Deep neuromuscular blockade and neuromuscular reversal : applications and implications

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Section 1

Surgical conditions

Chapter 2

Evaluation of surgical conditions during laparoscopic surgery in patients with moderate *versus* deep neuromuscular blockade

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ABSTRACT

Background

The routine use of neuromuscular blocking agents reduces the occurrence of unacceptable surgical conditions. In some surgeries, such as retroperitoneal laparoscopies, deep neuromuscular block (NMB) may further improve surgical conditions compared to a moderate NMB. In this study, the effect of deep NMB on surgical conditions was assessed.

Methods

Twenty-four patients undergoing elective laparoscopic surgery for prostatectomy or nephrectomy were randomized to receive moderate NMB (train-of-four 1–2 twitches, induced by atracurium and mivacurium) or deep NMB (post-tetanic count 1–2 twitches, induced by a high dose rocuronium). After surgery, NMB was reversed with neostigmine (moderate NMB), or sugammadex (deep NMB). During all surgeries, one surgeon scored the quality of surgical conditions using the five-point Leiden - surgical rating scale (L-SRS) ranging from 1 (extremely poor conditions) to 5 (optimal conditions). Video images were obtained and 12 anaesthetists rated a random selection of images.

Results

Mean (SD) SRS was 4.0 (0.4) during moderate and 4.7 (0.4) during deep NMB ($p < 0.001$). Moderate NMB resulted in 18% of scores at the low end of the scale (scores 1–3); deep block resulted in 99% of scores at the high end of the scale (scores 4 and 5). Cardiorespiratory conditions were similar during and after surgery in both groups. Between anaesthetists and surgeon, there was poor agreement between scores of individual images (average k statistic 0.05).

Conclusions

Deep NMB results in an improved quality of surgical conditions compared with moderate block in retroperitoneal laparoscopies, without compromise to the patients' peri- and postoperative cardiorespiratory conditions.

INTRODUCTION

Administration of muscle relaxation is essential in a variety of procedures since it causes an improvement of surgical conditions. For example, King *et al.* demonstrated that the routine use of muscle relaxants reduced the frequency of unacceptable surgical conditions in radical prostatectomies.[1] Improvement of surgical conditions may be even more important when the surgeon has to work in a narrow space surrounded by muscles such as in case of retroperitoneal laparoscopic surgery. It may be argued that in retroperitoneal laparoscopic surgery, a deep neuromuscular block (NMB), with train-of-four (TOF) values of 0 and a post-tetanic-count (PTC) of 1-2, would further improve working conditions. However, the use of deep NMB may come with complications including long-reversal times, incomplete recovery of neuromuscular function compromising respiratory and upper airway function, or the return of NMB following a period of seemingly normal neuromuscular function (re-curarization).[1-3]

The development of sugammadex enables rapid reversal of deep NMB. Sugammadex is a modified γ-cyclodextrin, especially created to bind the free plasma molecules of the muscle relaxant rocuronium to which is has high affinity.[4] Recent studies demonstrate that sugammadex produces rapid reversal of deep NMB following administration of high dose rocuronium.[5] Theoretically, the combination of rocuronium and sugammadex makes it possible to achieve deep NMB and consequently further improve surgical conditions in retroperitoneal laparoscopic surgery without the fear for prolonged reversal times or incomplete recovery of neuromuscular function. However, the association between the depth of NMB and surgical conditions has not been evaluated as yet.

In the current study we investigated the effect of a deep neuromuscular block (TOF count 0, PTC 1-2 twitches) against a moderate block (TOF count 1-2 twitches) on surgical conditions in patients undergoing retroperitoneal laparoscopic surgery for a prostatectomy or (partial) resection of a kidney. Surgical conditions were rated using a 5-point surgical rating scale (SRS) by one dedicated surgeon with ample experience in such surgery (RB). We hypothesize that deep NMB is associated with improved ratings by the surgeon. Secondary end-points of our study included the assessment of the level of agreement between anaesthetists (the providers of the NMB agents and consequently responsible for a significant part of surgical conditions) and surgeon in terms of their rating of the surgical conditions. To that end, 30-s video images of the surgical field, obtained at the time of scoring by the surgeon, were rated by the anaesthetists.

METHODS

The study (acronym BLISS study: effect of deep BLock on Intraoperative Surgical conditions, perioperative hemodynamic status and respiratory parameters following reversal with Sugammadex in patients undergoing laparoscopic renal and prostate surgery. was carried out between November 2012 and February 2013 at the Leiden University Medical Centre (Leiden, the Netherlands) and was performed according to guidelines of Good Clinical Practice and Good Research Practice. Approval of the protocol was obtained from the institutional review board (Commissie Medische Ethiek, Leiden, the Netherlands). Patients scheduled to undergo an elective laparoscopic prostatectomy or nephrectomy (partial or total), were approached 2 weeks prior to surgery and received oral and written information about the study. All patients who were willing to participate gave written informed consent before enrolment. The study was registered at clinicaltrials.gov (NCT01361149); the protocol was published earlier online.[6] The design of the study was randomized (deep neuromuscular block against standard or moderate block) and blinded (the surgical team, the research team and the anaesthetists that scored the video were all blinded to the treatment); the attending anaesthetist was not blinded. Randomisation was performed using a computer-generated randomisation code. The code was presented to the attending anaesthetist who prepared the medication and took care of patient dosing during anaesthesia.

Patients enrolled in the study had prostate or renal disease and were all eligible for surgical resection by laparoscopic approach. All procedures were performed by one surgeon (RB). Excluded from participation were patients with ASA class > III, age < 18 years, inability to give informed consent, known or suspected neuromuscular disease, allergy to medication to be used during anaesthesia, a (family) history of malignant hyperthermia, renal insufficiency (serum creatinine > 2 times normal or urine output < 0.5 $mL.kg^{-1}.h^{-1}$ or glomerular filtration rate < 60 $mL.h^{-1}$, or proteinuria), previous retroperitoneal surgery, and a body mass index of 35 $kg.m^{-2}$ or greater.

Perioperative protocol

All patients received total intravenous anaesthesia with propofol and sufentanil. During the procedure routine monitoring was applied: electrocardiography, blood pressure, heart rate, electroencephalographic monitoring using a bi-spectral index (BIS) module (*Philips*, Eindhoven, the Netherlands). Propofol dosing was such that BIS values remained within the range of 40 to 50. Additionally, the cardiac output was measured non-invasively using an inflatable finger cuff attached to the Nexfin haemodynamic monitor (*bmeye*, Amsterdam, the Netherlands).

With respect to neuromuscular blockade the patients were randomly assigned to one of two treatment groups:

Group 1: Moderate neuromuscular block, in which the goal was to realize a moderate neuromuscular block (train-of-four 1-2 twitches). Neuromuscular blockade was induced with a bolus dose of atracurium 0.5 $mg.kg^{-1}$, followed by a continuous infusion of mivacurium 0.5 $mg.kg^{-1}.h^{-1}$. In case of deviations from the target train-of-four values, the pump speed could be increased or decreased, or a bolus dose could be given. This was left to the discretion of the attending anaesthetist. We used atracurium/mivacurium in Group 1 rather than low-dose rocuronium, as this combination is the current standard of care in our hospital. This approach enables us to compare our current local practice against a new paradigm, which is deep NMB for the chosen surgical procedures.

Group 2: Deep neuromuscular block, in which the goal was to realize a block of zero twitches in the train-of-four but 1-2 twitches in the post-tetanic-count. To that end, patients received a loading dose of rocuronium 1.0 $mg.kg^{-1}$ followed by a continuous infusion of 0.6 $mg.kg^{-1}.h^{-1}$. In case of deviations from the target train-of-four and post-tetanic-count, the pump speed could be increased or decreased, or a bolus dose could be given. This was left to the discretion of the attending anaesthetist.

In case of poor or extreme poor surgical conditions (as scored by the surgeon, see below), mivacurium or rocuronium infusion rates were increased by 20% after the administration of a bolus dose of 15 mg.

At the end of surgery all patients received a reversal agent: neostigmine following a moderate NMB block (neostigmine 1-2 mg combined with atropine 0.5-1 mg) and sugammadex (4 $mg.kg^{-1}$) following a deep NMB block. Extubation occurred when the train-of-four ratio > 0.9.

Administration of all drugs was performed by the attending anaesthetists and not corresponded to the surgical team or the anaesthesia research team.

Monitoring

Neuromuscular function using an acceleromyograph was measured at the wrist (TOF-watch-SX, *MSD* BV, Oss, the Netherlands). The TOF-watch delivers an electrical stimulus to the ulnar nerve and measures contractions of the adductor pollicis muscle (causing adduction of the thumb) through a sensor attached to the tip of the thumb. The thumb was placed in a flexible adaptor that applied a constant preload to the thumb. Before administration of any NMB agent the device was calibrated according the specifications of the manufacturer. To that end, before administration of any neuromuscular blocking agent, but after induction of general anaesthesia, the following procedures were conducted to standardize the neuromuscular monitoring: (1) application of a tetanic ulnar nerve stimulation (50 Hz for 5 seconds); (2) calibration of the TOF watch; and (3) performing a series of TOF measurements ensuring that the TOF ratio differs by less than 5% between measurements. If the TOF ratio differed by more than 5% the TOF watch was recalibrated. The TOF ratio was normalised to the baseline values obtained during the calibration procedure. After these steps the neuromuscular blocking agent was administered according to protocol. The number of thumb twitches upon electrical stimulation of the ulnar nerve was measured and recorded. At 15-min intervals the train-of-four was measured and in case of TOF count = 0, this was followed by the post-tetanic-count. In our study a TOF count of 1-2 twitches reflects a standard block and a PTC of 1-2 twitches reflects a deep NMB. Finally, when a TOF count of 4 twitches was present, the ratio of the fourth to the first twitch was determined (the TOF ratio).

Leiden - Surgical Rating Scale (L-SRS)

During the laparoscopic procedure the surgeon scored the surgical working conditions at 15 min intervals according to a 5-point ordinal scale ranging from 1 (extremely poor conditions) to 5 (optimal conditions); Table 1. Extremely poor (score 1) indicates that the surgeon is unable to work due to coughing or due to the inability to obtain a visible field because of inadequate muscle relaxation; poor (score 2) indicates that there is a visible field but the surgeon is severely hampered by inadequate muscle relaxation with continuous muscle contractions and/or movements; acceptable (scores 3) indicates that the there is a wide visible field but muscle contractions and/or movements occur regularly; good (score 4) indicates a wide working field with sporadic muscle contractions and/or movements; and optimal (score 5) indicates a wide visible working field without any movement or contractions. In case of a sudden deterioration of conditions additional measurements could be added. The feasibility of this method of scoring was investigated during 5 surgical procedures not included in the study.

Table 1. The Leiden- surgical rating scale (L - SRS)

1	**Extremely poor conditions:** The surgeon is unable to work due to coughing or due to the inability to obtain a visible laparoscopic field because of inadequate muscle relaxation. Additional muscle relaxants must be given.
2	**Poor conditions:** There is a visible laparoscopic field but the surgeon is severely hampered by inadequate muscle relaxation with continuous muscle contractions and/or movements with the hazard of tissue damage. Additional muscle relaxants must be given.
3	**Acceptable conditions:** There is a wide visible laparoscopic field but muscle contractions and/or movements occur regularly causing some interference with the surgeon's work. There is the need for additional muscle relaxants to prevent deterioration.
4	**Good conditions:** There is a wide laparoscopic working field with sporadic muscle contractions and/or movements. There is no immediate need for additional muscle relaxants unless there is the fear for deterioration.
5	**Optimal conditions:** There is a wide visible laparoscopic working field without any movement or contractions. There is no need for additional muscle relaxants.

Video Images

Each time the surgeon rated the surgical conditions a video image of 30 seconds was captured using a camera connected to the endoscopic probe placed in the retroperitoneal surgical space. The procedure was such that the images collected give a visual indication of the surgical condition at the time of scoring. A randomized subset of these images (*n* = 10) was presented to twelve anaesthetists with ample experience in giving anaesthesia for urological laparoscopic procedures. They were asked to give a rating to the surgical condition using the same 5-point scale as used by the surgeon. These anaesthesia experts were blinded to the level of neuromuscular blockade and goals of the study.

Data Acquisition

The following clinical variables were collected on the case record form for further analysis: anaesthesia-related parameters (drug dosages, bi-spectral index, time from reversal to optimal extubation conditions (TOF ratio > 0.9)), haemodynamic parameters (blood pressure, heart rate, cardiac output, cardiac index), ventilatory parameters (tidal volume, breathing rate, breathing pressure), surgical parameters (L-SRS, intra-abdominal pressure, duration of surgery) and post-anaesthesia care-related parameters (time spent in the post-anaesthesia care unit, respiratory rate, oxygen saturation, pain score (on an 11-point numerical rating scale from 0, no pain, to 10, most severe pain imaginable), occurrence of nausea/vomiting and sedation (on a 5-point scale ranging from 0, normal alertness to 5, not aroused by a painful stimulus)). Recurrent observations were made at 15-min intervals both during anaesthesia and in the post-anaesthesia care unit.

Sample Size and Statistical Analysis

The sample size was based on the expectation of the surgeon for the distribution of the surgical ratings between the two treatment conditions: rating during the moderate block = 5 occurs in 10% of cases, 4 in 20%, 3 in 55% 2 in 10% and 1 in 5%; rating during the deep block = 5 in 70% of cases, 4 in 20%, 3 in 10%, 2 in 0% and 1 in 0%. These anticipated frequencies result in an odds ratio of 21 for optimal conditions (SRS 5) *versus* non-optimal conditions (SRS < 5). Ten-thousand simulations were performed to obtain the power for a given sample size with moderate block as a fixed distribution and a simulated distribution of the deep block condition assuming proportionality of the odds ratio with an odds ratio of 21 and analysing the results with a proportional odds model using the score test. The power ranged from 82% at a sample size of 14 (7 in each group) to 97% (*n* = 12/group). A sample size of 24 was chosen to take into account any margin of uncertainty around the effect size.

The data analysis was based on the intent-to-treat approach. The primary end-point of the study was the influence of the depth of the neuromuscular block on the surgical rating scale. For each patient the final score was the average of all 15-min SRS values.

The treatment effect on the final score was tested using a *t*-test (SigmaPlot version 12.5, Systat Software Inc., San Jose, CA, USA). Secondary end-points were (1) the assessment of the level of agreement between anaesthetists and surgeon in terms of their rating of the surgical conditions; and (2) the effects of level of neuromuscular block on haemodynamic variables during surgery, time to TOF > 0.9, and relevant variables in the post-anaesthesia care unit (pain rating, sedation levels, cardiorespiratory variables). All variables were averaged over time to get an indication of their mean value. Treatment effects were evaluated on the average data by *t*-test.

The scores of each of the 12 anaesthetists were compared with that of the surgeon's score using the kappa statistic (also known as Cohen's kappa) and population Bland Altman analysis.[7-9] The kappa statistic calculates the agreement between a pair of scores over and above what is expected from chance, where kappa = [P(A) – P(E)]/[1 – P(E)], P(A) is the proportion of scores that agree and P(E) the proportion of scores that would agree by chance.[7, 9] Kappa values between 0 and 0.2 are indicative of poor to slight agreement, values between 0.2 and 0.4 indicate fair agreement, 0.4 to 0.6 moderate agreement, 0.6 to 0.8 substantial agreement, and 0.8 to 1 near complete to complete agreement.[10] Bland Altman plots give the difference between paired measurements (scores) against the mean of the values, which results in values for bias and limits of agreement to describe how closely measurements from two sources are related.[8]

All values presented are mean ± SD unless otherwise stated. p-values < 0.05 were considered significant.

RESULTS

A total of thirty patients were screened. In four patients one or more exclusion criteria were met. The others were randomized. Two patients withdrew consent before treatment; two others replaced them. See Fig. 1 for the flow chart of the study. Patient characteristics are given in Table 2 showing that the two treatment groups were similar in physical characteristics, gender, types of surgery and haemodynamic variables. Duration of surgery was similar between treatment groups and ranged from 80 to 240 min with average surgical times of 141 and 144 min for standard care and deep NMB, respectively (Table 3).

Anaesthesia

Depth of anaesthesia, as measured by the bi-spectral index of the electroencephalogram (BIS), was similar between treatment groups (moderate block 42 (5) *vs.* deep block 44 (6)). Neuromuscular block in patients receiving a standard treatment was moderate with an average TOF count of 2.2 (0.9) twitches during surgery. Patients receiving a deep neuromuscular block had zero twitches in the TOF and 1.6 (1.5) twitches in the post-tetanic count. During surgery the dosages of the anaesthetic (propofol) or analgesic (sufentanil), the intra-abdominal pressure and haemodynamic variables were similar between treatments (Table 3).

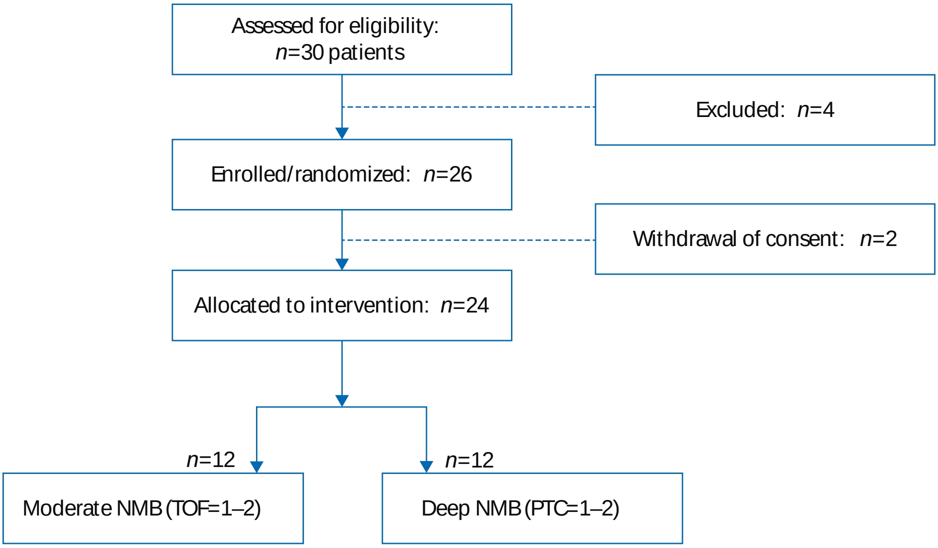

Figure 1. Study flow chart.

Table 2. Patient characteristics and screening measurements

	Moderate NMB (*n* = 12)	**Deep NMB** (*n* = 12)
Prostate surgery (*n*)	7	7
Renal surgery (*n*)	5	5
Gender (M/F)	10/2	10/2
Age (median, range)	59 (28-74)	60 (24-70)
Weight (kg)	83 (14)	83 (10)
Height (cm)	180 (10)	180 (9)
BMI (kg.m^{-2})	25.8 (3.2)	25.9 (3.9)
BP systolic (kPa)	19.6 (2.1)	18.9 (1.5)
BP systolic (mm Hg)	147 (16)	142 (11)
BP diastolic (kPa)	11.2 (2.2)	11.5 (1.6)
BP diastolic (mmHg)	84 (15)	86 (12)
HR (min^{-1})	71 (12)	73 (15)
CO (L.min^{-1})	5.9 (1.6)	5.8 (2.4)
CI (L.min^{-1}.m^{-2})	3.0 (0.8)	3.1 (1.0)

BMI is body mass index, BP: blood pressure, HR: heart rate, CO: cardiac output and CI: cardiac index. Haemodynamic measurements were obtained prior to induction of anaesthesia. Values are mean (SD) unless stated otherwise.

Table 3. Measurements during surgery

	Moderate NMB	Deep NMB
Duration of surgery (min, range)	141 (80-240)	144 (90-195)
BIS	42 (5)	44 (6)
Propofol (g)	1.6 (0.8)	1.6 (0.4)
Sufentanil (μg)	73 (30)	78 (22)
Rocuronium (mg)	-	223 (81)
Atracurium (mg)	37 (10)	-
Mivacurium (mg)	41 (24)	-
Train-of-four count	2.2 (0.9)	0
Post-tetanic-count	-	1.6 (1.5)
Leiden – surgical rating scale	4.0 (0.4)	4.7 (0.4) *
Retroperitoneal pressure (kPa)	1.5 (0.5)	1.4 (0.2)
BP systolic (kPa)	15.3 (2.6)	15.4 (1.7)
BP systolic (mmHg)	115 (20)	116 (13)
BP diastolic (kPa)	9.1 (0.9)	9.2 (1.2)
BP diastolic (mmHg)	68 (7)	69 (9)
HR (min^{-1})	67 (10)	69 (13)
CO ($L.min^{-1}$)	4.9 (1.4)	5.6 (2.0)
CI ($L.min^{-1}.m^{-2}$)	2.5 (0.8)	2.8 (0.9)

* $p < 0.001$ *vs.* moderate NMB.
NMB: neuromuscular block, BIS: bi-spectral index, TOF: train-of-four, PTC: post-tetanic-count, L-SRS: 5-point Leiden - surgical rating scale, BP: blood pressure, HR: heart rate, CO: cardiac output and CI: cardiac index. Values are mean (SD) unless stated otherwise.

Rating of surgical conditions during laparoscopic surgery

The rating of the surgical field was significantly different between treatments with a mean rating of 4.0 ± 0.4 (range 3.5 to 4.5, median 3.9) during a moderate NMB with TOF count of 1-2 twitches and 4.7 ± 0.4 (range 4.0 to 5.0, median 4.9) during a deep block with PTC of 1-2 twitches ($p < 0.001$, Figure 2). The distribution of all ratings taken during surgery is given in Figure 3. From these data the significant difference between the moderate (TOF count 1-2 twitches) and deep (PTC 1-2 twitches) blocks is apparent from the fact that 18% of scorings during moderate block was in the SRS range of 1-3 (scores rated as less than good), while 99% of scoring in the deep block was in the SRS range 4-5 (good and excellent scores). Variability in the individual ratings was higher for a block with TOF count = 1-2 twitches (mean coefficient of variation of ratings of surgical sessions 26%) compared to block with TOF = 0 and PTC = 1-2 (5%).

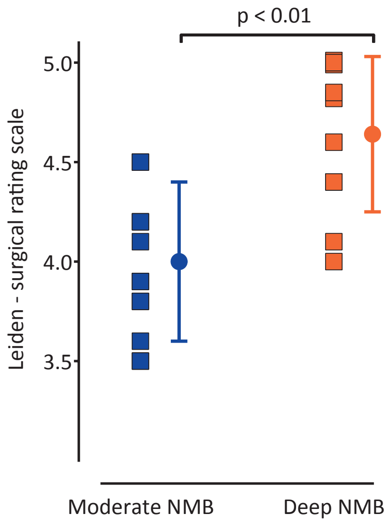

Figure 2. Surgical ratings by the surgeon during laparoscopic surgeries using the 5-point Leiden - surgical rating scale (see Table 1). Squares denote the individual mean ratings obtained during surgery. Circles are the mean of the means ± SD. NMB: neuromuscular block

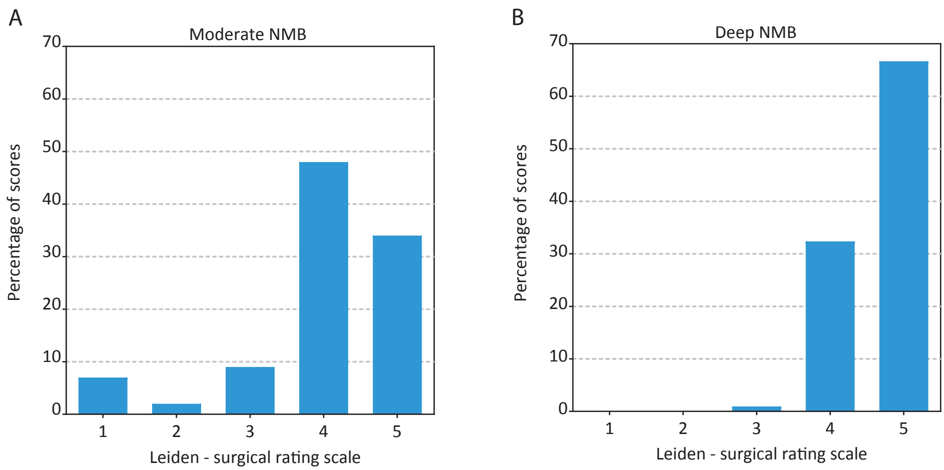

Figure 3. Distribution of the surgical ratings obtained during standard of care (**A**) and during deep neuromuscular block (**B**). NMB is neuromuscular block.

Measurements following surgery

Reversal of the neuromuscular block in patients with a deep block with sugammadex resulted in acceptable extubation conditions (TOF ratio > 0.9) after 5.1 (2.4) min. In contrast, similar extubation conditions were obtained after 10.9 (4.9) min ($p < 0.01$) in patients with a TOF count of 1-2 twitches and reversal with neostigmine. In the post-anaesthesia care unit, no differences were observed in respiration, pain and sedation levels (Table 4).

Table 4. Measurement following surgery

	Moderate NMB	Deep NMB
Sugammadex (mg)	-	380 (101)
Neostigmine (mg)	1 (0)	-
Time to TOF ratio > 0.9 (min)	10.9 (4.9)	5.1 (2.4)
Time in PACU (min)	86 (19)	86 (25)
SpO_2 (%)	98.6 (1.8)	98.2 (1.4)
Breathing rate (min^{-1})	14.5 (2.2)	14.5 (2.2)
Pain score (11-point scale)	2.6 (1.6)	2.1 (2.2)
Sedation score (5-point scale)	2.0 (0.6)	1.3 (1.0)

TOF is train-of-four count, PACU: post-anaesthesia care unit and SpO_2: arterial haemoglobin oxygen saturation. Values are mean (SD).

Rating of surgical condition by anaesthetists

A random set of 10 video images was scored by 12 anaesthetists. The distribution of the surgeon's ratings of these 10 images is given in Figure 4A; the corresponding distribution of ratings of the anaesthetists is given in Figure 4B. Compared to the surgeon their ratings were skewed to the right and agreement with the surgeon's ratings was poor (agreement between scores ranged from 0 to 40%). The kappa statistic was 0.05 (range -0.25 to 0.25). The Bland Altman analysis resulted in a significant bias of -0.43 (0.21; p = 0.03) and large limits of agreement of 2.87 and –3.72, and a between-subject variance of 0.25 (Figure 4C).

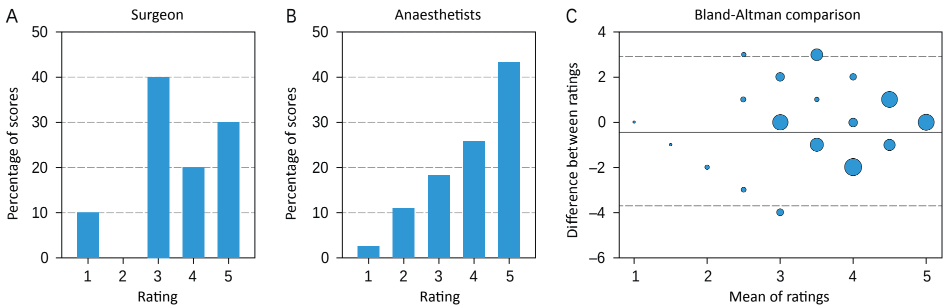

Figure 4. A. Distribution of scorings obtained from a random sample of 10 video snippets scored by the surgeon. **B.** Distribution of scorings obtained from a random sample of 10 video snippets scored by the surgeon and a group of 12 anaesthetists. **C.** Population Bland Altman analysis of the scorings from anaesthetists and surgeon. The continuous horizontal line is the bias; the dotted line the limits of agreement. The size of the dots represents the number of (overlapping) data points, which range from 1 for the smallest dots (1,0) and (1.5,-0.5), to 16 for the largest dot (4,-2).

DISCUSSION

This is the first study to assess the impact of a deep neuromuscular block (PTC 1-2 twitches) on surgical working conditions. The main results of our study are: (1) A deep neuromuscular block (TOF count = 0 and PTC 1-2 twitches) is associated with higher (*i.e.* improved) ratings from the surgeon compared to a moderate neuromuscular block (TOF count of 1-2 twitches) during laparoscopic prostatectomies and nephrectomies, indicating a significant improvement of surgical conditions; (2) Ratings from anaesthetists and surgeon of video images of the surgical field showed little agreement. In the current study, we chose to study retroperitoneal laparoscopic surgeries for two urological procedures (prostatectomy and (partial) nephrectomy) as these procedures are confined to a narrow working space where adequate (deep) muscle relaxation is of high importance and an effect of less optimal muscle relaxation on the quality of the surgical field is rapidly apparent.

The Leiden - surgical rating scale

The 5-point rating scale used in our study was developed in close cooperation with the surgeon involved in our project, who has ample experience in the performed procedures. It was decided that, while the scoring system should integrate all qualitative aspects that are important to the surgeon when judging the surgical working field, it should remain as simple as possible. A scoring system with more than 5 points was initially considered, such as an 11-point numerical quantitative scale (for example, numerical rating or visual analogue scales from 0 to 10, *cf.* Ref. 9), however, it was decided to rank the surgical field qualitatively from extremely poor, *via* poor, acceptable, good to optimal conditions (see Table 1 for an explanation of the different ratings). Further, to reduce variability in scoring between assessors just one surgeon was requested to score the surgical field in our study. Our system is similar to other scoring systems. For example, the Clinical Global Impression (CGI) rating scale is a 7-point qualitative scale in which physicians rate the severity of a patient's mental illness relative to the physician's past experience.[11] The GCI and our scoring systems are subjective but in our case the ample experience of the surgeon gives credibility to the procedure. Indeed the results of our study indicate that the surgeon was able to discriminate between a moderate and a deep neuromuscular block. The difference of 0.7 points (a difference of 18%) was regarded as important and clinically significant by the surgical team. We argue that the ability of our scoring system to discriminate between two distinct anaesthetic regimes indicates the validity of the 5-point surgical rating scale we developed.

Our study should be considered a proof-of-concept trial and further validation of the surgical rating scale is mandatory. Therefore, one should be cautious in extrapolation of our results to other procedures and other surgeons. Other surgeons may rate the surgical condition differently and other procedures may require a different anaesthetic and/or surgical approach. In an attempt to get an indication of the ability of other surgeons with ample experience in laparoscopic surgery to apply the scoring system, we invited eight surgeons, specialized in laparoscopic surgery for gastroenterological procedures, to score the 10 videos earlier presented to the anaesthetists. Their kappa statistic was on average 0.50 indicative of moderate agreement. As expected this agreement is substantially greater than that between surgeon and anaesthetists. It further shows that different surgeons (in this case with a different subspecialty) rate the surgical field differently. The current study was specifically aimed at scoring urological procedures performed in narrow retroperitoneal space. The results show a clinically relevant benefit of deep neuromuscular block for the surgeon involved in this study. Whether this benefit will also be relevant to other surgeons performing similar surgeries and possibly even for other laparoscopic procedures, such as for bariatric laparoscopic surgery is the topic of further research.

Deep neuromuscular block

Our *a priori* estimation of SRS distributions was satisfactory for the deep neuromuscular block but was underestimated for the moderate block. Good and optimal conditions were achieved during standard care (good 48% and optimal 34%) although at a lower frequency than during deep NMB (good 32% and optimal 67%). This indicates that in 82% of measurements during standard care and in 99% during deep NMB conditions were good to optimal. However, variability in ratings was high for moderate NMB compared to deep NMB: 26%, *versus* 5%. Also, in the deep NMB group, the range of scores (mean ranged from 4 to 5) was considered high and is still open for improvement. Further improvement may be obtained by (more) strictly controlling anaesthetic depth, analgesic state and arterial carbon dioxide concentrations. In the current study respirator settings were such that end-tidal carbon dioxide concentrations were between 4.4 and 6 kPa (33 and 56 mmHg). High arterial carbon dioxide concentrations stimulate the respiratory neuronal pool in the brainstem, which activates the phrenic nerve.[12] As a consequence, diaphragm contractions may persist despite a deep NMB. The neuromuscular block at the diaphragm is less intense than at the adductor pollicis muscle.[13, 14] Indeed, some of the video images showed movement related to diaphragm contraction unrelated to the ventilator-induced inspiration-expiration sequence or cardiac contractions despite train-of-four values of zero. The surgeon scored such conditions at the low end of the L - SRS. In laparoscopic bariatric surgery the working space volume and visibility increased in response to neuromuscular blockade.[15] In the current study, the retroperitoneal pressure was kept constant to 1.3-1.5 kPa (9-11 mmHg) in both groups and it may be assumed that the working space volume was greater in the deep NMB group. However, the scoring by the surgeon is only in part based on the perceived volume of the retroperitoneal space. Other factors similarly influence the surgeon's working conditions and consequently play an additional role in his scoring. For example, muscle contractions (including the diaphragm) and resultant movement of other structures are important as well. Further studies should address these issues.

We tested deep *versus* moderate block using two different drug regimens. The reason for this was that this approach enabled us to compare our current practice with atracurium and mivacurium with an approach that not only allows us to induce a deep neuromuscular block but also allows rapid reversal of that deep block. Since our end-point was to compare the depth of the neuromuscular block irrespective of the drugs used to induce that state, we do not believe that this influenced our outcome significantly. We observed that full reversal after deep NMB occurred after 5 min. It is importantto realise that measurements were made at 5-min intervals and full reversal with TOF ratio's > 0.9 may have occurred earlier (for sugammadex reversal to TOF ratio > 0.9 is expected after 2-3 min).

Scoring by anaesthetists of the surgical field

An important finding in our study is that the agreement of scores between the anaesthetists and surgeon was poor. This indicates that the anaesthetists are less well able to measure the quality of surgical conditions from the video images and hence derive insufficient information from these images regarding the working conditions of the surgeon. It may be argued that in our study observing a 30-s video image does not provide sufficient input to assess the quality of surgical condition in non-surgically skilled personnel. This may be true, but in our study, and possibly also in clinical practice, the anaesthetists base their impression of the surgical field primarily on the volume of the working space and the visibility of retroperitoneal tissues (most importantly related to the absence or presence of blood in the image obscuring relevant structures) without addressing muscle contractions and other movements visible on the video image. In our hospital, life video images of the laparoscopic field are available to the anaesthetists during each case and these, together with his/her clinical experience and interaction with the surgeon, form the basis of the anaesthetic regimen, including the additional use of muscle relaxants when surgical conditions are deemed poor. Some anaesthetists may not be willing to induce a deep neuromuscular block. This may be related to their inability to adequately judge the operating field from the video screen or to their fear for suboptimal post-surgical conditions. This may be the cause of some discussion in the operating room. To prevent such situations, we suggest that surgeons and anaesthetists communicate their wishes and intentions prior to the procedure (*e.g.* during preoperative *time-out*) and closely cooperate in obtaining optimal working conditions. Here we show that providing a deep neuromuscular block improves surgical conditions.

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