**Incidence and related factors for failed spinal anaesthesia for lower limb arthroplasty - a controlled prospective cohort subanalysis.**

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**Summary**

**Background** Spinal anaesthesia is the preferred choice for total hip- and knee arthroplasty (THA/TKA), due to the claimed superior outcome profile, relative simple technique and without the need for advanced airway support. However, choosing and informing about spinal anaesthesia should also include the risk for failed spinal anesthesia with associated pain, discomfort and suboptimal settings for airway management. Small scale studies suggest incidences from 1-17%, however no multi-institutional large data exists on failed spinal incidence and related factors during THA/TKA, hindering evidence based information and potential anaesthesia stratification.

**Methods** Data from a prospective study on spinal anaesthesia for THA/TKA were examined for incidence of conversion to general anaesthesia. Potential perioperative factors (age, gender, American Society of Anaesthesiologist (ASA) score, height, weight, BMI, hip vs knee, bupivacaine dosage and duration of time from spinal administration until end of surgery) were analyzed with logistic regression for relation to failed spinal anaesthesia.

**Results** 1451 patients were included for analysis, whereof 57 (3.9%) had failed spinal anaesthesia. Spinal failure patients were significantly younger (61 vs 67 yr, p=0.003), and operation time longer in the failed spinal group vs no- failure, respectively (133 vs. 89 min, p<0.001). No significant differences were found with regard to bupivacaine volume, gender, ASA-score, height, weight, BMI or THA vs TKA.

**Conclusion** Failed spinal anaesthesia for THA and TKA is a relatively frequent occurrence and identification of risk patients is not feasible. These results should be considered when choosing anaesthesia and included in the information to patients

**Keywords:**

Spinal anaesthesia, hip arthroplasty, knee arthroplasty, adverse events, failed

Spinal anaesthesia is often the preferred anaesthetic choice for lower limb surgery, due to the relative simple technique which, when effective, offers excellent analgesia and muscle relaxation without the need for advanced airway support. Choosing the ideal anaesthesia for total hip- or knee arthroplasty (THA/TKA) requires weighing the risk and benefits between spinal- and general anaesthesia where spinal anaesthesia so far has been considered superior with regards to outcomes1;2 . However, the acclaimed benefits of spinal anaesthesia has been challenged by recent smaller RCTs with modern general anaesthesia3;4 and reviews5;6 and some studies suggest an even higher cardiovascular risk with neuroaxial blockade7.

Choosing and informing about spinal anaesthesia should also include the risk of conversion to general anaesthesia with obvious discomfort or pain to the patient and suboptimal settings for airway management with inherent risk for difficult intubation or laryngeal mask placement 8. Failed spinal anaesthesia for various reasons has been known since the very first spinal by *August Bier* 9 and include incidences from 1% to 17%, with an overall incidence of about 2-4% across procedures 10-12. To our knowledge the largest dataset includes a multicenter prospective study of spinal anaesthesia in 1214 patients, with 531 “orthopedic procedures” (no details) where a 3% incidence of failure was seen especially in younger patients13. However, the majority of studies are from single centers or small series with heterogeneous surgical procedures 11;14 precluding specific information for THA/TKA, and potential identification of risk factors to enable patient stratification for optimization of anaesthesia. Thus, we aimed to describe the incidence of failed spinal anaesthesia and related factors and confirm previous findings in a large controlled prospective trial of THA and TKA in high volume expert centres .

**Methods**

Data were retrieved from a prospective multicenter study regarding the safety of discharging patients from the postanaesthesia care unit (PACU) without assessing motor function after spinal blockade for THA and TKA 15. The study was approved by the regional ethics committee and data handling authorities and registered at ClinicalTrials.gov (NCT02134496). The study took place at 5 Danish orthopedic centers (Farsø-, Gentofte-, Vejle-, Holstebro- and Viborg Hospitals, Denmark) from June, 2014 to august 28, 2015. Patients were included after written and verbal informed consent if scheduled for THA or TKA, ≥ 18 years, able to understand Danish, and scheduled for spinal anaesthesia. Patients were assessed for eligibility during the study-independent clinical examination preceding surgical admission at the orthopedic departments. The choice of anaesthesia (spinal/general) was made by the anaesthetist during consultation with the patient, reflecting clinical practice. Patients were excluded post-inclusion if spinal anaesthesia could not be performed or was contraindicated (technical, infection, other reason) or if general anaesthesia was chosen by the patient (waived participation). Only procedures were bupivacaine had been considered injected intrathecally were included. Thus, unsuccessful dural puncture attempts were not included as failures and failed spinal anaesthesia identified before the start of surgery was neither included. Patients were given a preoperative multimodal analgesia including oral paracetamol and celecoxib and 125 mg i.v.methylprednisolone (TKA only). Spinal anaesthesia was performed using 0.5% isobaric bupivacaine (preferably 1.8-2.5 ml. i.e. 9.0 -12.5 mg) or 0.5% hyperbaric bupivacaine (preferably 1.5-2,0 ml. i.e. 7.5-9.0 mg), based upon the anaesthetists clinical practice.

Primary outcome: we adopted the original definition of failed spinal anaesthesia as proposed by Levy et al 14: ”If a patient required general anaesthesia at any time during the surgical procedure, this was considered a failure. Pain and associated complaints persisting throughout the procedure, despite the frequent administration of narcotics or tranquilizers or both, were under suspicion but did not constitute failure for the purposes of this study”. Thus, supplemental sedation or analgesia with propofol or remifentanil was allowed per protocol, if it did not result in the need for advanced airway management to secure oxygenation (i.e. tracheal intubation, laryngeal mask placement to secure oxygenation).

Factors assessed in relation to failed spinal anaesthesia where; age, gender, American Society of Anaesthesiologist (ASA) score, height, weight, BMI, THA vs TKA, bupivacaine dosage and duration of time from spinal administration until end of surgery,

The main outcome was descriptive and based upon a sub-analysis of the original study 15. Thus, no formal power analysis with regard to spinal failure was performed.

Statistics: Data were analyzed using IBM SPSS statistics ver. 22 software. Data were presented using descriptive statistics including mean, median standard deviation and range where appropriate. Univariate analysis was performed for continuous data by students t-test (if normally distributed as per the Kolmogorov-Smirnov test) or by non-parametric tests (Mann-Whitney U test) if not normally distributed. Differences in distribution were assessed by Chi2-test. A binary logistic regression analysis was performed with a significance level of 5%.

**Results**

Inclusion of patients are detailed in figure 1, where 2317 patients were screened, 1511 patients included in the study and 1451 patients included in analysis for failed spinal. Thus, 60 patients were excluded from analysis and where the case of asystole needs special mentioning: loss of consciousness developed 10 minutes after intrathecal injection of 3 ml bupivacaine. Cardio-pulmonary resuscitation was commenced lasting approximately 2 minutes before consciousness was regained. The patient was classified as ASA II (well controlled hypertension and asthma, 92 kg, 174 cm height), and subsequent investigations found no other cause for the asystole, including preceding hypotension.

740 patients (51%) were women and 784 (54%) having a THA. The mean age was 67.4 years (SD 9.9), 1320 (91%) had an ASA-score of I or II. Average weight was 84 kg (SD 16.8), and BMI 28.4 (4.9). Mean bupivacaine 0.5 mg/ml dosage was 2.3 ml (SD 0.58), and average time from intrathecal administration to end of surgery (spinal-operating time) was 90 minutes (SD 22 min).

Spinal anaesthesia failure was seen in 57 (3.9%) cases with a range from 2.2% to 7.1% between the 5 participating centers (*P* = 0.003). No adverse events from conversion to general anaesthesia were noted. Laryngeal mask was the preferred airway management technique (51/57, 89.5%).

Distribution of potentially relevant factors for failed spinal anaesthesia is shown in table 1, including univariate tests for assessing significant differences. Spinal failure patients were significantly younger (61 vs 67 years, p = 0.003). The average spinal-operating time (time from intrathecal injection until end of surgery) was significantly longer (133 vs. 89 min, p<0.001) in the group with failed spinal anaesthesia vs. no-failure. These findings were confirmed in the logistic regression analysis including all variables (table 1) (age p=0.002, spinal-operating time <0.001). However, the relationship between failed-spinal and operating time was not linear, evidenced by the finding of maximum spinal-operating time of 230 minutes in the non-failure group vs. 176 minutes in the spinal-failure group (table 1.). There were no statistical differences with regards to bupivacaine 0.5% volume, gender, weight, ASA-class, height, BMI or THA vs TKA.

**Discussion:**

Our data confirms previous findings of spinal failure in about 3-6% of lower extremity procedures 14;16;17, although with a relatively large variation between our 5 participating centers. These numbers are conservative as we chose only to include patients were conversion to general anaesthesia was necessary, thus not considering those cases where supplement of analgesics or propofol were necessary to continue with the procedure, but not requiring intubation/laryngeal mask placement, or those where an attempt of intrathecal injection failed. Previous smaller studies have reported zero cases of failed spinal anaesthesia18, potentially due to lack of power (n=45),. As per protocol, we excluded the procedures where a conversion to general anaesthesia was done prior to surgery, thus the reported average incidence of ~4% spinal failure would be ~6% if the cases of exclusion *for technical reasons* or *pre-incision* *conversion due to no effect* were included in the analysis. It would have been ideal to further discriminate between the cases were the spinal was considered effective to commence surgery, but immediately turned out not to be, and those that “wore-of” during the operation, but due to the nature of the study this information was not available.

We confirmed age as a significant factor13, although the absolute differences between groups was small (average 6 years difference) and presumably not clinically meaningful. Our finding of longer procedure times in the spinal failure group may seem logical as a simple analgesia-duration effect, but a too simple explanation for the failure itself. First of all, as per protocol we have no data to support when the failure occurred (beginning, mid or end of surgery), only that it occurred after the incision. Secondly, the conversion to general anaesthesia itself may have prolonged the procedure. Furthermore, several procedures in the non-failure group exceeded the longest procedure in the failure group. Also, the available literature suggests that a spinal anaesthesia may not be as simple as claimed. Thus, a recent study has shown difficulties in performing a subarachnoid block in 29% of cases (especially in patients with high BMI) and in 11% resulting in change to general anaesthesia either before or during surgery 19.

Information about the potentially most relevant reasons for failed spinal anaesthesia are not easily available to the clinician, including large variations in bupivacaine concentrations in the lumbar cerebrospinal-fluid (CSF)20;21 , CSF volume variation22-25 and intrathecal septae 26. Despite administration of the same volume of bupivacaine, a 8-16 fold difference in CSF concentrations may occur and concentrations resulting in the same block level to vary six-fold 20. Studies in patients with failed spinal anaesthesia suggest that (too) low concentrations of local anaesthetics (LA) are the main reason for failed spinal anaesthesia21. However, in 60% of patients a LA concentration above what should be sufficient for blockade was found, leaving the question unanswered as to why some spinal blocks fail21. Potential explanations for the variation in concentrations include non-uniform distributions in the subarachnoid space, and especially variations in CSF volume which range 2-fold from 43 to 81 ml 24;25. These findings may also explain why no relation to failed spinal anaesthesia and administered bupivacaine, height, weight or BMI was seen in our study.

Our findings add to the discussion of spinal versus general anaesthesia in relation to outcomes. Thus, spinal anaesthesia is presumed superior due to the afferent input blockade resulting in analgesia, reducing the endocrine metabolic stress response and sympathetic blockade resulting in reduced bleeding and thromboembolic complications1;2. However, these data come from older randomized studies using non-modern analgesic agents or large epidemiological databases 1;2;27-31 without specific information on type of general anaesthesia, pain management or care-principles. Newer studies have questioned the validity of the acclaimed benefits of spinal anaesthesia when comparing to modern general total intravenous anaesthesia and fast-track care principles with regard to analgesia, opioid use 3;4 and complications 6;7. Furthermore, several complications to spinal anaesthesia exists, including postoperative urinary retention 32;33, hypotension, nausea, post-dural headache, and - although rare - neurological sequelae 34 and death 35;36. In our series we had 1 patient developing a pre-incission clinical cardiac arrest, and 3.9% requiring conversion to general anaesthesia despite a presumed pre-selection of patients eligible for spinal anaesthesia during the initial pre-operative consultation with the anaesthetist. These findings should be measured against the potential complications from general anaesthesia including airway management, negative inotrope and chronotrope cardiac effects from anaesthetics, aspiration 30;31 and the occurrence of accidental awareness 37.

Our study has limitations, mainly relating to the it being a subanalysis of data from another prospective study15 with the inherent lack of power calculation, however it is to our knowledge by far the largest series concerning THA and TKA with detailed characterization of patients and procedures. Another important factor is that we cannot give details on the technical reasons for failed spinal anesthesias, which has been emphazised as one of the most important factors previously. However, in our study we decided to exclude patients were a spinal was not deemed adequate to initiate surgery, thus excluding cases without intrathecal injection and loss of injectate, Furthermore, although we could not describe the relationship between the anaesthetist’s expertise and risk for failure, the participating centers are all high-volume, and specific selection of investigators would compromise the external validity of our data. We did not include or describe spinal anaesthesia’s where supplemental analgesics were required, nor did we asses when the failure occurred and this information should be collected in future trials to complete the assessment of the efficacy of spinal anaesthesia for THA and TKA. Finally our study only relates to spinals with bupivacaine without adjuvants, so any effect from other combinations of intrathecal dugs is not assessed, but given the fact that intrathecal opioids is not considered optimal due to the side-effects mainly (urinary retention and pruritus), the effect of adjuvants is considered purely speculative.

In conclusion, failed spinal anaesthesia for THA and TKA is a relatively frequent occurrence and preoperative identification of risk patients is not feasible. The information from the current study should be considered when choosing type of anaesthesia and included in the patient information.

**Legend:** Figure 1. Study inclusion flow-chart. GA: general anaesthesia, Uni-knee: Uni-compartment knee arthroplasty

**Authors contributions**

Eske Kvanner Aasvang, MD, Ph D: Designed the study, collected data, analyzed data, participated in manuscript writing

Mogens Berg Laursen, MD, Ph D: collected data, participated in manuscript writing

Jacob Madsen, MD: collected data, participated in manuscript writing

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Annette Elisabeth Skøtt, MD: collected data, participated in manuscript writing

Henrik Kehlet MD, Ph D: Designed the study, analyzed data, participated in manuscript writing

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**Conflicts on Interests:**

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article, thus we declare no conflicts of interst

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