

- 26 Walton B, Farrow C, Cook TM. A national survey of epidural use and management in elderly patients undergoing elective and emergency laparotomy. *Anaesthesia* 2006; **61**: 456–61
- 27 Saunders DI, Murray D, Pichel AC, Varley S, Peden CJ; UK Emergency Laparotomy Network. Variations in mortality after emergency

laparotomy: the first report of the UK Emergency Laparotomy Network. *Br J Anaesth* 2012; **109**: 368–75

- 28 National Emergency Laparotomy Audit. *National Institute of Academic Anaesthesia*. Available from <http://www.niaa.org.uk/article.php?article=775> (accessed 4 February 2013)

*British Journal of Anaesthesia* **111** (3): 331–3 (2013)  
doi:10.1093/bja/aet200

## EDITORIAL IV

# Does anaesthetic technique really matter for total knee arthroplasty?

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Total knee arthroplasty (TKA) is a common, painful surgical procedure requiring good quality anaesthesia and postoperative analgesia to provide best patient care and facilitate effective rehabilitation. More than 70 000 knee replacements are performed in the UK each year and this is projected to increase as the population ages and osteoarthritis, the most common reason for TKA, becomes more prevalent. Given ever increasing pressure on resource utilization the quality and the type of anaesthesia and postoperative pain relief can have a significant impact on ability to meet rehabilitation goals.<sup>1–3</sup> Studies have also demonstrated that poor pain control after knee replacement is associated with development of chronic pain<sup>4</sup> although our understanding of this area is only starting to develop.<sup>5</sup>

The anaesthetic management of patients undergoing TKA has undergone several refinements and transitions. In the past, general anaesthesia (GA) with systemic opioid analgesia alone was commonly used. Spinal anaesthesia, uniquely suited to lower extremity orthopaedic procedures, has gained prominence with several landmark studies demonstrating the superiority of spinal anaesthesia over GA in terms of morbidity and mortality.<sup>6,7</sup> Contemporary studies have continued to reinforce these data with recent epidemiological studies using large databases indicating a reduction in risk of morbidity and mortality with the use of neuraxial anaesthesia.<sup>8,9</sup> The mechanisms underlying these benefits remain to be fully understood but may include improvements in blood flow, cardiorespiratory benefits and a possible reduction in surgical stress response.<sup>9</sup> Outcomes such as pain relief, opioid consumption, and length of hospital stay (LOS) also favour spinal anaesthesia.<sup>2,10</sup> However, neuraxial anaesthesia is not without risk, and although rare, does have potential for spinal haematoma, infection, or abscess in contemporary practice.<sup>11</sup>

Therefore, despite the perceived benefits of neuraxial anaesthesia, newer methods of providing anaesthesia for knee replacement need to be evaluated and existing techniques challenged.

In this issue of the *British Journal of Anaesthesia*, Harsten and colleagues<sup>12</sup> compare recovery from TKA after GA [specifically with total-i.v. anaesthesia using target-controlled infusions (TCI) of propofol and remifentanyl] with spinal anaesthesia with bupivacaine in a randomized study of 120 patients. The authors demonstrate that patients in the GA group had a shorter time to meet discharge criteria (46 vs 52 h), less nausea and vomiting, better pain control (except for the first two postoperative hours), and less dizziness compared with the spinal anaesthesia group. The findings of this paper appear to contradict previous recommendations regarding spinal anaesthesia for TKA<sup>13</sup> and prompt an assessment of the reasons for disparity with previous results.

A closer examination of the study reveals both strengths and limitations. A major strength of this study is the comparison of a state-of-the-art general anaesthetic technique including multimodal analgesia with a basic spinal technique. Both of these relatively straightforward and common methods of anaesthesia would be feasible in all hospitals where total knee replacement procedures are currently performed. Many institutions across the world are unable to provide consistent, high-quality regional anaesthesia for their patients and in this regard demonstration of the effectiveness of a GA with multimodal analgesia technique is timely. The recovery time and time to reach discharge criteria are impressive in both groups and is currently faster than that achieved in many centres.

Some criticisms and observations with the techniques used in this study should be noted. First, the authors use a spinal

anaesthetic technique without additional adjuvant and it is therefore not surprising that the spinal group had severe pain on block resolution. Most practitioners using spinal anaesthesia for TKA would institute adequate opioid-related analgesia before spinal resolution either by adding a dose of intrathecal hydrophilic opioid such as morphine, diamorphine, or hydromorphone,<sup>13</sup> or by giving opioid analgesics by another effective route. Although the use of intrathecal opioids is associated with adverse effects such as pruritis, urinary retention, and respiratory depression, their addition will provide long lasting analgesia after resolution of the local anaesthetic effect. The post-surgical pain that the patient experiences with the rapid regression of spinal anaesthesia can be intense, particularly when limited provisions for analgesia are made such as omitting peripheral nerve blocks,<sup>1 2</sup> neuraxial opioids,<sup>13</sup> or other systemic analgesia and this certainly contributed significantly to the poor pain control that the spinal group reported in this study.

Secondly, the duration of effectiveness of the local infiltration analgesia (LIA) technique was surprisingly short. Given the recent excitement for the potential of LIA as a simple method of pain relief after knee replacement<sup>14</sup> it was disappointing to see how poorly it performed in this study. Personal clinical experience of using LIA has given the impression of an effective but short-lasting effect. The study by Harsten and colleagues<sup>12</sup> reinforces our impression because although the LIA appeared to provide good early analgesia in the GA group by the time the sensory block had resolved in the spinal group, the analgesic effectiveness of LIA appears to have disappeared.

It is also interesting to note that despite availability of rescue analgesia, the spinal group continued to experience significantly more pain for 2 days after surgery. The landmark editorial by Wall<sup>15</sup> who coined the term preoperative pre-emptive analgesia and more recent work on preventive analgesia<sup>16 17</sup> also note the 'protective' effect of opioids and other analgesics such as N-methyl D-aspartate receptor antagonists on pain control well beyond the clinically expected duration of these drugs. The seemingly prolonged analgesic effect of an intra-operative dose of oxycodone appears also to have provided some 'preventive' analgesic effect in the GA group. Conversely, there is no evidence of a hyperalgesic effect from remifentanyl infusion that has previously been demonstrated.<sup>18</sup> Finally, although a significant difference in LOS was demonstrated between the GA and spinal group, a 6 h differential may be of limited clinical or practical significance in most institutions and might not actually influence the day of discharge.

Several important messages can be taken from this paper. First, despite current beliefs, it appears that a good quality GA technique such as the TCI method can in fact provide effective anaesthesia and transition to reasonable postoperative analgesia after knee replacement. This may be a very useful option in centres that are currently unable to provide consistent high-quality regional anaesthesia such as neuraxial anaesthesia, continuous peripheral nerve blocks, or both.<sup>1 2 19</sup> Secondly, the importance of multimodal analgesia in facilitating good pain control is underscored by the fact that all patients

were given acetaminophen and celecoxib. The better pain control in the GA group reflects the important role that long-acting opioids continue to play in the context of multimodal postoperative analgesia especially when given before recovery of anaesthesia. Finally, the transient and disappointing effect of the LIA technique was especially evident in the spinal anaesthesia group and continues to call into question the overall utility of this method<sup>20</sup> especially when used alone without systemic or spinal opioids.

TKA is a common and painful surgical procedure that requires effective, safe anaesthesia and good postoperative pain control to facilitate best outcomes including reduction in LOS and chronic pain after surgery.<sup>4</sup> Harsten and colleagues<sup>12</sup> demonstrate that the TCI GA technique used compares favourably with a very limited spinal anaesthesia technique. However, better regional anaesthesia methods are available in centres that have the expertise and resources to provide them.<sup>1 2 19</sup> Regional anaesthesia including neuraxial techniques continue to provide short-, medium-, and long-term outcome<sup>1 2 8 9 21 22</sup> benefits for patients having TKA. Although Harsten and colleagues provide thought provoking data they do not really compare their GA technique with the standard of care for spinal anaesthesia<sup>13</sup> not to mention peripheral nerve block techniques.<sup>1 2 19</sup> Further studies are required to continue to investigate the best method of anaesthesia and postoperative analgesia for patients undergoing TKA (including GA techniques) before significant change in guidance can be advised.

## Authors' contributions

Both authors contributed to the writing of this editorial.

## Declaration of interest

None declared.

## References

- Carli F, Clemente A, Asenjo JF, et al. Analgesia and functional outcome after total knee arthroplasty: periaicular infiltration versus continuous femoral nerve block. *Br J Anaesth* 2010; **105**: 185–95
- Ilfeld BM, Mariano ER, Girard PJ, et al. A multicenter, randomized, triple-masked, placebo-controlled trial of the effect of ambulatory continuous femoral nerve blocks on discharge-readiness following total knee arthroplasty in patients on general orthopaedic wards. *Pain* 2010; **150**: 477–84
- Buvanendran A, Kroin JS, Della Valle CJ, et al. Perioperative oral pregabalin reduces chronic pain after total knee arthroplasty: a prospective, randomized, controlled trial. *Anesth Analg* 2010; **110**: 199–207
- Puolakka PA, Rorarius MG, Roviola M, et al. Persistent pain following knee arthroplasty. *Eur J Anaesthesiol* 2010; **27**: 455–60
- Rakel BA, Blodgett NP, Bridget Zimmerman M, et al. Predictors of postoperative movement and resting pain following total knee replacement. *Pain* 2012; **153**: 2192–203
- 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. *Br Med J* 2000; **321**: 1493

- 7 Macfarlane AJ, Prasad GA, Chan VW, Brull R. Does regional anaesthesia improve outcome after total knee arthroplasty? *Clin Orthop Relat Res* 2009; **467**: 2379–402
- 8 Memtsoudis SG, Sun X, Chiu YL, et al. Utilization of critical care services among patients undergoing total hip and knee arthroplasty: epidemiology and risk factors. *Anesthesiology* 2012; **117**: 107–16
- 9 Memtsoudis SG, Sun X, Chiu YL, et al. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients. *Anesthesiology* 2013; **118**: 1046–58
- 10 Capdevila X, Bathelet Y, Biboulet P, et al. Effects of perioperative analgesic technique on the surgical outcome and duration of rehabilitation after major knee surgery. *Anesthesiology* 1999; **91**: 8–15
- 11 Brull R, McCartney CJ, Chan VW, El-Beheiry H. Neurological complications after regional anesthesia: contemporary estimates of risk. *Anesth Analg* 2007; **104**: 965–74
- 12 Harsten A, Kehlet H, Toksvig-Larsen S. Recovery after total intravenous general anaesthesia or spinal anaesthesia for total knee arthroplasty: a randomized trial. *Br J Anaesth* 2013; **111**: 391–9
- 13 Fischer HB, Simanski CJ, Sharp C, et al., PROSPECT Working Group. A procedure-specific systematic review and consensus recommendations for postoperative analgesia following total knee arthroplasty. *Anaesthesia* 2008; **63**: 1105–23
- 14 Kerr DR, Kohan L. Local infiltration analgesia for total knee arthroplasty. *Br J Anaesth* 2011; **107**: 487–9
- 15 Wall PD. The prevention of postoperative pain. *Pain* 1988; **33**: 289–90
- 16 Katz J, McCartney CJ. Current status of pre-emptive analgesia. *Curr Opin Anesthesiol* 2002; **15**: 435–41
- 17 McCartney CJ, Sinha A, Katz J. A qualitative systematic review of the role of N-methyl-D-aspartate receptor antagonists in preventive analgesia. *Anesth Analg* 2004; **98**: 1385–400
- 18 Guignard B, Bossard AE, Coste C, et al. Acute opioid tolerance: intraoperative remifentanyl increases postoperative pain and morphine requirement. *Anesthesiology* 2000; **93**: 409–17
- 19 Andersen HL, Gyrn J, Møller L, Christensen B, Zaric D. Continuous saphenous nerve block as supplement to single-dose local infiltration analgesia for postoperative pain management after total knee arthroplasty. *Reg Anesth Pain Med* 2013; **38**: 106–11
- 20 McCartney CJL, McLeod GA. Local infiltration analgesia for total knee arthroplasty. *Br J Anaesth* 2011; **104**: 487–9
- 21 Pugely AJ, Martin CT, Gao Y, Mendoza-Lattes S, Callaghan JJ. Differences in short-term complications between spinal and general anesthesia for primary total knee arthroplasty. *J Bone Joint Surg Am* 2013; **95**: 193–9
- 22 Memtsoudis SG, Stundner O, Rasul R, et al. Sleep apnea and total joint arthroplasty under various types of anesthesia: a population-based study of perioperative outcomes. *Reg Anesth Pain Med* Advance Access published on April 3, 2013, doi: 10.1097/AAP.0b013e31828d0173

*British Journal of Anaesthesia* **111** (3): 333–7 (2013)  
doi:10.1093/bja/aet131

## EDITORIAL V

# Ventilator associated pneumonia: can we ensure that a quality indicator does not become a game of chance?

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Critical care was an early focus of national quality improvement (QI) programmes, driven first by the US-based Institute for Healthcare Improvement (IHI) (<http://www.ihl.org>) and later adopted in the UK by initiatives such as the Patient Safety First initiative (<http://www.patientsafetyfirst.nhs.uk/Content.aspx?path=/interventions/Criticalcare/>) and Scottish Patient Safety Programme (<http://www.scottishpatientsafetyprogramme.scot.nhs.uk>). Much emphasis has been placed on nosocomial infection, of which the most prevalent in the intensive care unit (ICU) is ventilator associated pneumonia (VAP).<sup>1</sup> Ideally, indicators for QI should be person-centred, safe, effective, efficient, equitable, and timely. VAP rates

fulfil most of these criteria, because they are relevant to all ICUs, are associated with adverse patient outcomes, and result in greater use of broad-spectrum antibiotics.<sup>1</sup> In principle, measuring VAP rates seems straightforward, does not increase risk to patients, and can be undertaken in all ICUs at low cost.

Various interventions decrease the incidence of VAP when introduced effectively. The quality of evidence for some of these is weak, such as nursing in the head-up position, avoiding frequent ventilator circuit changes, using heat and moisture exchange circuit humidification, and hand-washing, but as these interventions are inexpensive they are strongly

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

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## Editor's key points

- Regional anaesthesia is often recommended for total knee arthroplasty (TKA).
- General anaesthesia (GA) and spinal anaesthesia (SA) were compared in a study of short term recovery parameters.
- The GA group had higher immediate pain scores, but shorter length of hospital stay, and reduced postoperative nausea and vomiting, pain and morphine consumption.
- GA has a more favourable recovery profile than SA in a fast-track protocol.

**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 remifentanyl (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

Accepted for publication: 26 February 2013

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.<sup>1</sup> Consequently, RA with the intrathecal technique has been recommended.<sup>2</sup> 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 Håssleholm Hospital, Sweden. It was registered with ClinicalTrials.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, Håssleholm Hospital, Sweden, were

† This article is accompanied by Editorial IV.



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, 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, Uppsala, Sweden) during the first 24 h. All subjects received 1 g of tranexamic acid i.v.

Subjects in the SA group received intrathecal (L<sub>4</sub>–L<sub>5</sub>) administration (using a 25 G Quinke needle, Spinocan®, B.Braun AG, Germany) consisting of bupivacaine 0.5%, 3 ml. They were also given an infusion of propofol 10 mg ml<sup>-1</sup> to induce light sedation during surgery, breathing spontaneously with supplemental oxygen 2 litre min<sup>-1</sup>.

Subjects in the GA group were anaesthetized using target controlled infusion (TCI) with propofol and remifentanyl.<sup>3 4</sup> Rocuronium bromide 0.6 mg kg<sup>-1</sup> was given to facilitate intubation. Ventilation was with oxygen/air targeting an end-tidal CO<sub>2</sub> of 4.5 kPa. At the end of surgery glycopyrronium 0.5 mg and neostigmine 2.5 mg was given i.v., with i.v. bolus dose of oxycodone 10 mg 20 min before the end of surgery.

All subjects received cloxacillin 2 g i.v. (or clindamycin 600 mg i.v. if penicillin allergy) before surgical incision. The

preoperative fasting period was 6 or 2 h before surgery for solid food or clear fluids, respectively.<sup>5</sup>

Towards the end of surgery, all subjects received infiltration of local anaesthetic in the perisurgical area<sup>6</sup> consisting of 150 ml of ropivacaine (0.2%) with epinephrine (10 µg ml<sup>-1</sup>) (i.e. 148.5 ml ropivacaine 2 µg ml<sup>-1</sup>+1.5 ml epinephrine 1 µg ml<sup>-1</sup>). The mixture was injected using a systematic technique to ensure uniform delivery of 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 had 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 h.

All subjects were before operation familiarized with a patient controlled analgesia (PCA) device for postoperative pain medication during the first postoperative 24 h. The PCA pump (Abbott GemStar™ PCA Pump) delivered i.v. morphine in doses of 20 µg kg<sup>-1</sup> and with a lock out time of 10 min.<sup>6</sup> After 24 h the PCA device was disconnected and subjects received slow-release oxycodone (OxyContin®) 10 mg orally twice daily. After 24 h oxycodone (OxyNorm®) 10 mg orally was used as rescue medication. The PCA device was fitted to subjects as they left the operating theatre, and was removed 24 h later and the amount of morphine administered registered. The number of requested and 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 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, repeat bladder scan within 1 h;
- (4) ≥500 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.<sup>7</sup>

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  $SpO_2 > 94\%$  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 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 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 Håssleholm 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 Shapiro–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 25–75% interquartile range (IQR).  $P < 0.05$  was assigned statistical significance.

## Results

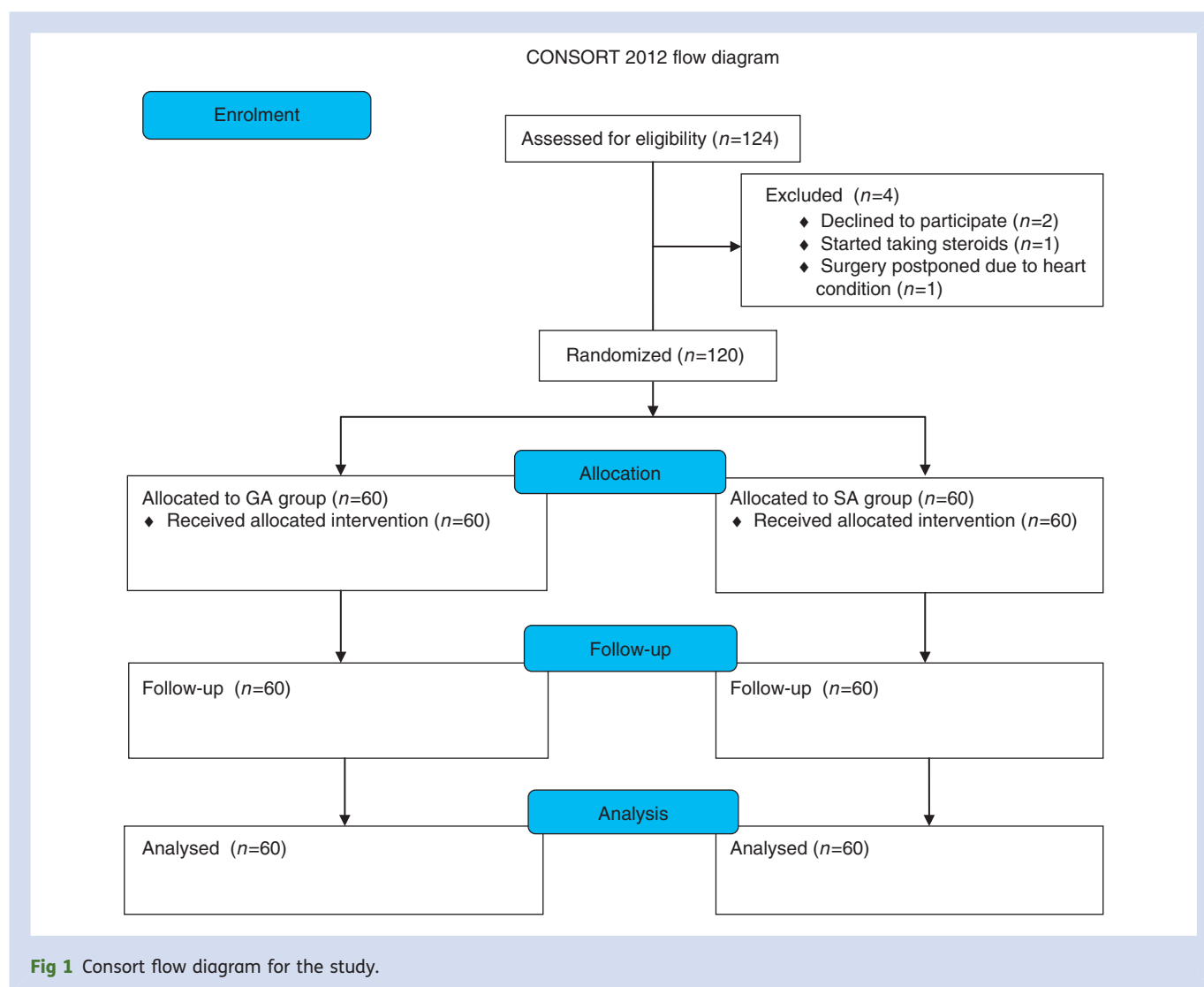
Patients were recruited between September 2011 and June 2012. One hundred and twenty-four consecutive patients were assessed for eligibility by 2 orthopaedic surgeons and 120 were included after the preoperative visit by the anaesthetist [Fig. 1 (CONSORT flow diagram)]. The 6-month follow-up was completed 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

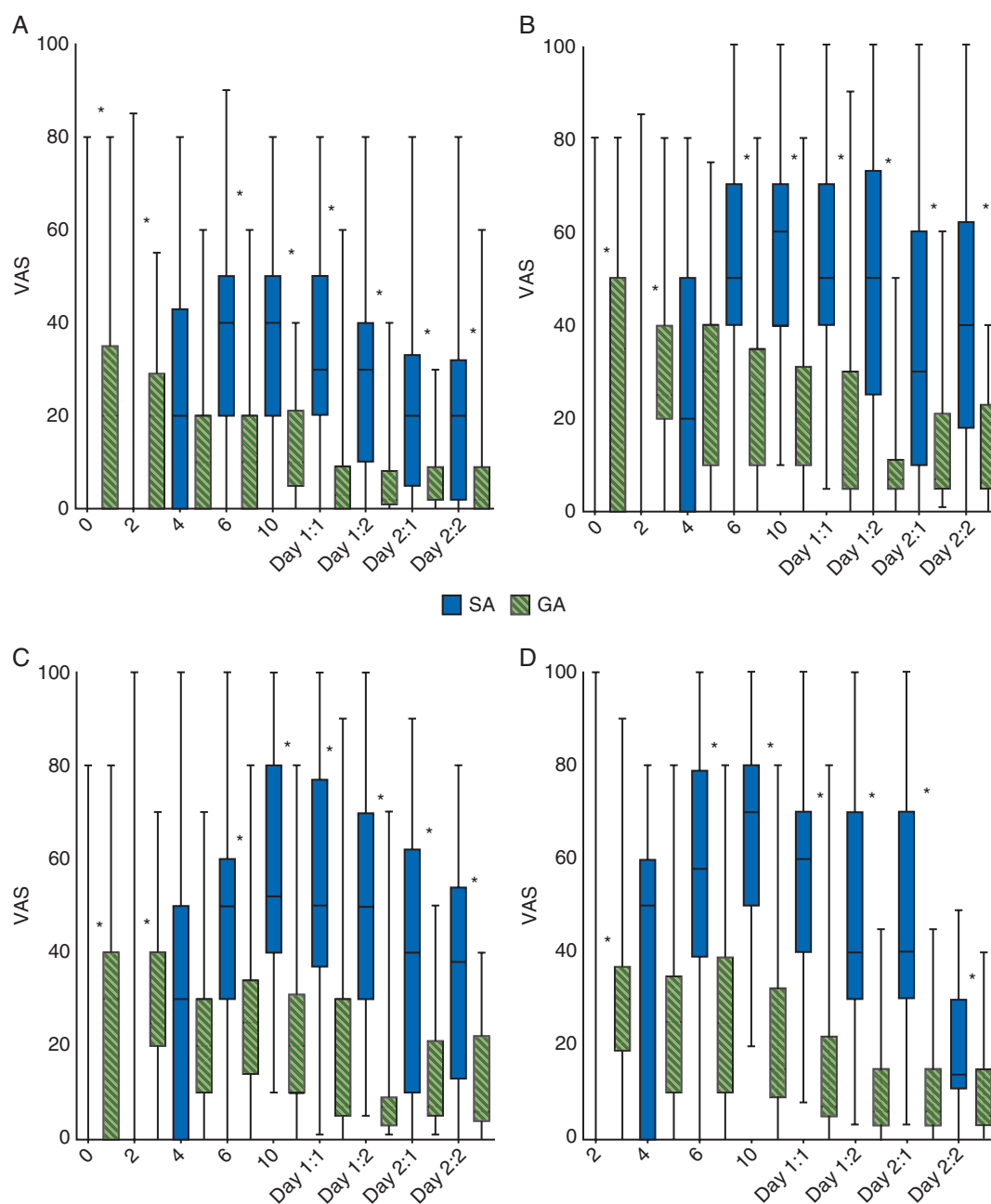


**Table 1** Weight, height, age, and duration of surgery presented as mean (sd). Operative bleeding presented as median (IQR). Gender and ASA status presented as numbers

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

**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

Discharge from the ward	According to criteria			Actual discharge		
	GA group n=60	SA group n=60	P-value	GA group n=60	SA group n=60	P-value
Day 1, 08:00	0	0	n.s.	0	0	n.s.
Day 1, 14:00	16	3	<0.01	1	1	n.s.
Day 2, 08:00	38	17	<0.01	1	1	n.s.
Day 2, 14:00	54	43	n.s.	23	25	n.s.
Day 3				49	44	n.s.
Day 4				56	53	n.s.



**Fig 2** Pain (VAS 0–100 mm) at (A) rest, (B) during knee flexion, (C) with the knee straight and hip flexion and (D) when walking. Green bars=GA and blue bars=SA. A line within the boxes indicates a median and the boxes indicate 25–75% IQR. Whiskers indicate range. \* $P < 0.001$ . Numbers indicate the hours 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 postoperative day.

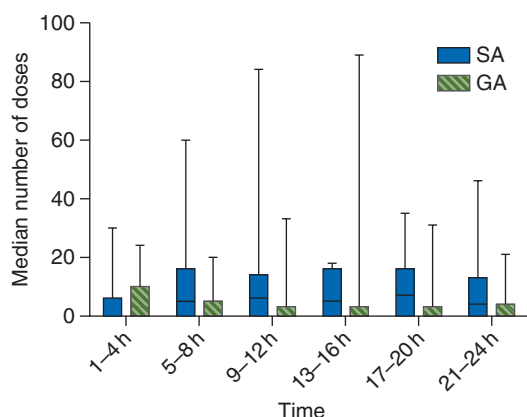
SA group ( $P < 0.001$ ). The distribution of the median (IQR) number of requested and administered PCA doses during the first 24 h after operation hours are shown in Figure 3.

Subjects in the SA group had higher dizziness scores ( $P < 0.05$ ) (Fig. 4). Orthostatic function was less affected in the GA group ( $\chi^2$ -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





**Fig 3** Median number of administered, and requested but not administered PCA doses during the first 24 h after surgery. A line within the boxes indicates median and boxes indicate 25–75% IQR. Whiskers indicate range.  $P < 0.001$  at all times.

median (IQR) number of redressings were 2 (0–3) in the GA group and 1 (0–3) in the SA group (n.s. Mann–Whitney).

Forty-two subjects in the GA group and 36 in the SA group were managed without bladder catheterization. Sixteen subjects in the GA group and 23 in the SA group had to have one or two intermittent catheterizations [ $P > 0.05$  between groups ( $\chi^2$ -test)].

There was no difference between groups in total anaesthesia satisfaction score. However, significantly more subjects in the SA group indicated that they would like to change the method of anaesthesia for a subsequent operation (14 vs 2,  $\chi^2$ -test,  $P < 0.05$ ).

There were no deaths during this study but a pulmonary embolus was diagnosed in two subjects, one 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 scale this procedure is increasing. For example, 550 000 TKAs were performed in 2007 in the USA.<sup>8</sup> A major challenge for the future will be to perform such a large number of operations not only with good medical outcome but also with acceptable economical and logistical quality.

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.<sup>9</sup> 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 Wu<sup>10</sup> 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.

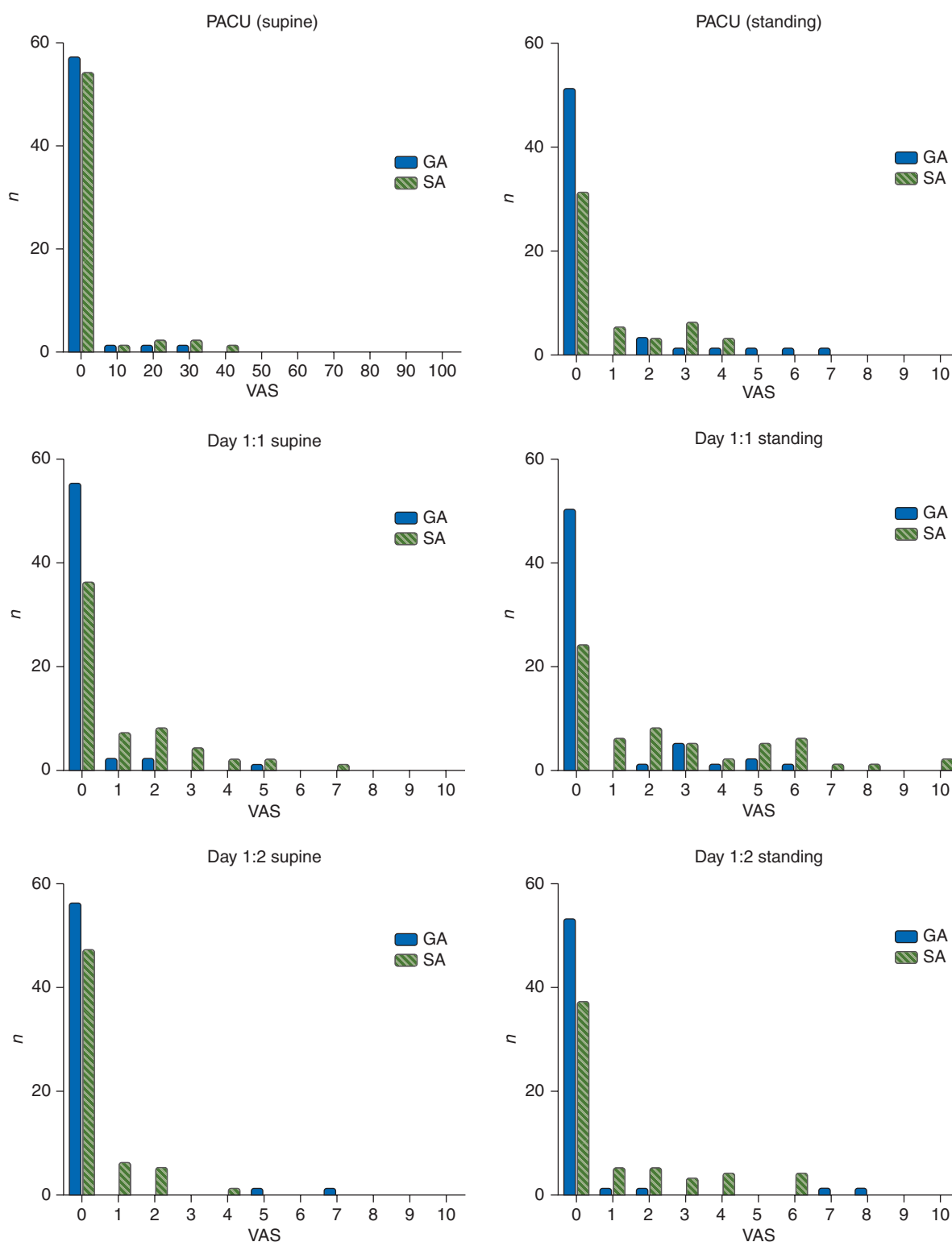
The main reasons for still being in hospital in spite of meeting discharge criteria in our study were exudation from the surgical wound and organizational causes. None of the subjects in our study had a tourniquet during surgery, which might have contributed to less pain but also to the increased postoperative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

A review by Macfarlane and colleagues<sup>12</sup> 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),<sup>13</sup> which has been widely used since 2008 in connection with TKA and which is more simple compared with many 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 as TCI is well tolerated with rapid and clear headed emergence.<sup>15</sup> 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 colleagues<sup>16</sup> 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 recommendations<sup>7</sup> 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 dysfunctions<sup>16</sup> and therefore calls for further large-scale studies.

In the SA group, intrathecal morphine was not used despite being recommended,<sup>1</sup> 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



**Fig 4** 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.

**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

	VAS score for nausea			Number of subjects vomiting		
	GA group n = 60	SA group n = 60	P-value	GA group n = 60	SA group n = 60	P-value
PACU	0 (0) [0–30]	0 (0–20) [0–100]	<0.01			
Day 1, 08:00 h	0 (0) [0–63]	17 (0–44) [0–90]	<0.001			
Day 1, 14:00 h	0 (0) [0–50]	0 (0–16) [0–100]	<0.01	4	15	<0.05
Day 2, 08:00 h	0 (0) [0–50]	0 (0–10) [0–50]	<0.05			
Day 2, 14:00 h	0 (0) [0–50]	0 (0) [0–50]	n.s.	1	5	n.s.

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 SA. However, the increase in dizziness among the SA subjects could not be explained by orthostatic dysfunction,<sup>17</sup> 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.<sup>18, 19</sup>

We found no difference between groups in bleeding during surgery, as suggested before.<sup>2</sup> 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<sup>20</sup> 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.<sup>21</sup> 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.<sup>22</sup> Major complications after RA are rare but sometimes serious (vertebral canal abscess or haematoma, meningitis, nerve injury, and cardiovascular collapse).<sup>23</sup> 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.<sup>2</sup> 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.<sup>24</sup>

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.

## Acknowledgements

We thank the staff at the Department of Anaesthesiology and the Department of Orthopedic Surgery, Håssleholm Hospital, Sweden, for helpful assistance.

## Declaration of interest

None declared.

## Funding

The study was supported with institutional grants.

## 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. *Br Med J* 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 American Society of Anesthesiologists Committee. 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 Anestesiol* 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 N Am* 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

Handling editor: H. C. Hemmings