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Comparing the safety of harmonic ACE and ACE+ around the recurrent laryngeal nerve in swine models

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Purpose: Among the various energy-based devices, ultrasonic shears are popular in thyroid surgeries. In this study, we tested the safety of Harmonic ACE and Harmonic ACE+ around the recurrent laryngeal nerve (RLN) in experimental swine models.
Methods: Harmonic ACE and Harmonic ACE+ were each tested in 4 piglets. Harmonic ACE and Harmonic ACE+ were activated at a 0- to 5-mm distance from the RLN. The function of the RLN was assessed using continuous electrophysiological monitoring.
Results: For Harmonic ACE, there was no adverse EMG event found when activated at 4- and 5-mm distances from the RLN. At a 2- to 3-mm distance, there were 4 adverse EMG events observed. In these 4 cases, adjacent tissue shrinkage occurred after 6 to 15 seconds of activation, and the RLN touched the Harmonic ACE. At a 1-mm distance, there were 2 adverse EMG events found after 25 seconds of activation. For Harmonic ACE+, there was no adverse EMG event observed when activated at 1- and 3-mm distances from the RLN. At a 0-mm distance, 2 adverse EMG events occurred after 6 to 10 seconds of activation.
Conclusion: The safe distance of Harmonic ACE and ACE+ was 4 and 1 mm, respectively, in the swine models. Harmonic ACE+ is safer than Harmonic ACE because it did not cause any tissue shrinkage. Surgeons need to understand the characteristics of devices for safe operation.
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Key Words: Thyroid, Recurrent laryngeal nerve, Neuromonitoring

INTRODUCTION

Energy-based devices (EBDs) have advantages of reduction of operative time, hospital stay duration, and incidences of blood loss and postoperative pain [1-8]. There are various types of EBDs, which have been widely used in laparoscopic and open surgeries. Especially in thyroid surgeries, a majority of the surgeons use EBDs because there are numerous small vessels around the thyroid glands, and meticulous hemostasis to prevent postoperative bleeding is essential. However, despite the usefulness of EBDs, surgeons should be careful in using them near the recurrent laryngeal nerve (RLN), since the RLN is vulnerable to thermal damage generated by EBDs [9].

Harmonic ACE (Ethicon, a subsidiary Johnson and Johnson, Cincinnati, OH, USA) uses ultrasonic vibrations for tissue cutting and cauterization, unlike other instruments using electric currents. It is one of the most popular EBDs used in thyroid surgery because of its minimal lateral thermal damage

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and its narrow and sharp blades. Harmonic ACE+ (Ethicon, a subsidiary Johnson and Johnson) was developed recently and has adopted a feedback mechanism to sense and respond to changes in patient tissue conditions. Harmonic ACE+ is superior to Harmonic ACE theoretically in that Harmonic ACE+ prevents unnecessary heat generation and helps avoid RLN thermal injuries during thyroid surgery. However, whether surgeons can use Harmonic ACE+ safely in closer distances from the RLN or for longer durations around the RLN than Harmonic ACE has not been studied yet.

In this study, we used swine models and applied Harmonic ACE and ACE+ at various distances from the RLN and for different durations to identify an optimal safety margin and duration of the devices. To monitor the intactness of the RLN, we used continuous intraoperative neuromonitoring (CIONM).

METHODS

Subjects

Permission to perform this experimental trial was obtained from the Institutional Animal Care and Use Committee under protocol number 2014-170. Yorkshire-Landrace-Duroc female piglets, weighing 30–40 kg, were housed one per cage and given 7 days to acclimate to the housing facility. Environmental conditions were a temperature of 23°C, humidity of 50%, lighting of 200 lux and a 12:12 light:dark cycle with lights on at 8:00 AM and off at 8:00 PM. Animals were housed in 880 × 1,360 × 950-mm cages and given access to maintenance food (Cargill Agri Purina Inc., Seongnam, Korea) and water. Eight piglets were used to evaluate the threshold of imminent thermal RLN injuries induced by Harmonic ACE and ACE+.

Anesthesia

Preoperatively, the pigs were fasted for 12 hours. After intramuscular preanesthetic medication with xylazine (1 mg/kg; Rompun, Bayer, Leverkusen, Germany) and zolazepam/tiletamine (7 mg/kg; Zoletil, Virbac S.A., Carros, France), the pigs were placed on an operating table in the supine position with a slight neck extension. A pulse oximeter and electrocardiogram were attached for vital sign monitoring. After vecuronium (0.15 mg/kg) was injected for muscle relaxation, the pigs were intubated with a 6-mm EMG endotracheal tube (Medtronic, Dublin, Ireland). The tidal volume and respiratory rate were set at 8 mL/kg and 15 breaths/min, respectively.

Equipment setting

We used the Ethicon Endo-Surgery Generator G11 (Ethicon Endo-Surgery, a subsidiary Johnson and Johnson), and the activation power of Harmonic ACE and ACE+ was set at level 5. For CIONM, the NIM 3.0 Nerve Monitoring Systems (Medtronic) and automated periodic stimulation (APS, 2 mm; Medtronic) electrode were used. The frequency, duration, and current of the stimulation were 1/sec, 100 μsec, and 1 mA, respectively. We regarded a 50% decrease in amplitude or 10% increase in latency as an adverse EMG change, and the visual and acoustic alarms were set accordingly.

Operation and study design

We created a midline, vertical cervical incision and subsequently exposed the trachea, thyroid glands, RLN, and vagus nerve. The RLN and vagus nerve were identified visually, and their intactness was confirmed using a handheld stimulation probe. After dissecting the vagus nerve free from the overlying soft tissue, we positioned the APS electrode on the vagus nerve.

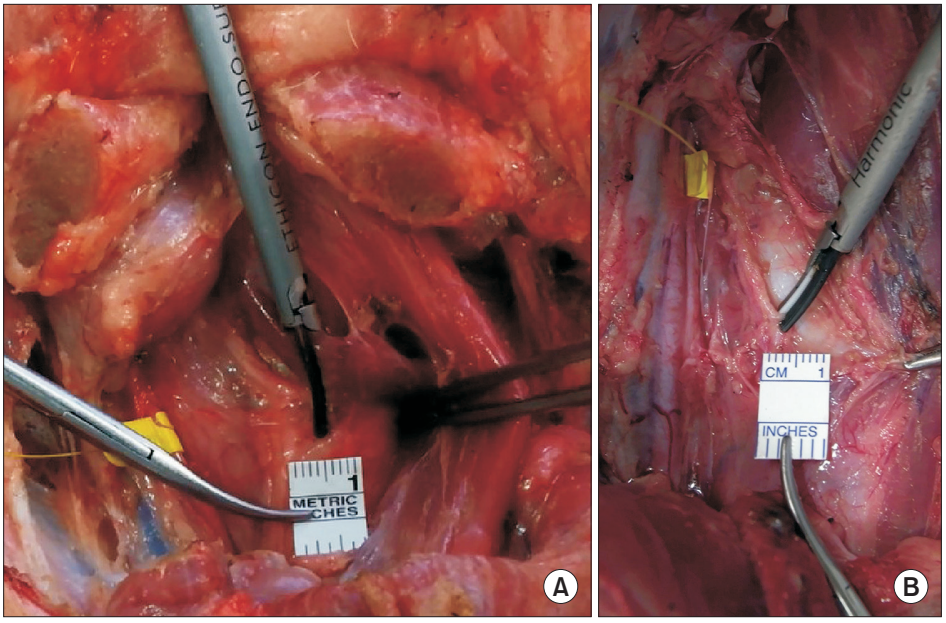

Fig. 1. Experiments of thermal injury of recurrent laryngeal nerve (RLN) induced by Harmonic ACE (Ethicon, a subsidiary Johnson and Johnson, Cincinnati, OH, USA) and Harmonic ACE+ (Ethicon, a subsidiary Johnson and Johnson) in swine model. (A) Harmonic ACE is activated at 2 mm from RLN. (B) Harmonic ACE+ is activated with direct contact to RLN.

Baselines of the amplitude and latency of the evoked response were calibrated automatically. Harmonic ACE was applied to the adjacent soft tissue around the RLN at a distance of 0 to 5 mm for duration of 10 to 25 seconds. When significant adverse EMG events such as amplitude decrease or latency increase did not occur at 5-mm distance from the RLN, the distance was shortened to 4, 3, 2, and 1 mm. Harmonic ACE+ was applied to the soft tissue at 3-mm distance from the RLN for a duration of 5 to 20 seconds and the distance was progressively shortened to 1 and 0 mm (Fig. 1). Each experiment was performed from the proximal to the distal part of the RLN.

When an adverse EMG event occurred, activation was halted, and the duration of activation was recorded. After any adverse EMG event had occurred, the EMG signals were monitored for 20 minutes to observe for recovery.

RESULTS

Harmonic ACE

Harmonic ACE was applied in four pigs with eight RLNs. The detailed study information, including the distance from the RLN, duration of activation, amplitude, latency, and loss of signal, is demonstrated in Table 1. Harmonic ACE was activated at 4- and 5-mm distances from the RLN for 10, 20, and 25

Table 1. EMG signal changes during thermal injury induced by harmonic ACE

Animal		Distance (mm)	Duration (sec)	Amplitude (μV)		Latency (msec)		AE	LOS
No.	Side			Baseline	Lowest, n (%)	Baseline	Highest, n (%)		
1	R	5	10	432	345 (80)	8.75	9.00 (103)	-	-
		4	10	432	348 (81)	8.75	8.80 (101)	-	-
		3	10	432	330 (76)	8.75	9.05 (103)	-	-
		2	6	432	216 (50)	8.75	8.75 (100)	+	-
1	L	5	15	554	470 (85)	8.38	8.38 (100)	-	-
		4	15	554	472 (85)	8.38	8.38 (100)	-	-
		3	15	554	450 (81)	8.38	8.40 (100)	-	-
		2	15	554	440 (79)	8.38	8.45 (101)	-	-
		1	15	554	439 (79)	8.38	8.50 (101)	-	-
2	R	5	20	372	305 (82)	9.00	9.18 (102)	-	-
		4	20	372	262 (70)	9.00	9.20 (102)	-	-
		3	15	372	9 (2)	9.00	0 (0)	+	+
2	L	5	25	683	601 (83)	8.38	8.58 (102)	-	-
		4	25	683	492 (72)	8.38	8.58 (102)	-	-
		3	20	683	252 (39)	8.38	8.63 (103)	+	-
3	R	5	10	333	266 (80)	8.75	9.00 (103)	-	-
		4	10	333	275 (83)	8.75	8.84 (101)	-	-
		3	10	333	263 (79)	8.75	9.12 (104)	-	-
		2	10	333	249 (75)	8.75	9.00 (103)	-	-
		1	10	333	230 (69)	8.75	8.84 (101)	-	-
3	L	5	15	278	236 (85)	10.38	10.38 (100)	-	-
		4	15	278	230 (80)	10.38	10.46 (101)	-	-
		3	15	278	205 (74)	10.38	10.89 (105)	-	-
		2	6	278	15 (5)	10.38	0 (0)	+	+
4	R	5	25	1018	1,018 (100)	5.38	5.38 (100)	-	-
		4	25	1018	1,015 (100)	5.38	5.38 (100)	-	-
		3	25	1018	1,015 (100)	5.38	5.38 (100)	-	-
		2	25	1018	1,003 (99)	5.38	5.43 (101)	-	-
		1	25	1018	0 (0)	5.38	0 (0)	+	+
4	L	5	25	313	281 (90)	5.5	5.56 (101)	-	-
		4	25	313	254 (81)	5.5	5.56 (101)	-	-
		3	25	313	247 (79)	5.5	5.67 (103)	-	-
		2	25	313	220 (70)	5.5	5.78 (105)	-	-
		1	25	313	0 (0)	5.5	0 (0)	+	+

EMG, electromyography; R, right; L, left; AE, adverse EMG event; LOS, loss of signal.

seconds, and there was no adverse EMG event observed (Fig. 2).

Of the 14 experiments at a 2- to 3-mm distance from the RLN, there were 4 adverse EMG events found. In these 4 cases, adjacent tissue shrinkage occurred after 6 to 15 seconds of activation, and the RLN touched the Harmonic ACE. The EMG signal did not recover after 20 minutes in two cases (Fig. 2).

Of the 4 experiments at a 1-mm distance from the RLN, there were 2 adverse EMG events, which occurred after 25 seconds of activation. The EMG signal also did not recover after 20 minutes.

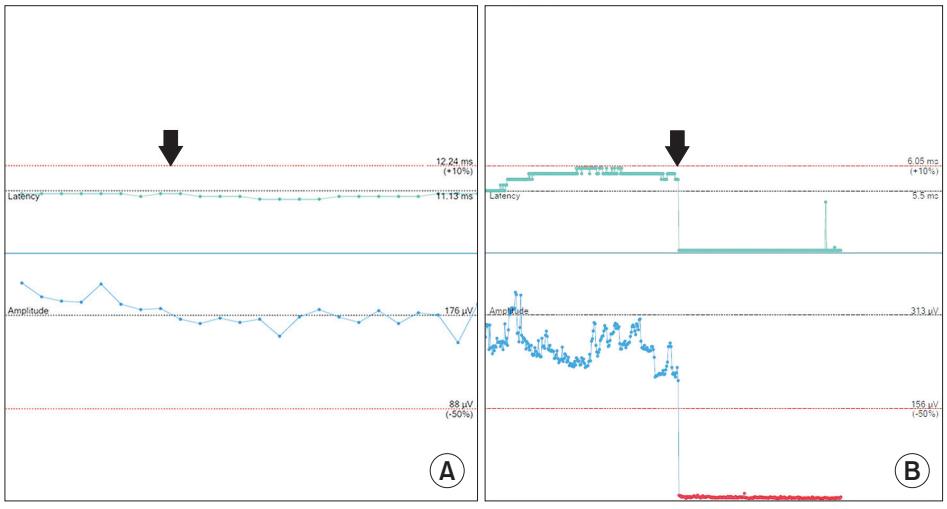

Fig. 2. Electromyography (EMG) signal changes in recurrent laryngeal nerve (RLN) during thermal injury in swine model. (A) The EMG signal remains stable during the Harmonic ACE (Ethicon, a subsidiary Johnson and Johnson, Cincinnati, OH, USA) activation (black arrow) at 3 mm from the RLN for 10 seconds. (B) EMG shows abrupt amplitude and latency decrease when Harmonic ACE is activated (black arrow) at 1 mm from RLN for 25 seconds. Amplitude and latency did not recover for 20 minutes.

Table 2. EMG signal changes during thermal injury induced by Harmonic ACE+

Animal		Distance (mm)	Duration (sec)	Amplitude (μV)		Latency (msec)		AE	LOS
No.	Side			Baseline	Lowest, n (%)	Baseline	Highest, n (%)		
1	R	3	5	330	325 (98)	8.88	8.88 (100)	-	-
		1	5	330	311 (94)	8.88	8.88 (100)	-	-
		0	5	330	280 (85)	8.88	9.15 (103)	-	-
1	L	3	10	1,223	1,211 (99)	6.63	6.63 (100)	-	-
		1	10	1,223	1,161 (95)	6.63	6.70 (101)	-	-
		0	10	1,223	966 (79)	6.63	6.76 (102)	-	-
2	R	3	10	554	543 (98)	8.38	8.38 (100)	-	-
		1	10	554	497 (90)	8.38	8.38 (100)	-	-
		0	6	554	37 (7)	8.38	0.75 (9)	+	+
2	L	3	20	410	377 (92)	8.63	8.75 (101)	-	-
		1	20	410	340 (83)	8.63	8.75 (101)	-	-
		0	10	410	12 (3)	8.63	0 (0)	+	+
3	R	3	5	366	362 (99)	8.75	8.75 (100)	-	-
		1	5	366	347 (95)	8.75	8.75 (100)	-	-
		0	5	366	304 (83)	8.75	8.75 (100)	-	-
3	L	3	10	1,340	1,327 (99)	4.25	4.25 (100)	-	-
		1	10	1,340	1,303 (97)	4.25	4.25 (100)	-	-
		0	10	1,340	992 (74)	4.25	4.34 (102)	-	-
4	R	3	10	1,013	962 (95)	10.13	10.13 (100)	-	-
		1	10	1,013	825 (81)	10.13	10.13 (100)	-	-
		0	10	1,013	710 (70)	10.13	10.25 (101)	-	-
4	L	3	20	1,021	921 (90)	9.88	10 (101)	-	-
		1	20	1,021	766 (75)	9.88	10.2 (103)	-	-
		0	20	1,021	664 (65)	9.88	10.2 (103)	-	-

EMG, electromyography; R, right; L, left; AE, adverse EMG event; LOS, loss of signal.

Harmonic ACE+

Harmonic ACE+ was also applied in 4 pigs with eight RLNs (Table 2). Of the 16 experiments at 1- and 3-mm distances from the RLN, there was no adverse EMG event observed during the 5 to 20 seconds of activation.

Of the 8 experiments at a 0-mm distance from the RLN, there were 2 adverse EMG events after 6 to 10 seconds of activation. The amplitude decreased to 3 to 7 percent, and the latency decreased to 0 to 9 percent.

DISCUSSION

In this study, we investigated safe distances and durations of Harmonic ACE and ACE+ around the RLN. Harmonic ACE was safely used for more than 10 seconds at 4- and 5-mm distances, whereas tissue shrinkage occurred at 2- and 3-mm distances, which resulted in an inadvertent contact with the RLN and adverse EMG events. However, tissue shrinkage did not occur in Harmonic ACE+, and there was no adverse EMG event observed.

Harmonic ACE generates a high-frequency mechanical energy at 55.5 kHz at the active blade to coagulate and cut soft tissues simultaneously [10,11]. This mechanical vibration causes collagen molecules within the tissues to become denatured and form a coagulum that seals the vessels [12]. This takes place at a relatively lower temperature and causes less thermal tissue injuries than other EBDs using electrocautery. Nonetheless, lateral thermal damage can still be transferred to the adjacent tissues that can cause thermal injuries, especially to the tissues vulnerable to heat injuries, such as the RLN. Furthermore, tissue shrinkage caused by Harmonic ACE activation for a long duration increased the risk of thermal injury in the RLN. In fact, the potential risk of tissue shrinkage by EBD use is well studied in a previous study [13]. In addition, it was also suggested that tissue shrinkage should be avoided because it can also delay wound healing [14].

The absence of tissue shrinkage in Harmonic ACE+ was because of the adaptive tissue technology applied to it. Such an adaptive tissue technology uses proprietary algorithms and provides the ability to monitor the thermal condition of the blade [15]. Using this technology, the generator decreases its power output and makes audible tone changes when minimal tissue remains in the jaw [16]. Therefore, it allows for an active monitoring to react to changes in tissue conditions while the instrument is in use and consequently helps surgeons avoid unnecessary heat transfers to the surrounding tissues near the RLN.

The RLN safety parameters of various ultrasonic devices were demonstrated by previous studies. In general, the safe distance of ultrasonic devices tended to shorten as new versions developed. One of the initial studies using the original version of Harmonic scalpel in canine models demonstrated that the safe distance around the RLN was 2 mm via laryngoscopic and microscopic examinations [17]. Another study using Harmonic ACE at the peritoneum of porcine models reported a safe distance of 1.5 mm [18]. The safe distance of the Harmonic Focus was shown to be 1 mm from a recent study using porcine models and CIONM [19].

This study was an animal model study with a small sample size. In addition, there is a limit to the fact that the thickness of tissue for each experiment is not constant; therefore, the current results should be applied in clinical settings with caution. In fact, the importance of this study does not lie in the exact safe distance itself, but in the suggestion that surgeons should be careful in using EBDs around the RLN during thyroid surgeries because EBD use for long durations may cause tissue shrinkage or thermal injury. In conclusion, Harmonic ACE requires a minimum distance of 4 mm from the RLN owing to the risk of tissue shrinkage, while Harmonic ACE+ could be safely used at a 1-mm distance. Surgeons need to understand the characteristics of each EBD and use it in an appropriate manner for safe operations.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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