Regional Anesthesia and Pain

Pain relief and functional status after vaginal hysterectomy: intrathecal *versus* general anesthesia

[Le contrôle de la douleur et l'état fonctionnel après l'hystérectomie vaginale : l'anesthésie intrathécale versus l'anesthésie générale]

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Purpose: We tested the hypothesis that the use of subarachnoid block (SAB) for vaginal hysterectomy produces superior postoperative analgesia and improves functional status at 12 weeks postoperatively.

Methods: In this randomized controlled trial 89 patients received either standardized general anesthesia vs SAB with bupivacaine, clonidine, and morphine. Postoperatively, patients in both groups received multimodal pain management. Primary outcomes included evaluation of pain and functional status (SF-36 Health Survey) over the 12 postoperative weeks.

Results: Pain was well controlled throughout the study, as judged from the average pain numerical scale scores of ≤ 3 in both groups, at all times studied. Intrathecal analgesia lessened pain and decreased the use of morphine both in the postanesthesia care unit (PACU) and over the first 12 hr after discharge from the PACU ($P < 0.001$). Although patients who received SAB had a lower frequency of postoperative nausea in the PACU than the patients in the general anesthesia group ($P = 0.021$), this effect was not extended beyond the PACU stay. Subarachnoid block did not affect the length of hospitalization. At the two-week follow-up 69% of patients in the SAB group and 48% patients in the general anesthesia group were pain free ($P = 0.044$). At all evaluation intervals patients' functional status was comparable between the SAB and general anesthesia group.

Conclusions: A significantly better immediate postoperative analgesia was present in the SAB group, and the duration was consistent with the expected action of intrathecally administered drugs. Two weeks after surgery a higher percentage of the patients in the SAB group reported no pain. However, SAB

had no effect on either length of hospitalization or patients' postoperative functional status.

Objectif : Nous avons vérifié l'hypothèse voulant que l'usage d'un block sous-arachnoïdien (BSA) pour l'hystérectomie vaginale produise une analgésie postopératoire supérieure et améliore l'état fonctionnel jusqu'à 12 semaines après l'opération.

Méthode : L'étude randomisée et contrôlée a porté sur 89 patientes qui ont reçu une anesthésie générale normalisée ou un BSA avec de la bupivacaine, de la clonidine et de la morphine. Après l'opération, toutes les patientes ont reçu un traitement de la douleur multimodal. La douleur et l'état fonctionnel (SF-36 Health Survey) ont été notés pendant 12 semaines postopératoires.

Résultats : La douleur a été bien contrôlée tout au long de l'étude, si l'on en juge par les scores moyens à l'échelle de douleur numérique ≤ 3 dans les deux groupes pour toutes les mesures prises. L'analgésie intrathécale a réduit la douleur et diminué l'usage de morphine à la salle de réveil (SDR) et pendant les 12 premières heures après le départ de la SDR ($P < 0,001$). Les patientes du groupe BSA ont eu moins de nausées postopératoires en SDR que les patientes sous anesthésie générale (AG), ($P = 0,021$), mais cet effet ne s'est pas prolongé au delà du séjour en SDR. Le BSA n'a pas permis d'écourter l'hospitalisation. Lors de l'examen de contrôle à la deuxième semaine, 69 % des patientes du groupe BSA et 48 % du groupe d'AG n'avaient plus de douleur ($P = 0,044$). Pendant toute l'étude, l'état fonctionnel a été comparable entre les groupes.

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Conclusion : Une analgésie postopératoire immédiate significativement meilleure a été notée avec le BSA et de durée conforme à l'action attendue des médicaments intrathécaux administrés. Deux semaines après l'opération, un plus fort pourcentage de patientes du groupe BSA était sans douleur. Le BSA n'a cependant pas modifié la durée de l'hospitalisation ou l'état fonctionnel postopératoire des patientes.

THERE are several potential advantages associated with regional anesthesia compared with general anesthesia,¹⁻³ but quantifying such benefits in terms of relevant, longer term patient outcomes remains elusive.⁴ For example, there has been a considerable interest in improving the quality of postoperative analgesia with regional techniques, and there is little doubt that these techniques can be quite effective in the treatment of immediate postoperative pain.^{3,5-11} The majority of research in regional anesthesia and analgesia focuses on traditional outcomes such as pain scores and opioid use. However, it is less known whether better pain management or other mechanisms can affect clinically-relevant long-term outcomes, such as functional status following hospital discharge. Indeed, there are relatively few studies evaluating the effect of regional techniques on outcomes measured after hospital discharge.^{8,11,12} Some studies find benefit of regional anesthesia. Carli *et al.*¹¹ found improved functional status in patients who received perioperative epidural analgesia at six weeks after surgery, while Gottschalk *et al.*¹² reported better pain control at 9.5 postoperative weeks in patients who received neuraxial opioids. These findings imply that a relatively short perioperative intervention may have prolonged benefit. However, most studies examine the effects of using regional techniques to supplement general anesthesia^{8,11,12} and few compare outcomes after general *vs* regional anesthesia alone.

In our surgical practice, subarachnoid block (SAB) has gained popularity as a technique to provide anesthesia to patients undergoing vaginal hysterectomy. With the addition of adjuvants such as clonidine and morphine, SAB is relatively simple and reliable, and provides duration of postoperative analgesia well suited to the typical duration of hospitalization after this procedure. Examination of this practice provided an opportunity to evaluate the impact of this common regional anesthetic technique on several short-term (e.g., pain control, nausea, pruritus) and long-term (e.g., functional status) outcomes. General categories

of functional status were assessed from the Health Related SF-36 functional scale, which was widely validated in numerous outcome studies in surgery, oncology, internal medicine, etc. The SF-36 questionnaire measures general perception of health by self-assessing various health concepts, among others physical activity, pain, energy, fatigue, and provides a global assessment of functional status.^{13,14} The purpose of this randomized clinical trial was to test the hypothesis that, compared with general anesthesia, SAB for vaginal hysterectomy would improve postoperative pain and functional status. The SF-36 Health Survey, used in this study to assess the functional status, was validated in nearly 4,000 publications so far (<http://www.sf-36.org/tools/SF36.shtml>, accessed February 8, 2006).

Materials and methods

Recruitment

Following approval by the Mayo Clinic Institutional Review Board, ASA physical status I–III patients scheduled for elective vaginal hysterectomy with or without repair of cystocele and rectocele were screened for enrollment in the study. Exclusion criteria included: 1) gross neurologic impairment, 2) chronic painful disorders with or without preoperative opioid use, 3) morphine allergy, 4) suspected difficult airway requiring awake fiberoptic intubation, 5) serum creatinine > 1.3 mg·dL⁻¹, 6) ages < 35 or > 85 yr, 7) preoperatively determined need for postoperative intensive care unit care, 8) any condition which would preclude from conducting regional anesthesia, such as bleeding tendencies (due to either primary disease or the use of anticoagulant drugs), and 9) a likelihood of conversion to an abdominal approach.

After written informed consent was obtained, a research assistant administered the SF-36 Health Survey (described below) and introduced the scoring systems used for pain assessment. Patients were randomized to receive either general anesthesia or SAB using a sealed envelope determined by a computer-generated list.

Protocol

INTRAOPERATIVE MANAGEMENT OF SAB

After standard anesthesia monitors were applied, sedation with *iv* midazolam (maximum 0.03 mg·kg⁻¹) and propofol (up to 1.5 mg·kg⁻¹), was administered simultaneously with the administration of lactated Ringer's solution (10 mL·kg⁻¹). With a patient in the lateral position, the lumbar region was prepared and draped in a sterile fashion and 1% lidocaine infiltrated subcutaneously in one of the lumbar interspaces between

the third and fifth vertebral bodies. After free flow of cerebrospinal fluid was confirmed, a mixture of 0.75% hyperbaric bupivacaine (15 mg), preservative-free clonidine ($1 \mu\text{g}\cdot\text{kg}^{-1}$), and morphine ($2 \mu\text{g}\cdot\text{kg}^{-1}$, up to maximum 200 μg) was slowly injected into the subarachnoid space through a 25-G Whitacre needle. After confirmation of an adequate dermatomal level of blockade (to at least the T_8 dermatome), the surgeon was allowed to proceed. Additional intraoperative sedation was accomplished at the discretion of the attending anesthesiologist using *iv* midazolam (up to $0.03 \text{ mg}\cdot\text{kg}^{-1}$) and propofol (maximum infusion rate of $75 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$); intraoperative use of *iv* opioids was not permitted. Each patient received 30 mg ketorolac *iv* at the end of surgery. Intraoperative fluid and vasopressor management were left to the discretion of the primary anesthesiologist.

INTRAOPERATIVE MANAGEMENT OF GENERAL ANESTHESIA

After preoxygenation, and administration of up to $2 \mu\text{g}\cdot\text{kg}^{-1}$ of fentanyl, general anesthesia was induced with sodium thiopental ($\leq 4 \text{ mg}\cdot\text{kg}^{-1}$) and succinylcholine ($1 \text{ mg}\cdot\text{kg}^{-1}$) to facilitate tracheal intubation. Muscle paralysis was maintained with vecuronium bromide titrated by using the twitch monitor to maintain $\leq$ two twitches of a train-of-four. Isoflurane (0.5–1.5% end-tidal concentration), and nitrous oxide (50% inspired) were used to maintain general anesthesia. All patients received morphine sulphate $0.1 \text{ mg}\cdot\text{kg}^{-1}$ *iv* administered in divided doses and no additional doses of morphine were allowed to be given intraoperatively. The concentration of isoflurane and the timing of the morphine administration were left at the discretion of the attending anesthesiologist. At the conclusion of surgery, neuromuscular block was reversed, isoflurane and nitrous oxide were discontinued, and the tracheas were extubated. As in the regional group, each patient received ketorolac 30 mg *iv* at the end of surgery. Intraoperative fluid and vasopressor management were left to the discretion of the primary anesthesiologist.

Postoperative management

At the conclusion of the operation the patient was taken to the postanesthesia care unit (PACU). Management in the PACU included supplemental oxygen as needed to maintain oxyhemoglobin saturation above 94%. In the PACU, the patients were allowed to receive morphine sulphate, 2 mg *iv* every five to ten minutes, as needed for a numerical pain score (NPS) > 3 ,¹⁵ in accordance with recently proposed JCAHO guidelines for pain management (www.jcaho.org, accessed

October 12, 2005). (JCAHO did not specify a target pain score; however, at Mayo Clinic, we aim for the $\text{NPS} \leq 3$ before the patient is discharged from the PACU). After satisfying clinical criteria for PACU discharge, the patients were transferred to the regular nursing floor. In addition to routine postoperative hemodynamic monitoring, respiratory rate and oxyhemoglobin saturation were recorded during the first 18 hr following regional block by floor nurses according to routine clinical practice for patients receiving intrathecal opioids. Postoperative pain in both study groups was managed with morphine patient-controlled analgesia (PCA): 1.0 mg every ten minutes with a four-hour lock-out maximum of 15 mg in the regional group, and 30 mg in the general anesthesia group. The reduction in maximum allowable morphine in the SAB group was designed to decrease the likelihood of delayed respiratory depression given the use of intrathecal opioid. If this regimen did not provide sufficient analgesia (defined as a $\text{NPS} \leq 3$), additional morphine was administered *iv* at the discretion of the attending physician. Thus, the amount of morphine allowable for a given time period was not different in the SAB compared to the general group, but it required a physician's evaluation to ensure the absence of respiratory depression. All patients had the opportunity to self-administer morphine via PCA *iv* for a minimum of 24 hr. Intramuscular ketorolac (30 mg) was prescheduled every six hours from approximately the time of arrival on the floor until the morning of postoperative day three. After 24 hr of *iv* PCA morphine, oral analgesics were administered providing that the patient was tolerating oral liquids. The oral analgesics consisted of acetaminophen and codeine (650 mg/30 mg) every six hours as needed. This multimodal pain management, including administration of non-steroidal antiinflammatory drugs, reflected the current practice at our institution at the time of the study design.

Pruritus was managed initially with diphenhydramine (25–50 mg *iv* every six hours, as needed) and then naloxone infusion ($20 \mu\text{g}\cdot\text{hr}^{-1}$ *iv* up to 30 hr after intrathecal opioid injection) if symptoms persisted. Nausea and emesis were managed initially with droperidol (0.625 mg *iv*, every six hours) (in the later stage of the study droperidol was substituted with ondansetron), and then naloxone (same dosing/administration route as for pruritus) if symptoms continued to persist.

Study assessments

Pain and functional status were the primary outcomes. Pain was assessed by an 11-point verbal pain numeri-

cal rating score (NPS) with “0” indicating no pain and “10” indicating the worst pain imaginable. This is a well-validated instrument for the assessment of pain.^{16–18} Pain assessment was performed preoperatively by a research assistant and at 0600, 1400, and 2200 ($\pm$ 2) hours by floor nursing staff when patients were in the hospital, for up to three days postoperatively. Patients were asked to score pain at the time of assessment (current pain). Postoperative morphine requirements were also recorded. Secondary outcomes were also examined. Respiratory depression was defined as a respiratory rate less than 8 breaths·min⁻¹ that required treatment with naloxone or mechanical ventilation. We compared fluid administration between the two groups as well as the need for vasopressors, as assessed by the primary anesthesiologist in charge of the case. We counted the number of vasopressor doses given during anesthesia course, one dose being either 5 mg of ephedrine or 100 μ g of phenylephrine. Patients receiving pharmacologic intervention for nausea/emesis or pruritus or an epidural blood patch for postdural puncture headache were considered to have experienced that side effect. Other perioperative outcomes assessed included an unexpected need for postoperative intensive care, hospital length of stay, and mortality. At discharge from hospital patients were asked to rate the quality of their general anesthesia care and pain relief by rating it on the following scale: very satisfied, satisfied, not very satisfied and not at all satisfied.

To assess functional status, the SF-36 Health Survey was administered by a research assistant at the time of enrollment and at 12 weeks postoperatively (questionnaire filled at 12-weeks was mailed to us). The SF-36 Health Survey measures perceived health status by assessing eight health components: 1) physical functioning - limitation in physical activity including self-care activities; 2) social functioning - limitations in social activities due to emotional problems; 3) role-physical - work and activity limitations due to physical problems; 4) role-emotional - work and activity limitations due to emotional problems; 5) bodily pain - limitations due to pain; 6) mental health - emotional symptoms (e.g., nervous, depressed); 7) vitality - energy *vs* fatigue; and 8) general health - overall self-rated health.¹³ In addition, there are two SF-36 summary composite scores based on the eight domains: physical composite score and mental composite score.¹³ The eight SF-36 scales and the summary physical and mental components were scored using published software.^{13,14} To adjust for age and sex differences, the SF-36 scores were standardized using the published age- and sex-specific reference norms for the general U.S. adult population.¹³ SF-36

subscale scores are age- and sex-adjusted and scaled to have a mean of 50 and a standard deviation of 10 for the reference sample. The average health-related quality of life of the U.S. adult population is represented by a scaled T score of 50, with T scores higher than 50 reflective of better reported health than the general population, and T scores lower than 50 reflective of worse health than the general population. This questionnaire is a validated method of determining bodily pain and functional status over a four-week time period.^{13,14} For the two-, four- and eight-week assessments we conducted the telephone interviews and the 11-point pain scale was used to characterize the level of pain. Patients were asked to score the level of pain at the time of telephone interview (current pain), and to score an *average pain* they experienced over the last 24-hr period before the interview.

Statistical analysis

SAMPLE-SIZE / POWER CALCULATIONS

Sample size requirements were determined based on findings of an earlier study of preemptive analgesia for patients undergoing radical prostatectomy.¹² For our primary aim, we hypothesized significantly different pain scores between treatment groups at 12-week postoperative follow-up. Gottschalk *et al.*¹² found that compared to the control group a significantly higher percentage of patients receiving preemptive analgesia reported no pain at 9.5 weeks following surgery (86% *vs* 47%). Based on these findings, we hypothesized that 45% of patients in the general group would report no pain at week 12. Based on this assumption, a sample size of 50 patients in each group (100 patients total) would provide statistical power of 90% to detect a 30 percentage point increase (i.e., 75% reporting no pain) for the intrathecal group.

Statistical analyses

This study employed a simple randomized design with no stratification factors. The data were analyzed using a two-sample intention-to-treat approach. Postoperative pain scores (NPS), morphine use, and other continuous variables were compared between treatment groups using the rank sum test. Dichotomous outcomes (e.g., treatment for nausea) were compared between treatment groups using the Chi-square test or Fisher's exact test. SF-36 subscale scores at baseline were compared between treatment groups using the two-sample t test and SF-36 data at 12-week follow-up were analyzed using analysis of covariance with the baseline score included as the covariate. In all cases, two-sided tests were performed with *P*-values $\leq$ 0.05 considered statistically significant.

FIGURE 1 Flow chart of the clinical trial.

Results

During the recruitment period between April 2001 and February 2005, 470 patients were screened at the Methodist Hospital, Rochester, Minnesota as potential candidates for this study (Figure 1). Enrollment was closed before the target number of patients was achieved because of a low rate of recruitment and the prolonged enrollment period. Twenty-four patients were excluded based on predefined exclusion criteria (5.1%), and 353 declined participation (of these the vast majority expressed clear preference in anesthetic and analgesic technique). Ninety-three (20%) patients agreed to participate; of those one patient was subsequently excluded due to protocol violation (randomized to SAB, but received general anesthesia), while in three patients the surgery was cancelled. Of the remaining 89 patients, 45 underwent surgery under SAB, and 44 under general anesthesia. In three patients in the SAB group, the block failed and the patient received general anesthesia. For all analyses presented in this report these patients are included in the SAB group (intention-to-treat). Patient characteristics and types of operations performed are shown in Table I. There were no differences in major preoperative co-morbidities (cardiovascular, hypertension, pulmonary, etc.) between the two groups (as defined by the diagnostic criteria described by Hosking *et al.*,¹⁹ data not shown). Preoperative health-related quality of life (SF-36) was comparable between the two groups and tended to be better than expected when compared to the age- and sex-matched U.S. population, as shown by the mean values exceeding 50 (Table II).

TABLE I Patient characteristics and types of surgery performed

Characteristic	Regional	General (n = 45)	P-value*
Age (yr)	52.2 ± 11.9	51.8 ± 12.8	0.693
Postmenopausal, n (%)	21 (47)	17 (39)	0.522
Height (cm)	163.3 ± 6.6	165.7 ± 6.2	0.089
Weight (kg)	75.7 ± 15.2	75.0 ± 16.1	0.566
Body mass index (kg·m ⁻²)	28.3 ± 4.7	27.3 ± 5.3	0.132
ASA status, n (%)			0.877
I	8 (18)	9 (20)	
II	34 (76)	33 (75)	
III	3 (7)	2 (5)	
Procedure			0.294
Hysterectomy only	27 (60)	27 (61)	
Hysterectomy + cystocele	1 (2)	1 (2)	
Hysterectomy + rectocele	4 (9)	9 (20)	
Hysterectomy + cystocele + rectocele	13 (29)	7 (16)	

*Groups were compared using the rank sum test for continuous variables and Chi-square test or Fisher's exact test for categorical variables.

Procedure related characteristics and postoperative pain scores in the two groups are summarized in Table III. The patients in the SAB group received significantly ($P = 0.012$) more doses of vasopressors intraoperatively (median 1, interquartile range 0–2.5) compared to those in the general anesthesia group (median 0, interquartile range 0–1). Intravenous fluid administration was comparable in two groups (Table III). The durations of anesthesia, PACU stay, and hospitalization were not significantly different between the two groups. The patients in the general anesthesia group received more morphine in the PACU ($P < 0.001$) compared to patients receiving SAB. Compared to the general anesthesia group, patients receiving SAB also required significantly less morphine over the first 12 hr after PACU discharge ($P < 0.001$). Subsequent morphine requirement was not significantly different between groups. Compared to the general anesthesia group, a smaller percentage of patients receiving SAB required treatment for nausea while in the PACU ($P = 0.021$), but the percentage of patients requiring nausea treatment at any time during hospitalization did not differ between groups. There were no intensive care admissions or mortalities in either study group.

Protocol goals for pain control were generally achieved, as reflected by mean current NPS values of ≤ 3 at all time points except at the time of arrival to the floor in the patients requiring general anesthesia (Table III). Numerical pain score values tended to

TABLE II Functional status at baseline and 12-week follow-up*

SF-36 subscale	Regional	General	P-value†
<i>Bodily pain</i>			
Baseline	54.1 ± 9.9	52.0 ± 8.8	0.291
12-week follow-up	56.3 ± 9.2	54.9 ± 7.8	0.465
<i>General health perceptions</i>			
Baseline	56.9 ± 6.6	55.7 ± 7.3	0.425
12-week follow-up	56.9 ± 6.6	55.1 ± 7.2	0.670
<i>Mental health</i>			
Baseline	55.2 ± 6.1	52.5 ± 7.6	0.073
12-week follow-up	56.6 ± 5.4	52.8 ± 8.0	0.146
<i>Physical functioning</i>			
Baseline	53.4 ± 7.7	53.3 ± 5.4	0.968
12-week follow-up	54.7 ± 6.8	54.7 ± 4.3	0.634
<i>Role - emotional</i>			
Baseline	54.0 ± 6.0	51.5 ± 8.1	0.113
12-week follow-up	54.6 ± 3.6	53.9 ± 5.4	0.615
<i>Role - physical</i>			
Baseline	51.9 ± 10.7	51.4 ± 7.7	0.810
12-week follow-up	52.3 ± 8.7	49.4 ± 9.5	0.201
<i>Social functioning</i>			
Baseline	52.3 ± 9.1	53.0 ± 7.3	0.712
12-week follow-up	55.2 ± 4.9	54.1 ± 7.1	0.448
<i>Vitality</i>			
Baseline	51.8 ± 11.1	49.9 ± 11.2	0.422
12-week follow-up	53.8 ± 9.3	51.8 ± 9.9	0.666
<i>Physical composite score</i>			
Baseline	53.1 ± 9.3	53.0 ± 7.9	0.972
12-week follow-up	54.2 ± 8.2	53.1 ± 7.4	0.872
<i>Mental composite score</i>			
Baseline	53.9 ± 6.2	51.5 ± 9.0	0.152
12-week follow-up	55.7 ± 4.9	53.3 ± 8.6	0.392

*This evaluation assesses functional status between eight and 12 weeks after surgery. Data are available for 87 subjects (44 regional, 43 general) at baseline and 76 subjects (41 regional, 35 general) at 12-week follow-up. Functional status was assessed using the SF-36 Health Survey questionnaire (see Methods for details; in brief subscale scores > 50 are reflective of better reported health than the general population and subscale scores < 50 are reflective of worse reported health than the general population). †The mean subscale scores at baseline were compared between groups using the t test. Subscale scores at 12-week follow-up were analyzed using analysis of covariance with the 12-week follow-up score as the dependent variable, treatment group as the independent variable, and baseline score included as a covariate.

be lower in patients receiving SAB compared to the general anesthesia group through 14:00 hr on postoperative day two (the day after surgery), with significant differences noted at the time of floor arrival and at 14:00 hr on postoperative day two. The frequency of pruritus noted at any time during hospitalization tended to be higher in patients receiving SAB compared to the general anesthesia group, but this difference was not statistically significant (14 *vs* seven patients; *P* < 0.091). There was no reported respiratory depression or positional headaches in patients receiving SAB.

There was no difference between the two groups in satisfaction with anesthetic care and pain management during hospitalization (Table IV).

Pain was well controlled during the 12-week postoperative follow-up. No significant differences between the two groups in the mean “current” or “average” NPS values were observed at any time (Table V), although there was some evidence (*P* = 0.052) suggesting lower pain values in patients receiving SAB at the time of evaluation at two weeks after surgery. Supplemental analyses found that at two-weeks postoperatively, significantly more patients in the SAB group compared to the general anesthesia group reported current NPS values of zero (i.e., were pain free) [69% (31/45) *vs* 48% (20/42) of patients for regional and general groups respectively, *P* = 0.044, Chi-square test, Figure 2]. No differences in the percentages of pain-free patients were observed at four, eight, or 12 weeks postoperatively. None of the eight subscales or two composite scores of the SF-36 health survey was significantly different between the two groups at either baseline, or at 12 weeks after surgery (Table II). When data were reanalyzed after excluding the three patients who had failed SAB, findings remained unchanged.

Discussion

Although pain was well controlled in both patient groups, a significantly higher proportion of patients reported being pain free at the two-week interval after receiving SAB for vaginal hysterectomy with or without repair of cystocele and/or rectocele. However, the clinical relevance of this difference, which was not sustained after this time, is unclear given that both groups reported low pain scores. There were no differences between groups in pain or functional status at 12-week follow-up.

In theory, regional anesthesia and analgesia may have multiple beneficial effects on postoperative outcome, a topic that has been the source of numerous reviews.^{1,3} This includes the possibility of “preemptive analgesia”, in which interruption of nociceptive afferent activity could produce improvement in postoperative analgesia.^{2,3,9,20} Nonetheless, when studied in larger clinical trials, definitive demonstration of such benefits has remained elusive.⁸ One of the methodological challenges in the area has been a wide variation in patient population and anesthetic techniques between studies. Further, as discussed by Wu *et al.*,⁴ there is a need to examine longer term outcomes such as functional status that are of primary interest to patients and society. Of note, the majority of studies have examined the addition of regional

TABLE III Procedure characteristics and perioperative outcomes during hospital stay

Outcome	Regional		General		P-value*
	n	Mean $\pm$ SD	n	Mean $\pm$ SD	
Duration of anesthesia, minutes	45	131 $\pm$ 38	44	137 $\pm$ 41	0.525
Intraoperative fluids (mL)	45	1672 $\pm$ 624	44	1649 $\pm$ 642	0.740
Intraoperative pressors, # doses†	45	1.6 $\pm$ 2.9	44	0.4 $\pm$ 0.7	0.012
Duration of PACU stay	45	131 $\pm$ 58	44	120 $\pm$ 40	0.783
Total morphine administered in PACU (mg)	45	1.0 $\pm$ 3.0	44	9.0 $\pm$ 7.3	< 0.001
Any morphine in PACU, n (%)	45	5 (11)	44	31 (70)	< 0.001
Treated for nausea in PACU, n (%)	45	6 (13)	44	15 (34)	0.021
Pain after PACU discharge, NPS‡					
Arrival to floor	45	1.4 $\pm$ 2.3	44	4.9 $\pm$ 2.4	< 0.001
22:00 - day of surgery	45	2.0 $\pm$ 1.8	44	2.8 $\pm$ 2.0	0.098
6:00 - postoperative day one	45	1.9 $\pm$ 1.7	43	2.6 $\pm$ 1.9	0.060
14:00 - postoperative day one	45	2.1 $\pm$ 1.7	44	3.0 $\pm$ 2.1	0.040
22:00 - postoperative day one	42	2.7 $\pm$ 2.1	40	2.6 $\pm$ 1.6	0.989
6:00 - postoperative day two	42	1.8 $\pm$ 1.5	40	2.2 $\pm$ 1.6	0.386
14:00 - postoperative day two	26	2.6 $\pm$ 2.1	23	2.3 $\pm$ 1.6	0.614
22:00 - postoperative day two	24	2.4 $\pm$ 2.0	21	3.0 $\pm$ 2.8	0.579
Morphine use after PACU discharge, mg					
0–12 hr	45	7.9 $\pm$ 8.3	44	14.8 $\pm$ 11.2	< 0.001
12–36 hr	45	18.6 $\pm$ 15.0	43	23.5 $\pm$ 21.2	0.261
36–60 hr	40	10.8 $\pm$ 8.0	38	12.2 $\pm$ 9.8	0.798
At any time during hospitalization					
Treatment for pruritus, n (%)	45	14 (31)	44	7 (16)	0.091
Treatment for nausea, n (%)	45	32 (71)	44	30 (68)	0.764
Duration of hospital stay (days)	45	2.6 $\pm$ 0.6	44	2.5 $\pm$ 0.8	0.403

PACU = postanesthesia care unit; NPS = numerical pain score. *Groups were compared using the rank sum test for continuous variables and the Chi-square test for categorical variables. †Median (interquartile range) number of intraoperative pressor doses was 1 (0, 2.5) for the regional group and 0 (0, 1) for the general group. Ephedrine 5 mg or phenylephrine 100 μ g were counted as a single pressor dose, each. ‡Pain was assessed using a 0 to 10 numeric pain scale.

anesthetic techniques to general anesthesia,^{7,8,11,12,21,22} and less frequently compared the effects of regional anesthesia and analgesia as a sole anesthetic to general anesthesia.^{23–25}

In the present study we examined both short and longer term outcomes following vaginal hysterectomy with or without repair of cystocele and/or rectocele. Short-term outcomes included the quality of analgesia and side-effects associated with analgesic techniques. We found that the short-term effects of SAB were limited to the expected duration of the intrathecally-administered drugs. The patients receiving SAB required significantly less morphine in the PACU, which may have contributed to a lesser need for nausea therapy in the PACU. Those receiving SAB were also significantly more comfortable upon arrival to the floor. However, by 22:00 hours on the day of surgery, pain was well-controlled in both groups (mean NPS $\leq$ 3.0), and morphine requirement did not differ after the first 12 hr postoperatively. Viewed over

the entire hospitalization, SAB did not decrease the proportion of patients requiring treatment for nausea, and was associated with a trend towards an increased frequency of pruritus, a well-recognized complication of intrathecal opioids. Overall, patients in both groups were equally satisfied with general anesthesia care and postoperative pain management.

For longer term outcomes, we were particularly interested in the association between the quality of postoperative analgesia and functional status as assessed by the SF-36 Health Survey^{13,14} at 12-week follow-up. Prolonged postoperative pain may affect quality of life by interfering with all daily activities and sleep.²⁶ This measure assesses physical, psychological and social factors that contribute to functionality and has been used in prior studies that examined the longer-term effects of regional analgesia.^{8,11,12} Fortunately for the patient, but perhaps unfortunately for purposes of the study, these patients reported surprisingly low pain scores, lower than hypothesized in the planning

TABLE IV Patient satisfaction with anesthesia care and pain management at the time of hospital discharge

	<i>Very satisfied</i>	<i>Somewhat satisfied</i>	<i>Not very satisfied</i>	<i>Not at all satisfied</i>
How satisfied were you with your anesthesia care? ¹				
SAB (% patients)	93	7	0	0
General anesthesia (% patients)	98	2	0	0
How satisfied were you with your pain relief following surgery? ²				
SAB (% patients)	71	29	0	0
General anesthesia (% patients)	71	20	9	0

SAB = subarachnoid block. Tested with Mantel-Haenszel Chi-square: P -value = 0.320¹ and P = 0.414.²

TABLE V Pain expressed on numerical pain score (numeric pain score scale) following hospital discharge

<i>Characteristic</i>	<i>Regional</i>		<i>General</i>		<i>P-value*</i>
	<i>n</i>	<i>Mean ± SD</i>	<i>n</i>	<i>Mean ± SD</i>	
Two-week follow-up	45		42		
Current pain		0.6 ± 1.2		1.0 ± 1.2	0.052
Average pain		0.9 ± 1.4		1.1 ± 1.2	0.129
Four-week follow-up	44		42		
Current pain		0.6 ± 1.0		0.7 ± 1.3	0.754
Average pain		0.9 ± 1.5		0.7 ± 1.2	0.668
Eight-week follow-up	43		41		
Current pain		0.1 ± 0.2		0.2 ± 0.6	0.341
Average pain		0.1 ± 0.2		0.2 ± 0.6	0.341
Twelve-week follow-up	39		40		
Current pain		0.1 ± 0.5		0.1 ± 0.3	0.986
Average pain		0.0 ± 0.2		0.1 ± 0.3	0.986

*Pain scores were compared between groups using the rank sum test.

of the study, diminishing the possibility that treatment effects could be detected. Nonetheless, a larger proportion of patients who received SAB were pain free at two-weeks compared to those who received general anesthesia, and the difference in current pain score at this time approached statistical significance. However, the clinical significance of this finding is likely to be minimal, given that mean pain scores were low in both groups. Unfortunately, to minimize respondent burden we did not assess functional status at this time to determine if these small differences might affect functional status, but this seems unlikely given the low pain scores. At subsequent times pain scores further declined, so that the possible impact of intraoperative anesthetic technique was minimal and, not surprisingly, functional status was similar. We can only speculate regarding the mechanism responsible for the small improvement in pain scores at two weeks postoperatively. It is tempting to invoke the concept of “preemptive” analgesia, but there was little evidence for such an effect while hospitalized in terms of improved pain scores and decreased opioid require-

ments. Further, it may be necessary to provide more prolonged interruption of afferent nociceptive activity to elicit a “preemptive” effect.^{20,27}

There are few studies available for comparison with these results. Three studies provide extended postoperative follow-up of patient functional status and pain.^{8,11,12} All examined the effect of regional analgesia when used during and after general anesthesia. Gottschalk *et al.*¹² found improved functional status at 3.5 weeks after dismissal in patients undergoing radical retropubic prostatectomy who received epidural analgesia before surgical incision (a “preemptive” strategy) and maintained for three days postoperatively compared with patients who received only postoperative epidural analgesia, not associated with improvements in pain. However, the “preemptive” strategy improved pain at 9.5 weeks without improving functional status.¹² Thus, the link between pain and functional status is unclear in their work. In patients undergoing radical retropubic prostatectomy, Brown *et al.*⁸ examined the effect of preoperative SAB with bupivacaine, morphine and clonidine (a regimen

FIGURE 2 Percentage of patients who reported no pain at the scheduled evaluation intervals. Pain was asked to be rated as current pain (pain at the time of telephone inquiry) or average pain (average pain during the two, four, eight, and 12-week period). At two weeks, 31 out of 45 patients *vs* 20 out of 42 patients in spinal and general groups, respectively, had no pain at the time of telephone interview (current pain, $P = 0.044$, Chi-square test) and 26 out of 45 patients *vs* 16 out of 42 patients in the spinal and general groups, respectively, reporting no pain during the 24-hr period preceding interview (average pain, $P = 0.067$, Chi-square test).

similar to that used in the current study) immediately before the induction of general anesthesia. They noted lower postoperative opioid requirement and better pain control for the expected duration of the intrathecally-administered drug, but not at later times. This is similar to our findings. However, unlike findings in the present study, Brown *et al.*⁸ found no differences in pain at two weeks after hospital discharge. Similarly to the current study, pain and functional status at 12 weeks postoperatively were not different between the two groups. A study by Carli *et al.*¹¹ examined the role of epidural analgesia on functional exercise capacity and health-related quality of life at three and six-weeks after colonic surgery. They found that epidural analgesia provided superior pain relief, as measured by improved in out-of-bed mobilization, bowel function, and food intake, and long lasting effects on exercise capacity and health-related quality of life. Furthermore, Carli *et al.*¹¹ found a dramatic

decrease in physical health and mental health in both groups with some recuperation by the last evaluation at six weeks. The SF-36 declined immediately postoperatively, and then returned to baseline by the sixth postoperative week, with the epidural group showing less deterioration. Interestingly, for mental health, the epidural group recuperated their baseline values and the PCA group did not. The contrast of these findings with our own may reflect differences in surgical procedure, or the shorter period of follow-up in the study of Carli *et al.*¹¹

Limitations

Our study has several limitations. First, the prerandomization exclusion rate was high due to patients' strong preference for a particular type of anesthesia, such that the study population may not reflect the general population of women undergoing vaginal hysterectomy. Second, it was impossible to blind either patients or study personnel to treatment assignment. Third, although limiting the study to one surgical type is scientifically desirable, any results found may not apply to the patients undergoing other types of operations. In addition, gender and hormonal status may influence nociception²⁸⁻³⁰ therefore, these findings may not apply to male subjects. Fourth, pain at 12 weeks after vaginal hysterectomy was less than originally anticipated during study design, decreasing the likelihood of finding treatment effects. Finally, the SF-36 is a measure of global functional status, and may not have been sufficiently sensitive to detect small differences due to anesthetic technique.

Conclusions

Compared with patients receiving general anesthesia, pain relief was improved in patients receiving SAB for vaginal hysterectomy for the expected duration of intrathecally used drugs only. Nonetheless, more patients receiving SAB were pain free at two weeks postoperatively, although pain was so well-controlled in both groups that this observation probably has little clinical significance. Anesthetic technique did not affect functional status at 12 weeks postoperatively. For patients desiring excellent analgesia in the immediate postoperative period, SAB can be recommended, but for this surgical procedure the choice of primary anesthetic has little influence on longer-term outcomes.

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