe pain on the day of the operation, while a continuous sciatic nerve block reduced moderate pain during mobilization on the first two postoperative days. Consumption of supplemental

opioids was significantly higher in patients without an additional sciatic nerve block.

Chapter 8

Poorly controlled severe postoperative pain has been identified as a key factor in the development of persistent pain in the long term after surgery. Therefore, we continued the previous trial (Chapter 7) with a follow-up whether an additional sciatic nerve block to a continuous femoral nerve block in patients undergoing total knee arthroplasty could improve long-term knee function and reduce pain after 3 and 12 months. Outcome was measured with two validated self reporting written questionnaires: The Western Ontario and McMaster Universities osteoarthritis (WOMAC) index questionnaire and the Oxford 12-item knee questionnaire (OKS). WOMAC index evaluates quality of life in the dimensions of pain (5 items), stiffness (2 items), and function (17 items). The OKS contains 12-items, assessing pain and physical disability). Pain was measured with the visual analogue scale (VAS) at rest and during mobilization. The collected WOMAC, OKS and VAS at 3 and 12 months were compared with preoperative baseline values. A post hoc median split analysis, based on the preoperative functional score (median baseline WOMAC index) was applied to test the hypothesis that only patients with severe disabilities and severe pain preoperatively (baseline WOMAC index < median baseline WOMAC index) might benefit from an improved postoperative pain management. Knee function improved greatly in all patients after TKA without any mid- and long- term effect of the addition of a sciatic nerve block (single injection or continuous) for patients undergoing total knee arthroplasty. Post-hoc subgroup analysis revealed that patients with poor preoperative knee function experienced less knee stiffness and pain during mobilization at the mid- and long term after addition of a sciatic nerve block for TKA. However, since groups and specially subgroups of poor preoperative functioning were small, it is entirely unclear whether this is a co-incidence by chance or a beneficial effect of the sciatic nerve block. Future research to long-term effects of an additional sciatic nerve block in preoperatively poor functioning patients undergoing total knee arthroplasty is recommended.

General Conclusion

Technical developments like ultrasound make performance of peripheral nerve blocks by anesthesiologists more effective. Guidance of ultrasound for peripheral nerve blocks need to be trained in a stepwise manner. Knowledge of site-specific anatomy is indispensible for the identification of sono-anatomy, but can be technically supported. From the perspective of patient comfort and safety, training methods of ‘learning by doing’ should be omitted.
Future inventive simulators may enhance training of ultrasound-guided nerve blocks and will accelerate the learning curve.
Use of ultrasound dramatically changes performance of peripheral nerve blocks concerning required amount of local anesthetics and corresponding duration of action, finding of most optimal patient posture and probe position for the optimal visibility and accessibility of the target nerves.
All these technical and clinical adjustments will definitively benefit patients with an indication for use of single of continuous peripheral nerve blocks after undergoing limb surgery and risk of suffering in severe postoperative pain while early mobilization is imposed.

Chapter 10

Samenvatting

Algemene conclusie

Samenvatting

Hoofdstuk 1

Het toepassen van een perifere zenuwblokkade vormt een belangrijk onderdeel van de regionale anesthesie en kent een groeiende belangstelling. Vroegere en huidige technische ontwikkelingen voor de uitvoering van de perifere zenuwblokkade komen aan bod in hoofdstuk 1. De meest belangrijke en recente uitvinding is de hoog frequente echografie voor de technische ondersteuning. Met hulp van echo is het mogelijk om de te blokkeren zenuwen, de aangrenzende vitale structuren, de naaldbeweging en de spreiding van het lokaal anestheticum te visulaliseren. Echter, deze techniek vereist volledig nieuwe vaardigheden van de anesthesioloog. Sinds het gebruik van echo is de klinische toepassing van de perifere zenuwblokkade sterk toegenomen. Grote groepen patiënten kunnen baat hebben bij een perifere zenuwblokkade: niet alleen tijdens een operatie maar vooral ook als vorm van postoperatieve pijnbestrijding na een pijnlijke ingreep aan één van de ledematen. Na implantatie van een totale knieprothese ervaren patiënten bij het toepassen van perifere zenuwblokkades aan het geopereerde been betere postoperatieve pijnbestrijding en minder pijn bij mobilisatie.

Hoofdstuk 2

In hoofstuk 2 wordt ingegaan op het leren van echogeleide technieken in de regionale anesthesie. Hiervoor werd het leerproces beoordeeld aan de hand van de 4 stappen die zijn aanbevolen door de European and American Society for Regional Anesthesia. Geschikte middelen voor het trainen bestaan uit modellen, fantomen, kadavers en simulators. Lesprogramma's waarbij met objectieve metingen de vorderingen gecontroleerd worden, geven over het algemeen betere resultaten. Toch bestaat er een dringende behoefte aan verder onderzoek waarbij verschillende trainingstechnieken worden vergeleken en waarbij simulators worden ontwikkeld, die in hoge mate de werkelijkheid nabootsen en die getest worden op hun efficiëntie. Onderwijsprogramma's moeten worden afgestemd op de individuele behoeften van een onervaren anesthesioloog. Uiteindelijk is het van belang om de effecten van verbeterde training programma's op de kwaliteit van patiënten zorg te onderzoeken.

Hoofdstuk 3

Het leren identificeren van de anatomie met echografie is een belangrijk onderdeel in het leerproces van echogeleide regionale anesthesie.

Een elektronische tutorial in het echoapparaat zou beginners kunnen ondersteunen bij het identificeren van de anatomie. Om deze reden hebben we in een gerandomiseerde gecontroleerde studie bij beginners onderzocht of het identificeren van anatomische structuren correcter en sneller verloopt als een dergelijke elektronische tutorial wordt gebruikt. De beginners namen deel aan een cursus over de anatomie van de plexus brachialis en de bijpassende echobeelden. Na het oefenen in het gebruik van een echoapparaat en het trainen van de hand-oog coördinatie, werden de deelnemers gerandomiseerd in een groep met een standaard echoapparaat en een groep met hetzelfde type echo apparaat, dat bovendien was uitgerust met elektronische tutorial. De structuren werden vaker correct geïdentificeerd met hulp van de elektronische tutorial, maar dit ging ten koste van de tijd. Mogelijk was meer tijd nodig door de onbekendheid met de tutorial.

Hoofdstuk 4

Een aantal jaren geleden werd een percutane elektrische zenuwstimulatie pen geïntroduceerd voor het non-invasief lokaliseren van oppervlakkige zenuwen. Deze techniek zou de uitvoering van een zenuwblokkade vereenvoudigen. De functie van de pen is gebaseerd op de theoretische lineaire relatie tussen de drempelwaarde van de stroom en de afstand tussen de elektrode en de zenuw. De relatie stroom-afstand is zelden lineair vanwege variërende elektrische impedantie in organische weefsels. Aangezien de betrouwbaarheid van een percutane elektrische zenuwstimulatie pen nooit was onderzocht, hebben we de stimulatiedrempels en de impedantie van de plexus brachialis met de pen systematisch vastgelegd op 49 locaties van de huid ter hoogte van de interscalene groeve bij vrijwilligers. Deze waarden vergeleken we met de afstand van de huid tot plexus, gemeten met echo op dezelfde locaties. Slechts bij 10% van de locaties werd een relatie gevonden tussen de stimulatiedrempels en afstanden. Hieruit bleek dat het gebruik van de percutane elektrische zenuwstimulatie pen niet kan worden aanbevolen.

Hoofdstuk 5

Bij het uitvoeren van een echogeleide plexus brachialis blokkade ter hoogte van de axilla kan de n. radialis, die hier vaak verborgen ligt achter de a. axillairis, beperkt zichtbaar zijn in de gebruikelijke positie van de arm met de schouder en elleboog 90^{o} gebogen. Dientengevolge onderzochten we de invloed van de positie van de arm op de visualisatie van de plexus brachialis ter hoogte van de axilla bij vrijwilligers. In acht verschillende posities werd de zichtbaarheid van de zenuwen en de afstand tot de arterie geanalyseerd en gemeten op video-opnames door twee geblindeerde waarnemers. De zichtbaarheid van de n. radialis verbeterde niet in de verschillende posities van de arm. Echter de afstand tussen de n. radialis en de arterie was significant groter en de zichtbaarheid van de n. medianus and n. ulnaris aanzienlijk beter in een arm positie met de schouder in 180 ^{o} en een gestrekte elleboog vergeleken met de andere posities. Verschillende oorzaken van de matige zichtbaarheid van de n. radialis worden geanalyseerd in de discussie van hoofdstuk 5. Of deze zelfde resultaten ook bij oudere of adipeuze patiënten zouden worden gevonden is nog onbekend. Aanpassing van de traditionele arm positie kan het verrichten van een echogeleide plexus brachialis blokkade in het axilla vergemakkelijken.

Hoofdstuk 6

Eén van de voordelen van echogeleide perifere zenuwblokkade ten aanzien van de veiligheid is de visualisatie van de spreiding van het lokaal anestheticum, waardoor met een lagere dosis van het lokaal anestheticum kan worden volstaan. Onlangs werd onderzoek verricht naar het reduceren van lokale anesthetica bij het gebruik van echo tot een minimaal effectief volume, waarbij nog een adequate perifere zenuwblokkade gerealiseerd kon worden. Echter, de effecten van gereduceerde volumes op de werkingsduur van de zenuwblokkade waren nog onbekend. Derhalve onderzochten we in een prospectief gerandomiseerd onderzoek de werkingsduur van een eenmalige, echogeleide axillair plexus brachialis blokkade nadat het volume van een kortwerkend locaal anestheticum (mepivacaïne 1.5%) met 60% (15 vs 40 ml) was verlaagd. De totale duur van de sensorische en motorische blokkade was significant verminderd met respectievelijk 17% en 19%, terwijl de tijd tot de eerste vraag naar postoperatieve pijnstilling met 30% afnam. Bij de individuele zenuwen was de werkingsduur van de blokkade nog sterker afgenomen, variërend van 20% tot 40% voor de sensibiliteit en van 18% tot 37% voor de motoriek.
De voordelen van een verlaging in de dosis moeten worden afgewogen tegen een verkorte werkingsduur van een perifere zenuwblokkade. Effecten van een dosisverlaging bij lang werkende lokale anesthetica moeten in de toekomst nog onderzocht worden.

Hoofdstuk 7

Na een totale knieprothese kunnen patiënten ernstige postoperatieve pijn ervaren, waardoor vroege fysiotherapie en snelle revalidatie worden belemmerd. Een continue femorale zenuwblokkade tijdens de eerste postoperatieve dagen

verbetert de postoperatieve pijnbestrijding en revalidatie. Echter deze vorm van pijnstilling kan nog onvoldoende zijn voor het posterieure deel van de knie, dat geïnnerveerd wordt door de n. ischiadicus. We onderzochten in een gerandomiseerde gecontroleerde trial of de aanvulling van een n. ischiadicusblokkade (met een éénmalige injectie of continue) bij een continue femorale zenuwblokkade de tijd tot het gereed zijn voor ontslag verkort en of de vroege postoperatieve kniefunctie verbetert. Daarnaast hebben we de postoperatieve opioïd consumptie en de postoperatieve pijnscores van patiënten in rust en bij mobilisatie gemeten. Deze studie toonde aan dat een n. ischiadicus-blokkade (éénmalig of continue) als aanvulling bij een continue femorale zenuwblokkade niet de tijd tot het gereed zijn voor ontslag en niet het herstel van de kniefunctie beïnvloedt. Echter, een éénmalige n. ischiadicus blokkade verminderde de ernstige postoperatieve pijn op de dag van de operatie significant, terwijl een continue ischiadicus-blokkade ook de matige pijn tijdens de mobilisatie in de eerste twee dagen na de operatie significant verminderde. Bovendien hadden patiënten zonder aanvullende n. ischiadicusblokkade een significant hoger gebruik van extra opioïden postoperatief.

Hoofdstuk 8

Onvoldoende behandelde ernstige postoperatieve pijn wordt beschouwd als een belangrijke factor bij de ontwikkeling van chronische pijn op de lange termijn na een operatie. Om deze reden continueerden we het vorige onderzoek (Hoofdstuk 7) met een follow-up bij patiënten met een totale knieprothese om de invloed van een n. ischiadicusblokkade bij een continue femorale zenuwblokkade op de kniefunktie en de pijn na 3 en 12 maanden te beoordelen. De kniefunktie werd gemeten met hulp van twee gevalideerde schriftelijke vragenlijsten: De Western Ontario en McMaster Universities artrose index vragenlijst (WOMAC) en de Oxford 12-item knie vragenlijst (OKS). De WOMAC index beoordeelt de kwaliteit van leven in de dimensies van pijn (5 items), stijfheid (2 items), en de functie (17 items). De OKS bevat 12-items, die pijn en fysieke beperkingen meet. De kniepijn werd apart gemeten met de visuele analoge schaal (VAS) in rust en tijdens de mobilisatie. De verzamelde gegevens van de WOMAC, OKS en VAS bij 3 en 12 maanden werden vergeleken met de preoperatieve uitgangswaarden. De kniefunctie verbeterde sterk bij alle patiënten op middellange en lange termijn, terwijl er geen significant effect werd aangetoond van de aanvullende ischiadicus blokkade (éénmalige injectie of continue).
Daarnaast pasten we een gesplitste post-hoc analyse toe, gebaseerd op de

mediane preoperatieve WOMAC score, om de hypothese te testen dat alleen patiënten met een ernstige preoperatieve beperking en pijn (uitgangswaarde WOMAC<mediane uitgangswaarde WOMAC) zouden kunnen profiteren van betere postoperatieve pijnbehandeling. Uit post-hoc analyse bleek dat patiënten met een slechte preoperatieve kniefunctie minder stijfheid en pijn tijdens de mobilisatie ondervonden op middellange en lange termijn na toevoeging van een n. ischiadicusblokkade voor een totale knie arthroplastiek. Echter, de groepen en de subgroepen waren klein, zodat het volstrekt onduidelijk is of dit een co-incidentie is of toch een gunstig effect van de n. ischiadicusblokkade. Verder onderzoek naar lange termijn effecten van een aanvullende n. ischiadicus-blokkade is aan te bevelen bij grotere patiëntengroepen met een preoperatief slechte kniefunktie, die een totale knie arthroplastiek ondergaan.

Algemene Conclusie

Technische ontwikkelingen zoals echografie maken de uitvoering van perifere zenuwblokkades door anesthesiologen effectiever. De technische uitvoering van echogeleide perifere zenuwblokkades vereist echter specifieke training, waarbij kennis van specifieke anatomie onontkoombaar is voor het identificeren van de weefselstructuren met echo. In de toekomst zouden simulators ontwikkeld moeten worden voor het trainen van echogeleide zenuwblok technieken, waardoor de leercurve versneld kan worden. De invloed van deze nieuwe trainingsmethoden op de kwaliteit van zorg zouden onderzocht moeten worden. De trainingsmethode ‘leren door te doen’ dient zoveel mogelijk te worden vermeden.
Het gebruik van echo heeft de uitvoering van perifere zenuwblokkades sterk veranderd ten aanzien van de hoeveelheid locaal anesthetica die gebruikt wordt en de daarbij passende werkingsduur, het vaststellen van de meest optimale houding van de patiënten voor een optimale zichtbaarheid en toegankelijkheid van de te blokkeren zenuwen.
Al deze technische en klinische aanpassingen en ontwikkelingen zullen beslist ten goede komen aan patiënten waarbij een éénmalig of continue perifere zenuwblokkade geïndiceerd is voor het ondergaan van een operatie aan een ledemaat met het risico op ernstige postoperatieve pijn, vooral als vroege mobilisatie noodzakelijk is.

Chapter 11

Dankwoord

Een bijzonder moment is aangebroken, want na een langdurig traject is dit proefschrift afgerond. Deze prestatie kon alleen gerealiseerd worden dankzij de samenwerking met en inzet en bijdrage van alle medeauteurs, waarvoor mijn grote dank!
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Curriculum Vitae Jessica Wegener

Jessica Wegener was born on 22 april 1961 in Bergen (NH). After finishing secondary school at the Wagenings Lyceum in 1979, she started one year Physical Science in Groningen, followed by one year Human Nutritition at the Wageningen University. Finally she studied medicine at the University of Utrecht and graduated in 1988. After two years of residency in intensive care and thoracic surgery, she entered her anesthesiology speciality training at the Erasmus University Medical Centre in Rotterdam under supervision of Prof. dr. W. Erdmann and stayed as a staff member in the Sophia Children Hospital and Erasmus University Hospital after qualification in 1996. From 1997 to 2004 she worked as a consultant for anesthesiology, intensive care and chronic pain treatment in 'het Westfriesgasthuis' in Hoorn. She also was involved in the development of group of caregivers for palliative care in the local area of Westfriesland.
Since 2004 she works as a staff anesthesiologist at the Academic Medical Centre in Amsterdam. From 2009 till 2013 she also worked as consultant for anesthesiology and chronic pain treatment one day a week at the Sint Maartenskliniek in Nijmegen. In the AMC she has set up a working group for locoregional anesthesia 'The Locals' together with interested colleagues.

Portfolio Jessica Wegener

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Poster presentations

Wegener JT, Ward CS, Preckel B, Lirk PB, Hollmann MW, Stevens MF, Frkovic V. Influence of arm position on ultrasound visibility of the axillary plexus. 32nd ESRA Congress 2013, Glasgow, 4-7 September, 2013

Wegener JT, Doorn van CT, Eshuis JH, Hollmann MW, Preckel B, Stevens MF. Value of an onboard electronic tutorial for ultrasound-guided regional anesthesia. 30th ESRA Congress, Dresden, 7-10 september 2011

Wegener JT, Boender ZJ, Preckel B, Hollmann MW, Stevens MF. Percutaneous electrical nerve stimulation (PENS) does not correlate with proximity or depth of the brachial plexus. 29 th ESRA Congress, Porto, 8-11 september, 2010

Wegener JT Ooij van B, Hollmann MW, Stevens MF, Preckel B. Long-term effects of sciatic nerve block in addition to femoral nerve block on functional outcome after total knee arhtroplasty (TKA) 29 th ESRA Congress, Porto, 8-11 september, 2010

Wegener JT, Stevens MF, Karayeva S, Hollmann MW, Preckel B. Sciatic nerve block in addition to femoral nerve block for postoperative analgesia after total knee arthroplasty. 28th Annual ESRA Congress, Salzburg, September 9-12, 2009

Wegener JT, Wandelen van RN, Woerkens van ECM, Aardweg vd M. Uptake of volatile anaesthetics; measures. PGA 47 th congress, New York, december 1993.

Wegener JT, Bouwmeester J. Postoperative pain assessment in children. The Pain Clinic, Istanbul, October 1996.

Oral presentations

Analgesie bij totale knie arthroplastiek. Pro/Con. XIIIth DARA/ESRA Nederland Symposium 1-2 februari 2013.

Analgesie bij TKP. XIIth DARA/ESRA Nederland Symposium 10-11 februari 2012.

Welk blok distaal van de elleboog? XIIth DARA/ ESRA Nederland Symposium 10-11 februari 2012

Anaesthesia meets surgery: Interaction between anesthesiologist and surgeon in knee surgery- the anaesthesiologists view. Euroanaesthesia 2011, Amsterdam, 11-14 june 2011.

Echo bij locoregionale anesthesie van de bovenste extremiteit. Echografie in de Anesthesie. Symposium AMC, Amsterdam, november 2009.

Several lectures, clinical presentations and workshops about acute and chronic pain, regional anesthesia and peripheral nerve blockade across the Netherlands.

PhD Courses

Basic Course Legislation and Organization, BROK,Amsterdam, 2012.

Introduction to Medical Statistics, Amsterdam, 2007.