Economic Analysis of Sugammadex for Neuromuscular Block Reversal for Laparoscopic Surgery from a Single Hospital System in China

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Background

- > Neuromuscular blockade (NMB) and pneumoperitoneum (PP) are important factors to ensure successful laparoscopic surgery.
- > Residual neuromuscular blockade (rNMB) may occur as long as neuromuscular blockade drugs are used. Clinically, rNMB is defined as the train-of-four ratio (TOFr) < 0.9 [1]. A real-world study in the Chinese population showed that the incidence of rNMB after tracheal extubation and arrival at post-anesthesia care unit (PACU) were 57.8% and 45.2%, respectively [2]
- > Many potential complications can be caused by rNMB, such as hypoxemia, airway obstruction, muscle weakness, pulmonary related complications due to ineffective cough, pharyngeal dysfunction, etc [3]
- > To provide a good surgical condition, PP must be made in laparoscopic surgery. But high-pressure PP can lead to potential side effects, such as nausea/vomiting, shoulder pain and others [4] [5]
- > Deep NMB (post-tetanic count = 1 or 2) and low-pressure PP (less than 10 mmHg) are recommended in laparoscopic surgery by Chinese clinical guidelines [3]. It not only can improve laparoscopic surgical condition, but also can reduce PP side effects [3].
- > Sugammadex can quickly reverse or moderate deep NMB compared with neostigmine [6] [7]. It can potentially reduce rNMB risk and at the same time, maintain a desirable deep NMB state during laparoscopic surgery.

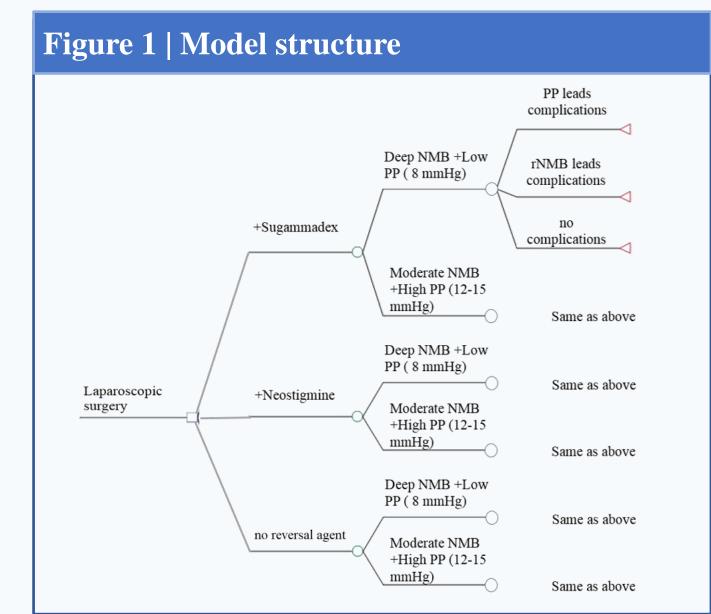
Objective

This study aims to compare the incidence of residual neuromuscular blockade (rNMB) and postoperative complications for patients undergoing laparoscopy in China, as well as assessing the impact on operating room (OR) and post anesthesia care unit (PACU) efficiency, and the potential cost savings with use of sugammadex, neostigmine (NEO) or no reversal agent from the hospital perspective.

Methods

Results

A decision tree model was developed with the time horizon across the whole hospitalization. 1000 patients were simulated for each treatment group within the model. The incidence of postoperative complications were calculated, including rNMB- and pneumoperitoneum (PP)-related complications and treatment-related adverse events. The time spent in OR and PACU were also reported. Data in the model were obtained from published literature, public data and expert interviews. Costs were expressed in 2023 CNY (¥).



Key dat	ta used in the decision model
Probabilit	ies of different surgical strategies
	Deen NMR + Low PP pressure (8 n

GIIG	Deep Tivib Low 11 pressure (6 mining)		
SUG	Moderate NMB + High PP pressure (12-15 mmHg)		KOL*
1,770	Deep NMB + Low PP pressure (8 mmHg)		
NEO	Moderate NMB + High PP pressure (12-15 mmHg)		
Spont	Deep NMB + Low PP pressure (8 mmHg)		
recov	Moderate NMB + High PP pressure (12-15 mmHg)	78.57%	
Relative re	ecovery times		
prolonged 1	hospital stay due to rNMB (days)	0.49	[8]
prolonged l	nospital stay due to high PP (days)	0.25	[9]
average operation duration of laparoscopic (minuties)		114.6	RWD
prolonged extubation time due to rNMB (minuties)		18	[11]
prolonged l	PACU stay due to rNMB (minuties)	6	[11]

^{*} based on input from 30 anesthesiologists, representing experiences from tertiary teaching hospitals in major metropolitan cities in China.

Drug Price				
Sugammadex (Brand)	¥980	List price		
Sugammadex (Generic)	¥225	List price		
Neostigmine /atropine	¥71/¥21			
Nothing	-	-		
Prop. of rNMB				
Sugammadex (Brand)	1.2%	[12]		
Sugammadex (Generic)	2.7%	assumptions		
Neostigmine /atropine	15.40%	[13]		
Nothing	34.00%	[12]		
Subgroup (elderly patients)				
Sugammadex (Brand)	10%	[14]		
Sugammadex (Generic)	17%	assumptions		
Neostigmine /atropine	49%	[14]		
* the difference of the pro	h rNMR hetween	hrand-		

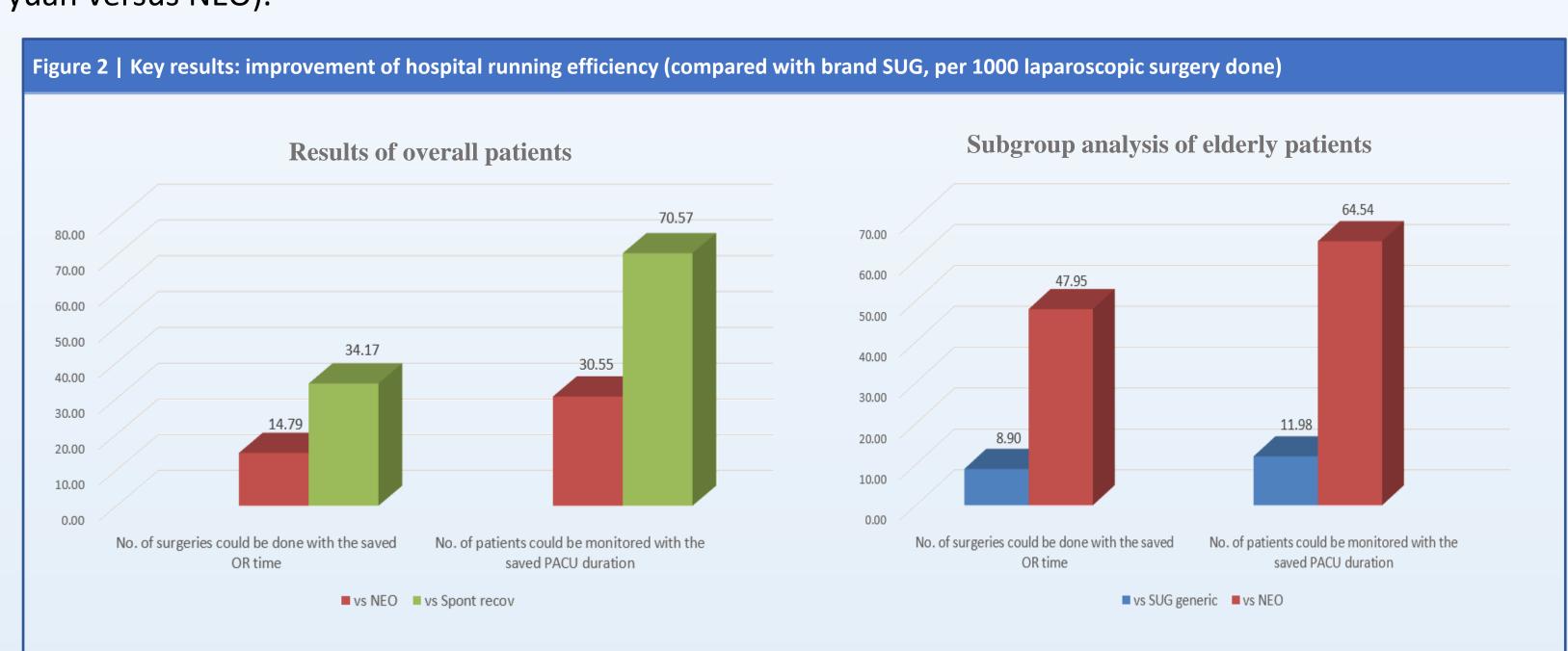
^{*} the difference of the prob.rNMB between brandname sugammadex and generic sugammadex was assummed base on affinity data (the affinity of the generic sugammadex with rocuronium bromide is about 58% of the brand-name sugammadex).

NMB / PP related complicati	ons related inputs						
	PP rel	PP related complications			PP related complications cost		
	< 12 mmHg	12-15 mmHg	Sources	prob. of intervention	Cost (Yuan)	Sources	
Shoulder pain	6.5%	14.4%	[15]	61.21%	172	KOL	
Nausea & Vomiting	2.5%	25.0%	[16]	77.41%	139	KOL	
	rNMB r	elated complications	rNMB related complications cost				
	rNMB	No rNMB	Sources	prob. of intervention	Cost (Yuan)	Sources	
Upper airway obstruction	8.42%	1.68%	[17]	63.90%	216		
Upper airway obstruction	1.58%	0.32%	[17]	88.45%	266		
Mild-moderate hypoxemia	23.00%	4.00%	[17]	91.03%	1,295		
Severe hypoxemia	7.00%	1.00%	[17]	85.86%	139		
Respiratory failure*	8.00% / (14.29%)	1.00% / (1.79%)	[17]/[22]	99.66%	781		
Muscular weakness*	16.00%/ (28.57%)	1.00% / (1.79%)	[17]/[22]	99.31%	29,494	KOL	
Pharyngeal dysfunction*	28.00% / (3.16%)	13.00% / (14.29%)	[18]/[22]	86.55%	1,467		
Pneumonia*	25.2% / (44.21%)	0.80% / (1.43%)	[19]/[22]	100.00%	1,050		
Unplanned reintubation*	1.6% / (1.89%)	0% / (0%)	[20]/[22]	100.00%	31,200		
ICU admission rate	3.3%	1.5%	[21]	100.00%	4,313		

^{*} Subgroup analysis data of elderly patients

Compared with NEO and spontaneous recovery, brand-name sugammadex would lead to 292 and 397 fewer postoperative complications respectively. Additionally, the OR time saw an decrease with brand-name SUG use (35.5 hours versus NEO and 82.0 hours versus spontaneous recovery), which could be used to perform 15 and 34 extra laparoscopic surgery respectively. The PACU time was also estimated to decline by 42.6 hours and 98.4 hours respectively. Total time saved in PACU with brand-name SUG could be used to monitor 31 and 71 extra patients. Compared to the finding in the overall patients groups, SUG was found with more encouraging efficacy in eldery subgroups, and with higher subsequent economic benefits and OR/PACU running efficiency for Chinese hospital (mean net monetary gain were 442 yuan versus generic SUG and 4,887yuan versus NEO).

	vs NEO	vs Spont recov
difference of the frequency of postoperative complications (rNMB / PP)	-292	-397
OR time saved with SUG (minutes)	2,130	4,920
PACU time saved with SUG (minutes)	2,556	5,904
No. of surgeries could be done with the saved OR time	14.79	34.17
No. of patients could be monitored with the saved PACU duration	30.55	70.57
Subgroup analysis for elderly patients (≥ 60 years)		
	vs SUG generic	vs NEO
difference of the frequency of postoperative complications (rNMB / PP)	-44	-364
OR time saved using SUG (minutes)	1,086	5,850
PACU time saved using SUG (minutes)	1,303	7,020
No. of surgeries could be done with the saved OR time	8.90	47.95
No. of patients could be monitored with the saved PACU duration	11.98	64.54
Mean Net monetary gain (CNY, ¥)	442	4,887



Conclusions

Sugammadex could effectively avoid postoperative complications compared with either NEO or spontaneous recovery, meanwhile reducing both the OR and PACU occupancy, despite a substantially higher medication cost might be followed. It indicates that sugammadex is likely to be an acceptable reversal agent choice in laparoscopy from the Chinese hospital perspective.

Limitations

- > The study assumed that the incidence of rNMB / PP related complications in laparoscopic surgery for different diseases was the same. However, via the interviews, more than 50% of KOLs believed that the incidence of rNMB / PP related complications in laparoscopic surgery for different diseases was the same so we deemed this an appropriate assumption.
- The cost data and proportion of intervention of this study were estimated based on input from 30 anesthesiologists, representing experiences from tertiary teaching hospitals in major metropolitan cities in China. In the future, a nation level study for cost should be carried out to improve the quality of data.
- > Finally, the difference of the probability between brand-name sugammadex and generic sugammadex was assummed base on affinity data (the affinity of the generic sugammadex with rocuronium bromide is about 58% of the brand-name sugammadex).

Reference

[1] Murphy, G.S. and S.J. Brull, Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. Anesthesia & Analgesia, 2010. 111(1): p. 120-128.

[2] Buwei, Y., et al., Incidence of postoperative residual neuromuscular blockade after general anesthesia: A prospective, multicenter, anesthetists-blind, observational study. Current Medical Research & Opinion, 2015. 32(1): p. 1.

[3] 吴新民. 2017版肌肉松弛药合理应用的专家共识. 2017. 人民卫生出版社. http://www.csaol.cn/a/xuehuigongzuo/linchuangzhinan/2017/1213/13706.html

[4] J. Sroussi, 2017, Low pressure gynecological laparoscopy (7 mmHg) with AirSeal1 System versus a standard insufflation (15 mmHg): A pilot study in 60 patients

[5] 胡建, 张蕊,鲍红光,等. FloTrac/Vigileo监测不同CO2气腹压对腹腔镜妇科手术患者血流动力学的影响[J]. 临床麻醉学杂志, 2012, 28(10):981-984.

[6] Wu, X., et al., Rocuronium blockade reversal with sugammadex vs. neostigmine: randomized study in Chinese and Caucasian subjects. Bmc Anesthesiology, 2014. 14(1): p. 1-10.

[7] Yu B, Wang X, Helbo-Hansen HS, Huang WQ, Askeland B, et al. (2014) Sugammadex 4.0 mg kg-1 Reversal of Deep Rocuronium-Induced Neuromuscular Blockade: A Multicenter Study in Chinese and Caucasian Patients. J Anesth Clin Res 5: 408.

[8] Grabitz S D, Rajaratnam N, Chhagani K, et al. The Effects of Postoperative Residual Neuromuscular Blockade on Hospital Costs and Intensive Care Unit Admission[J]. Anesthesia & Analgesia, 2019,128(6):1129-1136.

[15] 冯娟, 许巧玲. 腹腔镜人工气腹手术并发症与护理[J]. 临床护理杂志, 2015(1):46-48.
[16] 胡建, 张蕊, 鲍红光, 等. 监测不同CO2气腹压对腹腔镜妇科手术患者血流动力学的影响[J]. 临床麻醉学杂志, 2012,28(10):981-984.
[17] Norton M, Xará D, Parente D, et al. Residual neuromuscular block as a risk factor for critical respiratory events in the post anesthesia care unit[J]. Rev Esp Anestesiol Reanim, 2013,60(4):190-196.
[18] Sundman E, Witt H, Olsson R, et al. The incidence and mechanisms of pharyngeal and upper esophageal dysfunction in partially paralyzed humans: pharyngeal videoradiography and simultaneous manometry after atracurium[J]. Anesthesiology, 2000,92(4):977-984.
[19] Martinez-Ubieto J, Ortega-Lucea S, Pascual-Bellosta A, et al. Prospective study of residual neuromuscular block and postoperative respiratory complications in patients reversed with neostigmine versus sugammadex[J]. Minerva Anestesiol, 2016,82(7):735-742.
[20] Errando C L, Garutti I, Mazzinari G, et al. Residual neuromuscular blockade in the postanesthesia care unit: Observational study of a multicenter cohort[J]. Minerva Anestesiologica, 2016,82(12):1267-1277.
[21] Grabitz S D, Rajaratnam N, Chhagani K, et al. The Effects of Postoperative Residual Neuromuscular Blockade on Hospital Costs and Intensive Care Unit Admission: n: A Population-Based Cohort Study [J]. Anesthesia & Analgesia, 2019,128(6):1129-1136.

[13] Nemes R, Fülesdi B, Pongrácz A, et al. Impact of reversal strategies on the incidence of postoperative residual paralysis after rocuronium relaxation without neuromuscular monitoring: A partially randomised placebo controlled trial. Eur J Anaesthesiol. 2017;34(9):609-616.

[12] Martinez-Ubieto J, Ortega-Lucea S, Pascual-Bellosta A, et al. Prospective study of residual neuromuscular block and postoperative respiratory complications in patients reversed with neostigmine versus sugammadex. Minerva Anestesiol. 2016;82(7):735-742.

[14] Togioka B M, Yanez D, Aziz M F, et al. Randomised controlled trial of sugammadex or neostigmine for reversal of neuromuscular block on the incidence of pulmonary complications in older adults undergoing prolonged surgery[J]. 2020,124(5):553-561.

[22] Carron M, Tessari I, Linassi F. Sugammadex compared with neostigmine in reducing postoperative pulmonary complications in older patients: a meta-analysis. Br J Anaesth. 2022;128(4):e259-e262.

[7] Yu B, Wang X, Helbo-Hansen HS, Huang WQ, Askeland B, et al. (2014) Sugammadex 4.0 mg kg—1 Reversal of Deep Rocuronium-Induced Neuromuscular Blockade: A Multicenter Study in Chinese and Caucasian Patients. J Anesth Clin Res 5: 408. [8] Grabitz S D, Rajaratnam N, Chhagani K, et al. The Effects of Postoperative Residual Neuromuscular Blockade on Hospital Costs and Intensive Care Unit Admission[J]. Anesthesia & Analgesia, 2019,128(6):1129-1136. [9] Ortenzi M, Montori G, Sartori A, et al. Low-pressure versus standard-pressure pneumoperitoneum in laparoscopic cholecystectomy: a systematic review and meta-analysis of randomized controlled trials[J]. Surg Endosc, 2022,36(10):7092-7113. [10] 陈昊, 焦博, 鲁佩, 等. 舒更葡糖钠逆转深度神经肌肉阻滞对腹腔镜术后肺部并发症的影响[J]. 中国医院药学杂志, 2021,41(19):1993-1997 [11] Min X, Dong-Xin W, and Zhi-Yu G. Prevalence and Risk Factors of Postoperative Residual Curarization in Patients Arriving at Postanesthesia Care Unit after General Anesthesia: A Prospective Cohort Study[J]. J Anesth Perioper Med, 2014:72-78..