Laparoscopic Surgery and Muscle Relaxants: Is Deep Block Helpful?

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It has been hypothesized that providing deep neuromuscular block (a posttetanic count of 1 or more, but a train-of-four [TOF] count of zero) when compared with moderate block (TOF counts of 1–3) for laparoscopic surgery would allow for the use of lower inflation pressures while optimizing surgical space and enhancing patient safety. We conducted a literature search on 6 different medical databases using 3 search strategies in each database in an attempt to find data substantiating this proposition. In addition, we studied the reference lists of the articles retrieved in the search and of other relevant articles known to the authors. There is some evidence that maintaining low inflation pressures during intra-abdominal laparoscopic surgery may reduce postoperative pain. Unfortunately most of the studies that come to these conclusions give few if any details as to the anesthetic protocol or the management of neuromuscular block. Performing laparoscopic surgery under low versus standard pressure pneumoperitoneum is associated with no difference in outcome with respect to surgical morbidity, conversion to open cholecystectomy, hemodynamic effects, length of hospital stay, or patient satisfaction. There is a limit to what deep neuromuscular block can achieve. Attempts to perform laparoscopic cholecystectomy at an inflation pressure of 8 mm Hg are associated with a 40% failure rate even at posttetanic counts of 1 or less. Well-designed studies that ask the question "is deep block superior to moderate block vis-à-vis surgical operating conditions" are essentially nonexistent. Without exception, all the peer-reviewed studies we uncovered which state that they investigated this issue have such serious flaws in their protocols that the authors' conclusions are suspect. However, there is evidence that abdominal compliance was not increased by a significant amount when deep block was established when compared with moderate neuromuscular block. Maintenance of deep block for the duration of the pneumoperitoneum presents a problem for clinicians who do not have access to sugammadex. Reversal of block with neostigmine at a time when no response to TOF stimulation can be elicited is slow and incomplete and increases the potential for postoperative residual neuromuscular block. The obligatory addition of sugammadex to any anesthetic protocol based on the continuous maintenance of deep block is not without associated caveats. First, monitoring of neuromuscular function is still essential and second, antagonism of deep block necessitates doses of sugammadex of ≥4.0 mg/kg. Thus, maintenance of deep block has substantial economic repercussions. There are little objective data to support the proposition that deep neuromuscular block (when compared with less intense block; TOF counts of 1–3) contributes to better patient outcome or improves surgical operating conditions. (Anesth Analg 2015;120:51–8)

In the clinical literature, there is no consensus as to the meaning of terms such as "deep" or "moderate" neuromuscular block. To avoid confusion, we have defined depth of block as follows:

- Extreme block: a posttetanic count (PTC) of zero.
- Deep block: a PTC 1 or more; but a train-of-four (TOF) count of zero. Synonymous with profound or intense block.
- Moderate block: a TOF count of 1–3.
- Shallow block: a TOF count of 4 with fade.

There are clearly places in the practice of anesthesia where producing deep neuromuscular block is advantageous. Obtaining conditions favorable to tracheal intubation is an obvious example.[1] There are also situations where maintaining deep block until the very end of a surgical procedure may enhance patient safety and decrease morbidity. Examples might include open-eye surgery under general anesthesia and intracranial surgery.[2,3] However, as a general rule, because of the limited ability of anticholinesterases to antagonize deep nondepolarizing block, most clinicians wisely attempt to avoid deep block as the end of surgery approaches. More recently with the availability of sugammadex as an alternative to neostigmine, there has been renewed interest in other potential indications for the intraoperative maintenance of deep block, and especially on the potential advantages of maintaining

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[a]Available at: http://ispub.com/IJOS/7/2/7856. Accessed September 25, 2014.

[b]Available at: http://www.medscape.org/viewarticle/818024. Accessed September 25, 2014.

[c]Available at: http://www.medscape.org/viewarticle/814476. Accessed September 25, 2014.

[d]Available at: http://www.medscape.org/viewarticle/810637_transcript. Accessed September 25, 2014.

[e]Available at: http://publicationslist.org/data/jan.mulier/ref-357/Best%20practice%20in%20NMB%20management%209%2020121%20FARC%20ST%20Petersburg.pdf. Accessed September 25, 2014.

[f]Available at: http://publicationslist.org/data/jan.mulier/ref-355/deep%20block%20and%20enhanced%20surgical%20view%2022%206%202012%20EAES%20.pdf. Accessed September 25, 2014.

deep neuromuscular block for laparoscopic surgery.[4–9] Within the last 2 to 3 years, there has also been a flurry of education videos and conference panels on exactly this subject.[a–f]

There is some evidence that maintaining low inflation pressures during intra-abdominal laparoscopic surgery may reduce postoperative pain,[10] and many surgeons certainly believe that deep neuromuscular block improves the quality of surgical conditions compared with moderate block and thus may contribute to less postoperative morbidity. Unfortunately, the relationship between deep block and an optimized surgical space is now first being explored. In this review, we will attempt to evaluate the available data supporting the premise that deep neuromuscular block for laparoscopic surgery has benefits for both the patient and the surgeon.

SEARCH METHODOLOGY

With the help of a health science librarian, a literature search was conducted on Ovid Medline (from 1996 to present), Ovid Excerpta Medica Database (EMBASE, from 1974 to present), Scopus (from 1966 to present), Cochrane database, Web of Science—SciSearch (from 1966 to present), Web of Science—Conference Proceedings (from 1990 to present), Web of Science—Biosis Previews (from 1969 to present), and Web of Science—Biosis Citation Index (from 1969 to present). Last update was on June 10, 2014. The number of articles identified in each database was 148, 194, 320, 10, 246, 21, 62, and 62, respectively. The 3 search strategies used in each database search were (1) Laparoscopy [index term] or "laparoscop…" [keyword] AND Neuromuscular Blockade [index term] or "neuromuscul…" adj "block…" [keywords] AND "deep…" or "profound" or "intense" or "extreme," (2) Laparoscopy [index term] or "laparoscop…" [keyword] AND "abdominal" within 2 words of "relax…" [keywords], and (3) Laparoscopy [index term] or "laparoscop…" [keyword] AND "low…" within 2 words of "pressure" or "high…" within 2 words of "pressure" AND "pneumoperitoneum." The search was not restricted to the English language. In addition, we studied the reference lists of the articles retrieved in the search and of other relevant articles known to the authors.

The 2 authors independently screened the titles and abstracts of all papers identified in our search. We retrieved and assessed the full manuscripts of what we considered to be potentially relevant articles. We only included studies that were published in peer-reviewed journals, and to the best of our knowledge, we did not cite studies from "pay to publish" journals. Although we cite several studies from surgical journals related to operating conditions at high versus low insufflation pressures, we rejected many because they were simply repetitious or had no relevance to our central question: Does deep neuromuscular block for laparoscopy have potential benefits for surgeon and patient when compared to more moderate block? We also cite 1 recent abstract because it had in our opinion extraordinary relevance to this question.

NONLAPAROSCOPIC SURGERY: ARE RELAXANTS ALWAYS NECESSARY?

Satisfactory surgical conditions are the end product of multiple factors that may range from the level of general anesthesia administered to the personal relationship between the surgeon and the anesthesiologist. This is equally true for both conventional and minimally invasive surgery. We believe that lessons learned from general surgery have applicability to laparoscopic surgery as well.

A 1995 article by Tammisto and Olkkola[11] is instructive. They studied the intensity of neuromuscular block that was adequate for surgical relaxation at different end-tidal levels of enflurane during N_2O–O_2–fentanyl anesthesia in 30 patients undergoing upper abdominal surgery. All patients received vecuronium 0.07 mg/kg to facilitate tracheal intubation and thereafter the neuromuscular block was allowed to dissipate. Patients were then divided into 3 groups of 10 each, where end-tidal enflurane was maintained at 0.30, 0.60, or 1.2 percent. Additional increments of vecuronium were administered if (1) the surgeon complained about relaxation; (2) there were motor responses, e.g., coughing, bucking; or (3) there was a 30% increase in spontaneous electromyograph (EMG) activity in the muscles of the neck.[12] The authors found a linear relationship between end-tidal concentration of enflurane and the degree of neuromuscular block required to produce adequate surgical muscle relaxation during abdominal surgery. As anesthesia deepened, less intense block was required.

Even major surgery does not necessarily require the continuous administration of neuromuscular blocking drugs. Gueret et al.[13] report a series of 87 consecutive patients undergoing cardiac surgery in which no further relaxants were required after an intubation dose of either atracurium or cisatracurium. The absence of continuous neuromuscular block did not have any negative impact on surgery and neither diaphragmatic contraction nor patient movement was an issue. Surgeons were not concerned by the absence of neuromuscular blockade, and at the end of surgery TOF ratios recovered spontaneously to 0.90 or above in all of their patients.

Similarly, Li et al.[14] question the need for neuromuscular blocking drugs during spinal surgery. They studied 86 patients under total IV anesthesia (TIVA) (average bispectral index = 50; range 40–60). In all patients, succinylcholine 2.0 mg/kg was used to facilitate tracheal intubation. Upon return of neuromuscular function, half of the subjects received atracurium 0.50 mg/kg (the frequency of or use of incremental doses was not reported). None of the surgeons realized that half of the patients had not received additional neuromuscular blocking drugs, and no patient in the control group required relaxant administration because of unsatisfactory operating conditions.

A rigorous and well-designed study of the need for neuromuscular block during abdominal surgery comes from King et al.[15] They studied 124 patients scheduled for radical prostatectomy. In all patients, anesthesia was induced with sodium thiopental and tracheal intubation facilitated with succinylcholine. Anesthesia was maintained with an average end-tidal concentration of 1.3% isoflurane and a continuous infusion of fentanyl. Patients were vigorously hyperventilated (end-tidal pCO_2 values of 26 ± 3 mm Hg). A mechanomyographic transducer was attached to the thumb for evoked force measurements of neuromuscular function in all patients. Both the anesthesia care team and the surgical team were blinded to this assessment by draping the hand. At this point, patients were divided into 2 groups. In the relaxant group, vecuronium 0.10 mg/kg

was administered. In the placebo group, patients received a bolus of saline. After abdominal fascia was incised, surgeons were asked to rate the surgical field on a scale of 1 (excellent) to 4 (unacceptable). Based on this rating, additional doses of either vecuronium or saline were administered. In the placebo group, a rating of 4 was followed by a rescue dose of vecuronium. The surgeons were asked to give a final field assessment at the time of fascial closure. Discontinuation of the isoflurane was at the discretion of the anesthesia care team. Seventeen of 61 patients in the placebo group (28%) required rescue doses of vecuronium. Thus, good to excellent surgical conditions for the duration of the procedure were achieved in approximately 70% of patients without the use of neuromuscular blocking drugs. The authors conclude, "These findings suggest that anesthesiologists should at least consider whether muscle relaxants should be used routinely… or whether more selective application when inadequate surgical conditions are actually present might be more appropriate."

MUSCLE RELAXANTS AND LAPAROSCOPIC SURGERY

Is There Something Special About Laparoscopic Surgery?

Perhaps anesthesia for routine abdominal laparoscopy is a special case. The rationale for promoting the use of extreme or deep neuromuscular block for laparoscopic and robotic surgeries is based on the assumption that it will improve surgical operating conditions and patient outcome while allowing lower abdominal inflation pressures to be used. Controlled ventilation would seem to be indicated because pneumoperitoneum is associated with reduced airway compliance, a decreased functional residual capacity, and increased airway pressures and carbon dioxide (CO_2) production. Thus, "common sense" would dictate that neuromuscular blocking drugs should play an important and perhaps critical role in anesthesia for abdominal laparoscopy. But is this necessarily always true?

Does Deep Neuromuscular Block Provide Better Laparoscopic Surgical Conditions Than Moderate Levels of Block?

Chassard et al.[16] studied 50 patients having laparoscopies for gynecological surgery under TIVA. Half of the patients received atracurium in doses sufficient to maintain twitch height at 10% of control as measured by EMG. The control group received no blocking drugs. Surgeons were unable to identify differences in operating conditions between the 2 groups. The authors pointed out that these results were compatible with an animal study they conducted in which they observed that high peak inspiratory airway pressures and intraabdominal pressures during laparoscopy were not affected by neuromuscular block.[17] Thus, they questioned the necessity of administering muscle relaxants in clinical anesthetic practice during laparoscopic surgery. Similarly, Putensen et al.[18] also using an animal model concluded that, "Neuromuscular blockade does not alter the elastic properties of the lungs, chest wall, or total respiratory system in mechanically ventilated pigs receiving sodium pentobarbital anesthesia to suppress spontaneous breathing efforts."

Chen et al.[19] report findings similar to Chassard et al.[17] in a larger study (n = 120) of gynecological laparoscopies also under TIVA anesthesia (remifentanil 0.25 μg/kg/min and propofol 75–125 μg/kg/min). In half the patients, a ProSeal™ laryngeal mask airway (LMA) was inserted after rocuronium 0.60 mg/kg (the authors do not make clear if incremental doses of rocuronium were ever administered or if neuromuscular function was monitored). In the remainder, the LMA was placed without relaxant facilitation. Ventilation was controlled in both groups. Satisfactory conditions for ventilation and operation were consistently achieved with and without muscle relaxants using LMAs in all patients. The authors could see no benefits (reduced operative or recovery times) in the use of neuromuscular blocking drugs for laparoscopy gynecological surgery.

Swann et al.[20] also questioned the requirement for muscle relaxant administration for gynecological laparoscopy. They studied 60 patients scheduled for very short (average duration < 15 minutes) laparoscopic procedures. Anesthesia in all subjects was induced with propofol 2.5 mg/kg and fentanyl 1.0 μg/kg. Anesthesia was maintained with 67% N_2O and enflurane 0.5% to 2.0% inspired. In half the patients, this was followed by insertion of an LMA. The remainder of subjects had an endotracheal tube placed after a 0.30 mg/kg dose of atracurium. Ventilation was spontaneous in the LMA group and controlled in the atracurium group. There were no clinically significant differences in the intraoperative conditions of the 2 groups. No adverse consequences were reported. It is unclear, however, if the authors' results are applicable to longer surgical procedures. We suspect that many clinicians would not opt for spontaneous ventilation via an LMA for laparoscopic procedures with anticipated durations of 20 to 30 minutes or more.

Williams et al.[21] also studied the necessity of neuromuscular blockade for procedures of short duration in 40 women scheduled for diagnostic laparoscopy or laparoscopic sterilization. Anesthesia in all patients was induced with propofol and fentanyl, and anesthesia was maintained with isoflurane 1% to 2% and nitrous oxide 66% in oxygen. In half the subjects, an LMA was then inserted and patients were allowed to breathe spontaneously during the procedure. In the remaining patients, endotracheal intubation was accomplished after atracurium 0.50 mg/kg. In this group, ventilation was controlled. Blinding of the surgeons was attempted by screening of the patient's airway and the anesthetic machine. However, despite this, the surgeons could identify the technique used by observing the abdominal movements of the patient. Although the surgical view was rated as similar in both groups, in 5 of 18 patients in the LMA group, the pneumoperitoneum was rated as inadequate for trocar insertion. In the atracurium group, the pneumoperitoneum was rated as adequate in all 19 cases. Thus, spontaneous ventilation via an LMA must be considered a suboptimal technique for pelvic laparoscopy. Had the authors used controlled ventilation via the LMA, perhaps their results might have been different.

A more universally applicable study comes from Paek et al.[22] They studied 56 subjects scheduled for laparoscopic pelvic surgery. In all patients, anesthesia was induced with propofol and remifentanil, and tracheal intubation

was facilitated with rocuronium 0.60 mg/kg. Anesthesia was maintained with TIVA. In half the patients (group A), incremental doses of rocuronium were given whenever the TOF count returned to 2, and block was maintained until the peritoneum was closed. In group B, no additional doses of rocuronium were administered. In this group, the fourth response to TOF stimulation returned in 72 ± 10 minutes. The total pneumoperitoneal time in both groups approximated 100 ± 20 minutes. Thus in group B, the level of block for the final 30 minutes of the pneumoperitoneum was minimal. There was no difference between groups in intraoperative hemodynamics, peak airway pressures, or arterial blood gases. "There were no occasions when difficulty, such as coughing, bucking, and any voluntary movement during the procedure, led to the withdrawal of a patient from the study. Moreover, there were no complaints from any of the participating surgeons." The authors concluded that supplemental muscle relaxants were not required for laparoscopy pelvic surgery under TIVA.

Martini et al.[5] randomized 24 patients undergoing elective laparoscopic surgery for prostatectomy or nephrectomy under TIVA to receive moderate neuromuscular block (n = 12; TOF count = 1–2) using the combination of atracurium/mivacurium, or deep neuromuscular block (n = 12; PTC = 1–2) using high-dose rocuronium. After surgery, neuromuscular block was antagonized with neostigmine (in patients in the moderate neuromuscular block group) or sugammadex (in patients in the deep neuromuscular block group). During all surgeries, 1 surgeon scored the quality of surgical conditions using a 5-point surgical rating scale ranging from 1 (extremely poor conditions) to 5 (optimal conditions). Video images were obtained and 12 anesthesiologists rated a random selection of images. On a rating scale of 1 to 5, the authors reported a mean value of 4.0 ± 0.4 during moderate and 4.7 ± 0.4 during deep neuromuscular block.

A recent study by Dubois et al.[7] also addressed this issue. The authors randomly assigned 100 women scheduled to have laparoscopic hysterectomies under 1 minimum alveolar concentration desflurane anesthesia into 2 groups. In group D (deep block; as defined by the authors), patients received rocuronium 0.60 mg/kg before tracheal intubation and top-up doses of 5 mg whenever the TOF-count (as determined by EMG) exceeded 2. In group S (shallow block), the intubation dose of rocuronium was 0.45 mg/kg and no further relaxant was administered unless surgical conditions were unacceptable. The senior surgeon in charge of the study (blinded to the EMG values) assessed the exposure of the surgical field on a 4-grade numerical scale: excellent (1), good but not optimal (2), poor but acceptable (3), or unacceptable and impossible to continue the operation (4). Multiple assessments (348 in group S; 306 in group D) were made as surgery progressed. In group S, there were 14 episodes where the surgical field score was 4. In the D group, there were no such scores. The authors concluded: "Inducing deep neuromuscular block (TOF count < 1) significantly improved surgical field scores and made it possible to completely prevent unacceptable surgical conditions." However, several points need to be remembered. First, the preceding quote notwithstanding, group D included individuals with TOF counts of 1 and 2. Thus, an unknown number of their surgical field score observations were made during moderate block, not deep block as we define it. Second, the average field scores between the S and D groups did not differ statistically (1.3 ± 0.8 vs 1.1 ± 0.4; $P > 0.10$). Half of the scores of 4 occurred at TOF ratios >0.40 (a point when no fade can be detected by tactile evaluation) and only 1 such score was associated with a TOF count <4. Thus, it was only when the TOF count was 3 or more that the surgical field score was not excellent in the shallow block group. Although the authors refer to group S as having "shallow block," that was not really the case. The average duration of surgery in that group was 74 ± 23 minutes. Within 25 minutes after rocuronium 0.45 mg, one would expect to see a TOF count of 4,[23] and by 45 minutes, twitch height was probably 90% of control.[24] Thus, for probably half the duration of surgery, the authors were comparing deep block with essentially no block at all. A more instructive study would have been a comparison of deep block with moderate block (TOF counts maintained at 1–3). The authors' results are entirely compatible with the premise that a less intense block would have produced comparable results. A study by Staehr-Rye et al.[6] raises a similar issue. The authors conclude, "Deep neuromuscular blockade was associated with surgical space conditions that were marginally better than with moderate muscle relaxation during low-pressure laparoscopic cholecystectomy." However, at a point half way through the surgical procedure, T1 in the "moderate NMB" group was 47% of control (a TOF count of 4 with fade), and at the 75% time point, T1 was 89% of control (a TOF ratio >0.40).[25] Thus, the authors were really comparing deep versus very shallow or minimal block for a considerable portion of the surgical procedure.

What is still missing from the peer-reviewed literature are studies of surgical operating conditions during deep versus moderate block at comparable levels of anesthesia and their respective effects on outcome and patient safety. However, a recent abstract by Barrio et al.[8] is a positive move in that direction. They attempted to compare the effect of 2 different levels of rocuronium-induced neuromuscular blockade on abdominal compliance (work space) during the pneumoperitoneum in 28 ASA 1 to 2 women under propofol- remifentanil anesthesia. Depth of block was monitored by acceleromyography. The volume-pressure relationship was measured twice during pneumoperitoneum establishment before surgery, once at moderate block (1–3 TOF responses) and 1 time at profound block (PTC 1–3). After the insertion of the abdominal trocar, all CO_2 introduced with the Verres needle was allowed to escape. Then, during insufflation at a flow of 1.5 L/min, the abdominal pressure was measured at delivered volumes of 1, 2, 3, and 4 liters during moderate block. After this first set of measurements, all CO_2 was again allowed to escape and the same protocol was repeated once deep block was established. Volume-pressure data were fit by a linear least-square regression to calculate the compliance and a paired t test was used for comparison. They concluded that abdominal compliance was not increased by a

significant amount when deep block was established when compared with moderate neuromuscular block.

Does Deep Neuromuscular Block Allow the Use of Lower Insufflation Pressures?

The list of undesirable physiologic consequences and potential side effects associated with pneumoperitoneum is lengthy and beyond the scope of this review.[26,27] It has been hypothesized that high insufflation pressures may exacerbate many of these effects; therefore, efforts to keep abdominal pressures at a minimum consistent with satisfactory surgical exposure may be beneficial. Because neuromuscular blocking drugs can decrease muscle tone in lightly or inadequately anesthetized patients, the hypothesis that deep neuromuscular block may allow laparoscopic surgery to proceed with lower CO_2 insufflation pressures is not unreasonable. However, we have not been able to find any clinical studies or data to substantiate this position. The surgical literature on the potential virtues of low versus high insufflation pressures that we reviewed generally provided little information on the respective studies' anesthetic protocol and often none on the management of muscle relaxant administration.

The recent article by Staehr-Rye et al.[6] demonstrates that there are limits to what even deep block can accomplish. The authors divided 48 patients scheduled for laparoscopic cholecystectomy under TIVA into 2 groups. In 25 patients, PTC was maintained at 0 to 1 responses. In 23 patients, only shallow to moderate block (as defined in the present manuscript) was maintained. The goal was to perform surgery at an inflation pressure of only 8 mm Hg. Although deep or extreme block allowed surgery to be completed with a 60% success rate (versus only 35% with less intense block), they still experienced a 40% failure rate. Even with intense block only 7 of 25 individuals (28%) were deemed to have optimal surgical space conditions during the entire procedure.

The above observations should not be interpreted to mean that muscle relaxants are never indicated. Certainly, they occupy an important place in the anesthesiologist's armamentarium. However, they should not be used as a substitute for adequate depth of anesthesia. More often than not resumption of respiratory efforts under anesthesia in the presence of 1 to 2 twitches to TOF stimulation should be viewed as an indication that the depth of anesthesia is inadequate or that minute ventilation needs to be increased.

Does the Low Pressure Pneumoperitoneum Offer Advantages over a Standard Pressure Pneumoperitoneum?

A Cochrane review[10] comparing the safety and effectiveness of low pressure (12 mm Hg) versus standard pressure (16 mm Hg) pneumoperitoneum in laparoscopic cholecystectomy (1092 patients from 21 trials) concluded that there was no difference between the 2 groups with respect to (1) surgical morbidity, (2) conversion to open cholecystectomy, (3) hemodynamic effects, (4) length of hospital stay, or (5) patient satisfaction. Operating time was about 2 minutes longer in the low pressure group than in the standard pressure group.

Oliguria is equally associated with low (10 mm Hg)[28] or standard pressure (15 mm Hg)[29] pneumoperitoneum, possibly due to reduction in renal cortical perfusion[30] and increases in plasma antidiuretic hormone levels.[31] Urinary output returned to normal levels after the release of pneumoperitoneum. Serum creatinine levels are not altered by pneumoperitoneum.[28] There is no evidence to suggest that a low pressure (10 mm Hg) pneumoperitoneum[32] would have less effect on venous hemodynamics than a standard pressure (13 to 15 mm Hg) pneumoperitoneum.[33] There is no evidence that low or standard pressure pneumoperitoneum is associated with a lower incidence of gas embolization. Gas embolization was not seen during laparoscopic partial nephrectomy with insufflation pressures of 30 mm Hg in the porcine model.[34]

Factors implicated in pain after laparoscopic surgery[35] include (1) distension-induced neurapraxia of the phrenic nerves, (2) acid intraperitoneal milieu during the operation, (3) residual intraabdominal gas after laparoscopy, (4) lack of humidity of the insufflated gas, (5) volume of the insufflated gas, (6) wound size, (7) presence of drains, and (8) sociocultural and individual factors. A clinically significant reduction in pain score is likely to result in shorter hospital stay, earlier return to normal activity and to work. However, the overall quality of evidence in this regard with respect to low pressure versus standard pressure pneumoperitoneum is equivocal.

Sandhu et al.[36] reported that there was no significant difference in shoulder pain in 140 patients undergoing elective cholecystectomy randomized to low (7 mm Hg) or standard pressure (14 mm Hg) pneumoperitoneum. Similar findings were reported by others.[37,38] In contrast, Bogani et al.[39] studied fewer patients (n = 42) undergoing laparoscopic hysterectomy and reported that the incidence of shoulder tip pain was reduced with low (8 mm Hg) as compared with standard pressure (12 mm Hg) pneumoperitoneum at 1 and 3 hours (but not 24 hours) postoperatively. There were no between-group differences in abdominal pain noted. Sarli et al.,[40] however, reported that shoulder tip pain scores after laparoscopic cholecystectomy were lower in patients randomized to low (9 mm Hg) rather than standard pressure (13 mm Hg) pneumoperitoneum at 12 and 24 hours, but not at 1, 3, 6, or 48 hours. Despite the higher incidence of shoulder pain, the analgesic requirements were not significantly different between low versus standard pressure groups in the aforementioned studies.[39,40] In a double-blind randomized controlled study, the use of low pressure (8 mm Hg) versus standard pressure (12 mm Hg) pneumoperitoneum for laparoscopic cholecystectomy was associated with significantly less postoperative pain. However, the authors noted that the use of low-pressure pneumoperitoneum was often associated with a substantial reduction in visibility and in available working space.[41] The authors hypothesized that these factors could negatively affect patient outcome in terms of increased difficulty in dissection and might result in increased risk of organ injury and operating time.

The Cochrane review[10] also concluded that low pressure pneumoperitoneum appeared to be associated with a decrease in the incidence of shoulder pain after laparoscopic cholecystectomy; however, there was no difference in the postoperative analgesic requirements between low (12 mm Hg) and standard (16 mm Hg) pressure pneumoperitoneum.

Because of the high risk of bias due to incomplete outcome data in 7 trials, it was not possible to make any conclusions about the safety of low pressure pneumoperitoneum in the Cochrane review. A very recent meta-analysis[42] also concluded that cholecystectomies performed under low pressure pneumoperitoneum were associated with a reduction in postoperative pain scores and postoperative analgesic consumption compared with those performed under standard pressure pneumoperitoneum. Donatsky et al.[43] in a systematic review of 12 papers investigating the effects of low versus high pressure pneumoperitoneum found that only half reported a reduction of shoulder pain after low pressure pneumoperitoneum. Residual CO_2 may be a contributing factor for shoulder pain. Extended assisted ventilation with an open umbilical trocar valve for 5 minutes after laparoscopic hysterectomy was found to be an effective and safe method to reduce postoperative abdominal and shoulder pain levels in patients undergoing laparoscopic hysterectomy.[44]

An article by Warlé et al.[45] demonstrates that the use of low insufflation pressures is not without potential drawbacks even in the presence of fairly deep neuromuscular block. The authors studied 20 kidney donors randomly assigned to either standard (14 mm Hg) or low (7 mm Hg) pressure laparoscopic nephrectomy. Anesthesia was maintained with IV propofol and remifentanil infusions and tracheal intubation was facilitated with rocuronium 0.80 mg/kg. In all subjects, if the TOF count exceeded 2 responses additional boluses of rocuronium 10 to 20 mg were administered. Surgery was successfully completed in both groups. The authors concluded "Our data show that low-pressure pneumoperitoneum during [laparoscopic nephrectomy] is feasible and may contribute to increased … donors' comfort during the early postoperative phase." However, skin-to-skin time in the low pressure group was significantly longer and more variable (147 ± 86 vs 111 ± 19 minutes, $P = <0.01$). Thus, low insufflation pressures apparently resulted in a less than optimal surgical field. Inferior operating conditions plus an increased duration of the procedure may be a recipe for an increased incidence of surgical complications. However, the study was probably inadequately powered ($n = 10$ per group) to address this issue.

REVERSAL OF DEEP BLOCK: CLINICAL IMPLICATIONS

As noted earlier, maintaining deep block until the termination of pneumoperitoneum is not a wise idea if antagonism with neostigmine is planned. Reversal of block with an acetylcholinesterase inhibitor at a time when no response to TOF stimulation can be elicited is slow and incomplete. When neostigmine 0.07 mg/kg is used to reverse rocuronium at a PTC of 1 to 2, the mean time to TOF ratio of 0.80 is 41 minutes (IQR = 26–56 minutes).[46] Since the average time interval from the end of pneumoperitoneum to the last skin stitch is rarely more than 15 minutes and often considerably less,[22] the potential for postoperative residual neuromuscular weakness in these circumstances is considerable. Thus, continuous maintenance of deep block during laparoscopic surgery should only be contemplated by clinicians who have access to sugammadex. However, even for those anesthesiologists fortunate enough to have this drug in their armamentarium, the obligatory addition of sugammadex to any anesthetic protocol based on the maintenance of deep block is not without associated caveats.

First, monitoring of neuromuscular function is still essential. Results from a study of Kotake et al.[47] in which intraoperative monitoring of neuromuscular block was not used are instructive. The authors studied 117 patients who were given sugammadex (2.0 to 4.0 mg/kg based on clinical signs) to reverse rocuronium-induced block. After tracheal extubation, the TOF ratio was measured by acceleromyography. The frequency of TOF values <0.90 was 4.3% (95% confidence limits 1.7%–9.4%). However, these values were not normalized and thus probably overestimate the extent of recovery. The incidence of TOF ratios <1.0 was 46% (CI 37%–56%). Finally, antagonism at PTCs of 1 to 3 necessitates a dose of sugammadex of at least 4.0 mg/kg. Thus, maintenance of deep block has important economic repercussions. The acquisition price for sugammadex approximates $100 (€73) for a 200 mg single dose vial. Adequate dosage for a 70 kg patient at a PTC of 1 to 2 would require opening 2 vials, an expenditure of $200 (€146). Consequently, the cost of the routine application of deep block for laparoscopic surgery becomes an issue of importance. This is especially true because the actual benefits of deep block may be nonexistent.

CONCLUSIONS

Although the depth of neuromuscular block is easy enough to measure objectively, there has been a paucity of research into the subject of what level of block is associated with optimal conditions for surgery. Nevertheless, work by de Jong[48,49] now almost 50 years-old deserves mention. He was able to demonstrate that when single twitch height (T1) at the hand as measured by EMG was in the range of 5% to 10% of control (equivalent to a TOF-count of 1) that 24 of 25 patients under halothane anesthesia (0.8%–1.3% inspired) were deemed to have excellent abdominal relaxation compared to only 4 of 25 when T1 was in the range of 51% to 75% (a TOF-count of 4 with fade). He concluded that "total [deep] neuromuscular block … is not a prerequisite for profound muscle relaxation, at least not in the adequately anesthetized patient." A half century later these words are no less true.

On the basis of our review of the relevant literature, there is little or no evidence to suggest that using deep block (as opposed to block of moderate degree) for laparoscopic surgery will improve surgical operating conditions. Even if deep block is maintained, it does not necessarily follow that surgeons will automatically ask for lower inflation pressures. Current practice in the United States where sugammadex is not available and deep block is not routinely practiced for laparoscopic surgery suggests that there is no pressing need to change current clinical routines.

DISCLOSURES

Name: Aaron F. Kopman, MD.
Contribution: This author helped write the manuscript.
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Name: Mohamed Naguib, MB, BCh, MSc, FCARCSI, MD.
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REFERENCES

1. Mencke T, Echternach M, Kleinschmidt S, Lux P, Barth V, Plinkert PK, Fuchs-Buder T. Laryngeal morbidity and quality of tracheal intubation: a randomized controlled trial. Anesthesiology 2003;98:1049–56
2. Werba A, Klezl M, Schramm W, Langenecker S, Müller C, Gosch M, Spiss CK. The level of neuromuscular block needed to suppress diaphragmatic movement during tracheal suction in patients with raised intracranial pressure: a study with vecuronium and atracurium. Anaesthesia 1993;48:301–3
3. Fernando PU, Viby-Mogensen J, Bonsu AK, Tamilarasan A, Muchhal KK, Lambourne A. Relationship between posttetanic count and response to carinal stimulation during vecuronium-induced neuromuscular blockade. Acta Anaesthesiol Scand 1987;31:593–6
4. Dubois PE, Mulier JP. A review of the interest of sugammadex for deep neuromuscular blockade management in Belgium. Acta Anaesthesiol Belg 2013;64:49–60
5. Martini CH, Boon M, Bevers RF, Aarts LP, Dahan A. Evaluation of surgical conditions during laparoscopic surgery in patients with moderate vs deep neuromuscular block. Br J Anaesth 2014;112:498–505
6 Staehr-Rye AK, Rasmussen LS, Rosenberg J, Juul P, Lindekaer AL, Riber C, Gätke MR. Surgical space conditions during low-pressure laparoscopic cholecystectomy with deep versus moderate neuromuscular blockade: a randomized clinical study. Anesth Analg 2014;119:1084–92
7. Dubois PE, Putz L, Jamart J, Marotta ML, Gourdin M, Donnez O. Deep neuromuscular block improves surgical conditions during laparoscopic hysterectomy: a randomised controlled trial. Eur J Anaesthesiol 2014;31:430–6
8. Barrio J, San Miguel G, Carrion JL, Pelegrin F. Does profound neuromuscular block improve abdominal compliance in laparoscopic surgery? Eur J Anaesthesiol 2013;30: e-supplement 51, page 146, Abstract 9AP3–3
9. Geldner G, Niskanen M, Laurila P, Mizikov V, Hübler M, Beck G, Rietbergen H, Nicolayenko E. A randomised controlled trial comparing sugammadex and neostigmine at different depths of neuromuscular blockade in patients undergoing laparoscopic surgery. Anaesthesia 2012;67:991–8
10. Gurusamy KS, Vaughan J, Davidson BR. Low pressure versus standard pressure pneumoperitoneum in laparoscopic cholecystectomy. Cochrane Database Syst Rev 2014;3:CD006930
11. Tammisto T, Olkkola KT. Dependence of the adequacy of muscle relaxation on the degree of neuromuscular block and depth of enflurane anesthesia during abdominal surgery. Anesth Analg 1995;80:543–7
12. Edmonds HL Jr, Paloheimo M. Computerized monitoring of the EMG and EEG during anesthesia. An evaluation of the anesthesia and brain activity monitor (ABM). Int J Clin Monit Comput 1985;1:201–10
13. Gueret G, Rossignol B, Kiss G, Wargnier JP, Miossec A, Spielman S, Arvieux CC. Is muscle relaxant necessary for cardiac surgery? Anesth Analg 2004;99:1330–3
14. Li YL, Liu YL, Xu CM, Lv XH, Wan ZH. The effects of neuromuscular blockade on operating conditions during general anesthesia for spinal surgery. J Neurosurg Anesthesiol 2014;26:45–9
15. King M, Sujirattanawimol N, Danielson DR, Hall BA, Schroeder DR, Warner DO. Requirements for muscle relaxants during radical retropubic prostatectomy. Anesthesiology 2000;93:1392–7
16. Chassard D, Bryssine B, Golfier F, Raupp C, Raudrant D, Boulétreau P. Gynecologic laparoscopy with or without curare [in French]. Ann Fr Anesth Reanim 1996;15:1013–7
17. Chassard D, Berrada K, Tournadre J, Boulétreau P. The effects of neuromuscular block on peak airway pressure and abdominal elastance during pneumoperitoneum. Anesth Analg 1996;82:525–7
18. Putensen C, León MA, Putensen-Himmer G. Effect of neuromuscular blockade on the elastic properties of the lungs, thorax, and total respiratory system in anesthetized pigs. Crit Care Med 1994;22:1976–80
19. Chen BZ, Tan L, Zhang L, Shang YC. Is muscle relaxant necessary in patients undergoing laparoscopic gynecological surgery with a ProSeal LMA™? J Clin Anesth 2013;25:32–5
20. Swann DG, Spens H, Edwards SA, Chestnut RJ. Anaesthesia for gynaecological laparoscopy–a comparison between the laryngeal mask airway and tracheal intubation. Anaesthesia 1993;48:431–4
21. Williams MT, Rice I, Ewen SP, Elliott SM. A comparison of the effect of two anaesthetic techniques on surgical conditions during gynaecological laparoscopy. Anaesthesia 2003;58:574–8
22. Paek CM, Yi JW, Lee BJ, Kang JM. No supplemental muscle relaxants are required during propofol and remifentanil total intravenous anesthesia for laparoscopic pelvic surgery. J Laparoendosc Adv Surg Tech A 2009;19:33–7
23. Wright PM, Caldwell JE, Miller RD. Onset and duration of rocuronium and succinylcholine at the adductor pollicis and laryngeal adductor muscles in anesthetized humans. Anesthesiology 1994;81:1110–5
24. Schultz P, Ibsen M, Østergaard D, Skovgaard LT. Onset and duration of action of rocuronium–from tracheal intubation, through intense block to complete recovery. Acta Anaesthesiol Scand 2001;45:612–7
25. McCoy EP, Connolly FM, Mirakhur RK, Loan PB. Nondepolarizing neuromuscular blocking drugs and train-of-four fade. Can J Anesth 1995; 42:213–6
26. Gerges FJ, Kanazi GE, Jabbour-Khoury SI. Anesthesia for laparoscopy: a review. J Clin Anesth 2006;18:67–78
27. Nguyen NT, Wolfe BM. The physiologic effects of pneumoperitoneum in the morbidly obese. Ann Surg 2005;241:219–26
28. Nishio S, Takeda H, Yokoyama M. Changes in urinary output during laparoscopic adrenalectomy. BJU Int 1999;83:944–7
29. Richards WO, Scovill W, Shin B, Reed W. Acute renal failure associated with increased intra-abdominal pressure. Ann Surg 1983;197:183–7
30. Chiu AW, Azadzoi KM, Hatzichristou DG, Siroky MB, Krane RJ, Babayan RK. Effects of intra-abdominal pressure on renal tissue perfusion during laparoscopy. J Endourol 1994;8:99–103
31. Le Roith D, Bark H, Nyska M, Glick SM. The effect of abdominal pressure on plasma antidiuretic hormone levels in the dog. J Surg Res 1982;32:65–9
32. Ido K, Suzuki T, Kimura K, Taniguchi Y, Kawamoto C, Isoda N, Nagamine N, Ioka T, Kumagai M, Hirayama Y. Lower-extremity venous stasis during laparoscopic cholecystectomy as assessed using color Doppler ultrasound. Surg Endosc 1995;9:310–3
33. Millard JA, Hill BB, Cook PS, Fenoglio ME, Stahlgren LH. Intermittent sequential pneumatic compression in prevention of venous stasis associated with pneumoperitoneum during laparoscopic cholecystectomy. Arch Surg 1993;128:914–8
34. Weld KJ, Ames CD, Landman J, Morrissey K, Connor T, Hruby G, Allaf ME, Bhayani SB. Evaluation of intra-abdominal pressures and gas embolism during laparoscopic partial nephrectomy in a porcine model. J Urol 2005;174:1457–9
35. Mouton WG, Bessell JR, Otten KT, Maddern GJ. Pain after laparoscopy. Surg Endosc 1999;13:445–8
36. Sandhu T, Yamada S, Ariyakachon V, Chakrabandhu T, Chongruksut W, Ko-iam W. Low-pressure pneumoperitoneum versus standard pneumoperitoneum in laparoscopic cholecystectomy, a prospective randomized clinical trial. Surg Endosc 2009;23:1044–7
37. Koc M, Ertan T, Tez M, Kocpinar MA, Kilic M, Gocmen E, Aslar AK. Randomized, prospective comparison of postoperative pain in low- versus high-pressure pneumoperitoneum. ANZ J Surg 2005;75:693–6
38. Chok KS, Yuen WK, Lau H, Fan ST. Prospective randomized trial on low-pressure versus standard-pressure pneumoperitoneum in outpatient laparoscopic cholecystectomy. Surg Laparosc Endosc Percutan Tech 2006;16:383–6
39. Bogani G, Uccella S, Cromi A, Serati M, Casarin J, Pinelli C, Ghezzi F. Low vs standard pneumoperitoneum pressure

during laparoscopic hysterectomy: prospective randomized trial. J Minim Invasive Gynecol 2014;21:466–71
40. Sarli L, Costi R, Sansebastiano G, Trivelli M, Roncoroni L. Prospective randomized trial of low-pressure pneumoperitoneum for reduction of shoulder-tip pain following laparoscopy. Br J Surg 2000;87:1161–5
41. Vijayaraghavan N, Sistla SC, Kundra P, Ananthanarayan PH, Karthikeyan VS, Ali SM, Sasi SP, Vikram K. Comparison of standard-pressure and low-pressure pneumoperitoneum in laparoscopic cholecystectomy: a double blinded randomized controlled study. Surg Laparosc Endosc Percutan Tech 2014;24:127–33
42. Hua J, Gong J, Yao L, Zhou B, Song Z. Low-pressure versus standard-pressure pneumoperitoneum for laparoscopic cholecystectomy: a systematic review and meta-analysis. Am J Surg 2014;208:143–50
43. Donatsky AM, Bjerrum F, Gögenur I. Surgical techniques to minimize shoulder pain after laparoscopic cholecystectomy. A systematic review. Surg Endosc 2013;27:2275–82
44. Radosa JC, Radosa MP, Mavrova R, Rody A, Juhasz-Böss I, Bardens D, Brün K, Solomayer EF, Baum S. Five minutes of extended assisted ventilation with an open umbilical trocar valve significantly reduces postoperative abdominal and shoulder pain in patients undergoing laparoscopic hysterectomy. Eur J Obstet Gynecol Reprod Biol 2013;171:122–7
45. Warlé MC, Berkers AW, Langenhuijsen JF, van der Jagt MF, Dooper PM, Kloke HJ, Pilzecker D, Renes SH, Wever KE, Hoitsma AJ, van der Vliet JA, D'Ancona FC. Low-pressure pneumoperitoneum during laparoscopic donor nephrectomy to optimize live donors' comfort. Clin Transplant 2013;27:E478–83
46. Jones RK, Caldwell JE, Brull SJ, Soto RG. Reversal of profound rocuronium-induced blockade with sugammadex: a randomized comparison with neostigmine. Anesthesiology 2008;109:816–24
47. Kotake Y, Ochiai R, Suzuki T, Ogawa S, Takagi S, Ozaki M, Nakatsuka I, Takeda J. Reversal with sugammadex in the absence of monitoring did not preclude residual neuromuscular block. Anesth Analg 2013;117:345–51
48. De Jong RH. Controlled relaxation. I. Quantitation of electromyogram with abdominal relaxation. JAMA 1966;197:393–5
49. De Jong RH. Controlled relaxation. II. Clinical management of muscle-relaxant administration. JAMA 1966;198:1163–6

0.7 units (4.7 ± 0.4 vs 4.0 ± 0.4, respectively). Furthermore, a potential weakness of this protocol was its small sample size (n = 12 per group). The rating scale used is, at best, a surrogate marker. The study did not find any differences in patient outcome. In fact, to the best of our knowledge, no study has identified that maintaining deep neuromuscular blockade improves surgical outcome or reduces complication rates. We are not convinced that it is reasonable to generalize from a single study of limited sample size showing a weak difference in surrogate markers in lieu of clinically important differences in patient outcomes or incidence of adverse events. Indeed, the utter lack of important differences in clinical outcomes or incidence of adverse events in any of the cited studies is more consistent with the evidence showing no benefit.

Regrettably, investigators keep asking the wrong questions. For example, we think it is rather pointless to compare clinical conditions for laparoscopy during deep neuromuscular block versus no block at all.[8,9] Such protocols do not reflect the reality of routine anesthetic practice. To summarize our position, with the exception of the article by Martini et al.,[4] we have not been able to identify any studies that compare operating conditions for laparoscopy performed under deep neuromuscular block versus moderate block maintained until the end of surgery. Thus, we stand by our statement that the relative benefits of a sustained deep neuromuscular block over a sustained moderate block for laparoscopy are as yet unproven. The available data suggest that there are no important clinical benefits.

In our practice, where sugammadex is not available, if the surgeon says conditions are less than satisfactory, we then take action. We administer additional relaxant, opioid, hypnotic, change the ventilatory pattern, or some combination of these. Problem solved. None of the cited studies consider the possibility that the surgeon and the anesthesiologist might actually communicate during surgery to maintain optimal surgical conditions without overdosing the patient.

Finally, de Boer et al. suggest that further studies regarding this question are required. We believe that a prerequisite for any additional research is identifying a clinical problem that needs to be addressed. We cannot countenance intentionally administering an overdose of rocuronium to research subjects undergoing laparoscopic surgery in hopes of solving a nonexistent problem.

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REFERENCES

1. Madsen MV, Staehr-Rye AK, Gätke MR, Claudius C. Neuromuscular blockade for optimising surgical conditions during abdominal and gynaecological surgery: a systematic review. Acta Anaesthesiol Scand 2015;59:1–16
2. Dubois PE, Putz L, Jamart J, Marotta ML, Gourdin M, Donnez O. Deep neuromuscular block improves surgical conditions during laparoscopic hysterectomy: a randomised controlled trial. Eur J Anaesthesiol 2014;31:430–6
3. Staehr-Rye AK, Rasmussen LS, Rosenberg J, Juul P, Lindekaer AL, Riber C, Gätke MR. Surgical space conditions during low-pressure laparoscopic cholecystectomy with deep versus moderate neuromuscular blockade: a randomized clinical study. Anesth Analg 2014;119:1084–92
4. Martini CH, Boon M, Bevers RF, Aarts LP, Dahan A. Evaluation of surgical conditions during laparoscopic surgery in patients with moderate vs deep neuromuscular block. Br J Anaesth 2014;112:498–505
5. Kopman AF, Naguib M. Laparoscopic surgery and muscle relaxants: is deep block helpful? Anesth Analg 2015;120:51–8
6. McCoy EP, Connolly FM, Mirakhur RK, Loan PB, Paxton LD. Nondepolarizing neuromuscular blocking drugs and train-of-four fade. Can J Anaesth 1995;42:213–6
7. Blobner M, Frick CG, Stäuble RB, Feussner H, Schaller SJ, Unterbuchner C, Lingg C, Geisler M, Fink H. Neuromuscular blockade improves surgical conditions (NISCO). Surg Endosc 2015;29:627–36
8. Van Wijk RM, Watts RW, Ledowski T, Trochsler M, Moran JL, Arenas GW. Deep neuromuscular block reduces intra-abdominal pressure requirements during laparoscopic cholecystectomy: a prospective observational study. Acta Anaesthesiol Scand 2015;59:434–40
9. Madsen MV, Gätke MR, Springborg HH, Rosenberg J, Lund J, Istre O. Optimising abdominal space with deep neuromuscular blockade in gynaecologic laparoscopy—a randomised, blinded crossover study. Acta Anaesthesiol Scand 2015;59:441–7

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Laparoscopic Surgery and Muscle Relaxants: Is Deep Block Really Not Helpful?

To the Editor:

I have read the review by Kopman and Naguib[1] with great interest! However, although comprehensively written by 2 of the most distinguished authors in their field, I dare to disagree with the format in which some of the studies are represented and with the review's conclusions. I will confine my detailed criticism to the 3 most relevant headings from the original review.

NONLAPAROSCOPIC SURGERY: ARE RELAXANTS ALWAYS NECESSARY?

The authors make the point that "lessons learned from general surgery have applicability to laparoscopic surgery as well."[1] The first reference discussed in detail is a study by Tammisto and Olkkola,[2] which concludes that "as anesthesia deepened, less intense block was required." In the context of volatile-based anesthesia, this is not surprising. However, I would like to draw attention to a quote from the same article[2]: "We conclude that there is a linear relationship between the end-tidal concentrations of enflurane and the degree of neuromuscular block … However, due to huge interindividual variation, certain 'overdosing' of neuromuscular blocking drugs is necessary to guarantee adequate muscle relaxation of abdominal muscles during all stages of upper abdominal surgery." Depth of anesthesia therefore appears to be not

sufficiently predictive to avoid unsatisfactory operating conditions. The discussion of the study also states that tightness of abdominal muscles might have gone unnoticed because surgeons only complained when surgical conditions were grossly unacceptable (i.e., coughing). Therefore, I agree with the review's authors that lessons can be learned from this study; however, my conclusion would be that depth of anesthesia is an unreliable predictor of surgical working conditions. It may also be mentioned that in the light of ongoing intense (and admittedly controversial) research into the possible side effects of "too deep" anesthesia, mentioning deep anesthesia as an easy way to improve surgical conditions may be seen as somewhat counterintuitive.

In the review article, the authors also quote an investigation by King et al.[3] as stating that 70% of patients did not require a neuromuscular-blocking agent to achieve good or excellent operating conditions. In response, I will highlight another statement by King et al.[3]: "Nonetheless, vecuronium significantly increased the proportion of patients in whom at least adequate (# grade 3) surgical field ratings were maintained throughout the procedure, from 72% (placebo group) to 98%." In my view, at least this significantly changes the representation of the study, because it implies the question of whether nonadequate surgical conditions can and should really be tolerated in 30% of patients.

DOES DEEP NEUROMUSCULAR BLOCK PROVIDE BETTER LAPAROSCOPIC SURGICAL CONDITIONS THAN MODERATE LEVELS OF BLOCK?

Kopman and Naguib[1] commence this section by quoting the study by Chassard et al.[4] as finding no differences in surgical conditions in patients receiving either a neuromuscular-blocking agent to a twitch depression of 10% of control or no blocking drugs. According to a previous article by Kopman et al.[5] as well as the authors' definition of block levels in their review, this constitutes at best a "moderate versus no block study" and may hence be misplaced in the section of the review. Another larger study by Chen et al.[6] is quoted in the same context. Although the review acknowledges many of the shortcomings of this article (i.e., no depth of block monitored), it quotes that "Satisfactory conditions for ventilation and operation were consistently achieved with and without muscle relaxants…"[1] The readers should know that this study makes no mention of a standardized assessment of surgical working conditions. Are "satisfactory" conditions optimal or even "good"? The latter remains speculative. Two further articles[7,8] referenced in the same context investigated paralyzed versus nonparalyzed patients. In both studies, nonparalyzed patients were allowed to breathe spontaneously throughout the procedure. However, in the trial by Williams et al.,[8] pneumoperitoneum was rated as inadequate for trochar insertion in 5 of 18 (28%) patients (versus adequate in 100% of the paralyzed patients). Although the latter is acknowledged in the review, the review speculates whether this may have been the result of the fact that the nonparalyzed patients were breathing spontaneously and conclude that this may be a suboptimal technique for laparoscopic surgery.[1] Would the lack of neuromuscular block not provide an alternative and perhaps even more likely explanation for unsatisfactory surgical conditions?

A study by Paek et al.[9] is quoted as "more universally applicable" in the argument against a significant benefit of deep block. In this study, patients received either no additional rocuronium (allowed to recover from the induction dose of 0.6 mg/kg) or incremental bolus doses to maintain a train-of-four (TOF) of 2 twitches. The authors state that "there were no complaints from any of the participating surgeons."[9] Besides the fact that the latter may not qualify as a standardized assessment of operating conditions, it should be highlighted that the "paralyzed" group in this study received a mere average of an additional 24 mg of rocuronium during procedures lasting approximately 103 minutes. The nonparalyzed group also only experienced a recovery of 4/4 twitches after 72 minutes! Because of the large dose of rocuronium administered to patients in both groups on induction, this study may have ultimately compared 2 very similarly blocked groups for the larger part of the operation. Hence, the results could in fact be seen as universally applicable to demonstrate the benefits of (albeit moderate) muscle relaxation.

I completely agree with the authors that well-designed trials comparing deep with moderate block are rare if not nonexistent. However, the review quotes 3 studies,[10–12] which at least attempt to provide such a comparison. First mentioned in the review is a trial by Martini et al.[10] comparing surgical working conditions on a well-defined 5-point scale under conditions of either moderate (TOF 1–2) or deep (post tetatic count [PTC] 1–2) neuromuscular block. The review mentions that the mean difference of 0.7 points (4 vs 4.7 points) on the 1 to 5 scale had been, although statistically significant, relatively small. However, it is worth noting that this 18% difference was rated as "important and clinically significant" by the participating surgeons.[10] Although this merely constitutes subjective opinion and not patient outcome, it should probably not be completely ignored. Furthermore, I would like to bring to attention that in this study, deep block resulted in 67% excellent surgical ratings, with moderate block, and this was found in only 34%. Despite this, conditions were rated "good" ("…a wide laparoscopic working field with sporadic muscle contractions, movements, or both")[10] in >80% of patients in the moderate-block group. However, although sporadic muscle contractions or movements may not prevent successful and safe surgery in many instances, it may be permitted to ask the question whether we can or should accept suboptimal surgical conditions in 2 of 3 patients when possibly dealing with higher risk procedures (i.e., robotic surgery). The same question applies when reading about the number of treatment failures (unacceptable surgical conditions; $n = 14$) reported by Dubois et al.[11] in patients in their shallow block group. It is of course correct that Kopman and Naguib point out that the depth of block in this group might have been outside the definition of a moderate block. However, it is still interesting that at least half of these events were recorded either before the recovery of 4 twitches ($n = 3$) or at least at relatively low TOF ratios (<40%; $n = 4$). Ultimately, this may be close to what the intention to maintain moderate block might produce in clinical reality. Although I also

agree with the review that some deep block patients were found paralyzed at more shallow levels (hence possibly better defined as moderate blocks), no treatment failure was reported at a TOF ≤1. Even when accepting that deep block in this study may have better been replaced with a moderate but a continuously monitored and maintained block, one can still conclude that allowing gradual recovery from deep to moderate neuromuscular block during laparoscopic surgery may result in undesirable operating conditions.

CONCLUSIONS

In their own conclusion, the authors of this review mention a study by De Jong[13] as a noteworthy argument for a profound block to be unnecessary to achieve excellent surgical conditions. Although De Jong indeed found excellent conditions at the level of moderate block in most of his patients, his methodology for muscle relaxation (i.e., continuous succinylcholine administration) may have been appropriate in the 1960s but may fit the description of being awkward in today's practice. Furthermore, it is left unclear whether and how the surgeons in this trial were blinded. As a matter of fact, the author never investigated whether a more profound block than the moderate block used in the study could have improved surgical conditions even more. In view of the findings by De Jong of increasing numbers of excellent ratings with increasing depth of neuromuscular block, one could at least hypothesize that this might have been the case.

Finally, the review concludes that "Current practice in the United States where sugammadex is not available and deep block is not routinely practiced for laparoscopic surgery suggests that there is no pressing need to change current clinical routines."[1] In my view, this circulus in probando is difficult to accept as the final word of this review. Current practice in the United States alone can certainly not explain why there is currently no need to change clinical practice. Only data from well-conducted trials could, but this is ultimately still missing. Therefore, I fully agree that we have not yet seen sufficiently well-designed studies to recommend an optimum level of neuromuscular block. However, in the meantime, and based on reviewing Kopman and Naguib's references in a slightly different light and as outlined earlier, I would personally adopt a slightly different conclusion. I may also refer to a recently published very balanced review about muscle relaxation in abdominal and gynecological surgery in my support.[14]

There is strong evidence that muscle relaxation per se improves laparoscopic surgical working conditions. Although a deep (versus moderate) block may theoretically be beneficial, well-designed trials have yet to establish a correlation with improved patient outcome. Thus, currently, there is no hard evidence to generally recommend a specifically deep neuromuscular block. However, maintenance of deep to moderate neuromuscular block (versus a one-off dose of a muscle relaxant on induction of anesthesia) throughout surgery seems to avoid undesirable surgical conditions. On first sight, this seems more feasible than it may actually be. With neostigmine-based reversal having just recently been (re-)confirmed to be problematic,[15,16] anesthesiologists without unhindered access to sugammadex may find even the maintenance of moderate block during laparoscopic surgery challenging. In this context, careful—ideally quantitative—neuromuscular monitoring is a crucial component of relaxant anesthesia. Because sugammadex is not yet available in the United States, I fully agree with Kopman and Naguib that at this point in time, a change of practice cannot, therefore, be recommended.

However, where neuromuscular monitoring is applied and where sugammadex is available, I would invite coworkers to experiment with deeper levels of block to gain their own experience and, by performing aforementioned missing studies, add to the scientific knowledge base of our specialty.

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REFERENCES

1. Kopman AF, Naguib M. Laparoscopic surgery and muscle relaxants: is deep block helpful? Anesth Analg 2015;120:51–8
2. Tammisto T, Olkkola KT. Dependence of the adequacy of muscle relaxation on the degree of neuromuscular block and depth of enflurane anesthesia during abdominal surgery. Anesth Analg 1995;80:543–7
3. King M, Sujirattanawimol N, Danielson DR, Hall BA, Schroeder DR, Warner DO. Requirements for muscle relaxants during radical retropubic prostatectomy. Anesthesiology 2000;93:1392–7
4. Chassard D, Bryssine B, Golfier F, Raupp C, Raudrant D, Boulétreau P. [Gynecologic laparoscopy with or without curare] [in French]. Ann Fr Anesth Reanim 1996;15:1013–7
5. Kopman AF, Klewicka MM, Neuman GG. The relationship between acceleromyographic train-of-four fade and single twitch depression. Anesth Analg 2002;96:583–7
6. Chen BZ, Tan L, Zhang L, Shang YC. Is muscle relaxant necessary in patients undergoing laparoscopic gynecological surgery with a ProSeal LMA™? J Clin Anesth 2013;25:32–5
7. Swann DG, Spens H, Edwards SA, Chestnut RJ. Anaesthesia for gynaecological laparoscopy—a comparison between the laryngeal mask airway and tracheal intubation. Anaesthesia 1993;48:431–4
8. Williams MT, Rice I, Ewen SP, Elliott SM. A comparison of the effect of two anaesthetic techniques on surgical conditions during gynaecological laparoscopy. Anaesthesia 2003;58:574–8
9. Paek CM, Yi JW, Lee BJ, Kang JM. No supplemental muscle relaxants are required during propofol and remifentanil total intravenous anesthesia for laparoscopic pelvic surgery. J Laparoendosc Adv Surg Tech A 2009;19:33–7
10. Martini CH, Boon M, Bevers RF, Aarts LP, Dahan A. Evaluation of surgical conditions during laparoscopic surgery in patients with moderate vs deep neuromuscular block. Br J Anaesth 2014;112:498–505
11. Dubois PE, Putz L, Jamart J, Marotta ML, Gourdin M, Donnez O. Deep neuromuscular block improves surgical conditions during laparoscopic hysterectomy: a randomised controlled trial. Eur J Anaesthesiol 2014;31:430–6
12. Staehr-Rye AK, Rasmussen LS, Rosenberg J, Juul P, Lindekaer AL, Riber C, Gätke MR. Surgical space conditions during low-pressure laparoscopic cholecystectomy with deep versus moderate neuromuscular blockade: a randomized clinical study. Anesth Analg 2014;119:1084–92

13. De Jong RH. Controlled relaxation. I. Quantitation of electromyogram with abdominal relaxation. JAMA 1966;197:393–5
14. Madsen MV, Staehr-Rye AK, Gätke MR, Claudius C. Neuromuscular blockade for optimising surgical conditions during abdominal and gynaecological surgery: a systematic review. Acta Anaesthesiol Scand 2015;59:1–16
15. McLean DJ, Diaz-Gil D, Farhan HN, Ladha KS, Kurth T, Eikermann M. Dose-dependent association between intermediate-acting neuromuscular-blocking agents and postoperative respiratory complications. Anesthesiology 2015;122:1201–13
16. Brueckmann B, Sasaki N, Grobara P, Li MK, Woo T, de Bie J, Maktabi M, Lee J, Kwo J, Pino R, Sabouri AS, McGovern F, Staehr-Rye AK, Eikermann M. Effects of sugammadex on incidence of postoperative residual neuromuscular blockade: a randomized, controlled study. Br J Anaesth 2015;pii:aev104

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Lawyers Choose Specific Experts for Many Different Reasons

To the Editor

Radvansky et al.[1] studied expert witness qualifications in one dimension, namely that of scholarly impact. I have reviewed, as an expert witness, approximately 500 medical malpractice cases over 44 years, and I think I understand the many varied reasons why lawyers pick specific expert witnesses. First, as Radvansky et al.[1] point out, a high scholarly impact in a particular field can be important and was undoubtedly a major factor in my being selected as an expert witness in many anesthesia for thoracic surgery, airway, and obstructive sleep apnea management cases. However, sometimes a single off-the-beaten-path article or a letter-to-the-editor can be the sole determinant of whether an expert is asked to review a case. For example, my single article about 4 cases of neural injury after interscalene block under general anesthesia[2] and 2 very short letters-to-the-editor on the hazards of externally pressurizing cell-saver reinfusion bags[3,4] were great magnets for lawyers to send me cases to review in these areas. As Radvansky et al.[1] point out, even though an individual's entire publication record may have nothing to do with the issues of a given case, a good publication record still makes the author appear to be a desirable expert witness.

Second, the expert who is chosen to testify must agree with the lawyer's position on the case. There are many experts who are not asked to participate in a given case after review because they cannot support the side they have reviewed the case for, a circumstance I have encountered many times in my career. This aspect of expert witness activity is completely unaccounted for by the article of Radvansky et al.[1]

Third, the ability to communicate with a jury is vitally important to the success of a given side, and in the minds of many lawyers, this consideration far outweighs the importance of publication record. As a possibly related factor, physical appearance may play a role in expert witness selection.

Fourth, many experts are chosen simply by good word-of- mouth from one lawyer to another, and so the selection by the second lawyer has nothing to do with publication record.

Fifth, many lawyers pick experts based on previous jury decisions in similar cases; thus, the lawyer knows beforehand the direction and quality of an expert's testimony with regard to a specific issue. Sixth, and related to this previous point, I have no doubt experts are sometimes chosen because the lawyer knows what the expert is going to say based on previous direct experience and work with the expert.

Seventh, any "expert" can become more "expert" on any given issue after he or she gets into the case; thus, selection of experts may be based on the experts' willingness to educate themselves. Cases involving pure judgment on general issues are often like this.

Eighth, a relatively obscure (and inexpensive) expert is picked in a few recurring situations: plaintiff lawyers will use such "experts" to simply file an affidavit supporting the case just to get the case going in the litigation process, but they never intend to use that expert to actually testify. Such "experts" may then aid plaintiff attorneys in getting nuisance awards and aid defense attorneys in reducing awards in hopeless cases by threatening a lengthy and expensive fight.

Ninth, some experts are chosen from private practice to simply opine on the practice in a given community.

Finally, some defendants want faculty from their residency to be their experts; scholarly impact is usually high.

Thus, the choice of experts by lawyers is a complex and multifactorial matter, and it will likely vary from case to case and from lawyer to lawyer. Scholarly impact, although an important determinant in some cases, may be relatively unimportant in many other cases.

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REFERENCES

1. Radvansky BM, Farver WT, Svider PF, Eloy JA, Gubenko YA, Eloy JD. A comparison of plaintiff and defense expert witness qualifications in malpractice litigation in anesthesiology. Anesth Analg 2015;120:1369–74
2. Benumof JL. Permanent loss of cervical spinal cord function associated with interscalene block performed under general anesthesia. Anesthesiology 2000;93:1541–4
3. Benumof JL. Minimizing venous air embolism from reinfusion bags. Anesthesiology 1999;91:1962
4. Benumof JL. Externally pressurizing salvaged blood reinfusion bags: predictable, preventable cause of fatal air embolism. Anesthesiology 2007;107:851

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In Response

We thank Benumof[1] for his interest in our analysis and for valuable commentary into some of the reasons why lawyers choose specific experts in malpractice litigation. His insights into the varied reasons experts contribute to cases complement our findings and

Correspondence Editor: **Jean-Francois Pittet**, Incoming Editor-in-Chief

Optimal Surgical Conditions in Laparoscopic Surgery: Just Relax and Lower the Pressure

To the Editor

In their recent review, Kopman and Naguib[1] suggest that the benefits of deep neuromuscular block (NMB) may be nonexistent. This is a surprising conclusion, given the increasing amount of literature on this topic that does show a significant clinical benefit from deep NMB. The most important study in this respect, by Martini et al.,[2] demonstrated in a blinded, randomized, controlled trial that the use of deep compared with moderate NMB is associated with an improved quality of surgical conditions in retroperitoneal laparoscopies (retroperitoneal prostatectomy, and nephrectomy) as determined by an experienced surgeon on a 5-point surgical rating scale.[2] Moreover, the peri- and postoperative cardiorespiratory conditions of the patients that received deep NMB were not compromised.

Another study showed that the use of deep NMB compared with no NMB improved surgical conditions for laparoscopic cholecystectomy by a motionless surgical field and better visibility.[3] Apart from inducing the absence of interfering muscle contractions, deep NMB at post-tetanic count values ≤2 may allow for increased intraabdominal volume at lower insufflation pressures.[4,5] This is important because a low pressure pneumoperitoneum (8 mm Hg) may be more advantageous than a standard pressure (12 mm Hg) in terms of the adverse impact on the surgical peritoneal environment.[6] Guidelines from the European Association for Endoscopic Surgery recommended the use of the lowest intraabdominal pressure possible rather than the use of a routine pressure.[7]

We contend that both surgeons and anesthesiologists agree that the level of NMB, assessed with quantitative neuromuscular monitoring, should be aimed at optimal surgical conditions with the lowest possible pressure. This would see the prospects of improved outcome, including the potential to minimize the adverse effects of high intraperitoneal pressure on inflammation/peritoneal fibrosis, and less pain in the days after surgery.[6,8]

However, in this interesting field of neuromuscular management in relation to cavity pressure, cavity volume, and patient outcomes, there are several challenges. When assessing surgical conditions, objective measures should be developed, which may result in eliminating the discrepancy between anesthesiologist and surgeon ratings of optimal surgical conditions. The surgical rating scale of Martini et al.[2] is a first step in this direction. Furthermore, it is important to find the correct balance between insufflation pressure and cavity volume. A deep NMB may result in larger volumes at the same pressure, leading to overexpansion of the patient. This pneumoperitoneum-associated expansion of the abdominal cavity is related to visceral pain and other physiological changes, affecting the postoperative outcome negatively.[8] Finally, in relation to the use of deep NMB laparoscopic surgical procedures, more data are required on objective end points regarding outcomes of interest, such as surgical time, incidence of complications, postoperative patient outcome, graft function, pain, or other outcomes specific to the type of patient and surgery.

The study by Martini et al.[2] provides unambiguous evidence of benefit in one setting to deep NMB. Indeed, while we agree that further studies are needed to confirm the benefits of deeper levels of NMB in laparoscopic surgery, a multidisciplinary approach in the development of this new paradigm in laparoscopic surgery will be beneficial to the patient.

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REFERENCES

1. Kopman AF, Naguib M. Laparoscopic surgery and muscle relaxants: is deep block helpful? Anesth Analg 2015;120:51–8
2. Martini CH, Boon M, Bevers RF, Aarts LP, Dahan A. Evaluation of surgical conditions during laparoscopic surgery in patients with moderate vs deep neuromuscular block. Br J Anaesth 2014;112:498–505
3. Blobner M, Frick CG, Stäuble RB, Feussner H, Schaller SJ, Unterbuchner C, Lingg C, Geisler M, Fink H. Neuromuscular blockade improves surgical conditions (NISCO). Surg Endosc 2015;29:627–36
4. Lindekaer A, Istre O, Springborg H. Deep neuromuscular blockade give the same intraabdominal volume at 8 mmHg as no blockade at 12 mmHg during laparoscopy. Anesthesiology 2012;117: A627
5. Madsen MV, Gätke MR, Springborg HH, Rosenberg J, Lund J, Istre O. Optimising abdominal space with deep neuromuscular blockade in gynaecologic laparoscopy—a randomised, blinded crossover study. Acta Anaesthesiol Scand 2015;59:441–7
6. Matsuzaki S, Jardon K, Maleysson E, D'Arpiany F, Canis M, Botchorishvili R. Impact of intraperitoneal pressure of a CO2 pneumoperitoneum on the surgical peritoneal environment. Hum Reprod 2012;27:1613–23
7. Neudecker J, Sauerland S, Neugebauer E, Bergamaschi R, Bonjer HJ, Cuschieri A, Fuchs KH, Jacobi Ch, Jansen FW, Koivusalo AM, Lacy A, McMahon MJ, Millat B, Schwenk W. The European Association for Endoscopic Surgery clinical practice guideline on the pneumoperitoneum for laparoscopic surgery. Surg Endosc 2002;16:1121–43
8. Gurusamy KS, Samraj K, Davidson BR. Low pressure versus standard pressure peritoneum in laparoscopic cholecystectomy. Cochrane Database Syst Rev 2009;CD006930

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Deep Neuromuscular Blockade for Laparoscopy: A Different View

To the Editor

We read with much interest the manuscript by Kopman and Naguib[1] reviewing the impact of deep neuromuscular blockade (NMB) on surgical conditions during laparoscopy. It represents an important contribution to the literature. However, we believe that clarification is necessary.

In their conclusion, the authors stated that "there is little or no evidence to suggest that using deep block (as opposed to block of moderate degree) for laparoscopic surgery will improve surgical operating conditions."[1] This statement contrasts with the conclusion of a recent systematic review by Madsen et al.[2] indicating that "there is a good evidence that deep NMB, compared to moderate NMB, is associated with optimal surgical conditions" during laparoscopy. This conclusion was based on the results of 3 randomized controlled trials showing beneficial effects of deep NMB during laparoscopic surgery.[3–5] In the study by Dubois et al.,[3] optimal to excellent surgical conditions occurred in 90% of patients receiving deep NMB (train of four [TOF] count ≤2) but only 66% of those receiving moderate NMB (TOF count >2). Deep NMB also significantly reduced the incidence of unacceptable surgical conditions.[3] Similarly, Staehr-Rye et al.[4] reported optimal surgical space conditions in 28% of patients with deep NMB (posttetanic count 0–1) but only 4% of those receiving moderate NMB (TOF count ≥2). In addition, Martini et al.[5] demonstrated a significantly higher incidence of poor surgical conditions with moderate NMB (TOF count 1–2) than that with deep NMB (posttetanic count 1–2): 18% and 1% of patients, respectively. Maintaining deep NMB at posttetanic count 1–5 is desirable for optimal surgical conditions during laparoscopic surgery.[6]

Optimal surgical conditions are the result of synergistic effects of anesthetics, analgesics, and neuromuscular blocking agents carefully titrated during general anesthesia. On the basis of the literature, deep, compared with moderate or shallow, NMB is emerging as a distinct opportunity to improve laparoscopic surgical conditions.

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REFERENCES

1. Kopman AF, Naguib M. Laparoscopic surgery and muscle relaxants: is deep block helpful? Anesth Analg 2015;120:51–8
2. Madsen MV, Staehr-Rye AK, Gätke MR, Claudius C. Neuromuscular blockade for optimising surgical conditions during abdominal and gynaecological surgery: a systematic review. Acta Anaesthesiol Scand 2015;59:1–16
3. Dubois PE, Putz L, Jamart J, Marotta ML, Gourdin M, Donnez O. Deep neuromuscular block improves surgical conditions during laparoscopic hysterectomy: a randomised controlled trial. Eur J Anaesthesiol 2014;31:430–6
4. Staehr-Rye AK, Rasmussen LS, Rosenberg J, Juul P, Lindekaer AL, Riber C, Gätke MR. Surgical space conditions during low-pressure laparoscopic cholecystectomy with deep versus moderate neuromuscular blockade: a randomized clinical study. Anesth Analg 2014;119:1084–92
5. Martini CH, Boon M, Bevers RF, Aarts LP, Dahan A. Evaluation of surgical conditions during laparoscopic surgery in patients with moderate vs deep neuromuscular block. Br J Anaesth 2014;112:498–505
6. Carron M. Deep neuromuscular blockade and laparoscopy: which level improves surgical conditions? Eur J Anaesthesiol 2015;32:64–5

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In Response

We appreciate Dr. Carron's interest in our article, and we agree that "Optimal surgical conditions are the result of synergistic effects of anesthetics, analgesics, and neuromuscular blocking agents carefully titrated during general anesthesia." However, in their letter, they quote the statement of Madsen et al.[1] that "there is good evidence that deep neuromuscular block compared to moderate neuromuscular block is associated with optimal surgical conditions." We do not concur with this assertion.

Of the 3 references[2–4] that Dr. Carron cites in support of Madsen et al.'s conclusion, 2 have serious flaws in their protocols.[2,3] We discuss these deficiencies at considerable length in our review.[5] To give 1 example, in the article by Staehr-Rye et al.,[3] the authors conclude that "Deep neuromuscular blockade was associated with surgical space conditions that were marginally better than with moderate muscle relaxation during low-pressure laparoscopic cholecystectomy." However, at a point half-way through the surgical procedure, twitch height (T1) in the moderate neuromuscular block group was 47% of control (a train-of-four count of 4 with fade); and at the 75% time point, T1 was 89% of control (a train-of-four ratio >0.40).[6] Thus, the authors were really comparing deep versus very shallow or minimal block for a considerable portion of the surgical procedure.

In response to de Boer et al., we think that they have misread our position. We do not deny that neuromuscular-blocking agents may have a valuable role to play in achieving satisfactory operating conditions for laparoscopic surgery. Thus, we fail to see the relevance of the study by Blobner et al.,[7] in which the authors compared surgical conditions under deep block with no block at all. To repeat, we do not believe that Madsen et al.'s article is authoritative. Simply labeling an article a "systematic review" does not guarantee that the study was conducted or reported with due rigor. A review and its conclusions can only be as good as the references it includes and the data it attempts to analyze. The article by Martini et al.[4] was the only study that Madsen et al. cites that reasonably supports the hypothesis that deep versus moderate block may achieve superior conditions for the surgeon. The mean difference (±SD) in the rating scores between deep block (a post-tetanic count of 1 or 2) and moderate block were, however, very modest—only

0.7 units (4.7 ± 0.4 vs 4.0 ± 0.4, respectively). Furthermore, a potential weakness of this protocol was its small sample size (n = 12 per group). The rating scale used is, at best, a surrogate marker. The study did not find any differences in patient outcome. In fact, to the best of our knowledge, no study has identified that maintaining deep neuromuscular blockade improves surgical outcome or reduces complication rates. We are not convinced that it is reasonable to generalize from a single study of limited sample size showing a weak difference in surrogate markers in lieu of clinically important differences in patient outcomes or incidence of adverse events. Indeed, the utter lack of important differences in clinical outcomes or incidence of adverse events in any of the cited studies is more consistent with the evidence showing no benefit.

Regrettably, investigators keep asking the wrong questions. For example, we think it is rather pointless to compare clinical conditions for laparoscopy during deep neuromuscular block versus no block at all.[8,9] Such protocols do not reflect the reality of routine anesthetic practice. To summarize our position, with the exception of the article by Martini et al.,[4] we have not been able to identify any studies that compare operating conditions for laparoscopy performed under deep neuromuscular block versus moderate block maintained until the end of surgery. Thus, we stand by our statement that the relative benefits of a sustained deep neuromuscular block over a sustained moderate block for laparoscopy are as yet unproven. The available data suggest that there are no important clinical benefits.

In our practice, where sugammadex is not available, if the surgeon says conditions are less than satisfactory, we then take action. We administer additional relaxant, opioid, hypnotic, change the ventilatory pattern, or some combination of these. Problem solved. None of the cited studies consider the possibility that the surgeon and the anesthesiologist might actually communicate during surgery to maintain optimal surgical conditions without overdosing the patient.

Finally, de Boer et al. suggest that further studies regarding this question are required. We believe that a prerequisite for any additional research is identifying a clinical problem that needs to be addressed. We cannot countenance intentionally administering an overdose of rocuronium to research subjects undergoing laparoscopic surgery in hopes of solving a nonexistent problem.

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REFERENCES

1. Madsen MV, Staehr-Rye AK, Gätke MR, Claudius C. Neuromuscular blockade for optimising surgical conditions during abdominal and gynaecological surgery: a systematic review. Acta Anaesthesiol Scand 2015;59:1–16
2. Dubois PE, Putz L, Jamart J, Marotta ML, Gourdin M, Donnez O. Deep neuromuscular block improves surgical conditions during laparoscopic hysterectomy: a randomised controlled trial. Eur J Anaesthesiol 2014;31:430–6
3. Staehr-Rye AK, Rasmussen LS, Rosenberg J, Juul P, Lindekaer AL, Riber C, Gätke MR. Surgical space conditions during low-pressure laparoscopic cholecystectomy with deep versus moderate neuromuscular blockade: a randomized clinical study. Anesth Analg 2014;119:1084–92
4. Martini CH, Boon M, Bevers RF, Aarts LP, Dahan A. Evaluation of surgical conditions during laparoscopic surgery in patients with moderate vs deep neuromuscular block. Br J Anaesth 2014;112:498–505
5. Kopman AF, Naguib M. Laparoscopic surgery and muscle relaxants: is deep block helpful? Anesth Analg 2015;120:51–8
6. McCoy EP, Connolly FM, Mirakhur RK, Loan PB, Paxton LD. Nondepolarizing neuromuscular blocking drugs and train-of-four fade. Can J Anaesth 1995;42:213–6
7. Blobner M, Frick CG, Stäuble RB, Feussner H, Schaller SJ, Unterbuchner C, Lingg C, Geisler M, Fink H. Neuromuscular blockade improves surgical conditions (NISCO). Surg Endosc 2015;29:627–36
8. Van Wijk RM, Watts RW, Ledowski T, Trochsler M, Moran JL, Arenas GW. Deep neuromuscular block reduces intra-abdominal pressure requirements during laparoscopic cholecystectomy: a prospective observational study. Acta Anaesthesiol Scand 2015;59:434–40
9. Madsen MV, Gätke MR, Springborg HH, Rosenberg J, Lund J, Istre O. Optimising abdominal space with deep neuromuscular blockade in gynaecologic laparoscopy—a randomised, blinded crossover study. Acta Anaesthesiol Scand 2015;59:441–7

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Laparoscopic Surgery and Muscle Relaxants: Is Deep Block Really Not Helpful?

To the Editor:

I have read the review by Kopman and Naguib[1] with great interest! However, although comprehensively written by 2 of the most distinguished authors in their field, I dare to disagree with the format in which some of the studies are represented and with the review's conclusions. I will confine my detailed criticism to the 3 most relevant headings from the original review.

NONLAPAROSCOPIC SURGERY: ARE RELAXANTS ALWAYS NECESSARY?

The authors make the point that "lessons learned from general surgery have applicability to laparoscopic surgery as well."[1] The first reference discussed in detail is a study by Tammisto and Olkkola,[2] which concludes that "as anesthesia deepened, less intense block was required." In the context of volatile-based anesthesia, this is not surprising. However, I would like to draw attention to a quote from the same article[2]: "We conclude that there is a linear relationship between the end-tidal concentrations of enflurane and the degree of neuromuscular block … However, due to huge interindividual variation, certain 'overdosing' of neuromuscular blocking drugs is necessary to guarantee adequate muscle relaxation of abdominal muscles during all stages of upper abdominal surgery." Depth of anesthesia therefore appears to be not