Recovery after total intravenous general anaesthesia or spinal anaesthesia for total knee arthroplasty: a randomized trial†

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Background. This study was undertaken to compare the effects of general anaesthesia (GA) and spinal anaesthesia (SA) on the need for postoperative hospitalization and early postoperative comfort in patients undergoing fast-track total knee arthroplasty (TKA).

Methods. One hundred and twenty subjects were randomly allocated to receive either intrathecal bupivacaine (SA group) or GA with target controlled infusion of propofol and remifentanil (GA group). Primary outcome was length of hospital stay (LOS) defined as time from end of surgery until the subject met the hospital discharge criteria. Secondary outcome parameters included actual time of discharge, postoperative pain, intraoperative blood loss, length of stay in the Post Anaesthesia Care Unit, dizziness, postoperative nausea and vomiting, need for urinary catheterization and subject satisfaction.

Results. GA resulted in shorter LOS (46 vs 52 h, P<0.001), and less nausea and vomiting (4 vs 15, P<0.05) and dizziness (VAS 0 mm vs 20 mm, P<0.05) compared with SA. During the first 2 postoperative hours, GA patients had higher pain scores (P<0.001), but after 6 h the SA group had significantly higher pain scores (P<0.001). Subjects in the GA group used fewer patient-controlled analgesia doses and less morphine (P<0.01), and were able to walk earlier compared with the SA group (P<0.001). Subjects receiving SA would request a change in the method of anaesthesia in the event of a subsequent operation more often than the GA subjects (P<0.05).

Conclusion. GA had more favourable recovery effects after TKA compared with SA.

Keywords: anaesthetic techniques; i.v.; outcome; subarachnoid

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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 is a strong risk factor for developing persistent pain. The operation is usually performed under regional anaesthesia (RA) or general (GA), and previous data have shown better outcome effect after RA.1 Consequently, RA with the intrathecal technique has been recommended.2 However, RA has not often been compared with modern GA techniques with multimodal non-opioid analgesia and a fast-track approach. RA produces good pain control in the first couple of postoperative hours, but the question is whether this advantage remains 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 trial to compare the effect of spinal anaesthesia (SA) and GA on length of hospital stay (LOS), postoperative pain, opioid requirements and other patient comfort factors in 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 subjects.

Study design

The study design was consecutive and randomized. Patients with osteoarthritis undergoing TKA at the Department of Orthopaedic Surgery, Hässleholm Hospital, Sweden, were...
eligible for participation in the study. One hundred and twenty-four consecutive patients were assessed by two orthopaedic surgeons between September 2011 and June 2012, and 120 subjects were enrolled after the preoperative visit to the anaesthetist. Inclusion criteria were ASA I–III, able to understand the given information, age >45 yr and <85 yr and having signed the informed consent. 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 stroke or psychiatric disease that 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 a computer-generated description of whether the patient should receive GA or SA. On the day of surgery a nurse, likewise not involved in the study, opened the appropriate envelope and prepared the procedures accordingly. Subjects and investigating doctors were blinded to treatment group until 1 h before surgery. After that, both subjects and personnel in the operation theatre were, for obvious reasons, aware of the method of anaesthesia being used. Once subjects left the operating theatre, staff responsible for monitoring and assessing home readiness were blinded as to treatment group.

Anaesthesia and perioperative care
Approximately 1 h before surgery all subjects received oral celecoxib 400 mg and acetaminophen 1 g, and thereafter 12-hourly (celecoxib 200 mg) and 6-hourly (acetaminophen 1 g). No subjects received an indwelling urinary catheter before surgery, (celecoxib 400 mg and acetaminophen 1 g, and thereafter 12-hourly). Approximately 1 h before surgery all subjects received oral celecoxib 200 mg, and thereafter 12-hourly (celecoxib 200 mg) and 6-hourly (acetaminophen 1 g). No drains were used.

A low-volume fluid regimen was used with 2000 ml of Ringer’s solution (Fresenius-Kabi AB, Uppsala, Sweden) during the first 24 h. All subjects received 1 g of tranexamic acid i.v.

Subjects in the GA group received intrathecal (L₄–L₅) administration (using a 25 G Quinke needle, Spinocan®, B.Braun AG, Germany) consisting of ropivacaine 0.5%, 3 ml. They were also given an infusion of propofol 10 mg ml⁻¹ to induce light sedation during surgery, breathing spontaneously with supplemental oxygen 2 litre min⁻¹.

Subjects in the SA group received an indwelling urinary catheter before surgery, and a thigh tourniquet was not used. No drains were used.

In order to prevent overdistension of the bladder ultrasound bladder scans were performed at least every third hour until subjects could control their urinary bladder and the following rules were observed:

1. Bladder volume < 300 ml, repeat bladder scan within 3 h;
2. 300–399 ml, repeat bladder scan within 2 h;
3. 400–499 ml, do intermittent catheterization. This can be repeated twice after which an indwelling urinary bladder catheter is used.

Assessments
All subjects were familiarized with a horizontal visual analogue scale (VAS, 100 mm) used for assessment of pain (0=no pain, 100=worst imaginable pain), postoperative nausea and vomiting (PONV), and dizziness (0=no symptoms, 100=worst symptoms possible).

Pain was registered before operation, on arrival to Post Anaesthesia Care Unit (PACU), after 2, 4, 6 and 10 h. The first and second day after surgery pain was assessed at 08:00 and 14:00 h. Pain was registered at rest, with 45° knee
flexion, with the knee straight and 45° hip flexion, and after walking 5 m.

Dizziness (and at the same time blood pressure) was recorded twice per day 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 were monitored in supine and upright standing position. Blood pressure (systolic and diastolic, mmHg) was also measured after standing, with the measurement of blood pressure commencing within 60 s. When analysing the data, mean arterial blood pressure (MAP) was used. Orthostatic function was defined as being able to walk 5 m at 6, 10, 24 and 48 h after operation.

Discharge criteria from PACU to the ward were assessed every 15 min until obtained by a nurse blinded to treatment group. Discharge criteria from PACU were: (i) sufficient level of consciousness (aroused by verbal stimuli), (ii) able to maintain a free airway, (iii) adequate breathing with $\text{SaO}_{2} > 94\%$ when administering a maximum of 5 litre $O_{2}$ min$^{-1}$ nasally, (iv) mild or no PONV ($<30$ mm), (v) pain control adequate (VAS $\leq 30$ mm at rest).

LOS was defined as the time from the end of surgery until the subject met the discharge criteria from the ward: (i) able to get in and out of bed, (ii) able to get dressed, (iii) able to sit down in a chair and get up again, (iv) able to walk 50 m with or without walking aids (crutches, etc.), (v) able to flex the knee to $\geq 70^\circ$, (vi) able to walk stairs, (vii) pain manageable with oral analgesics, (viii) acceptance to be discharged.

Discharge criteria were checked twice daily, at 08:00 and again at 14:00 h by a nurse blinded to treatment group. The actual time at which the subject 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.

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

Six months after operation, subjects 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 (SA or GA).

Surgery

Surgeries were performed via a ventral incision with a para-patellar medial incision 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 subjects. 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 per experimental subject. In a previous pilot study at Hässleholm Hospital, the response within each subject group was 72 h with standard deviation of 42. If the true difference between experimental and control means was 24 h, 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 testing of this null hypothesis is 0.05. To compensate for drop outs we decided to include 124 subjects.

Data analyses were performed using SPSS version 20.0 (SPSS, Chicago, IL, 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 (SD) or median (IQR) of administered PCA doses was 2 (0–7) in the GA group and 30 (20–41) in the SA 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 SA 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

Results

Patients were recruited between September 2011 and June 2012. One hundred and twenty-four consecutive patients were assessed for eligibility by 2 orthopaedic surgeons and 120 were included after the preoperative visit by the anaesthetist [Fig. 1 (CONSORT flow diagram)]. The 6-month follow-up was completed in December 2012. There were no differences in subject characteristics or surgical data (Table 1).

Sixty-six per cent of subjects 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 h) compared with the SA group (52 h, $P<0.001$), but without difference between groups in actual day of discharge ($\chi^{2}$-test Table 2). The reasons for not being discharged in spite of meeting discharge criteria were organizational (39 patients), general weakness (2), dizziness (3), and pain (5).

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

The median (IQR) 24 h postoperative consumption of morphine was 19 mg (11–28) in the GA group and 54 mg (37–78) in the SA 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 SA 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
Fig 1 Consort flow diagram for the study.

Table 1 Subject characteristics and surgical data

<table>
<thead>
<tr>
<th>Subject characteristics and surgical data</th>
<th>GA group n=60</th>
<th>SA group n=60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>82 (11)</td>
<td>83 (16)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172 (8)</td>
<td>170 (9)</td>
</tr>
<tr>
<td>Male/Female</td>
<td>31/29</td>
<td>28/32</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>68 (7)</td>
<td>67 (7)</td>
</tr>
<tr>
<td>ASA physical status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>18</td>
<td>11</td>
</tr>
<tr>
<td>II</td>
<td>35</td>
<td>39</td>
</tr>
<tr>
<td>III</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>44 (11)</td>
<td>49 (7)</td>
</tr>
<tr>
<td>Operative bleeding (ml)</td>
<td>208 (145–267)</td>
<td>218 (132–293)</td>
</tr>
</tbody>
</table>

Table 2 Cumulative number of subjects meeting discharge criteria from the ward at different postoperative times and the actual number of subjects that in fact were discharged ($\chi^2$-test, GA group vs SA group). Day 1 is the day after the day of surgery

<table>
<thead>
<tr>
<th>Discharge from the ward</th>
<th>According to criteria</th>
<th>Actual discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GA group n=60</td>
<td>SA group n=60</td>
</tr>
<tr>
<td>Day 1, 08:00</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Day 1, 14:00</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Day 2, 08:00</td>
<td>38</td>
<td>17</td>
</tr>
<tr>
<td>Day 2, 14:00</td>
<td>54</td>
<td>43</td>
</tr>
<tr>
<td>Day 3</td>
<td>49</td>
<td>44</td>
</tr>
<tr>
<td>Day 4</td>
<td>56</td>
<td>53</td>
</tr>
</tbody>
</table>
SA group ($P<0.001$). The distribution of the median (IQR) number of requested and administered PCA doses during the first 24 h after operation hours are shown in Figure 3.

Subjects in the SA group had higher dizziness scores ($P<0.05$) (Fig. 4). Orthostatic function was less affected in the GA group ($x^2$-test) as 57 subjects in the GA group and 18 in the SA group were able to walk 5 m after 6 h ($P<0.001$). After 10 h and 24 h the same figures were 59 and 60 subjects in the GA group and 40 and 59 in the SA group ($P<0.01$ at 10 h and n.s. at 24 h). There were no differences in MAP between the groups except on the first postoperative day at 14:00 h where MAP was significantly higher in the SA group when standing up [96 (10) mm Hg vs 90 (12) mm Hg, Student $t$-test, $P<0.05$].

PONV scores and number of subjects that vomited are given in Table 3; both were higher in the SA group. The
groups (396 550,000 TKAs were performed in 2007 in the USA.8 A major and on a global scale this procedure is increasing. For example, TKA is an effective treatment for end-stage knee osteoarthritis, Discussion

In this standardized study in TKA, subjects receiving GA had shorter LOS (time to reach discharge criteria), less dizziness and PONV, and better early orthostatic function compared with SA. Also, pain scores were lower after 6 h with an opioid-sparing effect in the GA group compared with the SA 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 catheterization between the groups.

At 14:00 h on the second day after the day of surgery, 79% of subjects met or had met the discharge criteria from the ward, which is in line with previous findings.9 More interesting is that the GA subjects seemed to be ready for discharge earlier than the SA subjects (36 vs 48 h), probably explained by reduced PONV and dizziness. In a systematic study by Liu and Wu10 the effect of anaesthesia technique on pain and outcome was investigated. They found that RA resulted in a modest reduction in pain scores accompanied by an increase in side-effects that was not perceived as an improvement.

The main reasons for still being in hospital in spite of meeting discharge criteria in our study were exudation from the surgical wound and organizational causes. None of the subjects in our study had a tourniquet during surgery, which might have contributed to less pain but also to the increased postoperative wound exudation.11 We refrained from the use of a thigh tourniquet due to its association with intraoperative, ischaemic nociception.11

A review by Macfarlane and colleagues12 reported reduced postoperative pain and morphine consumption among patients receiving RA compared with GA. However, most of the studies included in this review were done before the introduction of the high-volume local infiltration technique (LIA),13 which has been widely used since 2008 in connection with TKA and which is more simple compared with many other regional anaesthetic techniques.13 14 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 as TCI is well tolerated with rapid and clear headed emergence.15

Finally, all subjects received standardized opioid-sparing analgesia with cyclo-oxygenase-2 inhibitor and acetaminophen.

In the PACU, 73% of the SA and 59% of the GA patients met the PACU discharge criteria on arrival. Thus, many TKA patients can bypass PACU and go directly to the ward. Lunn and colleagues16 found in a recent study that 85% of the patients met PACU discharge criteria within 15 min, but their study and ours had slightly different discharge criteria compared with standard recommendations7 in that motor function was not taken into consideration. This change did not cause any complication on the ward in terms of respiratory or cardiovascular instability, decreases due to motor weakness or other organ dysfunctions16 and therefore calls for further large-scale studies.

In the SA group, intrathecal morphine was not used despite being recommended,1 which may slightly have influenced our results. However, the analgesic effects of intrathecal morphine are rather small, and in elderly patients the side-effects from intrathecal opioids can be undesirable for early recovery. Furthermore, we used a rather comprehensive multimodal non-opioid analgesic programme, 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 SA group, receiving a combination of opioid-sparing intrathecal local anaesthetics and the LIA technique.

We found that subjects in the SA group had significantly more dizziness compared with those in the GA group. As
Number of subjects having different levels of dizziness (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 h (Day 1:1) and at 14:00 h (Day 1:2). Area under the curve analysed for PACU–Day 1:1 and Day 1:1–Day 1:2 using Mann–Whitney test. Statistically significant differences (more subjects having higher scores in SA group), $P<0.05$, at both intervals.
Dizziness and muscle weakness are two of the major reasons for delayed discharge, and it might be possible to reduce these complaints by using GA instead of SA. However, the increase in dizziness among the SA subjects could not be explained by orthostatic dysfunction, because we only found differences in MAP at 14:00 h the first day after the day of surgery, which was higher in the SA group.

Lumbar SA might have more profound effect on urinary bladder dysfunction, but 68% in both groups managed without having their bladder catheterized. Provided that bladder scans are done regularly it might be an advantage to avoid urinary catheters as they are associated with a number of serious complications such as urinary tract infections and subsequently deep wound infections.

We found no difference between groups in bleeding during surgery, as suggested before. Furthermore, blood loss was limited in both groups in spite of the fact that tourniquet was not used. This is, in contrast, with a recent publication by Stundner and colleagues where neuraxial anaesthesia was associated with reduced blood transfusions. 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 a hypothetical situation of requiring surgery for a lower extremity orthopaedic problem they preferred RA. It is, therefore, interesting that we found no differences in satisfaction scores between groups, although more subjects in the SA group would prefer GA in the case of a future operation.

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

In conclusion, in TKA GA resulted in earlier recovery, less pain, dizziness and nausea and earlier ability to walk compared with SA. In addition, subjects preferred GA over SA in the event of another TKA.

Authors’ contributions
A.H. participated in the design of the study, did preoperative evaluation, enrolled patients, administered anaesthesia, performed statistical analyses and wrote the manuscript. H.K. and S.T.-L. designed and coordinated the study and participated in writing the manuscript.

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Declaration of interest
None declared.

Funding
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References

Table 3 Postoperative nausea and vomiting. Median (IQR) [range] score for postoperative nausea (Mann–Whitney). Number of subjects vomiting each day ($\chi^2$-test). Day 1 is the day after the day of surgery

<table>
<thead>
<tr>
<th>VAS score for nausea</th>
<th>Number of subjects vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GA group</td>
</tr>
<tr>
<td>PACU</td>
<td></td>
</tr>
<tr>
<td>0 (0) [0–30]</td>
<td>0 (0) [0–50]</td>
</tr>
<tr>
<td>Day 1, 08:00 h</td>
<td>0 (0) [0–63]</td>
</tr>
<tr>
<td>Day 1, 14:00 h</td>
<td>0 (0) [0–50]</td>
</tr>
<tr>
<td>Day 2, 08:00 h</td>
<td>0 (0) [0–50]</td>
</tr>
</tbody>
</table>


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