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Transversus abdominis plane block in robotic gynecologic oncology: A randomized, placebo-controlled trial

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HIGHLIGHTS

- Preoperative TAP blocks do not decrease narcotic use after robotic surgery in gynecologic cancer.
- TAP blocks are safe to use in an analgesic plan for gynecologic cancer patients regardless of BMI.
- Narcotic dosing should be adjusted based on age and BMI using a nomogram created by this data set.

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ABSTRACT

Objective. Although robotic surgery decreases pain compared to laparotomy, postoperative pain can be a concern near the site of a larger assistant trocar site. The aim of this study was to determine the efficacy of transversus abdominis plane (TAP) block on 24-hour postoperative opiate use after robotic surgery for gynecologic cancer.

Methods. Sixty-four subjects with gynecologic malignancies who were scheduled to undergo robotic surgery were enrolled into the study. They were randomized to receive a unilateral TAP block to the side of the assistant port via ultrasound guidance. The block was comprised of 30 cc of 0.25% bupivacaine with 3 mcg/mL epinephrine or saline. Opiate use was measured and converted into IV morphine equivalents. Patient-reported pain was measured using the Brief Pain Inventory (BPI) and Visual Analog Scale (VAS).

Results. The treatment group used a mean of 64.9 mg morphine in the first 24 h compared to 69.3 mg for controls (primary outcome, $p = 0.52$). After age-adjustment, the treatment group used a mean of 11.1 mg morphine less than controls ($p = 0.09$). Postoperative pain scores assessed by the BPI (6.44 vs. 6.97, $p = 0.37$) and the VAS (3.12 vs. 3.61, $p = 0.30$) were equivalent. Block placement was uncomplicated in 98.4% of participants with mean BMI of 35.3 kg/m^2. Linear regression revealed an approximate 8.1 mg decrease in morphine equivalents used per additional decade of life ($p = 0.0008$). There was a positive correlation between the amount of opiates and BMI with an additional 8.8 mg of morphine per 10 kg/m^2 increase in BMI ($p = 0.0012$).

Conclusions. TAP block is safe and feasible in this patient population with a large proportion of morbid obesity. Preoperative TAP block does not significantly decrease opiate use. However; based on these data, a clinically useful nomogram has been created to aid clinicians in postoperative opiate-dosing for patients based on age and BMI.

Introduction

Since the GOG-sponsored LAP2 study was published, the use of laparoscopic and robotic surgical techniques to treat gynecologic malignancies has increased dramatically [1–3]. Although many patient quality indicators are improved with minimally-invasive surgery [4–7], achieving adequate postoperative analgesia continues to be a barrier to patient recovery and satisfaction [8–10]. Some studies indicate that larger trocar size and closure of the deep fascial layer after the use of these trocars can contribute to increased postoperative pain [11–13]. In the authors' experience, patients who undergo a robotic surgical procedure often complain of postoperative lower quadrant pain

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related to the manually operated "assistant port" placed during robotic procedures.

The transversus abdominis plane (TAP) block is a peripheral nerve block technique used for postoperative pain control. The efficacy of this block has been well documented in the literature for a variety of procedures involving incisions of the lower abdomen including bowel resection, open appendectomy, laparoscopic cholecystectomy, retropubic prostatectomy, and cesarean deliveries [14–20]. Some of the studies employed bilateral TAP blocks and others unilateral. However, the recent data involving the TAP block in a multi-modality analgesia plan for laparoscopic benign hysterectomy, colorectal surgery, obesity surgery and nephrectomy have been mixed regarding improved pain scores and reduced systemic opiate use [21–24].

A review of the literature reveals no data to inform surgeons and patients regarding the utility of the TAP block for postoperative pain specifically in robotic surgery. One study from Denmark that was investigating the TAP block for patients undergoing robotic hysterectomy was closed prior to completion [25]. Even so, that study would have excluded patients with BMI >40 kg/m^2. Given the lack of evidence regarding this analgesic modality in both robotic surgery and in surgery for gynecologic malignancies and in the morbidly obese, this randomized controlled trial was developed to determine the effect of the TAP block on postoperative use and patient reported pain. We hypothesized that patients undergoing robotic surgery who received preoperative TAP blocks would have decreased 24 h opioid consumption, as well as improved pain scores when compared with placebo controls.

Materials and methods

The study was a randomized, double-blinded, placebo-controlled trial approved by the University of Wisconsin Institutional Review Board and the University of Wisconsin Carbone Cancer Center Protocol Review and Monitoring Committee. All women undergoing robotic-assisted laparoscopic surgery for an oncologic indication on the Gynecologic Oncology service at the University of Wisconsin between October 2011 and February 2013 were eligible. Other patient eligibility requirements included: (1) at least 18 years of age; (2) English speaking; (3) ability to understand visual and verbal pain scales; and (4) ASA physical status of 1 to 3. Patients were excluded from participation in the study if they met any of the following criteria: (1) known allergy to local anesthetics; (2) immunocompromised status; (3) known history of opioid dependence; (4) known history of chronic pain disorders; (5) pregnancy or lactation; (6) patient is a prisoner or incarcerated; and (7) significant liver disease that would inhibit prescription of opiate analgesics.

Potential subjects were introduced to the study during their preoperative clinic visit. After written informed consent was obtained, randomization was performed by the Pharmaceutical Research Center on the day of surgery using a random computer generated assignment without stratification. Subjects were considered enrolled in the study at the time of randomization.

The TAP block was placed using a standardized ultrasound-guided approach to the layers of the anterior abdominal wall [26]. This was performed in a dedicated block area prior to entering the operating room. Subjects assigned to the study group received 30 mL of 0.25% bupivacaine with 3 mcg/mL of epinephrine injected into the plane between the internal oblique and the transversus abdominis muscles. The sham block was placed in the same fashion using a placebo injection of 30 mL of sterile, preservative-free saline. All subjects then went on to receive a general endotracheal anesthetic for the planned surgical procedure according to the standard of care. No additional long acting opioids, ketamine, ketorolac, or local anesthetic infusions were administered during the surgical procedure. Infiltration of the laparoscopic port sites with 0.25% bupivacaine was performed on all subjects at the time of skin closure. Standard postoperative pain management with systemic IV and oral opiates and anti-inflammatories were given as needed.

On the day of surgery, the appropriate study solution was prepared and delivered to the assigned anesthesiologist in a blinded manner. The identity of the anesthetic solution (i.e. bupivacaine/epinephrine versus normal saline) was placed in a sealed envelope and delivered to the anesthesiologist to be opened only if an adverse reaction occurred. Following the procedure, the sealed envelope was retrieved by the research team. A unilateral TAP block was placed corresponding to the site of the 12 mm robotic assistant port (right-sided in all 64 cases). All blocks were placed with standard sterile preparation and under ultrasound guidance. If the necessary tissue planes could not be appropriately visualized for safe placement of the TAP block the subject was eliminated from the study per protocol ($n = 0$).

Measurement of postoperative pain following robotic-assisted laparoscopic surgery was performed using both the validated Visual Analog Scale (VAS) and Brief Pain Inventory (BPI) scales [27–29]. Pain data were collected using both scales once on the day of surgery and twice on the first day after surgery (POD1). At a point 24 h after surgery, the total IV and oral opioid consumption for each subject was tallied and converted to IV morphine equivalents. Following the third VAS/BPI pain assessment, subjects started a pain diary which was logged daily for a total of 14 days. One additional VAS/BPI pain assessment was collected at the time of the postoperative clinic visit.

Statistical considerations

The primary outcome of interest was 24-hour opioid use in IV morphine equivalents with a 50% reduction considered to be the minimal clinically important difference. In order to achieve 80% power to detect a 50% reduction in IV morphine equivalents, 68 patients were required with a 5% drop out rate and an $\alpha = 0.05$ for a two-sided test. The primary outcome of 24-hour opioid use was compared using a two-sample *t*-test on the logarithmic scale assuming equal variances. Secondary outcomes were analyzed using the chi-squared test and linear regression. All statistical calculations used a two-sided significance level of 0.05 ($p \leq 0.05$) and were calculated using the R Project for Statistical Computing [30].

Results

A total of 75 women agreed to participate in the study, and 64 women were enrolled and completed the study between October 2011 and February 2013 (Fig. 1). Eight patients did not meet inclusion criteria, 2 patients were excluded from the analysis secondary to intraoperative conversion to laparotomy, and 1 additional patient was excluded because the robot was unavailable.

Subject demographics, including the procedure performed and indications can be found in Table 1. Aside from subject age, the randomization resulted in balance between the treatment groups in regards to patient factors. The treatment group was younger than the placebo group (55.2 years versus 62.1, $p = 0.03$). The primary outcome of total 24-hour opiate consumption (IV morphine equivalents) was not significantly different between the treatment and placebo groups (64.9 mg vs. 69.3 mg, $p = 0.52$, Table 2). The calculated total opiate consumption values include administration during the surgery, in the post-anesthesia care unit (PACU), and on the general care floor. There was no difference in the average postoperative pain scores as assessed by the BPI (6.44 in the treatment group vs. 6.97 in the placebo group, $p = 0.37$) or by the VAS (3.12 in the treatment group vs. 3.61 in the placebo group, $p = 0.30$).

Subjects were asked to complete a daily pain and medication use diary for 14 days. Average pain diary scores were not significantly different (3.52 mg in the treatment group vs. 3.82 in the placebo group; $p = 0.56$). One final pain assessment was taken at each subject's post-operative clinic visit, at least 2 weeks following discharge home from the hospital. There was no difference in the final BPI score (1.69 in the treatment group vs. 2.14 in the placebo group, $p = 0.42$) or the final VAS score (0.86 in the treatment group vs.1.22 in the placebo group,

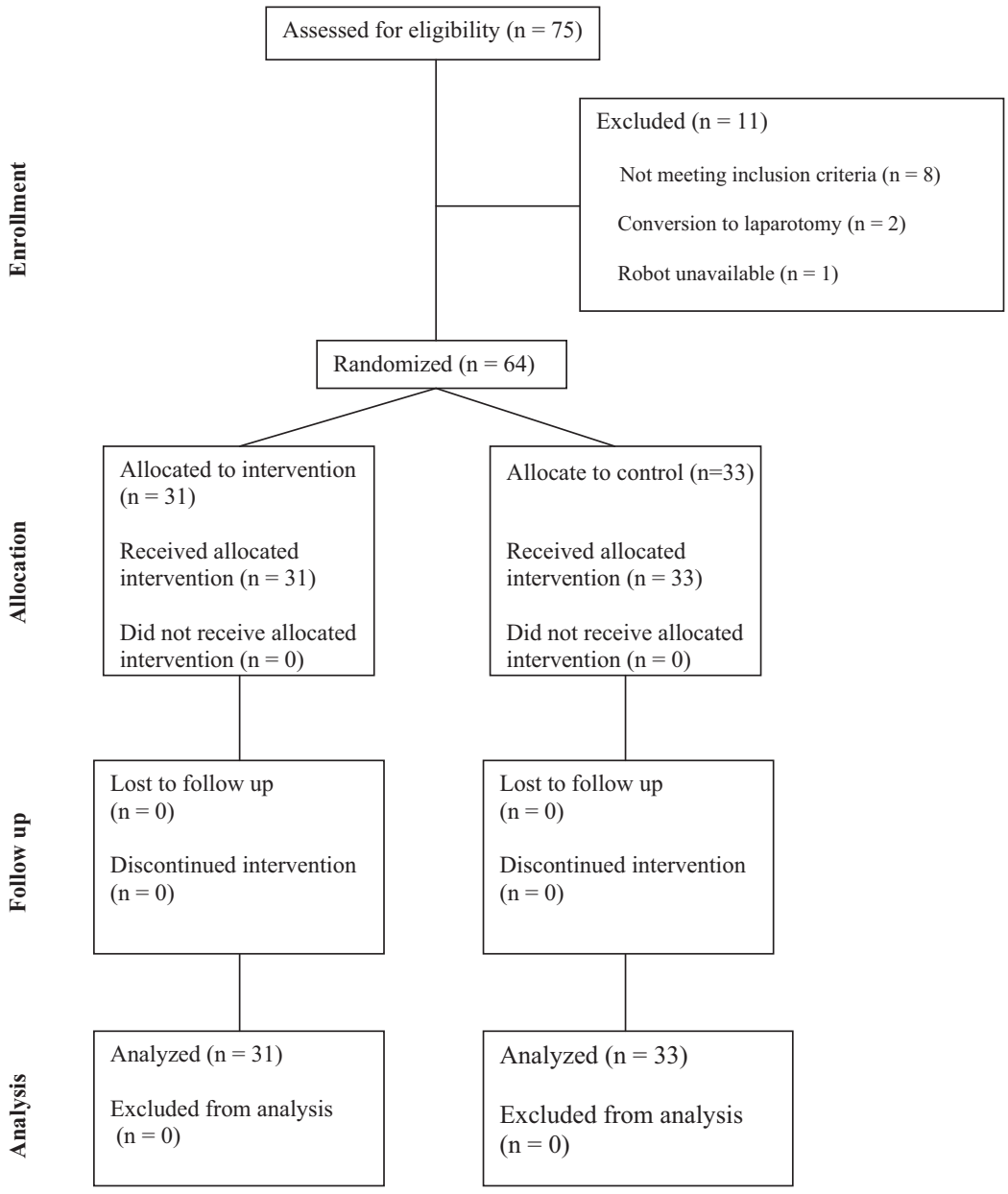

Fig. 1. CONSORT flow diagram.

$p = 0.40$) between subjects when they presented for their postoperative visit. This visit was conducted 2–4 weeks after surgery depending on surgeon preference. Length of hospital stay, postoperative complication rate, block placement time, ability to safely place the ultrasound-guided block, and patient satisfaction were similar between groups (Table 2).

Given the significant difference in age between the treatment and placebo groups, an analysis using age adjustment was performed. When adjusting for age, the 24-hour opiate use (morphine equivalents) for patients in the treatment group was 11.1 mg less than the placebo group ($p = 0.09$), where it was 4.4 mg less prior to age adjustment. None of the additional secondary analyses were significantly different following age adjustment.

This study demonstrated that the TAP block can be safely placed in a population consisting of morbidly obese patients. Mean BMI in this study was 35.3 kg/m^2 (range 18.3–66.6 kg/m^2) and block placement was accomplished without complication in all but one participant.

In the entire study population ($n = 64$), linear regression of total 24-hour opiate use showed a strong negative correlation with age. There was an approximate 8.1 mg decrease in morphine used per additional decade of age (Fig. 2, $p = 0.0008$). There was also a strong positive association with amount of opiate used and BMI. For each increase in 10 kg/m^2 of BMI, opiate use increased by an approximate 8.8 mg (Fig. 3, $p = 0.0012$). The use of additional morphine equivalents increased by 0.93 mg per BMI unit, with a 95% confidence interval of 0.38–1.48 ($p = 0.0016$). There was no observed correlation between age and BMI using linear regression ($p = 0.82$). The estimated effect of age on opiate consumption appears to hold across the spectrum of BMI in addition to the observed effect that increasing BMI increases opiate consumption for subjects of all ages. These strong associations would suggest that older women and women with lower BMI use less opiate pain medication, whereas younger women and women with higher BMI require more.

Table 1
Patient characteristics.

	TAP block ($n = 31$)	Saline control ($n = 33$)	p-value[a]
Age, years; mean (range)	55.2 (30, 75)	62.1 (29, 85)	0.028
Race			0.11
White	31	29	
Other	0	4	
BMI, kg/m^2; mean (range)	34.2 (19.1, 66.6)	36.3 (18.3, 53.6)	0.45
EBL, cc; mean (range)	88.7 (50, 200)	81.1 (25, 400)	0.58
Operating time, min; mean (range)	236 (133, 338)	228 (137, 476)	0.61
Primary diagnosis			0.65
Cervix	3	2	
Endometrial hyperplasia	3	1	
Grade 1 endometrial	12	19	
Grade 2–3 endometrial	12	9	
Other	1	2	
Procedure performed			0.44
Hyst without BSO	1	0	
Hyst + BSO	12	13	
Hyst ± BSO + LND	14	18	
Rad Hyst ± BSO + LND	3	1	
Trachel + BSO	1	0	
Trachel ± BSO + LND	0	1	

Abbreviations: Hyst = hysterectomy; BSO = bilateral salpingo-oophorectomy; LND = pelvic and paraaortic lymph node dissection; Rad Hyst = radical hysterectomy; Trachel = trachelectomy.

[a] t-test used to compare continuous variables and χ^2 for categorical variables.

Discussion

Unilateral TAP block does not significantly decrease total 24-hour opiate use or improve pain scores when compared to placement of control block with sterile saline. The TAP block does not appear to be an effective measure to decrease postoperative pain associated with the laparoscopic assistant port following robotic-assisted laparoscopic surgery for gynecologic malignancies. Block placement is costly due to the requirement of additional hospital resources including operative time, dedicated space for block placement, and anesthesiologist time and should not be routinely indicated in this patient population. Placement of bilateral blocks would likely take longer than the average of approximately 10 min in this study, although we do not have any data to make a comparison. However, placement of the ultrasound-guided TAP block appears to be feasible and safe in obese patients, with 63 of 64 blocks placed safely in this sample of patients with an average BMI of 35.3 kg/m^2. Therefore, the TAP block could be considered safely in a multi-modal analgesic plan if indicated by a patient-specific situation.

Although the effectiveness of the TAP block for laparoscopic procedures has been mixed across surgical specialties, a recent meta-analysis of 10 randomized trials concluded that TAP blocks decrease the amount of IV opiates required in the first 24 postoperative hours by 5.3 mg of IV morphine equivalents and decrease early and late resting pain [31]. Given our study shows a non-significant age-adjusted decrease of 11.1 mg of morphine for subjects receiving the TAP block, it is possible that a larger sample size would have resulted in statistical significance in accordance with the data from this meta-analysis. Although this outcome did not reach statistical significance, an 11.1 mg decrease may be considered a clinically significant amount.

Previous studies of TAP blocks in laparoscopy that have demonstrated improvement in pain scores and decreased systemic opiate-use employed bilateral blocks [14,22,24,32–36]. Our inability to achieve our primary endpoint may have been affected by the choice to utilize a unilateral block in this trial. Additionally, many of those studies also

Table 2
Narcotic use, pain scores and quality indicators.

	TAP block ($n = 31$)	Saline control ($n = 33$)	p-value[a]
24-hour opiate use; morphine eq (95% CI)	64.9 mg (54.8, 74.9)	69.3 mg (59.8, 78.7)	0.52
Brief Pain Index scores (95% CI)			
24 h after surgery	6.44 (5.56, 7.32)	6.97 (6.15, 7.79)	0.37
Post-surgical visit	1.69 (0.956, 2.42)	2.14 (1.28, 3)	0.42
Visual Analog Scale scores (95% CI)			
24 h after surgery	3.12 (2.48, 3.76)	3.61 (2.88, 4.35)	0.30
Post-surgical visit	0.862 (0.396, 1.33)	1.22 (0.495, 1.94)	0.40
Mean daily pain diary scores (95% CI)	3.52 (2.81, 4.23)	2.14 (1.28, 3)	0.56
Hospital length of stay			1.0
1 day	22	23	
2 days	7	7	
3 days	2	3	
Block placement time, min (95% CI)	9.29 (7.32, 11.3)	10.2 (8.53, 11.9)	0.47
Safe block placement			1.0
Yes	30	33	
No	1	0	
Patient satisfaction with analgesia (95% CI)	4.36 (3.97, 4.74)	4.17 (3.76, 4.57)	0.50

[a] t-test used to compare continuous variables and χ^2 for categorical variables.

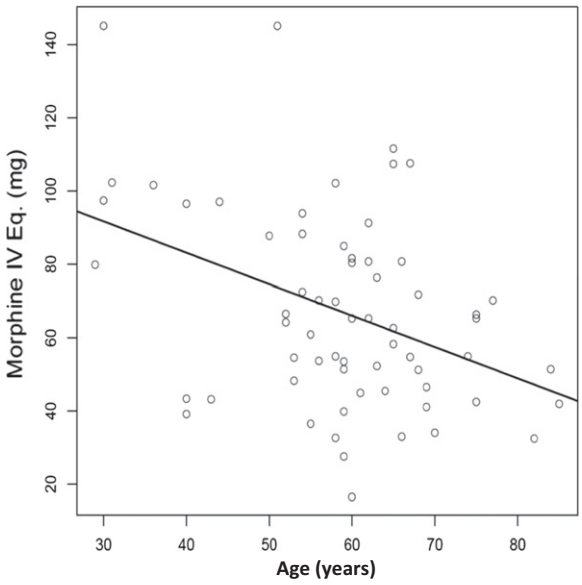

Fig. 2. Post-op IV morphine equivalents vs. age.

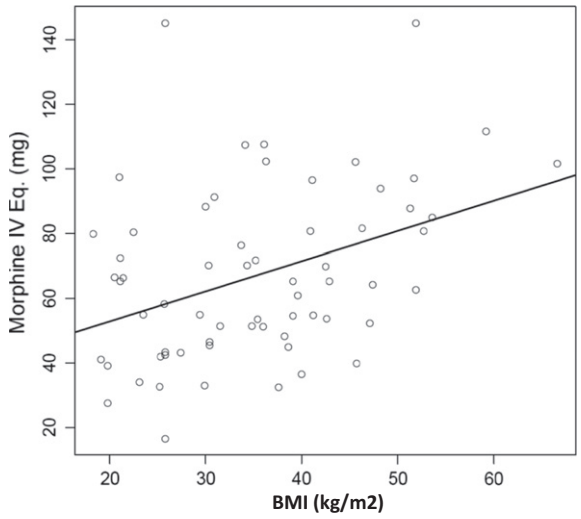

Fig. 3. Post-op IV morphine equivalents vs. BMI.

placed the blocks after induction of anesthesia [14,22,34–36] rather than pre-operatively. The choice of local anesthetic and concentration used has also varied throughout the literature. It is difficult to know how any of these factors contributed to the outcomes observed in this study; however, the surgeon/anesthesiologist team should be aware of these points in the context of published studies if considering a TAP block as part of a multi-modal analgesic plan.

BMI displayed a strong positive correlation with total 24-hour opiate use and age displayed a strong negative correlation with opiate use. This novel opiate requirement data may be extrapolated clinically to achieve more effective postoperative opiate dosing with the ability to improve pain control while maximizing the safety profile of these medications. We developed a nomogram of total 24-hour opiate use versus age by BMI group which may provide a baseline for clinical dosing of postoperative opiate medications (Fig. 4). This new dosing guideline will need to be validated and modified based upon underlying health conditions taking into account the extent of surgery and history of opiate use or abuse.

Using the data presented here, a clinician can compare the theoretical postoperative opiate requirement for a patient with a specific BMI across a spectrum of ages. Based on these data, a 35 year old female with a BMI of 30 will require 81.7 mg IV morphine in the 24-h following surgery, whereas a 75 year old female with the same BMI will require only 49.3 mg IV morphine. This represents a 40% decrease in opiate medication required for adequate pain control. In traditional practice, these two patients would likely receive the same pain medication on the same schedule. These data suggests that different opiate requirements may allow adjusted dosing based upon specific patient characteristics.

Because patients of increasing age display decreased drug metabolism, excretion and physical reserve, it is paramount to be mindful of the special circumstances surrounding the prescription of opiates to the elderly [37]. Research suggests that pain threshold may increase as a person ages [38], which may account for the decreased opiate requirement demonstrated by our data.

As noted above, there was an unexpected significant difference in age between the intervention and placebo groups in this study. There is no obvious explanation for this finding other than chance as the study was randomized. When corrected for age, the primary outcome of total 24-hour opiate consumption compared between the two groups approached significance with the TAP block group using an average of 11.1 mg less systemic opiates than the placebo group ($p = 0.08$). While the difference did not reach statistical significance, this may nonetheless represent a clinically significant decrease in opiate use. The trend also fits with the above-described relationships between age, BMI, and opiate requirement. The combination of these data may aid clinicians in making more appropriate dosing decisions regarding opiate medications to facilitate improved recovery and decreased incidence of dependence on these highly addictive substances.

The major strength of this study is the randomized, double-blinded, placebo-controlled design. The research protocol was generalizable to a gynecologic oncology population including those with BMI >35 kg/m^2, only three surgeons performed the surgeries so that perioperative care was similar across the study population, and objective measures were used for the primary outcome and many of the secondary outcomes. This is also the first report of using TAP blocks specifically for robotic surgery.

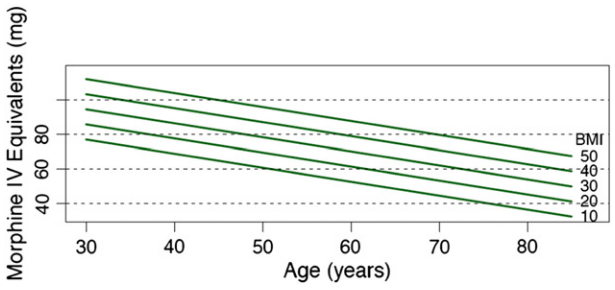

Fig. 4. Nomogram for narcotic consumption by age and BMI.

There are also limitations which merit mention. While methodologically sound to assess for impact on assistant-port pain, this study only assessed the ability of a unilateral block to decrease postoperative pain rather than a bilateral block. The unilateral block was chosen for this study for two reasons. First is because the assistant port was the only site requiring deep fascial closure which is known to cause increased postoperative pain [13]. Secondly, since the hypothesis was that a regional block would decrease the amount of pain at this site, the unilateral block was selected also to decrease anesthesiologist time and resources.

While the study groups were adequately powered to evaluate the hypothesized difference, the sample size remained relatively small and may not have been adequate to capture the smallest clinically important difference in opiate use. Also, data were collected from a single institution which led to significant homogeneity in the subjects.

Future areas of study should include evaluation of pain based upon assistant port location or for surgeries when no assistant port is used, evaluation in a more diverse patient population, and work to validate the associations between BMI, age and postoperative opiate use.

In conclusion, the unilateral TAP block does not significantly decrease total 24-hour opiate use or postoperative pain scores following robotic-assisted laparoscopic surgery for gynecology malignancy. We were unable to detect a difference in inpatient or outpatient pain scores, length of hospital stay, postoperative complications, or patient reported satisfaction. TAP block placement appears feasible and safe in obese populations while its analgesic effectiveness remains uncertain. This novel data set reveals a strong negative correlation between age and total opiate use, as well as a reciprocal strong positive correlation between BMI and total opiate use. These data have been organized into a nomogram that may assist clinicians in appropriate and safe postoperative dosing of opiate pain medications.

Conflict of interest statement

The authors indicated no potential conflicts of interest or financial disclosures. All authors have read and approved the manuscript.

IRB approval and informed consent

The study was approved by the human subjects committee prior to the research being conducted at each institution and all participants provided written informed consent.

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