

## Deep neuromuscular block does not improve surgical conditions in patients receiving sevoflurane anaesthesia for laparoscopic renal surgery

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### Abstract

**Background:** Deep neuromuscular block is associated with improved working conditions during laparoscopic surgery when propofol is used as a general anaesthetic. However, whether deep neuromuscular block yields similar beneficial effects when anaesthesia is maintained using volatile inhalation anaesthesia has not been systematically investigated. Volatile anaesthetics, as opposed to intravenous agents, potentiate muscle relaxation, which potentially reduces the need for deep neuromuscular block to obtain optimal surgical conditions. We examined whether deep neuromuscular block improves surgical conditions over moderate neuromuscular block during sevoflurane anaesthesia.

**Methods:** In this single-centre, prospective, randomised, double-blind study, 98 patients scheduled for elective renal surgery were randomised to receive deep (post-tetanic count 1–2 twitches) or a moderate neuromuscular block (train-of-four 1–2 twitches). Anaesthesia was maintained with sevoflurane and titrated to bispectral index values between 40 and 50. Pneumoperitoneum pressure was maintained at 12 mm Hg. The primary outcome was the difference in surgical conditions, scored at 15 min intervals by one of eight blinded surgeons using a 5-point Leiden-Surgical Rating Scale (L-SRS) that scores the quality of the surgical field from extremely poor<sup>1</sup> to optimal<sup>5</sup>.

**Results:** Deep neuromuscular block did not improve surgical conditions compared with moderate neuromuscular block: mean (standard deviation) L-SRS 4.8 (0.3) vs 4.8 (0.4), respectively ( $P=0.94$ ). Secondary outcomes, including unplanned postoperative readmissions and prolonged hospital admission, were not significantly different.

**Conclusions:** During sevoflurane anaesthesia, deep neuromuscular block did not improve surgical conditions over moderate neuromuscular block in normal-pressure laparoscopic renal surgery.

**Clinical trial registration:** NL7844 ([www.trialregister.nl](http://www.trialregister.nl)).

**Keywords:** laparoscopic surgery; Leiden-Surgical Rating Scale; neuromuscular block; propofol; sevoflurane; surgical conditions; volatile anaesthesia

### Editor's key points

- Deep neuromuscular block improves surgical working conditions for propofol anaesthesia, but whether the same is true for volatile anaesthetics, which potentiate muscle relaxation on their own, is unclear.
- The authors examined whether deep neuromuscular block improves surgical conditions over moderate neuromuscular block during sevoflurane anaesthesia in a single-centre, prospective, randomised, double-blind study.
- In contrast to propofol anaesthesia, deep neuromuscular block did not improve surgical conditions compared with moderate neuromuscular block with sevoflurane anaesthesia for laparoscopic renal surgery.

Neuromuscular blocking agents (NMBAs) are routinely administered during general anaesthesia to facilitate tracheal intubation and to optimise surgical conditions. Increasing data suggest superiority of deep neuromuscular block (defined by a post-tetanic count of 1–2 twitches) in creating optimal working conditions for the surgical team.<sup>1,2</sup> However, it is unknown whether other aspects of anaesthetic technique, most notably choice of anaesthetic (e.g. total intravenous vs inhalation anaesthesia), influence the relationship between the degree of the neuromuscular block and surgical conditions, particularly in laparoscopic surgery. Volatile anaesthetics are known to potentiate NMBAs,<sup>3,4</sup> an effect that is less evident with propofol.<sup>5</sup> We have shown that surgical working conditions in laparoscopic surgery during propofol anaesthesia are highly reliant on the degree of neuromuscular block.<sup>6,7</sup> Whether such a relationship also exists for inhalation anaesthetics is unknown. To investigate this, we conducted a prospective, randomised, double blinded study in which patients scheduled for laparoscopic renal surgery were randomised to receive either moderate or a deep neuromuscular block during sevoflurane anaesthesia. The primary outcome was intra-operative surgical condition assessed by a surgeon using the validated Leiden-Surgical Rating Scale (L-SRS).<sup>6,8</sup> We hypothesised that use of a volatile inhalation anaesthetic would obviate the need for deep neuromuscular block because of the intrinsic neuromuscular blocking agent potentiating properties of the anaesthetic to improve surgical working conditions.

## Methods

### Study design and patients

The study, known as BLISS4, was carried out between May 2018 and March 2020 at the Leiden University Medical Centre in Leiden, The Netherlands after approval of the local ethics committee (Medische Ethische Toetsingscommissie Leiden-Den Haag-Delft). The trial was performed according to Good Clinical Practice guidelines,<sup>9</sup> and was registered in the trial register of the Dutch Cochrane Centre (trialregister.nl; identifier NL7844). Eligible procedures were limited to elective laparoscopic renal surgeries. Data from previous studies showed that these procedures benefit from deep neuromuscular block in terms of improved surgical work conditions.<sup>6,7</sup> Eligible patients received oral and written information 2 weeks before surgery. If a patient was willing to participate, written informed consent was obtained. Inclusion criteria were: 18 yr of age or older, ASA physical status 1–3, and elective laparoscopic surgery (e.g. donor-nephrectomy, renal

tumour resection, or pyeloplasty). Exclusion criteria were inability to give informed consent, BMI >35 kg m<sup>-2</sup>, previous surgery at procedure site, neuromuscular disease, pregnancy, and contraindications to study medications. Just before surgery (in the operating room), subjects were randomised between a moderate neuromuscular block (train-of-four [TOF] count 1–3 twitches) or deep neuromuscular block (post-tetanic count 1–2 twitches). Randomisation was performed within the electronic data capture system CASTOR (<https://www.castoredc.com>) just before induction of anaesthesia. This system was also used for collection and storage of data. The attending anaesthesiologist was unblinded and was responsible for rocuronium administration. The study team and surgeons were fully blinded and remained so until all the data were analysed.

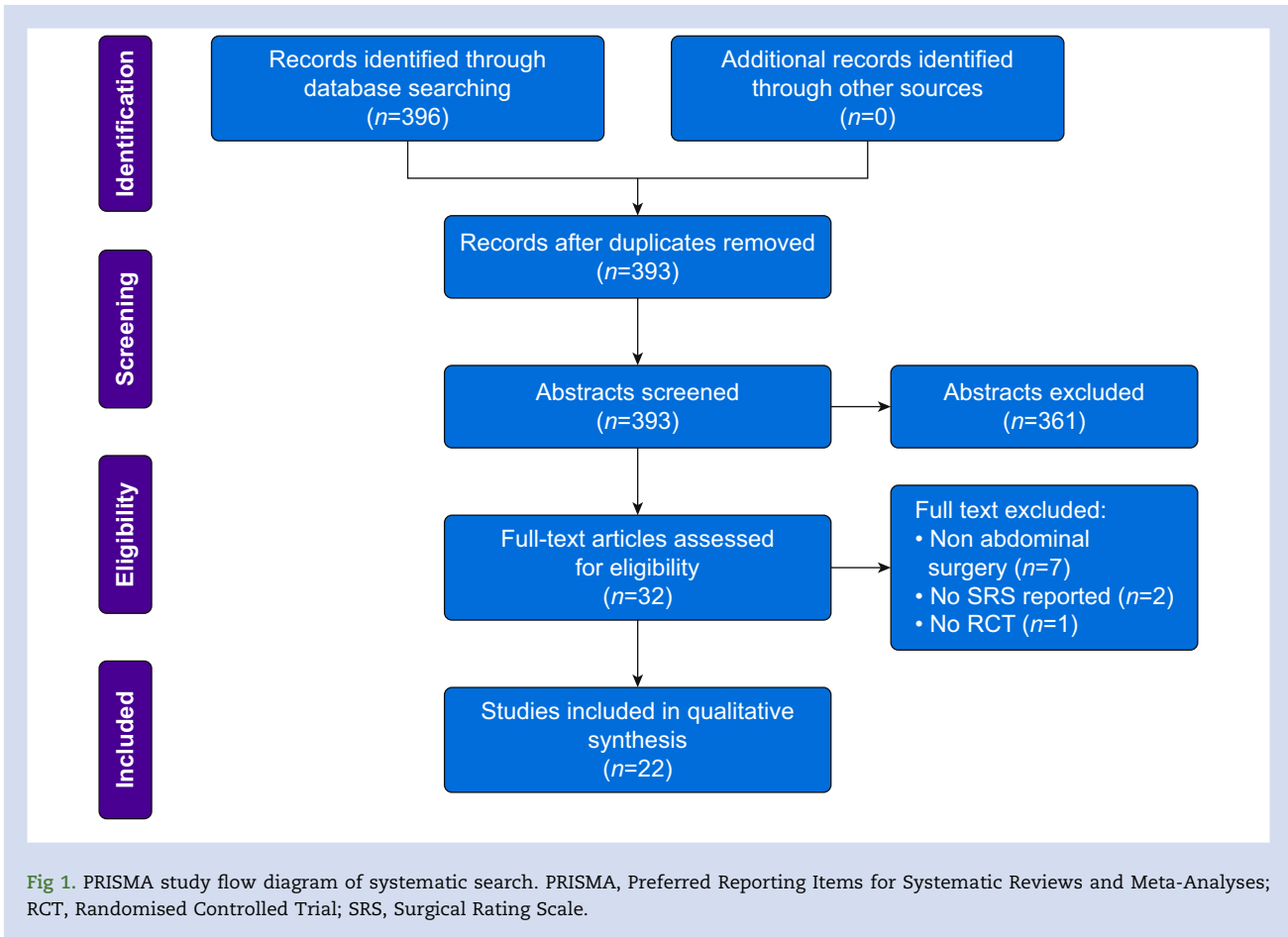
### Scoring of surgical conditions

The surgeon scored the quality of the intra-abdominal conditions at 15 min intervals using the L-SRS (see Martini and colleagues<sup>6</sup> and Boon and colleagues<sup>8</sup>). In brief, the L-SRS is a 5-point Likert scale that enables quantification of surgical conditions in a standardised fashion. The scale runs from 1 to 5: extremely poor (score=1), poor (2), acceptable (3), good (4), and excellent (5) surgical working conditions. The L-SRS has been internally and externally validated by our own group and other teams.<sup>6,10,11</sup> In our institution, surgeons have ample experience in using this scale. A dedicated team of eight surgeons performed all procedures and gave their L-SRS scores. As intra-abdominal pressure influences the quality of the surgical field, a target intra-abdominal pressure of 12 mm Hg was used in all cases.

### Perioperative protocol

All patients received standardised general anaesthesia with propofol/sufentanil/rocuronium for induction and sevoflurane/sufentanil/rocuronium for maintenance of anaesthesia. Routine monitoring was applied including bispectral index (BIS; Philips, Amsterdam, The Netherlands), noninvasive blood pressure, heart rate, ECG, pulse oximetry, and measurement of nasopharyngeal temperature. Sevoflurane administration was such that BIS values were kept between 40 and 50. Temperature was maintained between 36°C and 37°C with forced warm air blankets. In addition, nociception was monitored with the nociception level index (NOL; PMD200 Medasense, Ramat Gan, Israel).<sup>12</sup> Sufentanil was dosed during surgery aimed at keeping NOL between 10 and 25. Depth of neuromuscular block was measured with the TOF-Cuff brachial plexus compresso-myography (RGB Medical Devices, Madrid, Spain)<sup>13</sup> applied on an upper arm and calibrated according to the manufacturer's guidelines before administration of rocuronium. All data were collected at 15 min intervals during the procedure, simultaneously with the scoring by the surgeon.

Subjects received pre-emptive postoperative analgesia (acetaminophen 1 g i.v. and morphine 0.1–0.15 mg kg<sup>-1</sup> i.v.), 1 h before the end of surgery. After surgery, subjects were admitted to the PACU for routine monitoring. Data on nausea, vomiting, sedation level, oxygen saturation, and pain (visual analogue scale, 0–10) were collected at 15 min intervals. Pain scores represented overall pain level and were not related to body area (i.e. no distinction was made between shoulder vs abdominal pain). Intravenous morphine was the opioid of



choice for treatment of pain scores of 4 or greater. Data collection ended at the time of discharge to the ward, except for follow-up of (serious) adverse events, which continued for 7 days after surgery.

## Neuromuscular block and reversal

### Moderate neuromuscular block

In subjects randomised to receive moderate neuromuscular block, a bolus dose of rocuronium  $0.5 \text{ mg kg}^{-1}$  i.v. was administered, followed by intermittent injections of rocuronium 10–20 mg, aimed at keeping the TOF count at 1–2 twitches. At the end of the procedure, reversal of the neuromuscular block was by administration of sugammadex ( $2 \text{ mg kg}^{-1}$  i.v.). Patients were extubated when the TOF ratio reached 1.0, were breathing spontaneously, and were awake.

### Deep neuromuscular block

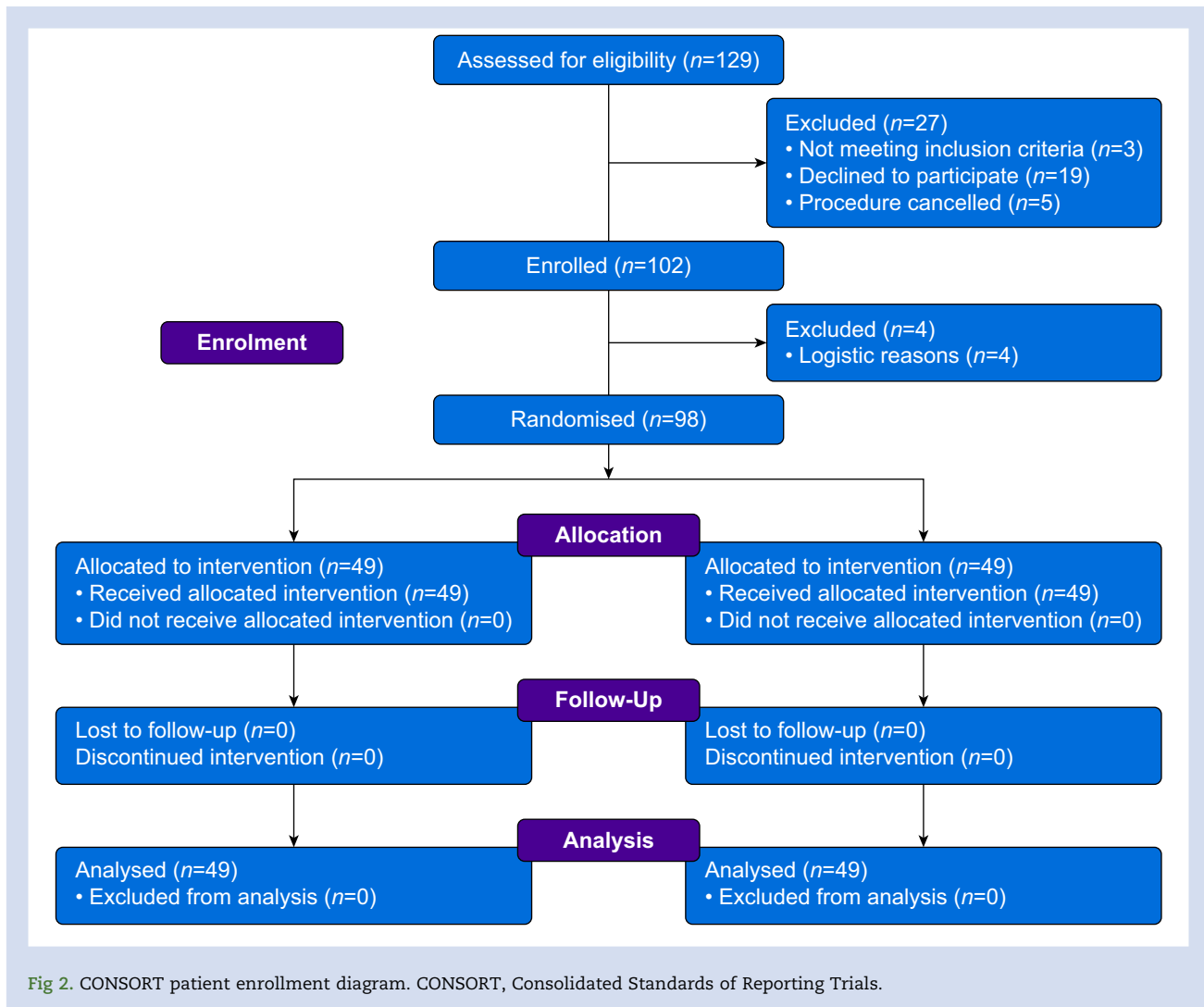
In subjects randomised to receive deep neuromuscular block, a bolus dose of rocuronium  $1.0 \text{ mg kg}^{-1}$  i.v. was administered, followed by a continuous infusion started at  $0.3 \text{ mg kg}^{-1} \text{ h}^{-1}$  and titrated to keep the post-tetanic count at 1–2 twitches throughout the procedure. In case the surgeon scored L-SRS at 1 or 2 (extremely poor or poor conditions), a bolus of rocuronium 10 mg could be administered. At the end of the procedure, reversal of the neuromuscular block was achieved with

administration of sugammadex  $2\text{--}4 \text{ mg kg}^{-1}$  i.v. Patients were extubated when the TOF ratio reached 1.0.

### Sample size calculation and data analysis

The study was powered to detect a minimum clinically relevant mean difference between the treatment groups of 0.5 point on the 5-point L-SRS scale. Assuming a standard deviation of 0.75, a sample size of 47 subjects per group would provide at least 90% power to observe the expected difference at  $\alpha=0.05$ . We chose to study 50 subjects per group to consider any margin of uncertainty around the effect size and standard deviation and possible subject withdrawal or loss of patients for other (e.g. logistic) reasons.

Generalised linear models were fitted to the data using the generalised estimating equations method (GEEGLM) in R (version 3.6.3, 2020, package 'geepack'; R Foundation for Statistical Computing, Vienna, Austria) to compare L-SRS data over time. Variability of the L-SRS was analysed by mean coefficient of variation of individual ratings. Comparisons of scores at fixed time points were analysed with the Mann–Whitney *U*-test. Other data were analysed with standard parametric or non-parametric tests as appropriate. Statistical analyses were performed using the SPSS statistical software package (version 26.0; IBM SPSS statistics, Armonk, NY, USA). A *P* value  $<0.05$  was considered significant. Data are presented as mean (standard deviation) unless otherwise stated.



### Systematic review

We performed a search on May 26, 2020 using PubMed to identify manuscripts that studied the effect of deep neuromuscular block on surgical working conditions, and examined their relationship with intravenous or inhalation anaesthesia. Only original randomised controlled trials, written in English, specifically assessing intraoperative surgical conditions during deep neuromuscular block were considered. Eligible manuscript titles and abstracts were screened independently by MH and MB; inconsistencies in final full-text selection were resolved by consensus. The search strategy and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) study selection flow chart are provided in Supplement 1 and Figure 1.

### Results

A total of 129 patients were screened for eligibility, of whom 102 were enrolled in the study. Reasons for exclusions were: not meeting inclusion criteria ( $n=3$ ), declining to participate ( $n=19$ ), or cancellation of the surgical procedure ( $n=5$ ). Four enrolled subjects were not randomised, and consequently not

studied, because of logistic reasons (e.g. postponement of surgery owing to the coronavirus disease 2019 [COVID-19] pandemic). The remaining 98 subjects were allocated, randomised, and treated according to protocol. All subjects were included in the data analysis and none were lost during follow-up. Figure 2 depicts the CONSORT (Consolidated Standards of Reporting Trials) flow chart of the study.

### Perioperative measurements

Baseline characteristics and intraoperative measurements did not differ between groups apart from depth of neuromuscular block (Tables 1 and 2). Importantly, depth of anaesthesia and NOL index were not significantly different between groups, both on average and at all individual time points (Table 2). Intraoperative opioid consumption was similar between groups. The median (inter-quartile range) level of neuromuscular block in the deep neuromuscular block group was PTC 2 (1–3) twitches and TOF 1 (1–1) twitches in the moderate neuromuscular block group.

The primary outcome, surgical working conditions as rated by surgeons on the L-SRS, was recorded 826 times during the

**Table 1** Subject baseline characteristics. Data are presented as mean (standard deviation) unless otherwise stated. NMB, neuromuscular block.

	Moderate NMB (n=49)	Deep NMB (n=49)
Procedure, n (%)		
(Donor) nephrectomy	36 (74)	45 (92)
Pyeloplasty	13 (26)	4 (8)
Sex (M/F)	21/28	20/29
Age (yr), median (range)	57 (20–77)	51 (22–84)
Height (m)	1.75 (0.1)	1.75 (0.1)
Weight (kg)	80.0 (13.5)	81.4 (13.9)
BMI (kg m <sup>-2</sup> )	26.2 (3.7)	26.4 (3.2)
ASA physical status, n (%)		
1	22 (45)	28 (57)
2	26 (53)	20 (41)
3	1 (2)	1 (2)

study: 394 scores during moderate neuromuscular block and 432 scores during deep neuromuscular block. The mean L-SRS was 4.8 (SD 0.3) in the deep neuromuscular block group and 4.8 (0.4) in moderate neuromuscular block group (GEEGLM  $P=0.94$ ). There were no significant effects of covariates (including surgeon,  $P=0.24$ ; surgery length,  $P=0.73$ ; and BMI,  $P=0.22$ ).

The distribution of scores was comparable between groups: L-SRS=5 was scored in 84.0% vs 83.6% during deep and moderate neuromuscular block, respectively; L-SRS <4 were not scored during deep neuromuscular block compared with 3.8% of all scores in the moderate neuromuscular block group. L-SRS <3 was not reported in any group. A graphical display of the results is available in [Supplementary Figure S1](#). The variability of ratings (mean coefficient of variation of ratings) was 2.8% in deep neuromuscular block

**Table 2** Data are presented as median (range) unless otherwise stated. \* $P<0.01$ . NMB, neuromuscular block; SD, standard deviation.

Intraoperative measurements	Moderate NMB (n=49)	Deep NMB (n=49)
Duration of surgery (min)	164 (70–251)	177 (84–298)
Train-of-four count	1 (1–3)	0
Post-tetanic count	–	2 (0–14)
Leiden-Surgical Rating Scale (1–5)		
Mean (SD)	4.8 (0.4)	4.8 (0.3)
Median [range]	5 (3–5)	5 (4–5)
Bispectral index	42 (33–50)	42 (29–51)
End-tidal sevoflurane concentration (vol%)	1.77 (1.5–2.2)	1.78 (1.4–2.3)
Minimum alveolar concentration	1.1 (0.8–1.2)	1.0 (0.8–1.4)
Mean arterial blood pressure (mm Hg)	84 (67–103)	85 (69–105)
Nociception level index	11 (1–42)	13 (4–27)
Total rocuronium (mg) *	110 (50–210)	206 (110–401)
Total sugammadex (mg) *	200 (150–400)	320 (200–600)
Total morphine (mg)	10 (5–15)	10 (5–15)
Total sufentanil (µg)	60 (30–100)	60 (40–115)

and 4.7% in moderate neuromuscular block group. In 5 out of 98 procedures the surgeon noted sudden deterioration of the surgical working field from L-SRS 5 to lower values (3 or 4). This happened four times during moderate neuromuscular block and once during deep neuromuscular block. In two cases (one in each group), the laparoscopic procedure was converted to an open procedure because of technical difficulties unrelated to the quality of the surgical field (e.g. uncontrollable bleeding).

### Postoperative measurements and outcomes

No statistically significant differences were observed in the PACU with regard to pain and total morphine requirement, sedation level, oxygen saturation level, and need for supplemental oxygen ([Table 3](#)). During the 7 day follow-up, five subjects (10%) in the moderate neuromuscular group suffered a serious adverse event: three subjects required prolonged hospital stay of which one was related to postoperative pneumonia and two subjects were readmitted after discharge because of ureter obstruction ( $n=1$ ) or postoperative infection ( $n=1$ ). In the deep neuromuscular block group, two subjects (4%) suffered a serious adverse event, in both cases prolonged hospital stay (one related to the conversion to open surgery and one because of deterioration of renal function). As judged by the local ethics committee, all adverse events were unrelated to the study.

### Systematic review

The literature search yielded 393 papers. After a careful selection process ([Fig. 1](#), PRISMA study selection flow chart), 22 papers were included in the review ([Table 4](#)). We identified 12 that used propofol as primary anaesthetic agent,<sup>6,10,19,25–33</sup> of which six found a benefit of deep neuromuscular block on surgical working conditions,<sup>6,10,19,25–27</sup> and six did not.<sup>28–33</sup> In addition, 10 studies were identified that used an inhalation agent.<sup>14–18,20–24</sup> Seven out of these 10 studies reported a benefit of deep neuromuscular block during inhalation anaesthesia on surgical working conditions.<sup>14–18,20,21</sup>

**Table 3** Measurements and drug administration in the PACU. Data are presented as mean (standard deviation) unless otherwise indicated. Discharge readiness at PACU is defined by time to an Aldrete score >9 and pain score <5 as measured by the numerical rating scale (NRS). Sedation score: Leiden Observer's Assessment of Alertness/Sedation; 7-point scale from 0 (no sedation) to 6 (not arousable). Differences are not statistically significant ( $P>0.05$ ). NMB, neuromuscular block; SpO<sub>2</sub>, blood oxygen saturation.

	Moderate NMB (n=49)	Deep NMB (n=49)
Time to discharge readiness (min)	51 (36)	53 (35)
NRS	2.9 (1.9)	3.2 (1.8)
Patients with NRS >5, n (%)	15 (31)	16 (33)
Sedation score	0.9 (0.6)	1.0 (0.6)
SpO <sub>2</sub> (%)	98 (1)	98 (1)
Oxygen dependency, n (%)	21 (43)	24 (49)
Nausea, n (%)	7 (14)	14 (29)
Total administered morphine (mg)	3.4 (4.8)	4.4 (4.6)

**Table 4** Overview of RCTs evaluating deep neuromuscular block (NMB) in abdominal surgery. \*Surgical working conditions not the primary outcome of the study. <sup>1</sup>Paediatric population. BIS, bispectral index; MAC, minimum alveolar concentration; SE, state entropy.

Authors	Surgical working conditions improved with deep NMB?	Comparator to deep NMB	Hypnotic agent	Depth of anaesthesia: BIS/MAC/vol. %	Low pressure pneumoperitoneum?
<i>Inhalation anaesthesia</i>					
Blobner and colleagues <sup>14</sup>	Yes	No NMB	Desflurane	BIS 40–50	No
Dubois and colleagues <sup>15</sup>	Yes	Single Shot	Desflurane	MAC 1.0	No
Fuchs-Buder and colleagues <sup>16</sup>	Yes	Moderate	Desflurane	4.0–6.0%	No
Kim and colleagues <sup>17</sup>	Yes*	Moderate	Desflurane	4.0–7.0%	Yes
Koo and colleagues <sup>18</sup>	Yes*	Moderate	Desflurane	BIS 40–60	Yes
Ozdemir-van Brunschot and colleagues <sup>20</sup>	Yes	Moderate	Sevoflurane	MAC 1.0	Yes
Yoo and colleagues <sup>21</sup>	Yes*	Moderate	Sevoflurane	BIS 40–60	Yes
Veelo and colleagues <sup>22</sup>	No	On Demand	Sevoflurane	MAC 1.0	No
Williams and colleagues <sup>23</sup>	No*	Moderate	Unknown	Unknown	No
Kim and colleagues <sup>24</sup>	No*	Moderate	Desflurane	4.0–8.0%	No
<i>Total intravenous anaesthesia</i>					
Koo and colleagues <sup>25</sup>	Yes*	Moderate	Propofol	Unknown	Yes
Koo and colleagues <sup>19</sup>	Yes*	Moderate	Propofol	Bis 40–50	Unknown
Madsen and colleagues <sup>26</sup>	Yes	Single shot	Propofol	SE 30–50	Not applicable
Martini and colleagues <sup>5</sup>	Yes	Moderate	Propofol	Bis 45–55	No
Rosenberg and colleagues <sup>27</sup>	Yes	Shallow (TOF ratio 0,1)	Propofol	Bis 40–50	Yes
Torensma and colleagues <sup>10</sup>	Yes	Moderate	Propofol	Bis 45–55	No
Baete and colleagues <sup>28</sup>	No	Moderate	Propofol	Unknown	No
Barrio and colleagues <sup>29</sup>	No	Moderate	Propofol	Bis 40–60	Yes
Bruintjes and colleagues <sup>30</sup>	No*	Single shot	Propofol	Bis 40–50	Yes
Klucka and colleagues <sup>31,i</sup>	No	Moderate	Propofol	Unknown	Yes
Soderstrom and colleagues <sup>32</sup>	No	No NMB	Propofol	Bis 40–60	No
Staehr-Rye and colleagues <sup>33</sup>	No	Single shot	Propofol	SE	Yes

## Discussion

Suboptimal surgical working conditions during procedures under general anaesthesia are commonly encountered.<sup>34</sup> These events are often benign and self-limiting but may potentially induce harm, especially when they occur unexpectedly at critical moments. Therefore, strategies that reduce these incidences may improve patient outcome.<sup>35</sup> Deep neuromuscular block prevents unanticipated deterioration of surgical conditions by inhibiting muscle contractions of the abdominal wall and diaphragm. Deep neuromuscular block is necessary to relax these resistant muscle groups fully.<sup>36</sup> Two recent meta-analyses of RCTs confirmed a benefit of deep neuromuscular block on surgical working conditions during laparoscopic surgery.<sup>1,2</sup> However, the meta-analyses were limited by small study sample sizes and significant inter-study heterogeneity, which impedes definitive conclusions. In addition, deep neuromuscular block may not always be feasible (e.g. because of drug allergies, limited access to sugammadex) or it may not be necessary, particularly when a volatile anaesthetic is used. Unlike intravenous anaesthetics such as propofol, volatile inhalation anaesthetics augment muscle relaxation<sup>3,4</sup> and suppress nociception-evoked motor responses through actions within the spinal cord via multiple receptor systems, ion-channel systems, or both that result in central spinal inhibition of motor neurone excitability and peripheral augmentation of NMBA potency at the neuromuscular junction.<sup>37–40</sup> In addition, clinical data support that immobility is less marked for propofol compared with inhalation anaesthetics.<sup>39,41</sup>

We hypothesised that the neuromuscular blocking agent properties of sevoflurane obviate the need for deep

neuromuscular block to obtain optimal surgical working conditions. Our data show that surgical working conditions during laparoscopic renal surgery were not significantly different between deep and moderate neuromuscular block when anaesthesia is maintained with sevoflurane and abdominal insufflation pressure is kept at 12 mm Hg. In addition, the majority of surgical ratings were good or excellent (L-SRS 4 or 5), even during moderate neuromuscular block.

The results of the current study contrast with a previously published study from our group.<sup>6</sup> In that study, the effects of deep vs moderate neuromuscular block on surgical working conditions were compared for similar types of surgical procedures, but differed with respect to the hypnotic that was used for maintenance (propofol vs sevoflurane in the current study).<sup>6</sup> When we compare the results of these two studies, the results of the deep neuromuscular block group during propofol anaesthesia are comparable with the results of the moderate neuromuscular block group during sevoflurane anaesthesia with similar L-SRS scores, distributions of scores, and low variability of individual ratings. Importantly, variability of ratings in the moderate neuromuscular block group during propofol anaesthesia was 26%, a sharp contrast with the current observation made during sevoflurane anaesthesia (3.3%). Although the current study did not directly compare the effect of depth of neuromuscular block during propofol vs sevoflurane and therefore does not allow for definitive conclusions, the general picture is that similarly optimal surgical conditions are obtained with moderate neuromuscular block during sevoflurane anaesthesia and deep neuromuscular block during propofol anaesthesia. Therefore, application of a deep neuromuscular block when using sevoflurane does not offer significant advantages in this respect.

In a systematic review of the literature, we considered papers that studied the effect of muscle relaxation on surgical working conditions based on the primary anaesthetic agent (i.e. propofol vs inhalation anaesthetic). Seven (of 10) studies reported improved surgical working conditions with deep neuromuscular block during inhalation anaesthesia.<sup>14–18,20,21</sup> At first, this appears to contradict with our current results; however, the context of these studies differed markedly from our study. For example four of the seven positive studies found a beneficial effect of deep neuromuscular block during low pressure pneumoperitoneum,<sup>17–18,20,21</sup> and two studies had an insufficient comparator to deep neuromuscular block (i.e. deep neuromuscular block was compared with groups in which no or single dose neuromuscular block was used).<sup>14,15</sup> One study showed that surgical conditions improved when switching from moderate to deep neuromuscular block in bariatric surgery during desflurane anaesthesia.<sup>16</sup> It may be that the beneficial effects of volatile anaesthetics on the quality of the surgical field are less pronounced when laparoscopic surgery is performed at a low insufflation pressure or in bariatric surgery, still requiring deep neuromuscular block for optimal surgical exposure in these settings. The degree of potentiation of neuromuscular block differs between various inhalation anaesthetics, with ethers being more potent than halogenated hydrocarbons<sup>42</sup> such that effects on surgical working conditions may likewise differ between various inhalation agents. However, we contend that for laparoscopic kidney surgery, and possibly other less complex laparoscopic procedures using a normal insufflation pressure, moderate neuromuscular block is sufficient when sevoflurane is used. Observations made during open surgery endorse a similar approach. For instance, King and colleagues<sup>43</sup> investigated the effect of muscle relaxation (vecuronium aimed at TOF count 1 twitch vs placebo) during open retroperitoneal prostatectomy under isoflurane–fentanyl anaesthesia. They found that surgical scores were acceptable without muscle relaxation; however, moderate neuromuscular block reduced the incidence of unacceptable surgical conditions.

Our systematic review identified 12 studies that used propofol as a primary anaesthetic, of which half found a benefit of deep neuromuscular block,<sup>6,10,19,25–27</sup> whereas the other half did not (Table 4).<sup>28–33</sup> Significant methodological differences and the large heterogeneity in surgical procedures prevents drawing definitive conclusions from these studies. However, the results of our current (sevoflurane) and previous (propofol) studies<sup>6,7</sup> give an indication of the differential effects of propofol and sevoflurane on surgical working conditions in laparoscopic renal surgery. The controlled anaesthesia protocol of the current study, using predetermined bispectral and nociception level index targets, decreased the chance of under- or over-dosing of sevoflurane and opioids. These aspects increase the likelihood that the absence of benefit of deep neuromuscular block was indeed determined by the choice for sevoflurane.

Our study has several limitations. First, the high degree of anaesthetic standardisation may limit generalisation to real-world practice, as this set-up may not always be possible. In addition, findings on the L-SRS are in essence subjective scorings, which have unclear relationships with other outcomes. Although there is subjectivity in every rating system, the L-SRS has shown good internal and external validity.<sup>6,10,11</sup> The current study, however, does not answer the question whether the absence of benefit of deep neuromuscular block on surgical working conditions translates into the absence of

benefit on other outcomes that were observed in earlier (exploratory) prospective and retrospective studies. For example earlier studies suggested that deep neuromuscular block is associated with less postoperative pain and reduced incidence of unplanned readmission.<sup>10,17,35</sup> The effect of deep neuromuscular block given with sevoflurane anaesthesia on other endpoints and under different circumstances (e.g. during low-pressure laparoscopy or bariatric surgery) needs to be addressed in future studies. Finally, the application of deep neuromuscular block may increase the risk for residual neuromuscular block or prolonged reversal times, especially if high doses of rocuronium are administered. Use of NMBAs in general and, application of deep neuromuscular block in particular, should only be used with guidance of TOF monitoring, and a threshold TOF ratio of 0.9 should always be regarded as minimum recovery before tracheal extubation is attempted.<sup>44</sup>

In conclusion, this study shows that during normal-pressure laparoscopic renal surgery, deep neuromuscular block has no benefit over a moderate neuromuscular block with regard to surgical working conditions when anaesthesia is maintained with sevoflurane.

### Authors' contributions

Data collection: GH, CM, RB, VH, IA, MN, MV, AD, MB

Statistical analysis: GH, EO, MV

Writing of the manuscript: GH, AD, MB

Inception of the study idea: CM, AD, MB

Study design: CM, EO, RB, VH, IA, MN, MV, LA, AD, MB

Revision of the manuscript: CM, EO, RB, VH, IA, MN, MV, LA

All authors approved the final manuscript.

### Declarations of interest

MB, AD, and CM received consultancy fees, speaker fees, or both from Merck Sharp Dome. The other authors have no conflicts of interest to declare.

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### Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.bja.2020.09.024>.

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