SUGAMMADEX ALWAYS FAST? PROBABLY YES, BUT IN LIVER TRANSPLANTATION

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rocuronium, neostigmine, reversal, recovery time, liver transplantation.
Abstract

Background: Rapid neuromuscular block reversal at the end of major abdominal surgery is recommended to avoid postoperative residual. To date, no study has evaluated sugammadex use and performance after rocuronium administration in patients undergoing liver transplantation. This is a randomized controlled trial with the primary objective of assessing the recovery time of neuromuscular transmission with sugammadex versus neostigmine after rocuronium administration in patients undergoing LTx.

Methods: The TOF-Watch SX® with calibration and linked to a portable computer with TOF-Watch SX Monitor Software® was used to monitor and record intraoperative neuromuscular block, maintained with a continuous infusion of rocuronium. Anaesthetic management was standardized as per our institution's internal protocol. At the end of surgery, neuromuscular moderate block reversal was obtained after administration of 2 mg/kg of sugammadex or 50 mcg/kg of neostigmine (plus 10 mcg/kg of atropine).

Results: Data from 41 patients undergoing liver transplantation were analysed. In this population, neuromuscular block recovery time was faster after administration of sugammadex than neostigmine, with a mean value±SD of 9.4±4.6 min vs. 34.6±24.9 min respectively (p<0.0001).

Conclusion: Neuromuscular block reversal after rocuronium continuous infusion was significantly faster with sugammadex than neostigmine and feasible in patients undergoing liver transplantation. It is important to note that sugammadex recovery time in this population was found to be considerably longer than in other surgical settings, an interesting finding that needs further studies to be fully explained and it should be taken into consideration in clinical practice.

Trial registration: ClinicalTrials.gov NCT02697929.

Keywords: rocuronium, neostigmine, reversal, recovery time, liver transplantation.
Background

Myoresolution plays a crucial role in laparotomic and laparoscopic general surgery, including orthotopic liver transplantation (LTx): it has been shown that a deep level of neuromuscular block (NMB) allows for better surgical conditions.\textsuperscript{1,2} Deep NMB, defined as \( \leq 2 \) responses after post-tetanic stimulation (or post-tetanic count - PTC), requires greater doses of neuromuscular blocking agent (NMBA) with a consequent higher risk for longer and unpredictable recovery times regardless of the agent used\textsuperscript{3-5}.

NMBA use, especially at high dosages, may be associated with postoperative residual curarization (PORC) leading to respiratory adverse events, pulmonary complications, and compromised extubation.\textsuperscript{6-8} Both the administration of NMBAs reversal agents at the end of surgery and the use of neuromuscular transmission monitoring (NMT) throughout the surgical procedure are key factors to counteract the adverse outcomes related to an impaired neuromuscular transmission after extubation.\textsuperscript{9-11,12}

International guidelines and expert opinions strongly recommend NMT to optimize dosages and administration timing of both the NMBAs and the reversal agent, thus providing an early and safe extubation. This is strongly encouraged also in the LTx settings, because it can directly affect the patient’s outcome as well as being a cost-effective practice.\textsuperscript{13-18}

Pharmacokinetics and pharmacodynamics of rocuronium bromide may be altered in patients with impaired liver function, with a longer half-life for drug elimination, a slower recovery from NMBA and an unpredictable behaviour.\textsuperscript{19,20}

The safety and speed of action of sugammadex has been investigated and validated in
different settings, including patients with liver disease.\textsuperscript{21-23} Fujita and colleagues demonstrated that sugammadex can be effective for the reversal of NMBA after rocuronium continuous infusion in patients with liver disorders undergoing liver resection surgery.\textsuperscript{24} Similar results were recently obtained by Abdulatif and colleagues that found a mean recovery time for sugammadex of 3.1 minutes given at 2 mg/kg for moderate block reversal in a cohort of cirrhotic patients.\textsuperscript{25} However, patients with end stage liver disease undergoing LTx, significantly differ from previous studies for a physiopathological, anesthesiological and surgical point of view.

To the best of our knowledge, no study has evaluated sugammadex use after rocuronium continuous infusion during LTx.

The primary objective of this study was to measure the time interval from the administration of the NMBA reversal agent (sugammadex or neostigmine) to the achievement of a Train of Four ratio (TOF\textsubscript{R}) \(\geq 0.9\) (called recovery time) in patients who have undergone LTx with intraoperative continuous rocuronium infusion.

The secondary objective was to determine possible relationships between the recovery times of the two drugs with pre-, intra- or postoperative variables.

\textbf{Methods}

\textbf{Materials and methods}

This is a single centre, unblinded, randomized controlled trial approved by the Ethics Committee of the University Hospital “Santa Maria della Misericordia” of Udine (n° 2016-O-015-ASUIUD) and registered at ClinicalTrials.gov (NCT02697929) prior to patient enrollment. This manuscript adheres to the applicable CONSORT guidelines and the study protocol conformed to the ethical guidelines of the Declaration of Helsinki.

After ClinicalTrial.gov registration, we evaluated consecutive LTx performed at Academic
Hospital “S. Maria della Misericordia”, Udine, Italy. When written informed consent was obtained before LTx starting, patients were randomly allocated to the sugammadex or neostigmine group using an online computer-generated table.

All clinical data were collected in an Excel spreadsheet (Microsoft Excel for Mac, Version 14.0.0, Microsoft Corporation, USA).

Inclusion criteria were as follows:
Age ≥ 18 years;
Neuromuscular transmission data acquired with TOF-Watch SX Monitor Software® (Organon, Dublin, Ireland. Version 1.2) from anaesthesia induction until extubation;

Exclusion criteria were as follows:
American Society of Anesthesiologists (ASA) status > 3;
Neuromuscular disease;
Other than rocuronium bromide used;
Body mass index (BMI) < 18 kg/m² or > 40 kg/m²;
Pre-operative impaired renal function, defined as an estimated glomerular filtration rate < 30 ml/min/1.73 m²;
Inner body temperature < 35 °C or thenar temperature < 32 °C at reversal administration;
Haemodynamic instability defined as norepinephrine dosage > 0.1 mcg.kg⁻¹.min⁻¹ and/or dobutamine > 3 mcg.kg⁻¹.min⁻¹ and/or epinephrine > 0.1 mcg.kg⁻¹.min⁻¹ at the time of reversal administration and/or mean arterial pressure < 60 mmHg and/or HR>100 bpm;
Acidosis defined as an arterial pH<7.30 at the time of reversal administration;
Incorrect dosage of reversal (50 mcg/kg for neostigmine and 2 mg/kg for sugammadex);

Pre-operative data included sex, age, weight, body mass index (BMI), liver disease, model for end stage liver disease (MELD), liver function, and renal function.

Intra-operative collected data included duration of surgery, intra-operative blood losses, packet red cells (PRC), fresh frozen plasma (FFP) and salvage blood transfused, platelets (PLT) use, fibrinogen administration, net fluid balance, cold ischaemia time (CIT), warm ischaemia time (WIT), total dose of rocuronium administered and total millilitres of crystalloids and colloids infused. Cardiac output, cardiac index and central temperature (values obtained from pulmonary artery catheter) with thenar temperature at the time of reversal administration were recorded. Adverse events reported in the anaesthesia sheet.
were recorded.

Anaesthesia was induced with propofol (1-1.5 mg/kg) and fentanyl (3-5 mcg/kg) or alfentanil (7-15 mcg/kg) after facial mask denitrogenation with $F_1O_2=0.8$. NMBA (rocuronium 0.6 mg.kg based on lean body weight) was administered at anaesthesia induction only after TOF Watch SX® calibration (Organon, Dublin, Ireland).

Maintenance of anaesthesia was provided by sevoflurane (ET% targeted to keep the bispectral index in the 40-60 range) and continuous infusion of remifentanil (0.05-0.3 mcg.kg$^{-1}$.min$^{-1}$), while neuromuscular block was maintained with rocuronium bromide (Esmeron® 50 mg/5 mL, MSD Italia S.r.l., Roma) intravenous continuous infusion (0.3-0.6 mg.kg$^{-1}$.h$^{-1}$) to keep $T_1<10\%$.

Haemodynamic monitoring with pulmonary artery catheter (CCombo catheter 777HF8; Edwards Lifescience, Irvine, California, USA) was targeted to optimize indexed oxygen delivery ($DOI_2>600\text{ m}\text{l}.\text{m}^2.\text{m}^{-1}$.min$^{-1}$) for the first 6 hours postoperatively.

All LTx were performed with the same surgical equipe dedicated to solid organ transplant surgery.

As per our routine practice for NMT monitoring with TOF-Watch, two electrodes were placed over the left ulnar nerve at the wrist and the acceleration transducer was put on the thumb, together with a hand adapter that immobilized the other fingers. Data was collected into a dedicated computer using the TOF-Watch SX Monitor Software® which registered the response to ulnar nerve stimulation every 15 s. After anaesthesia induction, but before rocuronium administration, the TOF-Watch SX was calibrated. Afterward, the rocuronium bolus for tracheal intubation was given, and continuous infusion was started.

At the end of surgery reversal agents - sugammadex 2 mg/kg based on actual body weight
(Bridion® 100 mg/mL, MSD Rome, Italy) or neostigmine 50 mcg/kg based on adjusted body weight plus 10 mcg/kg of atropine (Intrastigmina®, 0.5 mg/mL, Lusofarmaco S.p.a., Rozzano, Italy) were administered, according to randomization, after the appearance of three consecutive T_2 twitches (the so-called moderate neuromuscular block) detected by TOF Watch SX®.

Recovery time was defined as the time interval from the administration of the reversal agent to the achievement of 3 consecutive measurements of TOF_R ≥ 0.9.

Our secondary objective was to analyse the main possible correlations between factors that may have influenced recovery time of sugammadex and neostigmine: BMI, MELD, preoperative and postoperative liver and renal function, surgical procedure length, blood loss, intraoperative fluid balance, cold and warm ischaemia time, total amount of NMB delivered, millilitres of crystalloid and colloid infused, CO and CI when reversal was given.

Statistical Analysis

Illman and colleagues found a mean difference of 11.6 minutes between sugammadex and neostigmine, administered when two twitches were detectable, to reach a TOF_R>90%.^26^ Considering a 1:1 treatment ratio and an expected 5-minute reduction in the sugammadex group, with an alpha level of 0.05 and a power (1-ß) of 90%, the calculated sample size was 16 subjects for each group. Taking into consideration a dropout of 20%, and to increase the statistical significance, we decided to enroll at least 20 subjects per group.

Descriptive statistics (mean and standard deviation for quantitative variables, and absolute and relative frequencies for qualitative variables) were calculated for each group. To test for a difference of recovery times between the two groups with respect to the primary objective, we implemented a two-sided unpaired t test as well as an F-test to compare variances and to control for whether the t test assumptions were met. The same
test was applied to all remaining data. The alpha level of statistical significance for all applied tests was 0.05. No imputation of missing data was used for the analysis. Finally, to detect possible relationships between the recovery times of the two drugs with other variables, we performed both the Spearman rank and the Pearson correlation tests as their difference, or lack thereof, could provide additional information.

GraphPad Prism version 6.01 (GraphPad Software, California, USA) was used for the final statistical analysis.

Results

Between July 2016 and August 2017 we enrolled 41 patients: 21 treated with sugammadex and 20 with neostigmine, as shown in the study flowchart (Figure 1).

Baseline characteristics and end stage liver disease aetiology were comparable between the sugammadex and neostigmine groups (Table 1).

Additionally, there were no statistically significant differences in pre-, intra- and postoperative values regarding haemodynamics, liver and renal function (Table 1 and 2).

The rocuronium onset times were similar between the two groups, with 195±124 and 250±123 seconds for the sugammadex and neostigmine groups, respectively (p=0.20). The total dose of Rocuronium administered was 217±61 mg and 199±74 mg (p=0.41) for the sugammadex and neostigmine groups, respectively. The total amount of reversal administered was 147±25.5 mg and 3.7±0.6 mg respectively.

The mean core and thenar site temperature of patients treated with sugammadex, recorded at reversal administration, were 37±0.8°C and 35.2±1.3°C respectively, while they were 36.6±0.9°C and 35.2±1.4°C in the neostigmine group (core p=0.29, thenar site p=0.92).

Mean recovery times were significantly faster in patients treated with sugammadex than neostigmine: 9.4±4.6 min vs. 34.6±24.9 min, respectively (p<0.0001), as shown in Figure
2. Seven patients out of 21 (33%) in the sugammadex group required more than 10 minutes to achieve $\text{TOF}_R > 0.9$. One patient in the neostigmine group was an outlier with a recovery time > 100 minutes and was not included when mean recovery time was calculated (figure 2).

We also investigated the existence of correlations between recovery time and BMI, MELD, duration of surgery, WIT, CIT, PLT, fibrinogen, fluid balance, amount of intravenous fluids administered, liver function, creatinine clearance pre or post-surgery and total amount of NMBAs administered. No evidence for any strong correlations using Pearson and Spearman tests were found (Table 3). There was highlighted only a positive trend that could denote a possible moderate correlation between sugammadex recovery time and: AST post LTx ($r=0.61$, $p=0.003$), ALT post LTx ($r=0.50$, $p=0.02$), amount of colloids ($r=0.50$, $p=0.02$). In the group of neostigmine only length of surgery could denote a possible moderate correlation with its recovery time ($r=0.57$, $p=0.009$).

No adverse events were reported.

**Discussion**

This is the first randomized controlled trial that evaluates sugammadex use after rocuronium infusion in LTx settings. Our main finding is that sugammadex demonstrates, as expected, a considerably shorter recovery time than neostigmine, but within an unexpected quite longer absolute value compared to what was previously reported in the literature in other, non LTx, settings. The mean recovery time for sugammadex in our population was 9.4 min, which is pretty longer than reported in other studies after sevoflurane anaesthesia$^{15}$, with 33% of patients requiring more than 10 minutes to reach $\text{TOF}_R > 0.9$. This should be taken into account into the clinical practice when waking up the patient at the end of transplantation is desired.
However, sugammadex retained its well-known and broad advantage over neostigmine, which had a mean recovery time of 34.6 min. It is interesting to report that 19% of patients in the neostigmine group required more than 60 minutes for recovery from NMB, with a maximum value > 100 minutes, a very long time.

To understand this unexpected long recovery time of sugammadex, we performed Pearson and Spearman tests to explore possible correlations between peri-operative variables and recovery time, but no statistically significant strong correlations were found (Table 3). However post operative liver AST and ALT, and amount of intra-operative colloids demonstrated a positive trend with sugammadex recovery time, denoting a possible moderate correlation. It must be said that the sample size had not been calculated for this purpose, so any conclusion should be confirmed or refused only after a randomized controlled trial wiht adequate numerosity will be done.

In the literature, experimental studies investigated possible interactions between sugammadex and other drugs, and found that flucloxacillin, fusidic acid and tormifene had the potential for a displacement interaction with sugammadex. An in vitro study showed possible interferences of corticosteroids in the action of sugammadex but, on the contrary, Rezonja et al. published an in vivo randomized controlled trial where they demonstrated that dexamethasone did not alter sugammadex recovery time. In our study all patients received high intraoperative dose (3.5-5 mg/kg) of methylprednisolone hemisuccinate as immunosuppressant just before hepatic vascular unclamping. No study evaluated any possible interferences between methylprednisolone and sugammadex, however the molecular and structural form of methylprednisolone is similar to dexamethasone, so it may be unlikely that the administration of methylprednisolone interfered with the action of sugammadex. Further specific studies are needed to clarify
Rocuronium pharmacokinetic presents many variability in cirrhotic patients, and some authors noted an increased onset time and a long offset time.\textsuperscript{30-32} Given this premise, someone could argue against its use in patients undergoing LTx, in favour of a non-organ-specific metabolized NMB such as cisatracurium with a more favourable metabolism.\textsuperscript{33} However, the possibility to rapidly reverse rocuronium activity with sugammadex offers a useful opportunity to perform fast track surgery in general and in LTx in particular, so anaesthetists can extubate the patient in operating room or shortly after intensive care admission. There is evidence that early extubation after LTx improves patient outcome and saves costs\textsuperscript{17,18}; in light of the results of our study, it may be advisable to administer sugammadex with a reasonable margin of time (i.e. 15 minutes) before the actual extubation of the LTx recipient patient.

There are some limitations to our study. All LTx patients included are characterized by haemodynamic stability, so our findings can't be extended to patients with poor haemodynamic conditions.

Anaesthetic management can be an important confounder during LTx but, in our study, anaesthetic conduct was strictly adherent to the internal protocol used for every LTx, with consequent reduced anaesthetic variability; furthermore, no statistically significant difference in intra-operative variables were highlighted between the two groups of patients. Additionally, all LTx were performed with the same surgical team dedicated to solid organ transplant surgery, decreasing the potential treatment bias.

CONCLUSION

Sugammadex was superior to neostigmine in the LTx setting, offering anaesthetists a strong and safe tool for empowering a fast track anaesthesia protocol including extubation
in operating room in this kind of major and complex abdominal surgery. However, anaesthetists should take into account the need for longer recovery times compared to other settings, and know that NMT is mandatory.

Further larger randomized clinical trials are needed to confirm or refute our results and, possibly, to find any pre-, intra- or postoperative element that could explain the longer recovery time for sugammadex in the LTx setting, especially the possible role for steroids.

**List Of Abbreviations**

LTx = orthotopic liver transplantation, NMB = neuromuscular block, NMBA = neuromuscular blocking agent, PTC = post tetanic count, PORC = post operative residual curarization, NMT = neuromuscular transmission, TOFR = train of four ratio, BMI = body mass index, MELD = model for end stage liver disease, PRC = pure red cell, FFP = fresh frozen plasma, PLT = platelets, CIT = cold ischemia time, WIT = warm ischemia time, CO = cardiac output, CI = cardiac index.

**Declarations**

*Ethics approval and consent to participate:* this study was approved by the Ethics Committee of the University Hospital “Santa Maria della Misericordia” of Udine (n° 2016-O-015-ASUIUD). A written informed consent was obtained from every participant before LTx procedure.

*Consent for publication:* not applicable.

*Availability of data and material:* the datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
Competing interests: nothing to declare.

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All authors revised and approved the final version of the manuscript.

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Tables

Table 1. Demographics, biometrics, pre and postoperative liver and renal function data. Values are expressed as the mean±SD unless otherwise indicated. Postoperative data refers to laboratory tests conducted when the patient was admitted into the ICU after LTx.
|                                | Sugammadex  | Neostigmine |
|--------------------------------|-------------|-------------|
|                                | *n* = 21    | *n* = 20    |
| **Gender**                     |             |             |
| female, *n* and (%)            | 7 (33)      | 8 (40)      |
| male, *n* and (%)              | 14 (67)     | 12 (60)     |
| **Age (years)**                | 54.1 ± 9.8  | 54.1 ± 10.4 |
| **Weight (kg)**                | 73.9 ± 14.2 | 73.1 ± 14.7 |
| **Height (m)**                 | 1.7 ± 0.1   | 1.7 ± 0.1   |
| **BMI (kg/m²)**                | 25.2 ± 4.2  | 25.3 ± 3.9  |
| **Liver disease:**             |             |             |
| HBV-related cirrhosis ± HCC, *n* and (%) | 2 (9.5)     | 0 (0)       |
| HCV-related cirrhosis ± HCC, *n* and (%) | 9 (42.8)    | 6 (30)      |
| Alcohol-related cirrhosis ± HCC, *n* and (%) | 6 (28.5)  | 6 (30)      |
| Alcohol+HBV-related cirrhosis, *n* and (%) | 1 (4.7)     | 0 (0)       |
| Alcohol+HCV-related cirrhosis, *n* and (%) | 0 (0)       | 4 (20)      |
| HIV coexists, *n* and (%)      | 2 (9.5)     | 2 (9.5)     |
| Other disease, *n* and (%)     | 3 (14.2)    | 4 (19)      |

**Pre-operative liver and renal function**

|                                |                |              |
|--------------------------------|----------------|--------------|
| **MELD**                       | 16.8 ± 7.3     | 21.4 ± 9.1   |
| **AST (IU/l)**                 | 67.4 ± 39.1    | 122.8 ± 62   |
| **ALT (IU/l)**                 | 48.6 ± 41.1    | 89.7 ± 168.7 |
| **LDH pre-op (IU/l)**          | 485.3 ± 191.5  | 457.8 ± 368.4|
| **TBil (mg/dl)**               | 6.7 ± 10.2     | 11.5 ± 13.4  |
| **DBil (mg/dl)**               | 3.8 ± 6.1      | 6.1 ± 8.2    |
| **GGT (IU/l)**                 | 155 ± 340      | 75 ± 74      |
| **Albumin (mg/dl)**            | 29.9 ± 6.2     | 31 ± 6.4     |
| **ClCr (ml/min)**              | 86.5 ± 34.9    | 80.7 ± 36.8  |

**Postoperative liver and renal function**

|                                |                |              |
|--------------------------------|----------------|--------------|
| **AST (IU/ml)**                | 1246 ± 1060    | 1688 ± 1508  |
| **ALT (IU/ml)**                | 654 ± 348      | 1346 ± 1594  |
| **LDH (IU/l)**                 | 2986 ± 1699    | 3957 ± 5804  |
| **TBil (mg/dl)**               | 4.6 ± 2.5      | 6.9 ± 4.6    |
| **DBil (mg/dl)**               | 3.2 ± 2        | 4 ± 3.2      |
| **GGT (IU/l)**                 | 58 ± 47        | 77 ± 56      |
| **Albumin (mg/dl)**            | 19.8 ± 8       | 21.3 ± 6     |
| **ClCr (ml/min)**              | 86.2 ± 30.7    | 72.2 ± 29.1  |

**Abbreviations:** BMI, body mass index; MELD, Model for End-Stage Liver Disease; AST,
aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; TBil, total bilirubin; DBil, direct bilirubin; GGT, gamma glutamyl-transferase; ClCr, estimated creatinine clearance (Cockroft-Gault formula used).

Table 2. Intraoperative data. Cardiac output and index were evaluated at reversal administration.

Values are expressed as the mean±SD.

|                                      | Sugammadex (n=21) | Neostigmine (n=20) | p   |
|--------------------------------------|-------------------|--------------------|-----|
| **Duration of surgery (min)**        | 402±54            | 378±102            | 0.41|
| **Intra-op blood losses (ml)**       | 7278±6346         | 6039±5608          | 0.56|
| **PRC (ml)**                         | 1700±1325         | 2407±2475          | 0.28|
| **FFP transfused (ml)**              | 2981±2492         | 2933±3207          | 0.9 |
| **Salvaged blood transfused (ml)**   | 1825±1750         | 1650±2147          | 0.81|
| **PLT (unit)**                       | -                 | -                  |     |
| **Fibrinogen (g)**                   | -                 | -                  |     |
| **Fluid balance (ml)**               | 3374±2512         | 1612±1915          | 0.07|
| **CIT (h)**                          | 8.3±1.9           | 8.8±2.1            | 0.73|
| **WIT (min)**                        | 46.6±16.5         | 39±14.8            | 0.12|
| **Total crystalloid infusion (ml)**  | 8585±3224         | 6582±3095          | 0.06|
| **Total albumin 4% infusion (ml)**   | 2612±1314         | 1982±1199          | 0.14|
| **Cardiac Output (l/min)**           | 8.6±2.2           | 8.8±2.8            | 0.80|
| **Cardiac Index (l/min/m²)**         | 4.8±1.2           | 4.8±1.7            | 0.91|

Abbreviations: PRC, packet red blood cell; PLT, platelets; FFP, fresh frozen plasma; CIT, cold ischaemia time; WIT, warm ischaemia time.

Table 3. Correlations between recovery time and pre, intra and postoperative values. “Pre” refers to pre-operative while “post” to postoperative value.
|                | SUGAMMADEX |               | NEOSTIGMINE |               |
|----------------|------------|---------------|-------------|---------------|
|                | Pearson    | p             | Spearman    | p             |
| BMI            | -0.304     | 0.180         | -0.342      | 0.129         |
| MELD           | 0.0195     | 0.454         | 0.046       | 0.862         |
| AST pre        | 0.275      | 0.253         | 0.341       | 0.152         |
| AST post       | 0.611      | 0.003         | 0.569       | 0.007         |
| ALT pre        | 0.1633     | 0.504         | 0.329       | 0.167         |
| ALT post       | 0.4960     | 0.022         | 0.345       | 0.125         |
| GGT pre        | -0.061     | 0.815         | 0.335       | 0.186         |
| GGT post       | -0.242     | 0.317         | 0.037       | 0.878         |
| CI Cr pre      | 0.378      | 0.090         | 0.296       | 0.191         |
| CI Cr post     | -0.232     | 0.311         | -0.176      | 0.445         |
| Length surg    | 0.293      | 0.198         | 0.357       | 0.113         |
| Blood loss     | 0.423      | 0.063         | 0.355       | 0.123         |
| Fluid balance  | 0.293      | 0.270         | 0.209       | 0.436         |
| CIT            | -0.151     | 0.515         | -0.152      | 0.511         |
| WIT            | 0.461      | 0.036         | 0.372       | 0.097         |
| Tot NMBA       | 0.271      | 0.235         | 0.182       | 0.430         |
| Crystals       | 0.093      | 0.697         | 0.045       | 0.852         |
| Colloids       | 0.502      | 0.024         | 0.271       | 0.248         |
| CO             | 0.449      | 0.047         | 0.363       | 0.115         |
| CI             | 0.404      | 0.086         | 0.349       | 0.143         |

Abbreviations: BMI, body mass index; MELD, Model for End-Stage Liver Disease; CIT, cold ischaemia time; WIT, warm ischaemia time; CI Cr, clearance creatinine (Cockroft Gault); CO, cardiac output; CI, cardiac index; NMBA, neuromuscular blocking agent; AST, alanine aspartate transferase; alanine amino transferase; GGT, gamma glutamyl transferase.

Figures
Figure 1

Study flow-chart according to CONSORT. Abbreviations: LTx, orthotopic liver transplantation; GFR, glomerular filtration rate.
Figure 2

Recovery time for sugammadex and neostigmine. Mean value was 9.4 vs 34.6 minutes for sugammadex and neostigmine respectively (p<0.0001). Box plot comprehends median and interquartile (25th-75th) range, cross inside box plot represents mean value and whiskers represent minimun and maximum value. ° represents an outlier patient that was not taken into account when calculating recovery time because of its value > 100 minutes.

Supplementary Files

This is a list of supplementary files associated with the primary manuscript. Click to download.

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