Usefulness of vessel sealing devices for ≤7 mm diameter vessels: a randomized controlled trial for human thoracoscopic lobectomy in primary lung cancer

Masayuki Toishi, Kazuo Yoshida,* Takayuki Shiina, Masahiro Hashizume, Kazutoshi Hamanaka, Gaku Saito, Takashi Eguchi, Hiroyuki Agatsuma, Takao Sakaizawa

Department of Thoracic Surgery, Shinshu University School of Medicine

3-1-1 Asahi, Matsumoto 390-8621, Japan

*Corresponding author: Kazuo Yoshida, MD, PhD

Department of Thoracic Surgery

Shinshu University School of Medicine

3-1-1 Asahi, Matsumoto 390-8621, Japan

Tel: +81-263-37-2657

Fax: +81-263-37-2721

E-mail: kxy13@shinshu-u.ac.jp

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ABSTRACT

Objectives: Vessel sealing devices (VSD) are widely used for various surgical procedures, including thoracoscopic surgery, but very few reports have compared their safety and usefulness with human thoracoscopic lobectomy procedures not employing VSDs.

Methods: Primary lung cancer patients for whom a thoracoscopic lobectomy involving mediastinal lymph node dissection was planned in our department from April 2011 to March 2013 were recruited for the study. Patients were randomly allocated to a control group (n=14) or a VSD group (n=44), which constituted of three subgroups, namely, EnSeal (n=17), LigaSure (n=15), and Harmonic (n=12). The control group comprised of patients undergoing surgery solely with ligation and conventional electrocautery. EnSeal, LigaSure, and Harmonic were chosen because they are the 3 most popular disposable VSDs used in Japan. In the VSDs groups, the proximal side of pulmonary artery stumps (≤7-mm diameter) were ligated and then allocated to respective groups. Primary endpoints were burst pressure of the pulmonary artery stump (measured using resected specimens), operative time, intraoperative blood loss, instances of endostapler use, intraoperative surgeon stress (assessed by visual analog scale), and postoperative drainage volume and duration. As a secondary objective, the individual VSD groups were also compared with each other.

Results: The burst pressure of ligation-treated pulmonary artery stumps was higher than that of VSD-treated stumps (P<0.0001). The burst pressure of < 5-mm wide VSD-treated stumps was

higher than that of ≥ 5 mm wide stumps (*P*=0.0421). However, burst pressure for all groups and all vessel diameters was sufficient to withstand physiological pulmonary artery pressure. The VSD group demonstrated reduced intraoperative blood loss (*P*=0.0241), surgeon stress (*P*=0.0002), postoperative drainage volume (*P*=0.0358), and shortened postoperative drainage duration (*P*=0.0449). Operative time and the instances of endostapler use did not significantly differ. Comparison between each of the VSD groups revealed no significant differences. None of the patients experienced serious perioperative complications or died because of surgery.

Conclusion: VSD is simple and safe to use in thoracoscopic lobectomy involving mediastinal lymph node dissection for primary lung cancer. Further, none of the VSDs used in this study presented any observable differences in quality that could lead to clinical problems.

Keywords: Video-assisted thoracoscopic surgery; pulmonary lobectomy; vessel sealing; pulmonary artery; burst pressure; mediastinal lymph node dissection

INTRODUCTION

Thoracoscopic surgery has been widely used in recent years for pulmonary lobectomy and has not been reported to be inferior to open surgery even for early-stage lung cancer [1]. The incidence of intraoperative or postoperative fatal bleeding and other complications with thoracoscopic surgery are comparable to that of open surgery [1, 2]. Ligation has long been used for procedures such as small-diameter pulmonary arteriovenous treatment and treatment of blood and lymphatic vessels in lymph node dissection; however, ligation performed via a small, fixed thoracoscopic port is challenging. Moreover, it is considerably stressful to the surgeons performing it. Therefore, we infer that some instances of incomplete ligation, of the surgeon resorting to electrocautery usage due to the difficulty in ligation, and of damage from tugging, leading to complications such as oozing and lymphatic fistulae could have occurred in clinical practice.

Vessel sealing devices (VSDs) are proven to be effective in various fields including neck surgery, axillary dissection, and laparoscopic surgery [3-5]. They are also very useful in thoracoscopic surgery. Although the effectiveness of VSDs in human thoracoscopic lung resection has occasionally been reported [6-9], very few studies have described comparisons between VSD usage and conventional methods [10, 11]. To our knowledge, no studies on thoracoscopic lung resection have prospectively compared VSDs against conventional methods or compared different types of VSD.

Three types of VSDs have hitherto been used in our department; however, the decision to use a VSD

and the type of VSD used were based solely on the experience of the surgeon, and neither their usefulness compared to conventional methods nor the differences in quality between the various types of VSDs used had been assessed. This trial was planned with the aim of analyzing the usefulness of the three types of VSDs so that their choice is no longer based on experience or preference in clinical practice. The primary objective of our study was to prospectively examine the usefulness of VSDs in thoracoscopic lobectomy for primary lung cancer and, the secondary objective was to compare the use of different VSDs, with the aim to establish a simple and safe thoracoscopic lobectomy protocol.

MATERIALS AND METHODS

This study was approved by the institutional review board of Shinshu University School of Medicine (receipt number 1588) and registered in the UMIN Clinical Trials Registry (UMIN study ID: UMIN000004643). Informed consent was obtained from all patients enrolled in the study.

Patients and allocation

Patients planned to undergo thoracoscopic lobectomy involving mediastinal lymph node dissection for non-small cell lung cancer of clinical stage IIIA or less at the Department of Thoracic Surgery, Shinshu University School of Medicine from April 2011 to March 2013 were enrolled in the study. During this period, 97 eligible patients were identified. Patients were allocated to the VSD

(intervention) group and control group at a ratio of 3:1 to assess the primary endpoints. Patients in the VSD group were then assigned to the EnSeal® TRIO (“EnSeal”; advanced bipolar type; moderately curved tip, 3 mm in width; Ethicon Endo-Surgery, Guaynabo, Puerto Rico, USA), LigaSure™ Blunt Tip ("LigaSure"; advanced bipolar type; straight tip, 5 mm in width; Covidien, Mansfield, MA, USA), and Harmonic ACE™ ("Harmonic"; ultrasonic type, moderately curved tip, 2.8 mm in width; Ethicon Endo-Surgery, Guaynabo, Puerto Rico, USA) groups at a ratio of 1:1:1 to assess the secondary endpoints. These VSDs are the three most popular disposable VSDs used in Japan. Group allocation was achieved by simple randomization on the day before surgery by generating random numbers using the Microsoft Excel function RANDBETWEEN (Microsoft Japan, Shinagawa, Tokyo, Japan). This resulted in disproportionate number of patients being allocated to each of the groups. The surgeons did not have an opportunity to select their patients because the surgeon-patient combination had been determined before the patients were allocated to the individual groups. Patients were unaware of the group to which they were allocated, but the study was essentially not blinded.

The sample size was calculated using a visual analog scale (VAS)-based comparison of surgeon stress during LigaSure and conventional ligation procedures for thoracoscopic lobectomies performed in our department in 2009 (presented at the 26th Annual Meeting of the Japanese Association for Chest Surgery Symposium 3). A VAS score of 0 mm was defined as an entirely

stress-free state and 100 mm was defined as maximum imaginable stress. The rationale behind this selection criterion was that the surgeon should be comfortable enough during the procedure to obtain concrete clinical evidence substantiating the popularization of a device. From our empirical data collected in 2009, a 20-mm reduction in VAS was expected to yield substantial reduction in stress. Based on the mean VAS score of the intervention group (33), the control group (53), and standard deviation (13), the sample size required for control group was 10 and VSD group was 30. In addition, at the time of the calculation, we used α-error of 0.05 and power of 0.8.

Exclusion criteria and adverse events

Patients scoring 3 or higher on the American Society of Anesthesiologists Physical Status (ASA-PS) scale were excluded, as were patients from whom consent to participate was not obtained. We only wanted to evaluate patients who underwent completely thoracoscopic lobectomy involving mediastinal lymph node dissection using VSD and ligation. Although no adverse events were directly attributable to VSD usage and ligation, patients with modification to the procedure (conversion to open surgery, reduction of the lung resection range due to dissemination or the like, and reduction or omission of lymph node dissection) were treated as having not received intervention, as were patients treated solely with an endostapler without use of a VSD or ligation for pulmonary artery treatment. Instances of failure to conform to allocation in the control group,

resulting in usage of a VSD, were also excluded. Cases of advanced adhesion during intrathoracic observation were also excluded from analysis because it substantially influenced our measurement items.

The details of the allocation are shown in Fig. 1. Eighty-three cases were randomized. No intraoperative or postoperative bleeding thought to have been caused by incomplete vascular lumen closure by VSD usage or ligation was observed. Two patients were allocated, but then treated as having not received intervention based on conversion to open surgery due to bleeding (one caused by inappropriate use of the endostapler in the EnSeal group, and one caused by lymph nodes adherent to a pulmonary artery in the Harmonic group). No other evident adverse events were thought to directly result from VSD usage or ligation. No reoperations were required for hemorrhage or other reasons among the allocated patients. Excluding those not subjected to intervention and those not subjected to analysis, ultimately 44 patients in the VSD group (17 in the EnSeal group, 15 in the LigaSure group, and 12 in the Harmonic group) and 14 patients in the control group were analyzed.

Endpoints

Primary endpoints were burst pressure of the pulmonary artery stump treated with VSD or ligation (the burst pressure of VSD-treated pulmonary artery stumps measured to evaluate safety [7]), operative time, intraoperative blood loss, instances of endostapler use (VSD usage reportedly

reduces endostapler use and lowers surgical costs [12]), intraoperative surgeon stress (evaluated in 10 surgeons by VAS, as mentioned above), postoperative drainage volume, and postoperative drainage duration. Postoperative drainage volume was defined the volume measured until the morning of the second post-operative day because subsequent measurement in some cases was impossible due to drain removal. The criteria for postoperative drain removal were problem-free status with drainage ≤ 250 mL/day and lack of air leaks during coughing. Because our initial goal was to demonstrate that VSDs are useful, the three VSD groups were analyzed as one group to determine primary endpoints.

The abovementioned endpoints were compared between each of the VSD groups to determine the secondary endpoints. These secondary endpoints were assessed for their potential applicability to guide the choice of VSD for future use.

Surgery

Lateral decubitus was assumed for general anesthesia by differential lung ventilation. A 3- to 4-cm window in the lateral fourth intercostal space was established, as were three ports in the anterior and posterior sixth intercostal space and lateral eighth intercostal space, providing an approach from a total of 4 locations. Thoracoscopic surgery was performed with an inverted image using a 5-mm, 30° angled thoracoscope. Irrespective of the group allocations, treatment was carried out using an endostapler (ECHELON FLEX™ [Ethicon Endo-Surgery, Guaynabo, Puerto Rico, USA], 45mm,

white cartridge) on blood vessels greater than 7 mm. Pulmonary arteries treated with VSD were ≤7 mm in diameter. We measured the diameter of the pulmonary artery with a flexible ruler inserted into the thoracic cavity. Because intraoperative bleeding can occur due to stump contact with other instruments [7], in general, the proximal side was ligated using a 2-0 silk suture and then the allocated VSD was used to treat the pulmonary arteries. In the control group, the proximal side was double-ligated where possible, the distal side was ligated, and then scissors were used to separate the proximal and distal sides. Regarding lymph node dissection and treatment of other blood vessels and chords, surgery was stipulated to consistently conform to the allocations. With the VSD group, ligation was essentially only used for ligating the proximal side of the pulmonary artery. No detailed restrictions were provided regarding treatment of the bronchi and the lung parenchyma, but allocations were complied with in this regard as well. Conventional electrocautery and endostapler were employed in all groups, but no other special equipment was used.

Immediately after surgery, surgeons were asked to respond comprehensively regarding stress endured during vascular treatment, lymph node dissection, and treatment of other chords, for assessment on the VAS.

Measurement of pulmonary artery burst pressure

Burst pressure was measured using a pulmonary artery stump of the resected lung as previously

described [11]. Briefly, measurements were taken from VSD-treated stumps in the VSD group and from ligation-treated stumps in the control group. EnSeal and LigaSure can be used in vessels up to 7 mm in diameter, and Harmonic can be used in vessels up to 5 mm in diameter [13, 14]; however in all groups, vessels up to 7 mm were measured. Burst pressure was measured immediately following resection of the lung from the patient's thoracic cavity. After measurement of the stump vessel diameter, a 22-gauge plastic angiocatheter was cannulated near the stump from a site 5–10 mm from the distal side of the stump, and the proximal side of the insertion site was ligated with 2-0 silk suture (Fig. 2A). After filling an angiocatheter with physiological saline, it was connected to a digital pressure gauge (PG-208-103GP, Copal Electronics, Shinjuku, Tokyo, Japan; converted to mmHg from the kPa display by multiplication by 7.50062) and a pressurization device (Encore26 Inflation Device, Boston Scientific, Natick, MA, USA) using a three-way stopcock (Fig. 2B). The pressure was slowly increased until the physiological saline was ejected from the stump. The maximum pressure in the vessel lumen was recorded as the burst pressure. Pulmonary veins represent nearly all instances treated with an endostapler during lobectomy; therefore, in this study only pulmonary arteries were assessed.

Statistical procedures

Statistical analysis was conducted using Excel Statistics 2010 (SSRI, Shinjuku, Tokyo, Japan), which is an add-on software for Microsoft Excel. Continuous variables were expressed as mean ± standard

deviation; comparisons between two groups were conducted using Student's t-test or Welch's t-test, and comparisons between multiple groups were conducted using ANOVA. Categorical variables were expressed as number (percentage) and assessed using the chi-square test. $P<0.05$ was set as the threshold for statistical significance.

RESULTS

Primary endpoints

Patient characteristics

Patient characteristics are shown in Table 1. No significant differences in age, sex, tumor localization, surgical procedure, or clinical stage were observed between the VSD and control groups.

Measurement of pulmonary artery burst pressure

The results of burst pressure measurement are shown in Table 2. We measured burst pressure from multiple vessels when multiple pulmonary artery branches treated by VSD or ligation were apparent during an operation; therefore, the number of blood vessel measurements is higher than the number of patients. No significant difference was observed in the number of blood vessels with measured burst pressure or the mean diameter of measured vessels. The mean diameter of measured vessels was 4.5±1.2 mm. Blood vessel diameters <5 mm and those ≥5 mm were divided to further compare

whether vessel diameter led to any difference in burst pressure because the burst pressure of small pulmonary arteries has been reported as higher than that of thick pulmonary arteries [10]. In ligation-treated stumps, sites that were not stumps and indwelling needle puncture sites, which reached >1500 mmHg (200 kPa) pressure, as well as instances where pressure reaching 2250 mmHg (300 kPa), still failed to result in bursting. Overall, the burst pressure of ligation-treated stumps was higher (1142±486 mmHg) than that of VSD-treated stumps (309±193 mmHg; $P<0.0001$). Similarly, both diameter classes of ligation-treated stumps had higher burst pressure than VSD-treated stumps (<5 mm: 1218±466 mmHg vs. 351±187mmHg, $P=0.0002$ and ≥5 mm: 1044±530 mmHg vs. 254±191 mmHg, $P=0.0036$). The burst pressure of VSD-treated stumps < 5 mm (351±187 mmHg) was higher than that of stumps ≥ 5 mm (254±191 mmHg; $P=0.0421$). Even VSD-treated stumps ≥ 5 mm, which had the lowest burst pressure in this study, still had sufficient strength to withstand physiological pulmonary artery pressure.

Clinical data

The clinical data for the VSD and control groups are compared in Table 3. The VSD group demonstrated reduced intraoperative blood loss (122±98 mL vs. 217±157 mL, $P=0.0241$), reduced surgeon stress (47±20 vs. 69±16, $P=0.0002$), reduced postoperative drainage volume (437±213 mL vs. 613±320 mL, $P=0.0358$), and shortened postoperative drainage duration (4.1±2.0 days vs.

5.7±3.1 days, *P*=0.0449). No significant differences in operative time or the instances of endostapler use were observed.

Secondary endpoints

Patient characteristics in each of the VSD groups are shown in Table 1; none of the parameters demonstrated any significant difference. The results of burst pressure measurement in each of the VSD groups are shown in Table 2. As in the primary endpoint, the number of vessels measured does not match the number of patients. No significant differences were observed in the number of vessels measured, mean diameter of measured vessels, burst pressure, burst pressure at <5 mm, or burst pressure at ≥5 mm. The clinical data for each of the VSD groups are shown in Table 3. No significant differences were observed in operative time, intraoperative blood loss, instances of endostapler use, intraoperative surgeon stress, postoperative drainage volume, or postoperative drainage duration.

Postoperative complications

Postoperative complications occurring within 30 days of surgery are shown in Table 4. Atrial fibrillation, pulmonary fistula lasting ≥ 1 week, induction of home oxygen therapy, pleurisy, delayed onset pulmonary fistula, and postoperative pneumonia were observed. The overall incidence was

36.2% (21/58 patients), with 36.4% in the VSD group (16/44), and 35.7% in the control group (5/14) and therefore not significant (*P*=0.9649). Furthermore, no significant differences in incidence were observed between each of the VSD groups (*P*=0.8986). Atrial fibrillation was the most frequent (24.1% incidence, 14/58 patients) complication. No surgery-related deaths occurred within 30 days of surgery.

The median postoperative follow-up period (range) was 16.9 months (3.6–29.7 months) for all patients. The median postoperative follow-up period (range) was 17.1 months (3.6–29.6 months) for the VSD group versus 18.9 months (7.5–29.7 months) for the control group, which is not a significant difference (p=0.3088). Comparison between the individual VSD groups (p=0.1234) also did not yield significant differences, with the EnSeal group median follow-up at 18.1 months (3.6–29.6 months), LigaSure group 13.5 months (6.1–27.3 months), and the Harmonic group 18.4 months (8.4–28.4 months). Each group had one case where the patient was rehospitalized and treated for a respiratory disease other than primary lung cancer after the 30th postoperative day (one case of acute aggravation of the interstitial pneumonia in the EnSeal group, one case of bacterial pneumonia in the LigaSure group, and one case each of delayed-onset pulmonary fistula in the Harmonic group and control group). The rehospitalized patient in the EnSeal group died 5.1 months after surgery.

DISCUSSION

VSDs are not widely used in pulmonary vascular treatment during thoracoscopic lobectomy mainly because of the histological vulnerability of the pulmonary arteries due to the thinness of the tunica media and elastic lamina and because of concerns regarding major hemorrhagic morbidity and mortality, with the potential for bleeding to become a fatal complication. Thus, the primary concern is safety with regard to reliable closure of the vessel stumps. The burst pressure of vessel stumps is most directly indicative of this factor. Lesser et al. [10] compared the burst pressure of pulmonary artery stumps treated with LigaSure or conventional ligation in open lobectomy. Mean burst pressure of 3- to 5-mm pulmonary arteries was 315 mmHg for LigaSure vs. 1345 mmHg for ligation, and that of 6- to 8-mm stumps was 156 mmHg vs. 1007 mmHg, respectively, indicating that the burst pressure was higher in the ligation group and higher for small-diameter pulmonary arteries. Our examination yielded essentially the same results as the report by Lesser et al. regarding burst pressure in the VSD and ligation groups, with higher burst pressure in the VSD group for vessels with width <5 mm than for those with width ≥5 mm. However, pulmonary artery pressure, even when regarded as being extremely high, is on an average 45 mmHg or higher, indicating that even the burst pressure for vessels ≥ 5 mm in width in the VSD group in our investigation (the very worst condition) was sufficient to allow for safe clinical usage. These data represent immediate postoperative findings; therefore, additional studies are required to investigate the state of

VSD-treated vessel stumps a few days to several months after surgery. It might be interesting to create VSD treated vessel stumps in an experimental pig model and investigate the burst pressure and histological features of the stumps.

Kovács et al. [8] compared clinical data on VSD usage and endostapler use in partial lung resection. All items measured yielded equivalent results, leading them to conclude that VSD is easy and useful in reducing expenses. Yoshida et al. [11] also observed reduced intraoperative blood loss, postoperative drainage volume, and postoperative drainage duration in a VSD group vs. control group in pulmonary lobectomy. Our study results are consistent with those of Yoshida et al. and are inferred to be largely reflective of the usefulness of VSD in mediastinal lymph node dissection.

In lymph node dissection, full ligation and dissection of invisible blood and lymphatic vessels is very difficult in actual practice and even more challenging in thoracoscopic lobectomy. It is believed that these vessels are frequently treated with either conventional electrocautery or dissected bluntly or sharply. VSD usage, though not without some differences in each of the mechanisms, is consistent in that closure of the vascular and lymphatic lumen is obtained by protein denaturing [15]. However, the hemostatic effect of conventional electrocautery depends on thrombus formation or heat coagulation of blood present in the vascular lumen. Thus, the lumen retains patency, and obtaining lymphatic vessel closure is difficult. Thoracoscopic VSD usage enables simple and reliable vascular

and lymphatic closure and is believed to reduce oozing and lymphatic fistulae. This explains the usefulness of these devices as observed from the results of our study. Although very few studies have reported VSD use in lymph node dissection for primary lung cancer [16], their usefulness has already been proven in procedures such as lymph node dissection for breast cancer [4]. We also attempted to use VAS to assess surgeon stress in vascular treatments, lymph node dissection, and treatment of other chords. VSD usage reduced surgeon stress, which is thought to be largely attributed to the simplicity of lymph node dissection along with the reduced number of ligations made during pulmonary artery treatment and reduced intraoperative blood loss.

Regarding adverse events, Schuchert et al. [6, 12] investigated the usefulness of VSDs in 211 lung resections (among which 79 were thoracoscopic segmentectomies and 51 were thoracoscopic lobectomies) and found that they were associated with no artery dehiscence or conversion to open surgery due to bleeding. Complications were noted in 25.1% of cases, with atrial fibrillation being the most frequent. With no complications or deaths directly attributable to VSD usage, these authors concluded that the results of VSD usage were equivalent to that of endostapler usage. Our investigation was also without surgery-related deaths, and no intraoperative or postoperative observation of bleeding was thought to result from incomplete vascular lumen closure due to VSD usage or ligation. Incidence of complications in the VSD group was slightly higher than that reported in previous studies [6, 12], but the difference was not large given that mediastinal lymph node

dissection was performed in all cases. Comparison between the VSD and control groups revealed no significant difference in complication rates, and the types of complications were also consistent with other reports. Based on these findings, VSD usage appears to not be inferior to conventional methods in terms of adverse events.

We had anticipated that VSD usage may also reduce operative time, but failed to observe a significant difference in this parameter. One possible cause of the equivalent operative times is that VSD usage could require unexpected additional time for ligations placed on the proximal side to ensure safety. Whether VSDs can be used without proximally placed ligation remains a topic for future study. Because careful attention can prevent intraoperative bleeding due to contact with other instruments such as was reported by Tsunezuka et al. [7], proximal ligation is believed to be unnecessary if stump state remains problem-free in the long-term.

In addition to vessel treatment and lymph node dissection, interlobar fissure completion is an extremely important factor affecting operative time, and its effects are thought to be especially significant in thoracoscopic surgery. Interlobar fissure completion is also the most important factor determining the instances of endostapler use. We observed no difference the instances of endostapler use between the VSD and control groups. This similarity is attributed to the fact that the lung parenchyma was treated with an endostapler, essentially without the use of VSDs. Some reports have described VSD treatment of lung parenchyma in the case of partial resection [8], but there seem to

be very few reports addressing intersegmental division in segmentectomy or interlobar fissure completion in lobectomy [17], where its effects remain debatable. In the future, in the absence of safety concerns, the value of VSDs would be further increased if their usage can be actively compared for the lung parenchyma as well, to confirm that they can contribute to reducing operative time and endostapler usage.

This study also compared the individual VSDs as a secondary endpoint. Nearly all the literature in this area is based on animal experiments, and to the extent that reports in clinical practice are occasionally seen, to our knowledge, none have investigated human lung resections. For all devises, the burst pressure of up to 7 mm wide vessels was measured, and all VSDs demonstrated adequate strength, including the burst pressure of vessels ≥ 5 mm wide treated with Harmonic, with no significant differences observed among the three groups. Thus, it appears that any of these VSDs can be safely used provided that the pulmonary arteries being treated are not >7 mm wide.

Janssen et al. [18] systematically reviewed randomized controlled trials in abdominal surgery and compared the usefulness of LigaSure and ultrasonic VSD. In laparoscopic adrenalectomies, the LigaSure usage group demonstrated reduced operative time and intraoperative blood loss, but no differences were observed in laparoscopic colectomies and hepatic resections. The two groups did not differ in any of the surgical procedures regarding conversion to laparotomy, frequency of

complications, or length of hospital stay. Baldwin et al. [3] compared the use of EnSeal in thyroid surgery against past reports on LigaSure and Harmonic, and found that they were equivalent in terms of safety and efficacy. We also did not observe any significant differences in any of the measurement items, and all 3 VSDs were equivalent in terms of adverse events. Harmonic is thought to be inferior to advanced bipolar VSDs in terms of the occurrence of cavitation, but no findings were observed in this study that would have suggested this difference. Previous reports on advanced bipolar VSD usage have predominantly concerned LigaSure, and fewer address EnSeal [3, 19]; however, our investigation found equivalent results for EnSeal and LigaSure. Our data indicated no significant differences among the three groups, and at present we feel that selecting a VSD should depend on the ease of use for the surgeon and enabling less stressful procedures.

We expect that larger-scale controlled trials will be conducted in the future to confirm the usefulness of VSDs in terms of cost-effectiveness and long-term performance and to identify additional specific advantages of each VSD.

Limitations

This study required understanding and cooperation from surgeons, making it difficult to blind them. The authors themselves are surgeons. It would be difficult to run a study with a single surgeon, and undeniably the inclusion of multiple surgeons (10) imparts differences in the surgical procedure

itself, their proficiency, method of using the VSD, and how they perceive stress. Although the pulmonary artery burst pressure was measured by an individual not otherwise associated with this study, numerous doctors treated the resected sample blood vessels for measurement preparation. It is possible that the state of the vessels varied before measurement, which could create a bias. Moreover, we measured burst pressure from multiple vessels only in some patients, which could have induced correlation. Furthermore, an intention-to-treat analysis was not performed. Thus, future studies should focus on improvement of study design and randomization and on increasing the sample size to further validate the findings.

CONCLUSION

VSD usage reduced intraoperative blood loss, surgeon stress, postoperative drainage volume, and drainage duration compared to VSD non-usage. Pulmonary artery stumps had adequate strength in terms of burst pressure, and the incidence of adverse events was equivalent to that of VSD non-usage. The different VSDs demonstrated no difference in quality that could result in clinical complications. VSDs are safe and simple to use in thoracoscopic lobectomy involving mediastinal lymph node dissection for primary lung cancer.

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FIGURE LEGENDS

Fig. 1: Participant flow based on CONSORT 2010

Fig. 2: A, Burst pressure measurement. Plastic angiocatheter cannulated from the distal side toward the stump. The arrow indicates the pulmonary artery stump. B, Burst pressure measurement circuit. Digital pressure gauge and pressurization device connected using a three-way stopcock.

Table 1. Patient characteristics

			VSD (n=44)	Control (n=14)	*P* value	VSD (n=44)			*P* value
						EnSeal (n=17)	LigaSure (n=15)	Harmonic (n=12)	
Age (years)			66±10	63±9	0.4437	64±12	68±9	66±10	0.6445
Sex	Male		27 (61)	9 (64)	0.8444	9 (53)	9 (60)	9 (75)	0.4815
	Female		17 (39)	5 (36)		8 (47)	6 (40)	3 (25)	
Tumor localization	Right	Upper	13 (30)	3 (22)	0.9539	5 (29)	5 (33)	3 (25)	0.6188
		Middle	2 (5)	1 (7)		1 (6)	1 (7)	0	
		Lower	16 (36)	6 (43)		7 (41)	3 (20)	6 (50)	
	Left	Upper	5 (11)	2 (14)		2 (12)	1 (7)	2 (17)	
		Lower	8 (18)	2 (14)		2 (12)	5 (33)	1 (8)	
Surgical procedure	Lobectomy		39 (89)	11 (78)	0.3990	15 (88)	14 (93)	10 (83)	0.3853
	Lobectomy + partial resection		1 (2)	0		0	1 (7)	0	
	Lobectomy + segmentectomy		1 (2)	0		1 (6)	0	0	
	Bilobectomy		3 (7)	3 (22)		1 (6)	0	2 (17)	
Clinical stage	IA		18 (41)	8 (58)	0.5095	8 (47)	6 (40)	5 (42)	0.8885
	IB		12 (27)	1 (7)		4 (24)	4 (27)	3 (25)	
	IIA		7 (16)	2 (14)		3 (17)	2 (13)	2 (17)	
	IIB		1 (2)	1 (7)		0	0	1 (8)	

	IIIA	6 (14)	2 (14)	2 (12)	3 (20)	1 (8)

Continuous variables were expressed as mean ± standard deviation. Categorical variables were expressed as number (percentage).

Table 2. Burst pressure of treated stumps

	VSD (n=48)	Control (n=16)	*P* value	VSD (n=48)			*P* value
				EnSeal (n=18)	LigaSure (n=16)	Harmonic (n=14)	
<5 mm	27 (56)	9 (56)	1.0000	10 (56)	8 (50)	9 (64)	0.7317
≥5 mm	21 (44)	7 (44)		8 (44)	8 (50)	5 (36)	
Mean vessel diameter (mm)	4.5±1.1	4.6±1.4	0.8325	4.3±1.0	4.6±1.3	4.5±1.1	0.7490
Burst pressure (mmHg)	309±193	1142±486	<0.0001	309±177	351±249	259±129	0.4336
Burst pressure < 5mm (mmHg)	351±187*	1218±466	0.0002	363±172	402±246	291±142	0.4722
Burst pressure ≥ 5mm (mmHg)	254±191	1044±530	0.0036	241±170	300±258	201±86	0.6641

Continuous variables were expressed as mean ± standard deviation. Categorical variables were expressed as number (percentage). In the control group, stumps were treated with ligation.*, significantly higher than VSD-treated stumps ≥ 5 mm.

Table 3. Comparison of clinical data

	VSD (n=44)	Control (n=14)	*P* value	VSD (n=44)			*P* value
				EnSeal (n=17)	LigaSure (n=15)	Harmonic (n=12)	
Operative time (min)	242±83	278±109	0.1019	258±91	226±80	239±77	0.5557
Intraoperative blood loss (mL)	122±98	217±157	0.0241	122±106	95±73	155±110	0.2965
Instances of endostapler use	5.3±1.3	5.2±1.7	0.4266	5.5±1.5	5.0±1.3	5.3±1.2	0.5441
Surgeon stress (measured by VAS)	47±20	69±16	0.0002	46±25	47±16	48±19	0.9715
Drainage volume (mL)	437±213	613±320	0.0358	437±197	471±208	395±249	0.6625
Drainage duration (days)	4.1±2.0	5.7±3.1	0.0449	4.1±1.7	4.3±2.4	3.9±2.1	0.8639

Continuous variables were expressed as mean ± standard deviation. VAS, visual analog scale

Table 4. Postoperative complications within 30 days of surgery

	VSD (n=44)	**Control (n=14)**	***P* value**	**VSD (n=44)**			***P* value**
				EnSeal (n=17)	**LigaSure (n=15)**	**Harmonic (n=12)**	
Atrial fibrillation	10 (22.7)	4 (28.6)		4 (23.5)	4 (26.6)	2 (16.7)	
Pulmonary fistula lasting ≥ 1 week	2 (4.5)	1 (7.1)		1 (5.9)	1 (6.7)		
Home oxygen therapy	1 (2.3)					1 (8.3)	
Pleurisy	1 (2.3)			1 (5.9)			
Delayed-onset pulmonary fistula	1 (2.3)					1 (8.3)	
Postoperative pneumonia	1 (2.3)					1 (8.3)	
Total	16 (36.4)	5 (35.7)	0.9649	6 (35.3)	5 (33.3)	5 (41.6)	0.8986

Categorical variables were expressed as number (percentage).

Fig.1

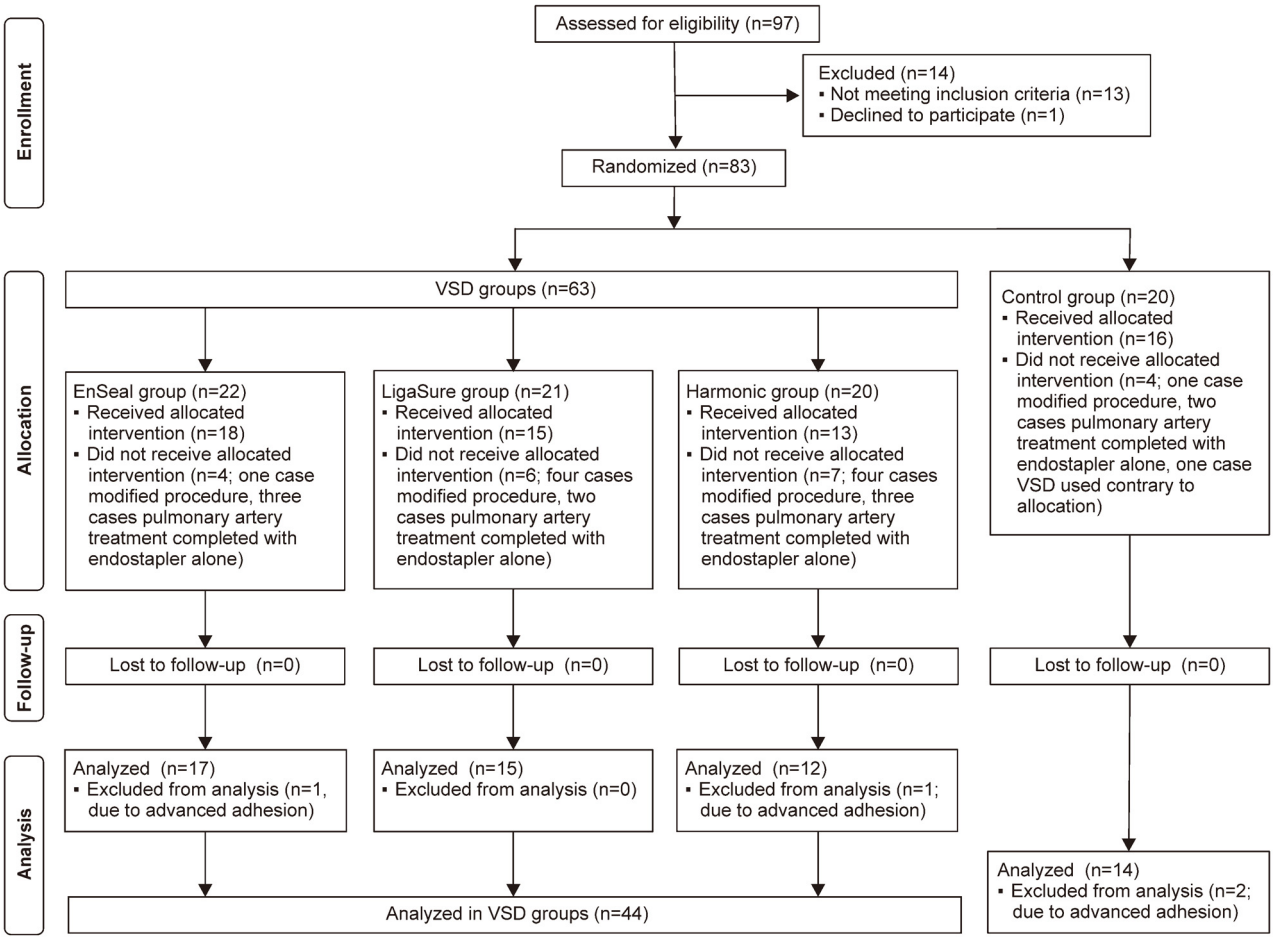
Enrollment
Assessed for eligibility (n=97)
Excluded (n=14)
▪ Not meeting inclusion criteria (n=13)
▪ Declined to participate (n=1)
Randomized (n=83)
Allocation
VSD groups (n=63)
Control group (n=20)
▪ Received allocated intervention (n=16)
▪ Did not receive allocated intervention (n=4; one case modified procedure, two cases pulmonary artery treatment completed with endostapler alone, one case VSD used contrary to allocation)
EnSeal group (n=22)
▪ Received allocated intervention (n=18)
▪ Did not receive allocated intervention (n=4; one case modified procedure, three cases pulmonary artery treatment completed with endostapler alone)
LigaSure group (n=21)
▪ Received allocated intervention (n=15)
▪ Did not receive allocated intervention (n=6; four cases modified procedure, two cases pulmonary artery treatment completed with endostapler alone)
Harmonic group (n=20)
▪ Received allocated intervention (n=13)
▪ Did not receive allocated intervention (n=7; four cases modified procedure, three cases pulmonary artery treatment completed with endostapler alone)
Follow-up
Lost to follow-up (n=0)
Lost to follow-up (n=0)
Lost to follow-up (n=0)
Lost to follow-up (n=0)
Analysis
Analyzed (n=17)
▪ Excluded from analysis (n=1, due to advanced adhesion)
Analyzed (n=15)
▪ Excluded from analysis (n=0)
Analyzed (n=12)
▪ Excluded from analysis (n=1; due to advanced adhesion)
Analyzed (n=14)
▪ Excluded from analysis (n=2; due to advanced adhesion)
Analyzed in VSD groups (n=44)

Fig.2