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**RECOVERY AFTER TOTAL INTRAVENOUS GENERAL**  
**ANAESTHESIA VS. SPINAL ANAESTHESIA FOR TOTAL KNEE**  
**ARTHROPLASTY; A RANDOMIZED TRIAL**

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Short title: regional or general anaesthesia for knee arthroplasty

## Abstract

**Background.** This study was undertaken to investigate if general anaesthesia compared to regional, would reduce the need for postoperative hospitalisation and improve early postoperative comfort for patients undergoing fast-track total knee arthroplasty (TKA).

**Methods.** One hundred and twenty patients were randomly allocated to receive either intrathecal bupivacaine (regional anaesthesia group, RA) or general anaesthesia with a target controlled infusion of propofol and remifentanyl (general anaesthesia group, GA). Primary outcome was length of hospital stay (LOS) defined as time from end of surgery until the patient met the hospital discharge criteria. Secondary outcome parameters included actual time of discharge, pain, intraoperative blood loss, length of stay at the Post Operative Care Unit, dizziness, postoperative nausea and vomiting, need for urinary catheterization and patient satisfaction.

**Results.** GA resulted in shorter LOS (46 hrs vs. 52 hrs,  $P < 0.001$ ), less nausea and vomiting (4 vs. 15,  $P < 0.05$ ) and dizziness (VAS 0 mm vs. 20 mm,  $P < 0.05$ ) compared to RA. During the first 2 postoperative hours GA patients had higher pain scores ( $P < 0.001$ ), but after 6 hrs the RA group had significantly higher pain scores ( $P < 0.001$ ). Patients in the GA group used fewer PCA doses and less morphine ( $P < 0.01$ ). GA patients were able to walk earlier compared to the RA group ( $P < 0.001$ ). Patients receiving RA wanted to change method of anaesthesia in the event of a subsequent operation more often than the GA patients ( $P < 0.05$ ).

**Conclusion.** GA may have favourable recovery effects after TKA compared with RA.

**Keywords:** anaesthetic techniques, i.v., subarachnoid

**Trial registry number:** NCT01312298

Total knee arthroplasty (TKA) is a common and painful procedure. Pain is not only unpleasant for the patient but the intensity of early postoperative pain a strong risk factor for developing persistent pain. The operation is usually performed under regional anaesthesia (RA) or general anaesthesia (GA) and where previous data have shown better outcome effect after RA <sup>1</sup>. Consequently, RA with the intrathecal technique has been recommended <sup>2</sup>. However, RA has often not been compared with modern GA technologies with multimodal non-opioid analgesia and fast-track setup. Without question, RA will produce good pain control in the first couple of postoperative hours, but the question is whether this advantage will remain for the first 1-2 postoperative days or whether a modern GA technique would be preferable in a fast-track set-up? Therefore, we conducted a prospective, randomized, controlled trial to compare RA and GA with regards to length of hospital stay, postoperative pain, opioid requirements and other patient comfort factors for patients undergoing TKA.

## Methods

This study was approved by the Research Ethics Committee at Lund University (no 2011/180) and was carried out at Hässleholm Hospital, Sweden. It was registered with ClinicalTrial.gov under the US National Library of Medicine (reg. no NCT01312298). Written informed consent was obtained from all patients.

### *Study design*

The study design was consecutive and randomized. Patients with osteoarthritis scheduled for TKA at the department of orthopaedic surgery, Hässleholm Hospital, Sweden, were eligible for participation in the study. 124 consecutive patients were assessed by 2 orthopaedic surgeons between September 2011 and June 2012 and 120 patients were enrolled after the preoperative visit to the anaesthetist. Inclusion criteria were ASA I-III, able to understand the given information, age > 45 yrs and < 85 yrs and having signed the informed consent document. Exclusion criteria were previous major knee surgery to the same knee, obesity (BMI > 35), rheumatoid arthritis, immunological depression and allergy to any of the drugs used in this study. Patients were also excluded if they were taking opioids or steroids or if they had a history of having had a stroke or psychiatric disease that potentially could affect the perception of pain.

### *Randomization and blinding procedure*

Randomization was performed by an employee, not involved in the study, who prepared non-transparent, sealed envelopes each containing a slip of paper with descriptions of whether the patient should receive GA or RA. The randomization was computerized. On the day of surgery a nurse, likewise not involved in the study, opened the appropriate envelope and prepared the procedures accordingly. Patients and investigating doctors were blinded to which of the

treatments each patient was allocated to until one hour prior to surgery. After that, both patients and personnel in the operation theatre were, for obvious reasons, aware of the method of anaesthesia being used. Once the patients left the operating theatre nurses and doctors responsible for monitoring and assessing home readiness were blinded as to what treatment was given.

### *Anaesthesia and perioperative care*

Approximately 1 h before surgery all patients received oral celecoxib 400 mg and paracetamol 1 g. Thereafter, it was administered 12-hourly (celecoxib 200 mg) and 6-hourly (paracetamol 1g). None of the patients received an indwelling urinary catheter prior to surgery and a thigh tourniquet was not used. No drains were used.

A low-volume fluid regimen was used with 2000 mL of Ringer's solution (Fresenius-Kabi AB, 751 74 Uppsala, Sweden) during the first 24 hrs. All patients received 1 g of tranexamic acid i.v.

Patients in the RA group received intrathecal (L<sub>4</sub>–L<sub>5</sub>) anaesthesia (using a 25 G Quinke needle, Spinocan®, B.Braun AG, Germany) consisting of bupivacaine 0.5%, 3 mL. The patients were also given an infusion of propofol 10 mg/mL to induce light sedation during surgery. All patients breathed spontaneously with supplemented oxygen 2 L/minute.

Patients in the GA group were anaesthetized using Target Controlled Infusion (TCI) with propofol 10 mg/mL and remifentanyl 40 µg/mL<sup>3,4</sup>. Rocuronium bromide 0.6 mg/kg was given to facilitate intubation. Ventilation was done with oxygen/air and aimed at EtCO<sub>2</sub> 4.5 kPa. At the end of surgery glycopyrronium 0.5 mg and neostigmine 2.5 mg was given. Twenty min before the end of surgery an i.v. bolus dose of oxycodone 10 mg was given.

All patients received cloxacillin 2 g iv (or clindamycin 600 mg iv if penicillin allergy) prior to surgical incision. The preoperative fasting period was 6 and 2 hrs before surgery for solid food and clear fluids, respectively<sup>5</sup>.

Towards the end of surgery the patients in both groups received infiltration of local anaesthesia in the perisurgical area <sup>6</sup> consisting of 150 ml of ropivacaine (0.2%) with epinephrine (10 µg/ml) (i.e. 148.5 ml ropivacaine 2 mg/ml + 1.5 ml Epinephrine 1 mg/ml). The mixture was injected using a systematic technique to ensure uniform delivery of the local anaesthetic to all tissues incised, handled or instrumented during the procedure. The first 50 ml were injected into the posterior joint capsule and both collateral ligaments after the bone cuts have been performed. After insertion of the prosthesis, 50 ml were injected along the borders of and into the capsule and cut quadriceps tendon, infra-patellar ligament, possible remnants of the fat pad, cruciate ligaments and soft tissues surrounding the joint. Another 50 ml were infiltrated into the subcutaneous tissues before wound closure <sup>6</sup>.

A Cryo-bandage (Iceband, Nordic Medical Supply A/S, Denmark) was applied directly after surgery and remained in place for 24 hrs.

All patients were preoperatively familiarized with a Patient Controlled Analgesia (PCA) device for post operative pain medication during the first postoperative 24 hrs. The PCA pump (Abbott GemStar™ PCA Pump) administered i.v. morphine in doses of 20 µg/kg and with a lock out time of 10 min <sup>6</sup>. After 24 hrs the PCA device was disconnected and the patients received slow-release oxycodone (OxyContin®) 10 mg orally twice daily. After 24 hrs oxycodone (OxyNorm®) 10 mg orally was used as rescue medication. The PCA device was fitted to the patients as they left the OR. 24 hrs later it was removed and the amount of morphine administered was registered. Furthermore the number of administered PCA-doses and requested, but not administered PCA-doses were registered along with the time at which these doses were requested. In order to prevent overdistension of the bladder ultrasound bladder scans were performed at least every third hour until the patients could control their urinary bladder. The following rules were observed:

1. bladder volume < 300 ml, repeat bladder scan within 3 hrs



2. 300 – 399 ml repeat the bladder scan within 2 hrs
3. 400 - 499 ml repeat the bladder scan within 1 h
4.  $\geq 500$  ml do an intermittent catheterization. This can be repeated twice after which an indwelling urinary bladder catheter is used.

### *Assessments*

All patients were familiarized with a horizontal Visual Analogue Scale (VAS, [100 mm]) used for assessment of pain (0 = no pain, 100 = worst imaginable pain), PONV and dizziness (0 = no symptom, 100 = worst symptom possible). Pain was registered preoperatively, on arrival to Post Anaesthesia Care Unit (PACU), after 2, 4, 6 and 10 hrs. The first and second day after surgery pain was assessed at 08.00 and 14.00 hrs. Pain was registered at rest, with 45° knee flexion, with the knee straight and 45° hip flexion and after walking 5 meters<sup>7</sup>. Dizziness (and at the same time blood pressure) was recorded twice per day. It was done by asking the patient to score his/her dizziness on a 100 mm VAS anchored with “no dizziness” and “worst possible dizziness”. Dizziness and blood pressure was monitored in supine and upright standing position. Blood pressure (systolic and diastolic, mm Hg) was also measured before standing, with the measurement of blood pressure commencing within 60 sec. When analysing the data, mean arterial blood pressure (MAP) was used. Orthostatic function was defined as being able to walk 5 meters at 6, 10, 24 and 48 hrs postoperatively.

Discharge criteria from PACU to the ward was assessed every 15 min until obtained and done by a nurse blinded to which treatment the patient had received. Discharge criteria from PACU were: 1. sufficient level of consciousness (aroused by verbal stimuli), 2. able to maintain a free airway, 3. adequate breathing with  $\text{SaO}_2 > 94\%$  when administering a max of 5 L  $\text{O}_2/\text{min}$ , 4. only mild or no PONV ( $< 30$  mm), 5. pain control adequate (i.e. VAS no more than 30 mm at rest).

LOS was defined as the time from the end of surgery until the patient met the discharge criteria from the ward: 1. able to get in and out of bed, 2. able to get dressed, 3. able to sit down in a chair and get up again, 4. able to walk 50 meters with or without walking aids (crutches etc), 5. can flex the knee to  $\geq 70^\circ$ , 6. able to walk stairs, 7. pain manageable with oral analgesics, 8. acceptance to be discharged.

Discharge criteria were checked twice daily, at 08.00 and again 14.00 hrs and done by a nurse blinded to which treatment the patient had received. The actual time at which the patient was discharged from the ward was noted and compared with LOS.

PONV was monitored using a 100 mm VAS for nausea anchored with “no nausea” and “worst possible nausea”. The number of vomiting occasions was recorded. PONV was monitored twice daily during the study.

Intraoperative blood loss was calculated by weighing the gauze and draping sheets together with the content in the surgical suction bottle corrected from the irrigation fluid volume.

Six months postoperatively, the patients were interviewed via telephone by an employee blinded to assigned treatment. They were asked to assess the anaesthesia they had received 6 months earlier on a 100 mm scale where 0 = worst imaginable experience and 100 = best possible experience. They were also asked what type of anaesthesia they would like to have in case of a subsequent TKA having the opportunity to choose between the 2 types of anaesthesia used in this study.

### *Surgery*

The surgeries were performed via a ventral incision with a parapatellar medial entrance to the joint. The patella was everted. A cemented single radius cruciate retaining (CR) total knee was used (the Triathlon™ Knee System [Stryker,

Mahwah, New Jersey, USA]) for all patients. Appropriate guide instruments were used according to the surgical-technique manual supplied with the knee system.

### *Statistical analyses*

Power and sample size calculation was done with

<http://biostat.mc.vanderbilt.edu/twiki/bin/view/Main/PowerSampleSize> .

We planned a study of a continuous response variable from independent control and experimental subjects with 1 control(s) per experimental subject. In a previous pilot study at Hässleholm Hospital the response within each subject group was 72 hrs with standard deviation of 42. If the true difference between experimental and control means was 24 hrs, we would need to study 49 experimental subjects and 49 control subjects to be able to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) 0,8. The Type I error probability associated with this test of this null hypothesis is 0,05. To compensate for drop outs we decided to include 124 patients.

Data analyses were performed using SPSS version 20.0 (SPSS, Chicago, USA). Data distribution was tested for normality with Sharpio-Wilks test and residual plots. According to data distribution either Student-t test or Mann-Whitney U-test for unpaired data was used. Chi Square test was used for binary data. Data are presented as mean ( $\pm$  SD) or median (25-75% interquartile range [IQR]. A P-value  $< 0.05$  was assigned statistical significance.

## Results

Patients were recruited between September 2011 and June 2012. 124 consecutive patients were assessed for eligibility by 2 orthopaedic surgeons and 120 were included after the pre operative visit by the anaesthetist (Fig 1 [CONSORT flow diagram]). The 6 months follow-up was completed in December 2012. There were no differences in demographic or surgical data (Table 1).

Sixty-six % of patients were ready to be discharged from PACU upon arrival without statistical differences between the groups (Mann-Whitney). LOS (fulfilling discharge criteria) was shorter in the GA group (46 hrs) compared to the RA group (52 hrs,  $P < 0.001$ ), but without difference between the groups in actual day of discharged ([Chi Square test] Table 2). The reasons for not being discharged in spite of meeting the discharge criteria were organizational causes (39 patients), general weakness (2), dizziness (3) and pain (5).

Preoperatively, there were no differences in the pain scores between GA and RA. In the early phase of the postoperative period the patients in the GA group had higher pain scores, but from 6 hrs and onwards the RA patients had higher pain scores (Figure 2).

The median (IQR) 24 hr postoperative consumption of morphine was 19 mg (11-28) in the GA group and 54 mg (37-78) in the RA group ( $P < 0.001$ ). The median number (IQR) of administered PCA doses was 12 (10-22) in the GA group and 30 (20-41) in the RA group ( $P < 0.001$ ). The median (IQR) number of requested, but not administered, PCA doses was 2 (0-7) in the GA group and 9 (1-26) in the RA group ( $P < 0.001$ ). The distribution of the mean (IQR) number

of requested and administered PCA doses during the first 24 postoperative hours are shown in figure 3.

The patients in the RA group had higher dizziness scores ( $P < 0.05$ ) (Fig 4) and orthostatic function was less affected in the GA group ([Chi-Square test] since 57 patients in the GA group vs 18 in the RA group were able to walk 5 meters after 6 hrs ( $P < 0.001$ ). After 10 and 24 hrs the same figures were 59 and 60 patients in the GA group and 40 and 59 in the RA group ( $P < 0.01$  at 10 hrs and n.s. at 24 hrs). There were no differences in MAP between the groups except on the the first post operative day at 14.00 hrs where MAP (mean  $\pm$  SD) was significantly higher in the RA group when standing up ( $96 \pm 10$  mm Hg vs.  $90 \pm 12$  mm Hg, [Student T-test,  $P < 0.05$ ]).

PONV scores and number of patients that vomited are shown in table 3 and both parameters were more common in the RA group. The median (IQR) number of redressings were 2 (0-3) in the GA group and 1 (0-3) in the RA group (n.s. Mann-Whitney).

Forty-two patients in the GA group and 36 in the RA group were managed without any urinary catheterization. 16 patients in the GA group and 23 in the RA group had to have 1 or 2 intermittent catheterizations ( $P > 0.05$  between the groups (Chi-Square test)).

There was no difference between the groups in the total anaesthesia satisfaction score. However, significantly more patients in the RA group indicated that they would like to change the method of anaesthesia if a subsequent operation was to be done (14 vs. 2, [Chi-Square test]  $p < 0.05$ ).

There were no deaths during in this study but a pulmonary embolus was diagnosed in 2 patients, 1 in each group. No other pulmonary or cardiac complications were diagnosed.

## Discussion

TKA is an effective treatment for end-stage knee osteoarthritis and on a global basis this procedure is increasing. Thus, 550 000 TKAs were performed in 2007 in the United States <sup>8</sup>. A major challenge for the future will probably be to be able to perform such a large number of operations not only with good medical outcome but also with acceptable economical and logistical quality.

In this standardised study in TKA, patients receiving GA had shorter LOS (time to reach discharge criteria), less dizziness and PONV and better early orthostatic function compared to RA. Also, pain scores were lower after 6 hrs with an opioid-sparing effect in the GA group compared to the RA group. Furthermore, patients in the GA group were more likely to favour the same type of anaesthesia if they had to have surgery again. No differences were found in length of PACU stay, blood loss and need for urinary catheterisation between the groups.

At 14.00 hrs the second day following the day of surgery 79% of our patients met or had met the discharge criteria from the ward, which is in line with previous findings <sup>9</sup>. More interesting is that we found that the GA patients seemed to be ready for discharge earlier than the RA patients (36 hrs vs. 48 hrs), probably explained by reduced PONV and dizziness. In a systematic by Liu et al the effect of anaesthesia technique on pain and outcome was investigated <sup>10</sup>. They found that, when using RA, a modest reduction in pain scores could be accompanied by an increase in side effects that was not perceived as an improvement.

The main reason for still being in hospital in spite of meeting the discharge criteria in this study were exudation from the surgical wound and organizational causes. None of the patients in our study had a tourniquet during surgery, which may have contributed to less pain but also to the increased postoperative wound exudation <sup>11</sup>. We refrained from the use of a thigh tourniquet due to its

association with intraoperative, ischemic nociception <sup>11</sup>.

In a review by Macfarlane et al they reported reduced postoperative pain and morphine consumption among patients receiving RA compared to GA <sup>12</sup>.

However, most of the studies included in this review were done before the introduction of the high-volume local infiltration technique (LIA) <sup>13</sup> started to be widely used in 2008 in connection with TKA and which is more simple compared to many of the other regional anaesthetic techniques <sup>13, 14</sup>. In our study both groups received the same type of LIA. Other differences compared with older studies are that we used TCI as the GA method since TCI is well tolerated with rapid and clear headed emergence <sup>15</sup>. Finally, all our patients received standardized opioid-sparing analgesia with COX-2 inhibitor and paracetamol.

73% of the RA and 59% of the GA patients met the PACU discharge criteria on arrival. The implication of this is that many TKA patients can bypass PACU and go directly to the ward. Lunn et al found in a recent study <sup>16</sup> that 85% of the patients met the PACU discharge criteria within 15 min, but their study and ours had slightly different discharge criteria compared to the standard recommendations <sup>7</sup> in the sense that motor function was not a criteria to be taken into consideration. This change did not cause any complication on the ward in terms of respiratory or cardiovascular instability, falls due to motor weakness or other organ dysfunctions <sup>16</sup> and therefore calls for further large-scale studies. In the RA group, intrathecal morphine was not used despite recommended <sup>1</sup>, which may slightly have influenced our results. However, the analgesic effects of intrathecal morphine are rather small and in these elderly patients the side effects from intrathecal opioids may be undesirable for early recovery.

Furthermore, we used a rather comprehensive multimodal non-opioid analgesic program, which we thought would reduce the need for intrathecal morphine. The GA group received intraoperative oxycodone at the end of surgery due to the shortlasting analgesic effects of the GA technique. In contrast, we found routine

intraoperative oxycodone inappropriate in the RA group, receiving a combination of opioid-sparing intrathecal local anaesthetics and the LIA technique.

We found that the patients in the RA group had significantly more dizziness compared to the patients in the GA group. Since dizziness and muscle weakness are two of the major reasons for delayed discharge <sup>9</sup> it might be possible to reduce these complaints by using GA instead of RA. However, the increase in dizziness among the RA patients could not be explained by orthostatic dysfunction <sup>17</sup>, since we only found differences in MAP at 14.00 hrs the first day after the day of surgery and then it was higher in the RA group.

A lumbar spinal anaesthesia may have more profound effect on urinary bladder dysfunction, but 68% in both groups managed without having their bladder catheterized at any time. Provided that bladder scans are done regularly it might be an advantage to avoid urinary catheters since they are associated with a number of serious complications such as urinary tract infections and subsequently deep wound infections <sup>18, 19</sup>.

We found no difference between the groups in bleeding during surgery, as suggested before <sup>2</sup>. Furthermore, the actual volumes of bleeding were fairly limited in both groups in spite of the fact that tourniquet was not used. This is in contrast with a recent publications by Stundner at al. where neuraxial anaesthesia was associated with lower rates of blood transfusions <sup>20</sup>. However, their study was retrospective and in one third of the cases analysed method of anaesthesia could not be determined.

When anaesthetists were asked if they would like GA or RA themselves in the hypothetical situation of requiring surgery for a lower extremity orthopaedic problem they preferred RA <sup>21</sup>. It is therefore interesting that we found no



differences in satisfaction scores between the groups although more patients in the RA group would prefer GA in case of a future operation.

One of the limitations of our study was that from 1 hour prior to the start of surgery until the patients reached the PACU patients and caregivers were, for obvious reasons, not blinded to which anaesthetic technique was being used. However, all nurses and doctors involved in the monitoring and registration were otherwise unaware of treatment allocation. Another limitation was that this study looked solely on comfort factors and not serious morbidity or mortality which will require a sufficiently powered prospective randomized trial to decide the primacy of RA or GA, although probably being minimal <sup>22</sup> . Major complications after RA are rare but sometimes serious (vertebral canal abscess or haematoma, meningitis, nerve injury, cardiovascular collapse) <sup>23</sup> . Other serious complications such as deep vein thrombosis, pulmonary embolism, pneumonia and respiratory depression was in a large systematic review reported being less frequent when using RA <sup>2</sup> . However, their conclusions were based on studies performed in the 1980s and 1990s. Today, with a fast track regimen early mobilisation and effective treatment of pain has reduced those outcomes <sup>24</sup> .

In conclusion, this TKA study shows that GA results in earlier recovery, less pain, dizziness and nausea and earlier walk ability compared to RA. In addition, the patients preferred GA over RA in case of a new TKA.

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## **Conflict of interest**

None declared

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## **Authors' contribution**

AH participated in the design of the study, did preoperative evaluation, included the patients, administered anaesthesia, performed statistical analyse and wrote the manuscript. HK and STL designed and coordinated the study and participated in writing the manuscript.

## REFERENCES

1. Fischer HB, Simanski CJ, Sharp C, et al. A procedure-specific systematic review and consensus recommendations for postoperative analgesia following total knee arthroplasty. *Anaesthesia* 2008; **63**: 1105-23
2. Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *BMJ* 2000; **321**: 1493
3. Marsh BJ, Morton NS, White M, Kenny GN. A computer controlled infusion of propofol for induction and maintenance of anaesthesia in children. *Can J Anaesth* 1990; **37**: S97
4. Minto CF, Schnider TW, Shafer SL. Pharmacokinetics and pharmacodynamics of remifentanyl. II. Model application. *Anesthesiology* 1997; **86**: 24-33
5. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology* 2001; **114**: 495-511
6. Andersen LO, Husted H, Otte KS, Kristensen BB, Kehlet H. High-volume infiltration analgesia in total knee arthroplasty: a randomized, double-blind, placebo-controlled trial. *Acta Anaesthesiol Scand* 2008; **52**: 1331-5
7. Lunn TH, Kristensen BB, Andersen LO, et al. Effect of high-dose preoperative methylprednisolone on pain and recovery after total knee arthroplasty: a randomized, placebo-controlled trial. *Br J Anaesth* 2011; **106**: 230-8
8. Buvanendran A, Kroin JS, Della Valle CJ, Kari M, Moric M, Tuman KJ. Perioperative oral pregabalin reduces chronic pain after total knee arthroplasty: a prospective, randomized, controlled trial. *Anesth Analg* 2010; **110**: 199-207
9. Husted H, Lunn TH, Troelsen A, Gaarn-Larsen L, Kristensen BB, Kehlet H. Why still in hospital after fast-track hip and knee arthroplasty? *Acta Orthop* 2011; **82**: 679-84
10. Liu SS, Wu CL. The effect of analgesic technique on postoperative patient-reported outcomes including analgesia: a systematic review. *Anesth Analg* 2007; **105**: 789-808
11. Estebe JP, Davies JM, Richebe P. The pneumatic tourniquet: mechanical, ischaemia-reperfusion and systemic effects. *Eur J Anaesthesiol* 2011; **28**: 404-11
12. Macfarlane AJ, Prasad GA, Chan VW, Brull R. Does regional anesthesia improve outcome after total knee arthroplasty? *Clin Orthop Relat Res* 2009; **467**: 2379-402
13. Kerr DR, Kohan L. Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. *Acta Orthop* 2008; **79**: 174-83

14. Kehlet H, Andersen LO. Local infiltration analgesia in joint replacement: the evidence and recommendations for clinical practice. *Acta Anaesthesiol Scand* 2011; **55**: 778-84
15. Wang Y, Yan M, He JG, et al. A randomized comparison of target-controlled infusion of remifentanyl and propofol with desflurane and fentanyl for laryngeal surgery. *ORL J Otorhinolaryngol Relat Spec* 2011; **73**: 47-52
16. Lunn TH, Kristensen BB, Gaarn-Larsen L, Husted H, Kehlet H. Post-anaesthesia care unit stay after total hip and knee arthroplasty under spinal anaesthesia. *Acta Anaesthesiol Scand* 2012; **56**: 1139-45
17. Jans O, Bundgaard-Nielsen M, Solgaard S, Johansson PI, Kehlet H. Orthostatic intolerance during early mobilization after fast-track hip arthroplasty. *Br J Anaesth* 2012; **108**: 436-43
18. Balderi T, Carli F. Urinary retention after total hip and knee arthroplasty. *Minerva Anesthesiol* 2010; **76**: 120-30
19. Hameed A, Chinegwundoh F, Thwaini A. Prevention of catheter-related urinary tract infections. *Br J Hosp Med (Lond)* 2010; **71**: 148-50, 51-2
20. Stundner O, Chiu YL, Sun X, et al. Comparative perioperative outcomes associated with neuraxial versus general anesthesia for simultaneous bilateral total knee arthroplasty. *Reg Anesth Pain Med* 2012; **37**: 638-44
21. Roy RC. Choosing general versus regional anesthesia for the elderly. *Anesthesiol Clin North America* 2000; **18**: 91-104, vii
22. Kettner SC, Willschke H, Marhofer P. Does regional anaesthesia really improve outcome? *Br J Anaesth* 2011; **107 Suppl 1**: i90-5
23. Cook TM, Counsell D, Wildsmith JA. Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists. *Br J Anaesth* 2009; **102**: 179-90
24. Husted H, Otte KS, Kristensen BB, Orsnes T, Wong C, Kehlet H. Low risk of thromboembolic complications after fast-track hip and knee arthroplasty. *Acta Orthop* 2010; **81**: 599-605

## **LEGENDS TO FIGURES:**

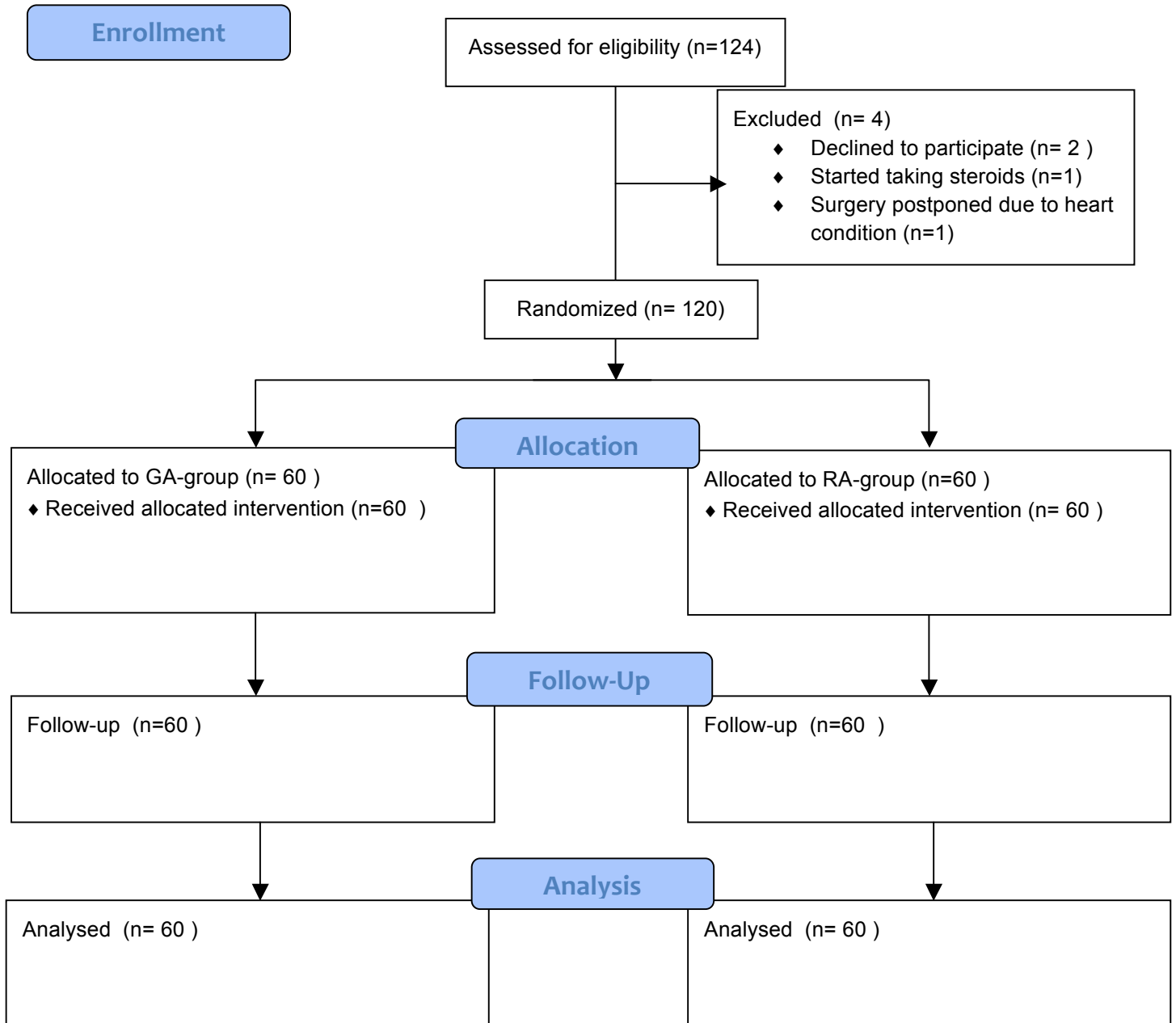
Figure 1: Consort Flow Diagram for the study.

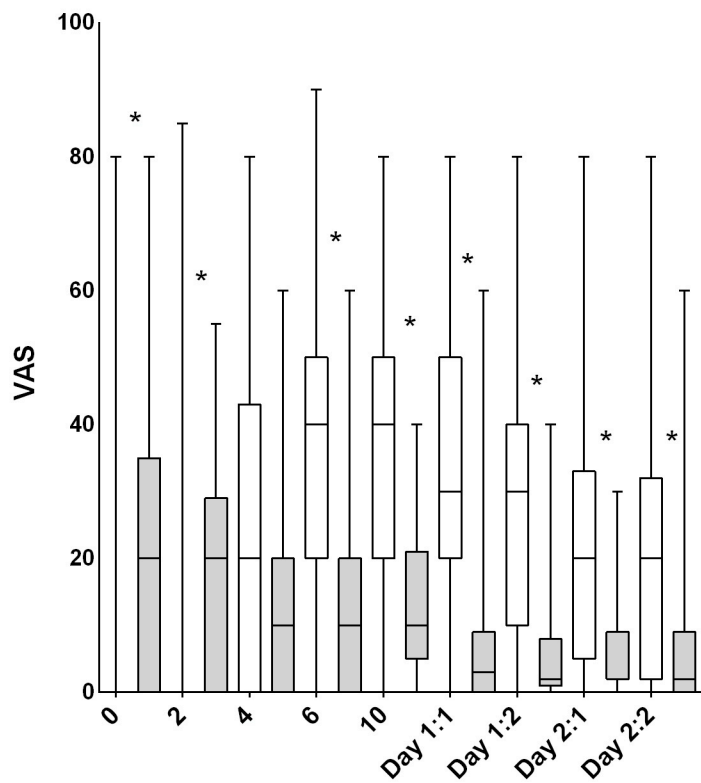
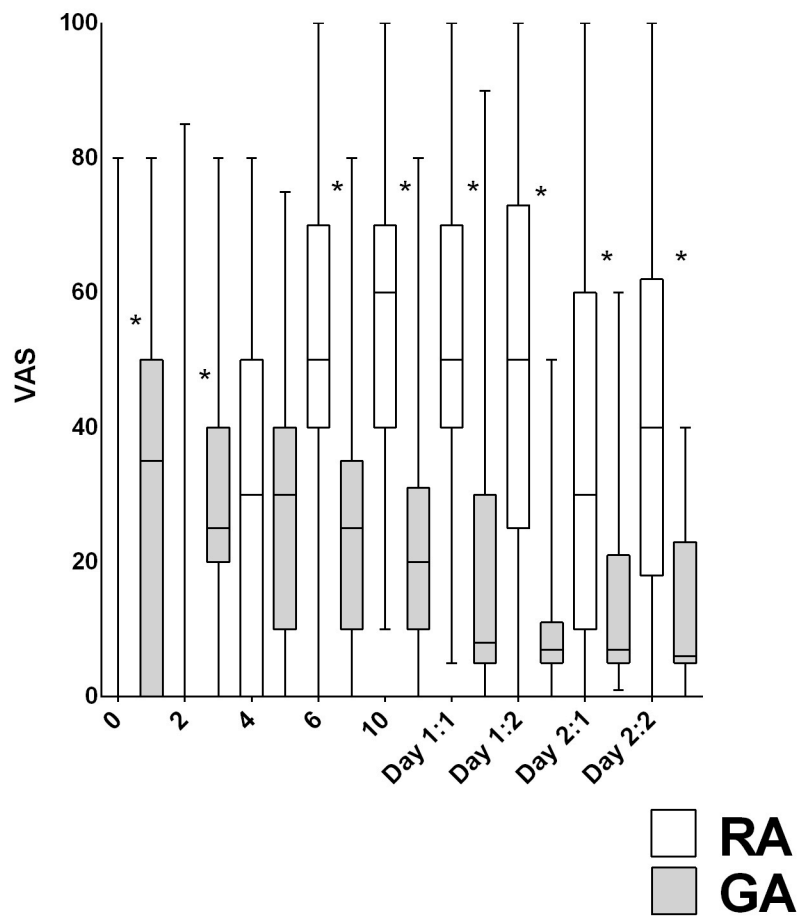
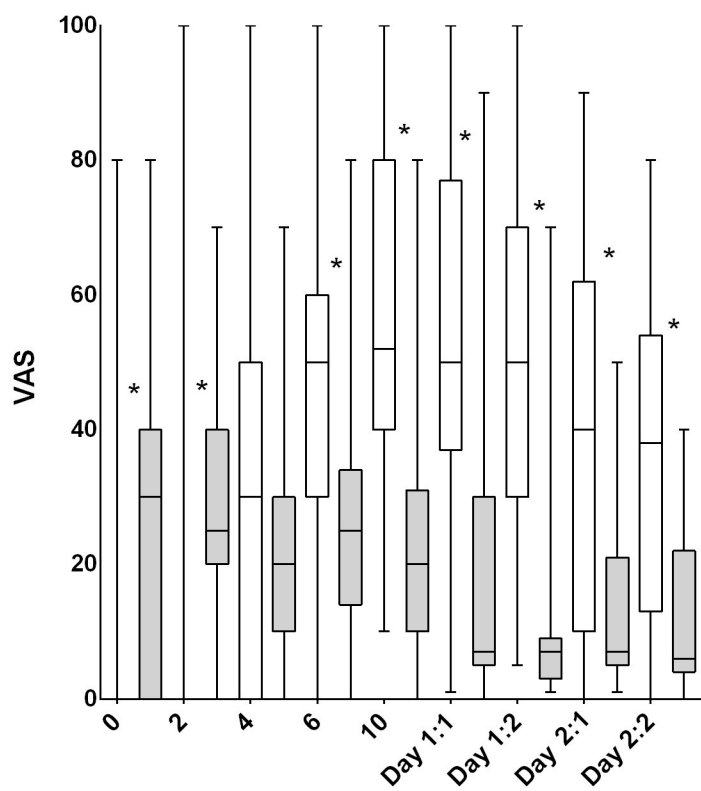
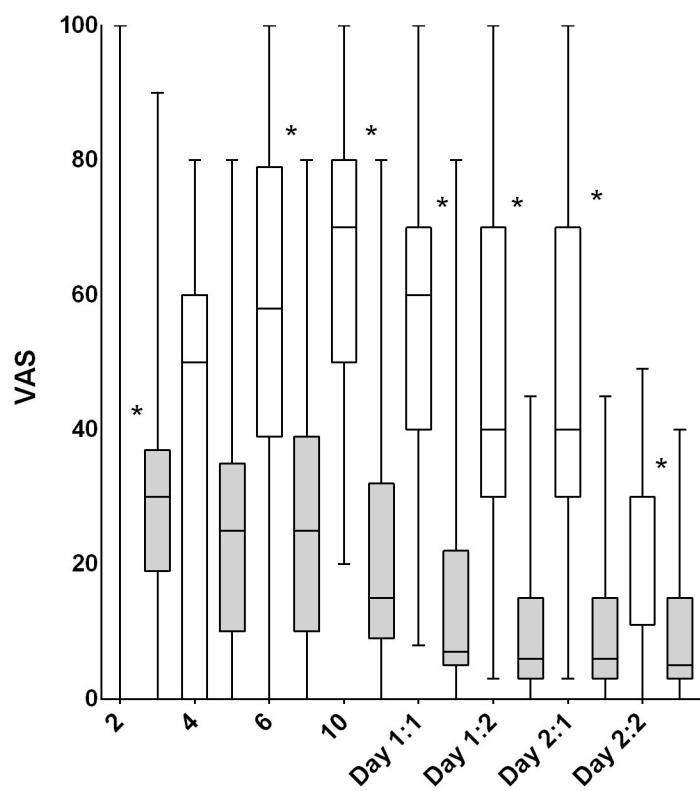
Figure 2: Pain (Visual Analogue Scale, VAS 0-100 mm) at (A) rest, (B) during knee flexion, (C) with the knee straight and hip flexion and (D) when walking. Filled bars = GA and non filled bars = RA. Line within the boxes indicate median and the boxes indicate 25-75% interquartile range (IQR). Whiskers indicate range. \* =  $p < 0.001$ . Numbers indicate the hrs after surgery. Day 1:1 and 1:2 is the day after the day of surgery at 08.00 and 14.00. Day 2:1 and 2:2 are the same times but the second post operative day.

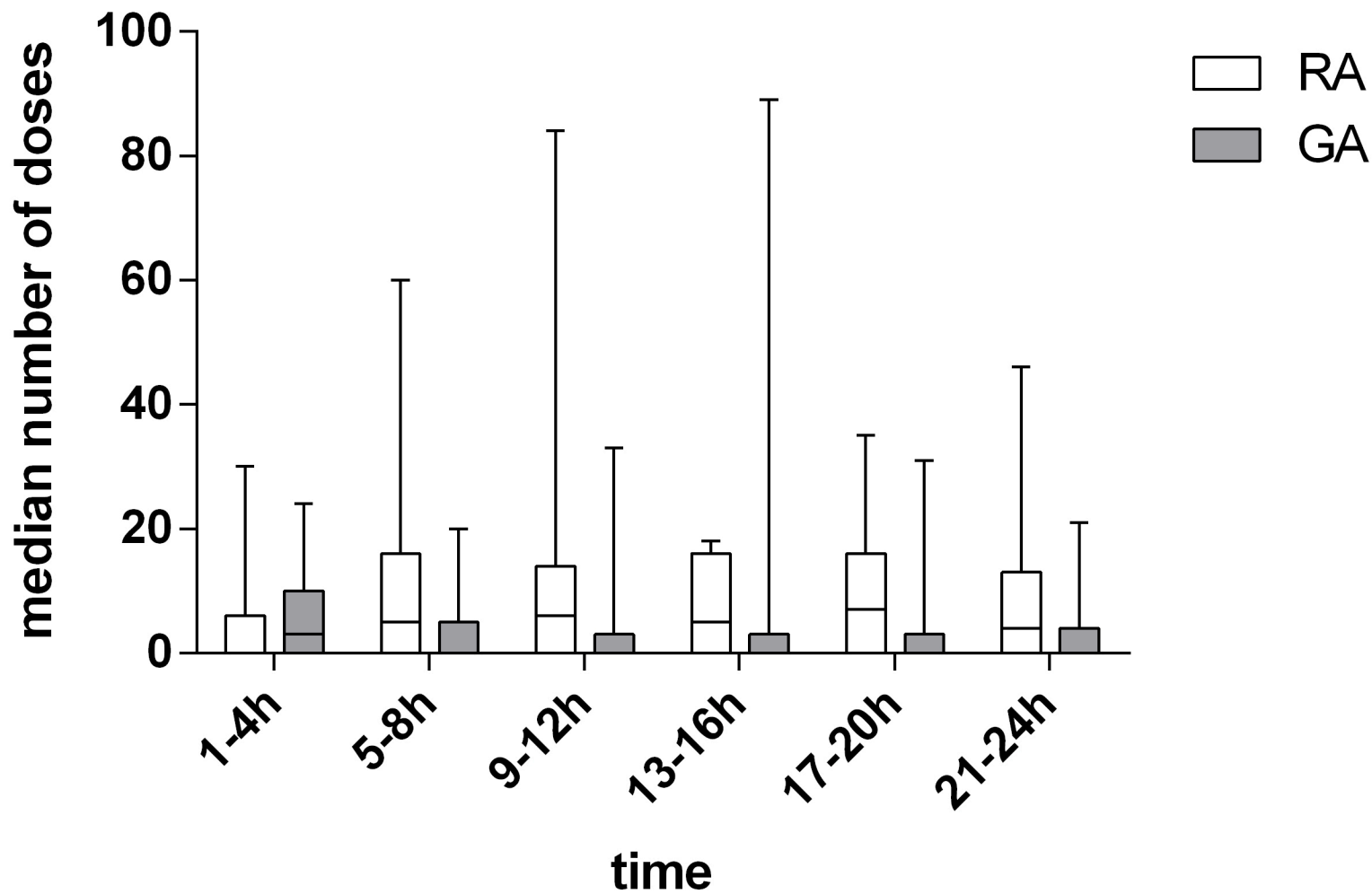
Figure 3: Median number of administered and requested, but not administered PCA doses during the first 24 hrs after surgery. Line within the boxes indicate median and boxes indicate 25-75% interquartile range (IQR). Whiskers indicate range.  $p < 0.001$  at all times.

Figure 4: Number of patients having different levels of dizziness (Visual Analogue Scale, VAS 0-100 mm) when in a supine or standing up position. Measurements made at PACU, the day after the day of surgery at 08.00 hrs (Day 1:1) and at 14.00 hrs (Day 1:2). Area under the curve analyzed for PACU - Day 1:1 and Day 1:1- Day 1:2 using Mann- Whitney test. Statistically significant differences (more patients having higher scores in RA group).  $P < 0.05$ , at both intervals.

## CONSORT 2012 Flow Diagram

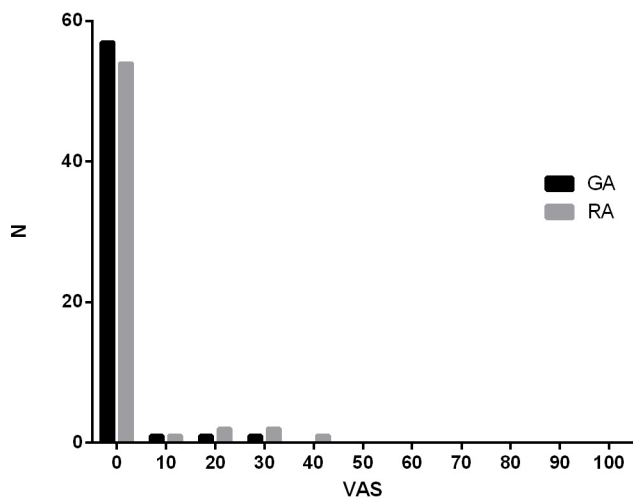


**A****B****C****D**

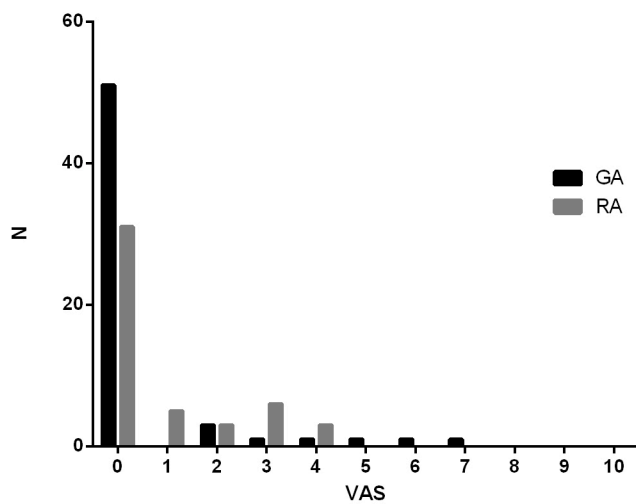




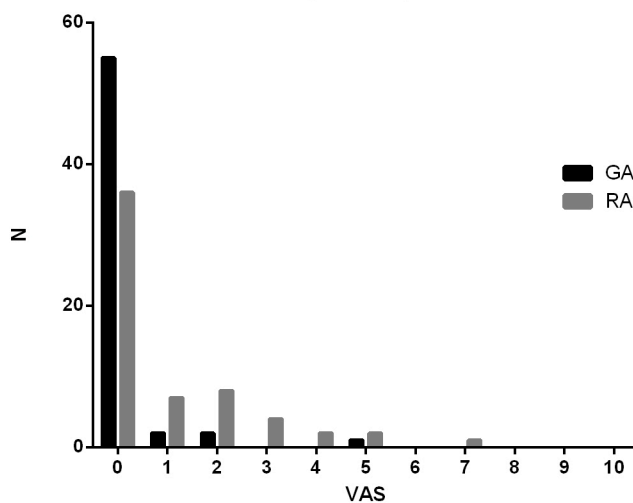
PACU (Supine)



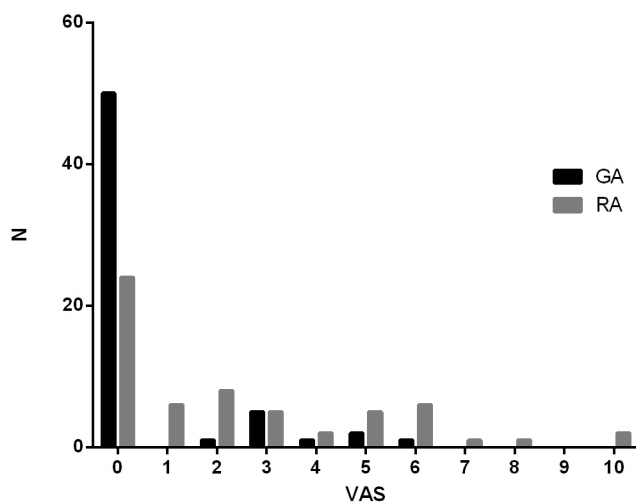
PACU (Standing)



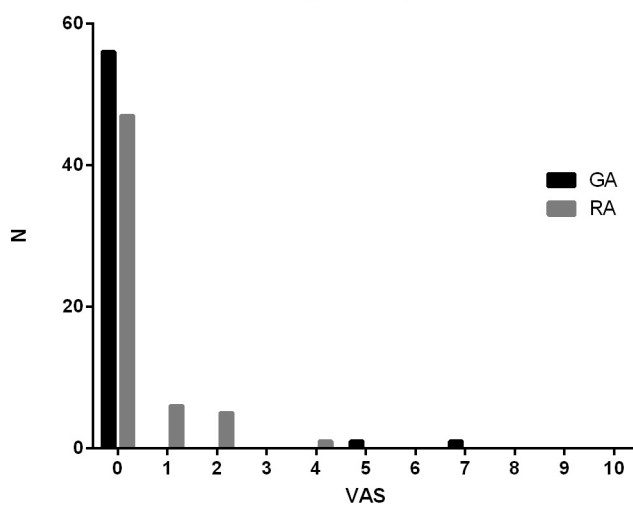
Day 1:1 Supine



Day 1:1 Standing



Day 1:2 Supine



Day 1:2 Standing

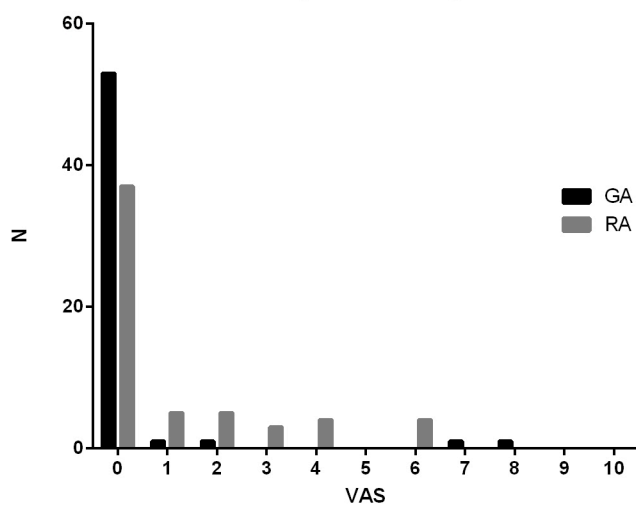


Table 1

Demographics and surgical data		
	GA-group <i>n</i> =60	RA-group <i>n</i> =60
Weight (kg)	82 ± 11	83 ± 16
Height (cm)	172 ± 8	170 ± 9
Male/Female	31/29	28/32
Age (yrs)	68 ± 7	67 ± 7
ASA physical status		
I	18	11
II	35	39
III	7	10
Duration of surgery (min)	44 ± 11	49 ± 7
Per-operative bleeding (ml)	208 (145-267)	218 (132-293)

Weight, height age and duration of surgery presented as mean ± SD. Per - operative bleeding presented as median (IQR). Gender and ASA status presented as numbers.

Table 2

Discharge from the ward	according to criteria			actual discharge		
	GA-group	RA-group	<i>P</i>	GA-group	RA-group	<i>P</i>
	<i>n</i> =60	<i>n</i> =60		<i>n</i> =60	<i>n</i> =60	
Day 1, 08.00 hrs	0	0	n.s.	0	0	n.s.
Day 1, 14.00 hrs	16	3	<0.01	1	1	n.s.
Day 2, 08.00 hrs	38	17	<0.01	1	1	n.s.
Day 2, 14.00 hrs	54	43	n.s.	23	25	n.s.
Day 3				49	44	n.s.
Day 4				56	53	n.s.

Cumulative number of patients meeting the discharge criteria from the ward at different post operative times and the actual number of patients that in fact were discharged (Chi-Square test, GA-group vs. RA-group). Day 1 is the first day following the day of surgery.

Table 3

Post operative nausea and vomiting						
	VAS score for nausea			Number of patients vomiting		
	GA-group	RA-group	<i>P</i>	GA-group	RA-group	<i>P</i>
	<i>n</i> =60	<i>n</i> =60		<i>n</i> =60	<i>n</i> =60	
PACU	0 (0) [0-30]	0 (0-20) [0-100]	<0.01			
Day 1, 08.00 hrs	0 (0) [0-63]	17 (0-44) [0-90]	<0.001			
Day 1, 14.00 hrs	0 (0) [0-50]	0 (0-16) [0-100]	<0.01	4	15	<0.05
Day 2, 08.00 hrs	0 (0) [0-50]	0 (0-10) [0-50]	<0.05			
Day 2, 14.00 hrs	0 (0) [0-50]	0 (0) [0-50]	n.s.	1	5	n.s.

Median (IQR) [range] score for post operative nausea (Mann-Whitney). Number of patients vomiting each day (Chi-Square test). Day 1 is the first day following the day of surgery.