Comparative Study of TOF-Cuff, a New Neuromuscular Blockade Monitor, and TOF-Watch, an Acceleromyography

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Train-of-four ratios were recorded to assess the agreement between the TOF-Cuff and TOF-Watch, and residual paresis was assessed to evaluate the clinical utility of TOF-Cuff. Train-of-four ratios were evaluated using Lin concordance correlation coefficient and Bland–Altman analyses. Measured train-of-four ratios demonstrated high accuracy and precision over the entire range of train-of-four ratios. Although precision and Lin concordance correlation coefficients decreased with train-of-four ratios >0.7, none of the patients showed signs of residual paresis. Because TOF-Cuff underestimated train-of-four ratios in the recovery period, the clinical safety of train-of-four ratios >0.9 indicated by TOF-Cuff is unclear; the issue of residual paresis requires future research that rigorously evaluates outcomes. (Anesth Analg 2019;129:e16–e19)

Quantitative or objective monitoring of neuromuscular blockade in patients under general anesthesia is now widely recommended. It is useful for optimization of the time to intubation[1] and to confirm full recovery of neuromuscular blockade before extubation.[2] However, it might be difficult to perform measurements using current neuromuscular monitors when the patient is placed in the prone position or with the arms against the body. Therefore, widespread use of quantitative neuromuscular blockade monitors may depend on how quick and easy they are to install.

Recently, a new neuromuscular blockade monitor (TOF-Cuff; RGB Medical Devices, S.A., Madrid, Spain) became commercially available, which only requires placement of a single cuff incorporated stimulating electrodes on the patient's arm. A response to nerve stimulation is detected by the change in the cuff's internal pressure.

We hypothesized that train-of-four ratios measured by the TOF-Cuff have high accuracy and precision and good agreement with those measured by the TOF-Watch (Bluestar Enterprises, Omaha, NE), which uses acceleromyography principles and is commonly used for neuromuscular monitoring in anesthetized patients

METHODS

This single-center, open-controlled clinical study was conducted after approval of the study protocol by the ethics committee of our institution (approval No. 272-183) and with the informed consent in writing from all participating patients. The trial was registered before patient enrollment at University hospital Medical Information Network Clinical Trial Registry database (No. R000028727, Principal investigator: M.Y., date of registration: November 24, 2016).

We enrolled American Society of Anesthesiologists physical status I–III patients undergoing general anesthesia and who were free from an underlying neuromuscular disorder. Exclusion criteria included patients who were <15 years and had hepatic or renal disorders.

Patients were administered a target-controlled infusion of propofol to maintain the bispectral index between 40 and 60, while breathing 100% oxygen with mask ventilation. The rectal temperature of the patients was maintained at 38°C using a warming blanket. Then, a TOF-Cuff was attached on arbitrary upper arm, while a TOF-Watch was attached to the distal forearm of the arm used for measurement of blood pressure.

Neuromuscular monitoring using the TOF-Watch was performed as previously described.[3] The same principles of measurement, including calibration, as the TOF-Watch were adopted for the TOF-Cuff. During induction of anesthesia or reversal of neuromuscular blockade, train-of-four ratios were measured by both devices at the same time every 30 seconds after administration of 0.6–1.0 mg/kg rocuronium or 2.0–4.0 mg/kg sugammadex, respectively. Extubation was performed when the train-of-four ratio was >0.9, as estimated by the TOF-Watch. In addition, 20 randomly selected patients were assessed by standardized examination to evaluate for symptoms of residual paresis within 5 minutes after extubation. The examination was designed based on the evidence by Kopman et al.[4] To ensure a uniform and consistent evaluation of all subjects, testing was performed by a single research assistant (blinded to the train-of-four ratio data). Patients were asked to perform 10 tests that included 5-second head lift, 5-second hand grip, 5-second eye opening, 5-second tongue protrusion, tongue depressor test, ability to swallow, ability to speak, ability to cough, ability to track objects with eyes, and ability to breathe deeply. Responses were recorded on a 10-point

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Table. Lin Concordance Correlation Coefficient (Above) and Bland–Altman Test (Below) for Assessment of Agreement Between All Train-of-Four Ratios and Train-of-Four Ratios >0.7 Measured by the TOF-Cuff and TOF-Watch

		Elapsed Time	Sample Size	Concordance Correlation Coefficient	99% CI for Concordance Correlation Coefficient	Pearson Correlation Coefficient, ρ (Precision)	99% CI for Pearson Correlation Coefficient
Overall train-of-four ratios	Induction of anesthesia	0 s	54	−0.01	−0.16 to 0.13	−0.03	−0.37 to 0.32
		30 s	53	0.77	0.59 to 0.88	0.79	0.60 to 0.89
		1 min	49	0.89	0.78 to 0.94	0.90	0.79 to 0.95
		1.5 min	40	0.95	0.89 to 0.98	0.96	0.90 to 0.98
		2 min	27	Not available	Not available	Not available	Not available
	Reversal of neuromuscular blockade	0 s	38	0.96	0.92 to 0.98	0.98	0.96 to 0.99
		30 s	35	0.95	0.89 to 0.98	0.97	0.93 to 0.99
		1 min	41	0.90	0.81 to 0.95	0.95	0.89 to 0.98
		1.5 min	35	0.28	−0.05 to 0.56	0.37	−0.06 to 0.69
		2 min	28	0.33	−0.12 to 0.67	0.36	−0.14 to 0.71
Train-of-four ratios >0.7	Induction of anesthesia	0 s	53	−0.01	−0.11 to 0.10	−0.03	−0.37 to 0.32
		30 s	50	0.35	0.00 to 0.62	0.36	0.00 to 0.64
		1 min	24	0.66	0.25 to 0.87	0.67	0.24 to 0.88
		1.5 min	1	Not available	Not available	Not available	Not available
		2 min	0	Not available	Not available	Not available	Not available
	Reversal of neuromuscular blockade	0 s	17	0.51	0.10 to 0.78	0.74	0.25 to 0.93
		30 s	20	0.58	0.17 to 0.83	0.71	0.26 to 0.91
		1 min	33	0.51	0.21 to 0.72	0.67	0.32 to 0.86
		1.5 min	35	0.28	−0.05 to 0.56	0.37	−0.06 to 0.69
		2 min	28	0.33	−0.12 to 0.67	0.36	−0.14 to 0.71

		Elapsed Time	Sample Size	Mean Difference (Bias)	SD of the Difference	Limit of Agreement		Linear Regression Coefficient (*r*)	99% CI for Linear Regression Coefficient
						Lower	Upper		
Overall train-of-four ratio	Induction of anesthesia	0 s	54	−0.01	0.12	−0.26	0.24	1.84	1.61 to 2.08
		30 s	53	0.02	0.06	−0.11	0.14	−0.17	−0.36 to 0.03
		1 min	49	0.02	0.12	−0.21	0.26	−0.12	−0.25 to 0.02
		1.5 min	40	0.02	0.08	−0.14	0.17	0.01	−0.09 to 0.11
		2 min	27	0.00	0.02	−0.04	0.05	2.00	2.00 to 2.00
	Reversal of neuromuscular blockade	0 s	38	0.05	0.06	−0.06	0.16	0.03	−0.03 to 0.09
		30 s	35	0.06	0.06	−0.07	0.19	−0.05	−0.13 to 0.04
		1 min	41	0.04	0.05	−0.06	0.15	−0.17	−0.27 to −0.07
		1.5 min	35	0.03	0.05	−0.07	0.14	−0.34	−0.81 to 0.13
		2 min	28	0.00	0.02	−0.03	0.04	−0.54	−1.07 to −0.01
Train-of-four ratios >0.7	Induction of anesthesia	0 s	53	0.01	0.03	−0.05	0.06	−1.92	−2.10 to −1.75
		30 s	50	0.01	0.06	−0.12	0.14	−0.07	−0.47 to 0.33
		1 min	24	−0.01	0.07	−0.16	0.14	−0.02	−0.42 to 0.37
	Reversal of neuromuscular blockade	0 s	17	0.06	0.05	−0.04	0.15	0.00	−0.43 to 0.43
		30 s	20	0.04	0.05	−0.06	0.14	0.12	−0.29 to 0.52
		1 min	33	0.04	0.05	−0.07	0.14	−0.54	−0.85 to −0.24
		1.5 min	35	0.03	0.05	−0.07	0.14	−0.34	−0.81 to 0.13
		2 min	28	0.00	0.02	−0.03	0.04	−0.54	−1.07 to −0.01

rating scale (0 = most severe muscle weakness, 10 = no muscle weakness).

STATISTICAL ANALYSIS

Using statistical software (R v3.2.4; R Core Team 2016; R Foundation for Statistical Computing, Vienna, Austria), Lin concordance correlation coefficient and Bland–Altman test were performed to evaluate agreement between train-of-four ratio measured by the TOF-Cuff and TOF-Watch. Bland–Altman analysis was performed to evaluate the trend of the difference between TOF-Cuff and TOF-Watch values.

Repeated measurements were performed for each patient by analyzing the 5 time points of 0 second, 30 seconds, 1 minute, 1.5 minutes, and 2 minutes from induction of anesthesia or reversal of neuromuscular blockade, and agreement was assessed at each time point. Type I error for each outcome variable was controlled at 5% by using a Bonferroni correction and reporting 99% CIs at each of the 5 time points. In addition, subgroup analysis was performed for groups with a train-of-four ratio >0.7. Sample size of approximately 50 appeared sufficient because in such scenarios, we were able to estimate the Lin concordance correlation coefficient with CI width ≤0.30 when the point estimate was larger than 0.50. However, with smaller n or point estimates, below 0.50 precision was rather poor.

RESULTS

Fifty-five patients were included in the analyses (Supplemental Digital Content, Document, http://links.lww.com/AA/C784). Patients' demographic characteristics

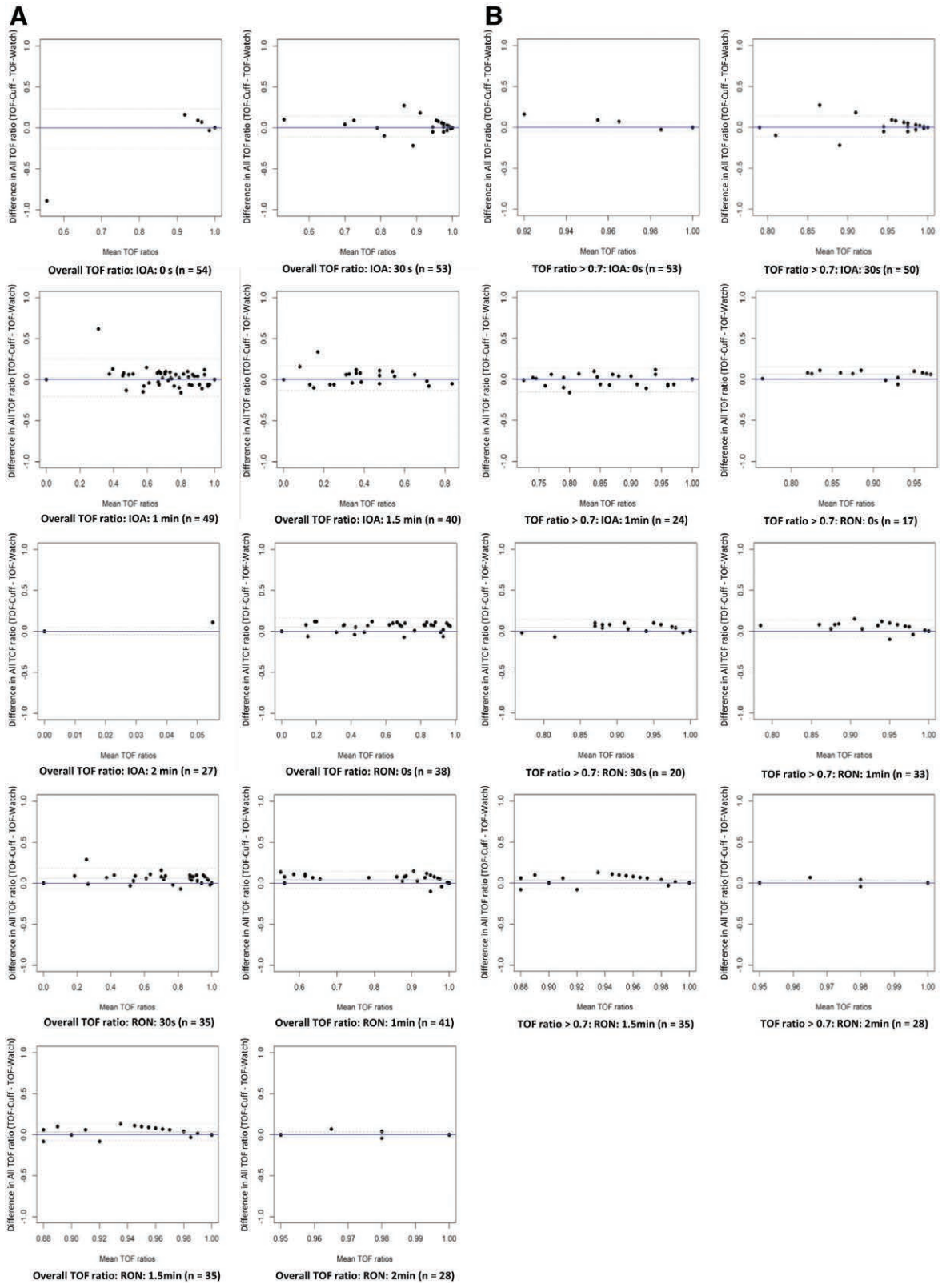

Figure. Assessment of agreement of train-of-four (TOF) ratios between the 2 devices (TOF-Cuff and TOF-Watch) using Bland–Altman analysis during induction of anesthesia or reversal of neuromuscular blockade (A, Overall TOF ratio, B, TOF ratios >0.7). As the number of observations was small, the data of measurements obtained 1.5 min and 2 min after the induction of anesthesia are not shown. The black dotted lines demonstrate the limits of agreement. The notation "n" in the title represents the number of observations and the number of patients. IOA indicates induction of anesthesia; RON, reversal of neuromuscular blockade.

were as follows: age, 54 years (39–67 years); and body mass index, 23 kg·m^{-2} (21–26 kg·m^{-2}). Surgeries included head and neck, abdominal, or gynecologic. In all the patients, sugammadex was given at a train-of-four count of 1–2.

When all the train-of-four ratios were analyzed, the lower limit of the Lin concordance correlation coefficient CI exceeded 0.90 in the group of measurements performed 0 second after reversal of neuromuscular blockade. Lin concordance correlation coefficient did not exceed 0.90, but there was relatively high lower limit of the Lin concordance correlation coefficient CI (0.80–0.89) in the group of measurements performed 1.5 minutes after induction of anesthesia and 30 seconds and 1 minute after reversal of neuromuscular blockade (Table). When analysis was limited to data of train-of-four ratio >0.7, there was no group of measurements in which the lower limit of the Lin concordance correlation coefficient exceeded 0.9. In addition, the width of the Lin concordance correlation coefficient CIs of train-of-four ratio >0.7 groups was also large compared to the analysis of all the train-of-four ratios. The TOF-Cuff underestimated train-of-four ratios in comparison with the TOF-Watch in the latter part of the recovery period (Table; Figure). A priori we decide that differences larger than approximately ±0.10 were clinically important, so estimated limits of agreement narrower than that represented good agreement. We found estimated limits of agreement to be within that range for variables of the group of measurements 2 minutes after induction of anesthesia for all the train-of-four ratio data and the group of measurements 2 minutes after reversal of neuromuscular blockade for all the train-of-four ratio data and train-of-four ratio >0.7 data. There was no fixed error for all groups, except for the groups with train-of-four ratio >0.7 at 1.5 and 2 minutes after the induction of anesthesia, for which the SD of the value could not be estimated. For the group of measurements 1 minute after reversal of neuromuscular blockade for all the train-of-four ratio data and train-of-four ratio >0.7 data, differences tended to become smaller as the mean of the 2 methods increased (estimated slope [95% CI] of −0.17 [−0.27, −0.07] for all the train-of-four ratio data and −0.54 [−0.85, −0.24] for train-of-four ratio >0.7 data). None of the patients showed signs of residual paresis on a standardized examination performed within 5 minutes after extubation (the average score was 9.9 on the 10-point scale).

DISCUSSION

This study showed agreement between the TOF-Cuff and TOF-Watch during both induction of anesthesia and reversal of neuromuscular blockade. Although train-of-four ratios by the 2 devices demonstrated high accuracy and precision over the entire train-of-four range, with a low bias and narrow limits of agreement, precision and Lin concordance correlation coefficient decreased remarkably for train-of-four ratios >0.7. Yet, there were no patients with signs of residual paresis on a standardized examination performed within 5 minutes after extubation. Some reports have stated that reversal of neuromuscular blockade with sugammadex eliminates residual neuromuscular blockade and the associated clinical symptoms of partial paralysis.[5,6] Hence, the differences between the 2 devices despite the absence of clinical differences could have been due to differences in the principles of measurement of the 2 devices. For example, there is a report that electromyography has higher plasticity of measurements compared to acceleromyography, and it is assumed that acceleromyography overestimates the train-of-four ratio in comparison with electromyography.[7] Although the TOF-Watch is considered to be the current gold standard among neuromuscular blockade monitors, 1 systematic review reports that the TOF-Watch is not suitable for pharmacological studies involving dose–response curves, and it is not interchangeable with mechanomyography. Moreover, TOF-Watch is not interchangeable with electromyography about train-of-four ratio.[8]

A limitation of the current study is that the TOF-Cuff utilizes the completely different measurement principle of acceleromyography. Therefore, it is not clear whether the clinically acceptable train-of-four ratio should be 0.9 or 1.0 measured with TOF-Cuff to ensure the absence of residual paresis and hence, postoperative complications, after discharge of the patient from the postanesthesia care unit. Also, no previous studies evaluating rigorous outcomes have included patients with a train-of-four ratio <0.9 or 1.0. In this study, residual paresis beyond 5 minutes after extubation was not evaluated, and the number of observations was also relatively small. Yet, the study results suggest that the TOF-Cuff may not be sufficient to evaluate significant residual paresis in all patients, and future research evaluating rigorous outcomes is necessary to prevent residual paresis.

DISCLOSURES

Name: Satoshi Kazuma, MD, PhD.
Contribution: This author helped draft the article and critically revise the article for important intellectual content.
Name: Keiko Wakasugi, MD.
Contribution: This author helped collect and assemble the data.
Name: Hiroya Hagiwara, MD.
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Name: Michiaki Yamakage, MD, PhD.
Contribution: This author helped conceptualize and design the study, analyze and interpret the data, and finally approve the article.
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