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# A randomized trial comparing deep and moderate neuromuscular blockade in patients undergoing ambulatory gynecologic laparoscopy

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## Abstract

**Background and aims:** Deep neuromuscular blockade (NMB) is known to improve surgical conditions, compared to moderate neuromuscular blockade (NMB), which is expected to improve postoperative quality of recovery (QOR). However, it is unknown whether deep NMB improves postoperative QOR in ambulatory gynecologic laparoscopy. Therefore, we compared the effects of deep and moderate NMB on postoperative QOR in ambulatory gynecologic laparoscopy.

**Methodology:** We included 80 female in this study. They were randomized into 2 equal groups: deep NMB (dNMB) and moderate NMB (mNMB) at constant pneumoperitoneum pressure of 12 mmHg. The primary outcome was QOR-40 at 24 h, and the secondary outcomes were duration of surgery, surgical rating scale (SRS) score, time to home discharge readiness, pain scores, and tramadol consumption.

**Results:** The SRS scores were significantly higher in dNMB group, compared with mNMB. Mean (95% CI) SRS scores in deep NMB were 4.55 (4.52-4.58) versus 4.15 (4.11-4.19) in moderate NMB, $p = 0.03$. However, there was no significant difference between the two groups in the QoR-40 scores, and other secondary outcomes.

**Conclusion:** We found no difference between deep and moderate NMB on postoperative QOR after ambulatory gynecologic laparoscopy. Therefore, deep NMB during ambulatory gynecologic laparoscopy may be unnecessary, at least in non-obese patients.

**Trial registration:** This study was registered at www.clinicaltrials.gov (NCT04105764).

**Keywords:** Gynecologic laparoscopy, Neuromuscular blockade, Ambulatory surgery, Postoperative quality of recovery, Surgical conditions

## Introduction

Gynecologic laparoscopic surgeries are commonly performed as an ambulatory basis (Lee 2017). One of the principal endpoints after ambulatory surgery is the postoperative quality of recovery (QOR). However, the pneumoperitoneum created during laparoscopy may cause postoperative pain (Madsen et al. 2016), which could result in poor QOR (Özdemir-van Brunschot et al. 2017). Poor QOR leads to prolonged hospital stay (Myles et al. 2000).

Deep NMB is known to improve quality surgical conditions and postoperative pain (Madsen et al. 2015; Donatsky et al. 2013).

Previous studies (Özdemir-van Brunschot et al. 2017; Kim et al. 2019) found that deep NMB does not improve the QOR after inpatient laparoscopic gastrectomy and nephrectomy. However, it is unknown whether deep NMB improves QOR in ambulatory gynecologic laparoscopy.

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Therefore, we compared the effects of deep and moderate NMB on postoperative QOR in ambulatory gynecologic laparoscopy. The primary outcome was QOR-40 at 24 h, and the secondary outcomes were duration of surgery, surgical rating scale (SRS) score, time to home discharge readiness, pain scores, and tramadol consumption.

## Methodology

This prospective, randomized, double-blind study was carried out after approval of the local hospital ethical committee (05/11/2016) and was registered at ClinicalTrials.gov: NCT04105764. All patients provided written informed consent. The study included 80 female of ASA PS I or II, aged 21-60 years, undergoing ambulatory gynecologic laparoscopy. Patients with BMI ≥ 30 kg $m^{-2}$, neuromuscular disease, and allergy to rocuronium were excluded.

Patients were randomized to one of two equal groups: deep NMB (dNMB) or moderate NMB (mNMB). Each group included 40 patients. Randomization was done by an independent investigator using a computer-generated table and delivered in number-coded, sealed envelopes. With the exception of attending anesthesiologists, the patient, surgeon, and outcome assessors were blinded for group allocation.

In addition to standard monitors, a bispectral index (BSI) and an acceleromyography were used to monitor the depth of anesthesia and depth of NMB, respectively.

Anesthesia was standard in both groups with the exception of NMB maintenance. Anesthesia was induced with fentanyl 1 μg $kg^{-1}$ and propofol 2 mg $kg^{-1}$. Following loss of consciousness, acceleromyography was caliberated as described by Fuchs-Buder et al. (Fuchs-Buder et al. 2007). Rocuronium 0.5 mg $kg^{-1}$ IV was given to facilitate tracheal intubation. Lungs were mechanically ventilated to maintain end -tidal CO2 between 35-45 mmHg.

Anesthesia was maintained with oxygen and air mixture (Fio2 = 0.4). Sevoflurane to maintain the BSI between 40 and 60. Remifentanil infusion 0.1 μg/kg/min to maintain the mean arterial pressure within 20% of baseline. Rocuronium infusion was initially 0.2 mg $kg^{-1}$ $h^{-1}$, then titrated to maintain the post-tetanic count (PTC) of 1 to 2 in the dNMB group, and the train of four (TOF) of 1 to 2 in the mNMB group (Fuchs-Buder et al. 2007).

All patients received lactated ringer (LR) at a rate of 5 mL $kg^{-1}$ $h^{-1}$ ketorolac 30 mg IV and ondansetron 4 mg IV were given for postoperative analgesia, postoperative nausea, and vomiting (PONV), respectively. Temperature was maintained at 36 -37 °C using forced-air warming devices. Pneumoperitoneum pressure was maintained at a constant pressure of 12 mm Hg.

At the end of surgery, all infusions were discontinued, and NMB was reversed with either sugammadex 4 mg $kg^{-1}$ or 2 mg $kg^{-1}$ for the dNMB group and mNMB group, respectively. Extubation was done after recovery of spontaneous breathing and TOF ratio > 0.9 (Fuchs-Buder et al. 2007).

The postoperative QOR was assessed using QOR-40 score (Myles et al. 2000), which measures 5 items: physical comfort (12 items), physical independence (5 items), pain (7 items), emotional state (9 items), and psychological support (7 items). Each item is scored from 1 to 5 (1, very poor; 5, excellent). The total score ranges from 40 to 200 (40, very poor recovery; 200, excellent recovery). At the admission to the hospital, all patients were provided with a QoR-40 score and instructed to answer the questionnaire at 24 h after the surgery.

The surgical conditions were assessed by surgeon using the SRS at the end of surgery. The SRS is a 5-point ranging from 1 to 5 (1, extremely poor conditions; 5, optimal conditions) (Table 1) (Martini et al. 2013).

In the PACU, abdominal pain at rest were assessed using a 10-point numeric rating pain scale (NRPS), ranging from 0 to 10 (0, no pain; 10, worst imaginable pain). Tramadol 20 mg IV was administered to maintain NPRS score < 4 or at patient request for analgesia. PONV was treated with 10 mg IV metoclopramide, followed by 4 mg IV ondansetron if necessary. Time to home discharge readiness was assessed by using the post anesthesia discharge scoring system (PADSS) (Marshall and Chung 1999) every 15 min until patients met discharge criteria. Patients with PADSS score ≥ 9 were eligible for discharge.

At discharge, all patients were instructed to record the highest NRPS scores (abdominal pain at rest and referred shoulder pain) and tramadol consumption. Postoperative pain was treated with oral ibuprofen 400 mg every 6 h and a combination of oral tramadol (37.5 mg) with acetaminophen (325 mg for NRPS score > 3). Patients were contacted by telephone at 24 h after the surgery were questioned regarding the highest abdominal and referred shoulder pain scores, analgesic consumption, and the QOR-40 questionnaire.

**Table 1** Leiden-surgical rating scale

1. Extremely poor conditions: The surgeon is unable to work due to coughing or due to the inability to obtain a visible laparoscopic field due to inadequate muscle relaxation.
2. Poor conditions: There is a visible laparoscopic field, but the surgeon is severely hampered by inadequate muscle relaxation with continuous muscle contractions, movements, or both with the hazard of tissue damage.
3. Acceptable conditions: There is a wide visible laparoscopic field but muscle contractions, movements or both occur regularly causing some interference with the surgeon's work.
4. Good conditions: There is a wide laparoscopic working field with sporadic muscle contractions, movements or both.
5. Optimal conditions: There is a wide visible laparoscopic working field without any movement or contractions.

*NMBA* neuromuscular blocking agent

The primary outcome of this study was the total QOR-40 at 24 h. The secondary outcomes were the duration of surgery, surgical rating scale (SRS) score, time to home discharge readiness, pain scores, and tramadol consumption.

### Statistical analysis

The primary outcome of this study was the total postoperative QOR-40. Based on previous study, the minimal clinically important difference is 10 for QOR-40 (9). With a standard deviation of 14, a sample size of 32 patients per group would be required to detect this difference at a power of 80% and a significance level of 5%. A total sample size of 80 patients were included to allow for a dropout rate of 20%, with 40 patients in each group.

Statistical analyses were performed using the SPSS software version 20. Data are presented as number, mean (SD), median (range), or mean (95% CI). Nominal data were compared using chi-square test. Parametric and non-parametric data were compared using independent student's *t* test and Mann-Whitney *U* test, respectively. *P* value < 0.05 was considered significant

## Results

We studied 80 female (Fig. 1). The demographic and anesthetic data are shown in Table 2. With the exception of rocuronium requirement, there was no significant difference between the two groups as regards demographic data and and anesthetic requirements.

QoR-40 scores at 24 h between the two groups (Table 3). Median total QOR-40 in dNMB group was 170 (range 150-183) versus 168 (range 155-188) in mNMB group, $p = 0.72$.

The SRS scores was significantly higher in dNMB group, compared with mNMB. Mean (95% CI) SRS scores in dNMB were 4.3 (4.03-4.57) versus 3.9 (3.64-4.16) in mNMB, $p = 0.028$ (Table 4). Patients distribution over the SRS scores in both groups are shown in Fig. 2, showing that good and optimal surgical conditions were 2 (30%) and 21 (52.5%) patients in dNMB group, compared with 21 (52.5%) and 9 (22.5%) patients in mNMB group, $p = 0.007$.

There was no significant difference in duration of surgery, time to home discharge readiness, pain scores, or tramadol consumption between the two groups (Table 4).

## Discussion

In this study, there was no significant difference in the total and subcomponents postoperative QOR at 24 h between deep and moderate NMB. However, deep NMB significantly improved surgical conditions in patients undergoing ambulatory gynecologic laparoscopy.

Few studies have investigated the effects of deep and moderate NMB on postoperative QOR. In one such study, Özdemir et al. (Özdemir-van Brunschot et al. 2017) found that deep NMB does not improve the QOR after laparoscopic nephrectomy under low [6 mmHg] and constant [12 mmHg] pneumoperitoneum pressure.

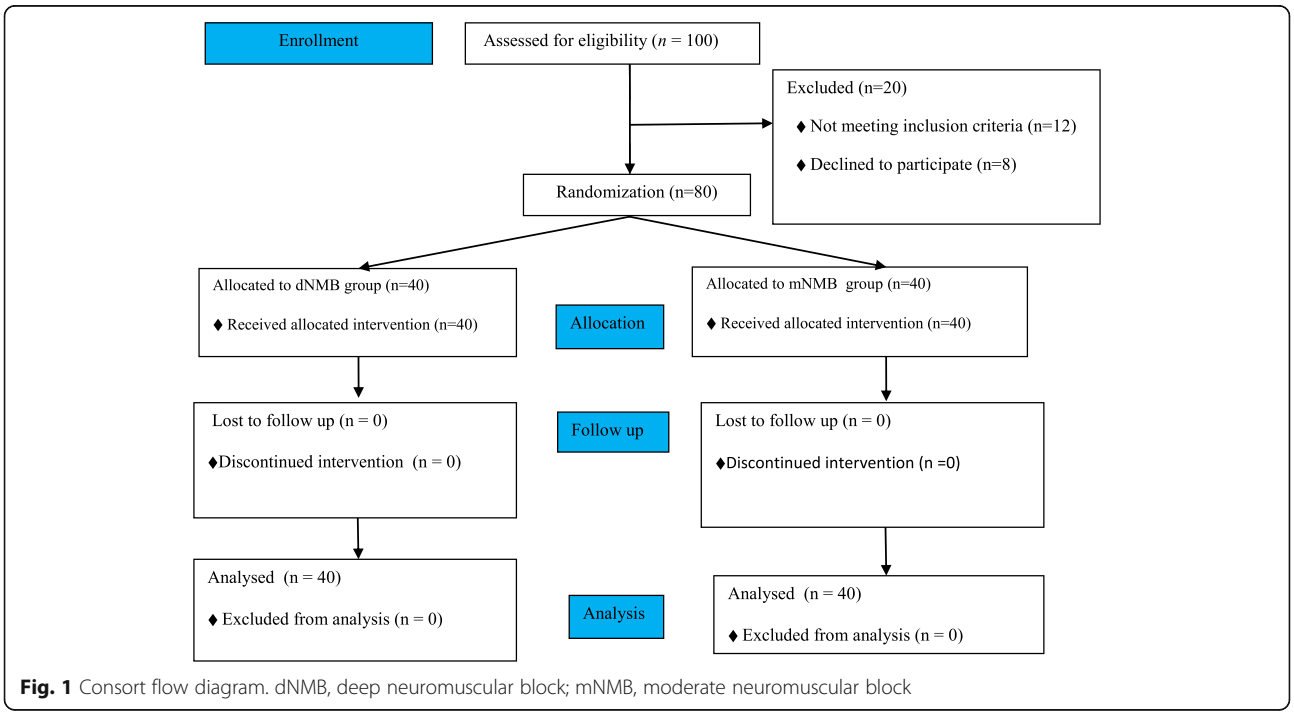


**Fig. 1** Consort flow diagram. dNMB, deep neuromuscular block; mNMB, moderate neuromuscular block

**Table 2** The demographic and anesthetic data between the groups. Values are mean (SD), median (range), or numbers

| | dNMB group ($n$ = 40) | mNMB group ($n$ = 40) | $P$ value |
|---|---|---|---|
| Age (year) | 43.5 (21-60) | 44 (27-60) | 0.72 |
| ASA grade I/II | 28/12 | 23/17 | 0.35 |
| Previous abdominal surgery (yes/no) | 13/27 | 10/30 | 0.80 |
| Body mass index (kg $m^{-2}$) | 26.0 (2.3) | 25.8 (1.6) | 0.65 |
| Type of laparoscopic gynecologic surgery | | | |
| • Excision of ovarian cyst | 12 | 14 | 0.81 |
| • Salpingo-oophorectomy | 13 | 16 | 0.64 |
| • Diagnostic laparoscopy | 10 | 7 | 0.31 |
| • Tubal ligation | 5 | 3 | 0.48 |
| Total dose remifentanil (μg) | 555 (490-700) | 567.5 (500-720) | 0.28 |
| Total dose rocuronium (mg $kg^{-1}$) | 0.96 (0.21) | 0.69 (0.11) | < 0.001* |
| Anesthesia duration (min) | 64.3 (10.2) | 66.57 (9.9) | 0.33 |

Abbreviations: *dNMB* deep neuromuscular block, *mNMB* moderate neuromuscular block, *ASA PS* American Society of Anesthesiologists physical status
*P < 0.05 considered significant

Similarly, Kim et al. (Kim et al. 2019), found that deep NMB does not improve the QOR after laparoscopic gastrectomy under constant [12 mmHg] pneumoperitoneum pressure. In line with these studies, the postoperative QOR in our study was similar between dNMB and mNMB groups.

Many studies (Van Wijk et al. 2015; Blobner et al. 2015; Rosenberg et al. 2017) have investigated the effect of deep NMB on surgical conditions in laparoscopic surgery. The use of deep NMB was reported to be effective in improving the surgical conditions in patients undergoing laparoscopic surgery. One study compared IAP (intraabdominal pressure) in laparoscopic cholecystectomy who received deep NMB or no block demonstrated that deep NMB could lower the intra-abdominal pressure (Van Wijk et al. 2015). Another study found that deep NMB, compared to no block improves surgical conditions in laparoscopic cholecystectomy (Blobner et al. 2015). In contrast, one study reported that deep NMB, compared to no block minimally increased the surgical space (Myles et al. 2000). These studies could induce a bias because they compared the superiority of deep NMB over a shallow or no NMB on surgical conditions, not the added value of routine use of deep NMB over moderate NMB.

The surgical conditions depend on the pneumoperitoneum pressure and the depth of NMB. Therefore, we maintained constant [12 mmHg] pneumoperitoneum pressure to rule out the effect of pneumoperitoneum pressure on surgical conditions (Rosenberg et al. 2017; Vijayaraghavan et al. 2014), and postoperative pain (Vijayaraghavan et al. 2014; Koo et al. 2016; Perrakis et al. 2003) which may affect the QOR negatively. Previous studies (Martini et al. 2013; Rosenberg et al. 2017; Vijayaraghavan et al. 2014; Perrakis et al. 2003) compared between deep and moderate NMB on surgical conditions under different pneumoperitoneum pressure, this may be a source of bias. In addition, deep NMB with low pneumoperitoneum pressure could not replace constant pneumoperitoneum pressure for better surgical conditions and associated with surgeon discomfort. Previous studies found that deep NMB with low pneumoperitoneum pressure [8 mmHg] marginally improved the quality of surgical conditions (Koo et al. 2016), and associated with surgeon dissatisfaction (Atkinson et al. 2017) compared with moderate NMB with constant pneumoperitoneum pressure [12 mmHg].

**Table 3** Subcomponents and total postoperative QOR-40 score. Values are median (range)

| | dNMB group ($n$ = 40) | mNMB group ($n$ = 40) | $P$ value |
|---|---|---|---|
| Pain | 31 (25-35) | 30 (28-35) | 0.79 |
| Comfort | 54 (45-56) | 53 (48-58) | 0.95 |
| Independence | 22 (20-25 | 21 (19-25) | 0.55 |
| Emotional | 37 (35-39) | 37 (35-42) | 0.25 |
| Psych | 26 (25-28) | 27 (25-28) | 0.34 |
| Total QOR-40 score | 170 (150-183) | 168 (155-188) | 0.72 |

Abbreviations: *QOR* quality of recovery, *dNMB* deep neuromuscular block, *mNMB* moderate neuromuscular block

**Table 4** Duration of surgery, surgical rating scale score and postoperative recovery, and medication use between the groups. Values are mean (95% CI), median (range), or numbers (proportion)

| | dNMB group ($n$ = 40) | mNMB group ($n$ = 40) | $P$ value |
|---|---|---|---|
| Duration of surgery (min) | 58.0 (6.0) | 60.6 (7.5) | 0.09 |
| Mean (95% CI) surgical rating scale score | 4.3 (4.03-5.57) | 3.9 (3.64-4.16) | 0.028 |
| Time to home discharge readiness (min) | 80.6 (15.5) | 82.9 (18.3) | 0.64 |
| Overall highest abdominal NRPS | | | |
| • At PACU | 4.0 (3.0-6.0) | 4.0 (3.0-7.0) | 0.78 |
| • At 24 h postoperative | 4.0 (1.0-5.0) | 4.0 (2.0-5.0) | 0.68 |
| Overall highest Referred Shoulder NRPS at 24 h postoperative | 1.0 (0.0-3.0) | 1.0 (0.0-4.0) | 0.23 |
| 24 h tramadol consumption | 98 (62.8) | 108.5 (76.2) | 0.5 |
| Antiemetic requirement, $n$ (%) | | | |
| • 0 | 25 | 21 | |
| • 1 | 9 | 7 | |
| • ≥ 2 | 6 | 12 | 0.28 |

Abbreviations: *dNMB* deep neuromuscular block, *mNMB* moderate neuromuscular block, *NRPS* numeric rating pain scale, *PACU* post anesthesia care unit

Our results are consistent with a previous study (Martini et al. 2013), which found that deep NMB improves the quality of surgical conditions. This is in contrast to a study (Baete et al. 2017) which found that no difference in surgical conditions between deep and moderate NMB, a constant [18 mmHg] pneumoperitoneum pressure in bariatric surgery. A possible reason for the discrepancy with our results could be the high pneumoperitoneum pressure applied by the authors, which above the recommended pneumoperitoneum pressure < 15 mmHg (Atkinson et al. 2017). Because high IAP may counteract the effects of moderate NMB, and the improvement in the surgical conditions has been obtained naturally.

Our results are in line with previous studies, which demonstrating that no difference between deep and moderate NMB in duration of surgery (Martini et al. 2013), hospital discharge time (Bruintjes et al. 2017), and postoperative pain [10, 21]. In contrast, one study (Donatsky et al. 2013) found that low pneumoperitoneum pressure (≤ 10 mmHg) results in decreased shoulder pain; however, there is still controversy if a low pneumoperitoneum pressure decreased postoperative pain (Vijayaraghavan et al. 2014).

Some limitations should be considered. First, the duration of surgery, time to home discharge readiness, pain scores, and tramadol consumption were similar between groups. However, the sample size calculation of our study was not based on these outcomes. Second, we did not compare the baseline QOR-40 score.

## Conclusion

We found no difference between deep and moderate NMB on postoperative QOR after ambulatory gynecologic laparoscopy. Therefore, deep NMB during ambulatory gynecologic laparoscopy may be unnecessary, at least in non-obese patients.

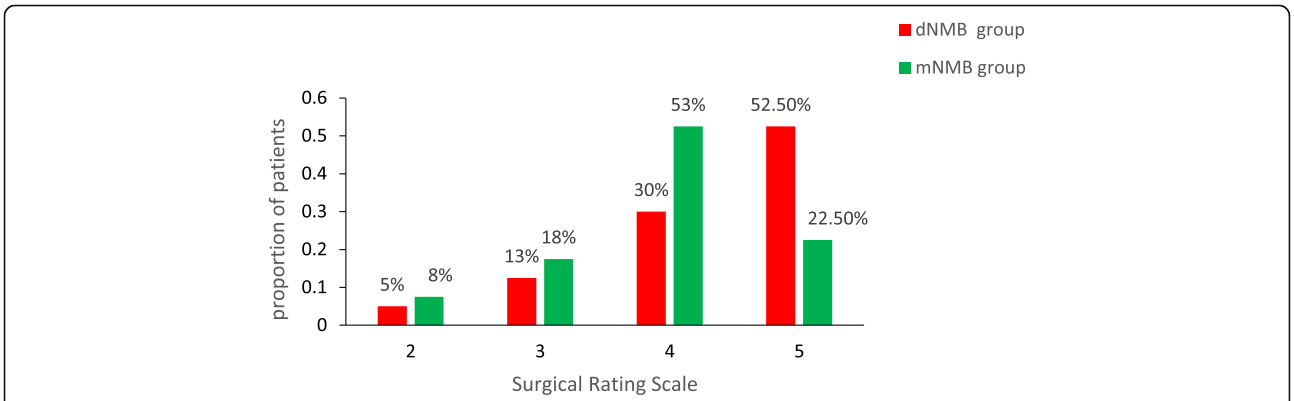


**Fig. 2** Proportion of patients distribution over surgical rating scale (SRS) scores in both groups. dNMB, deep neuromuscular block; mNMB, moderate neuromuscular block

**Abbreviations**
NMB: Neuromuscular blockade; QOR: Quality of recovery; dNMB: Deep NMB; mNMB: Moderate NMB; SRS: Surgical rating scale; BSI: Bispectral index; LR: Lactated Ringer; PTC: Post-tetanic count; TOF: Train of four; PONV: Post-operative nausea and vomiting; PADSS: Post-anesthesia discharge scoring system; NRPS: Numeric rating pain scale; IAP: Intraabdominal pressure

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**Author's contributions**
WB: concept, design, definition of intellectual content, literature search, experimental studies, data acquisition, data analysis, statistical analysis, manuscript preparation and manuscript editing, and manuscript review. The author(s) read and approved the final manuscript.

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**Availability of data and materials**
Data supporting findings can be obtained from the corresponding author.

**Ethics approval and consent to participate**
The study protocol was approved by Hospital Elite day surgery ((05/11/2016), and the study was conducted in accordance with the Helsinki declaration. A written informed consent from the participants was given before the study.

**Consent for publication**
Not applicable

**Competing interests**
The author declares that he has no competing interests.

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## Publisher's Note