Comparison of hand-assisted laparoscopic surgery (HALS) and conventional laparotomy in patients with colorectal cancer: Final results from a single center

TAKAYUKI TAJIMA[1], MASAYA MUKAI[2], DAIKI YOKOYAMA[2], SHIGEO HIGAMI[2], SHUJI UDA[2], SAYURI HASEGAWA[1], EIJI NOMURA[2], SOTARO SADAHIRO[1], SEIEI YASUDA[1] and HIROYASU MAKUUCHI[1,2]

[1]Department of Surgery, Tokai University School of Medicine, Isehara, Kanagawa 259-1193; [2]Department of Surgery, Tokai University Hachioji Hospital, Hachioji, Tokyo 192-0032, Japan

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Abstract. In recent years, the use of laparoscopic surgery has been expanded to include radical curative resection. In a previous study, 212 patients with primary colorectal cancer (stages I-III) underwent radical curative resection by hand-assisted laparoscopic surgery (HALS) (n=98) or conventional laparotomy (CL) (n=114) and were compared with respect to 3-year relapse-free survival (3Y-RFS) and 3-year overall survival (3Y-OS). The study included 210/212 patients who were followed up to 5 years, including 96 patients who underwent HALS and 114 treated with CL. The two groups were matched for stage, clinical background, and postoperative management. Patient characteristics were compared and the 5Y-RFS and 5Y-OS were determined. The 5-year follow-up rate was 97.6%. In stage I-III patients, 5Y-RFS and 5Y-OS showed no significant differences between HALS and CL. The patients with stage I disease accounted for 41.7% (40/96) of the patients undergoing HALS, while stage I patients only accounted for 23.7% (27/114) of the patients undergoing CL, and the difference was significant (P=0.005). Stage II patients undergoing CL were older than those treated with HALS (P=0.017). However, there were no differences in the characteristics of stage III patients undergoing HALS or CL. In conclusion, HALS achieved a similar survival to CL in patients with stage I to III colorectal cancer. Compared with CL, HALS was performed more safely and achieved superior cosmetic results.

Correspondence to: Dr Takayuki Tajima, Department of Surgery, Tokai University School of Medicine, 143 Shimokasuya, Isehara, Kanagawa 259-1193, Japan
E-mail: takayukitajima1970@yahoo.co.jp

Abbreviations: HALS, hand-assisted laparoscopic surgery; CRC, colorectal cancer; CL, conventional laparotomy; LACS, laparoscopy-assisted colorectal surgery

Key words: colorectal cancer, hand-assisted laparoscopic surgery, conventional laparotomy, laparoscopy-assisted colorectal surgery, laparoscopic surgery

Introduction

In recent years, the indications for laparoscopic surgery have been expanded to include radical curative resection of early to advanced colorectal cancer and palliative surgery for stage IV disease (1-6). In Japan, laparoscopy-assisted colorectal surgery (pure LACS) is widely used. However, pure LACS has several disadvantages, such as requiring at least 2 physicians who are familiar with the procedure and prolonging the operating time, as well as needing more staff and limiting the availability of operating theaters. Previously, it was reported that pure LACS achieves the same or better outcomes as conventional laparotomy (CL) with regard to wound infection, hospital stay, and survival, together with superior cosmetic results (7-10). In Europe and the USA, hand-assisted laparoscopic surgery (HALS) (HH) is more widely used than pure LACS. HH is characterized by: i) Providing the operator with palpation/tactile sensation, and allowing full grasping manipulation with the left hand and the possibility of smoothly removing even large and heavy tumors; ii) a shorter operating time than for pure LACS; and iii) a more rapid learning curve than for pure LACS (8,9,11-17).

In Japan, various surgical procedures are employed for colorectal cancer, including pure LACS (30-40%), CL (~50%), and other methods such as HALS and microincisional surgery (18). HALS is often regarded as being an optimal medium between CL and pure LACS (8,9,18-23). In Japan, HALS initially became popular for a short period of time during the introduction of pure LACS in 2000, possibly as a method of training for other procedures, prior to showing a marked decline in this function. Consequently, at present, single-center reviews of HALS are performed in countries other than Japan (9,24). Previously, 212 patients with primary colorectal cancer (stages I-III) underwent radical curative resection by hand-assisted laparoscopic surgery (HALS) (n=98) or conventional laparotomy (CL) (n=114) and were compared with respect to 3-year relapse-free survival (3Y-RFS) and 3-year overall survival (3Y-OS) (25). However

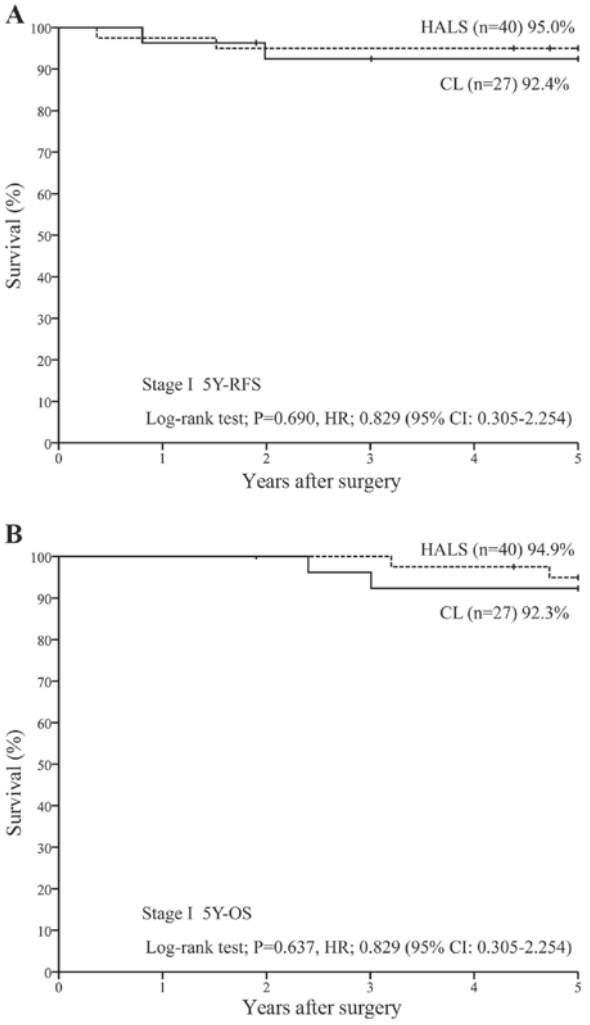

Figure 1. (A) The 5-year relapse-free survival rate (5Y-RFS) and (B) 5-year overall survival rate (5Y-OS) of stage I patients in the hand-assisted laparoscopic surgery (HALS) and conventional laparotomy (CL) groups. The Kaplan-Meier method was employed, followed by comparison with the log-rank test and hazard ratio (HR) [95% confidence interval (CI)].

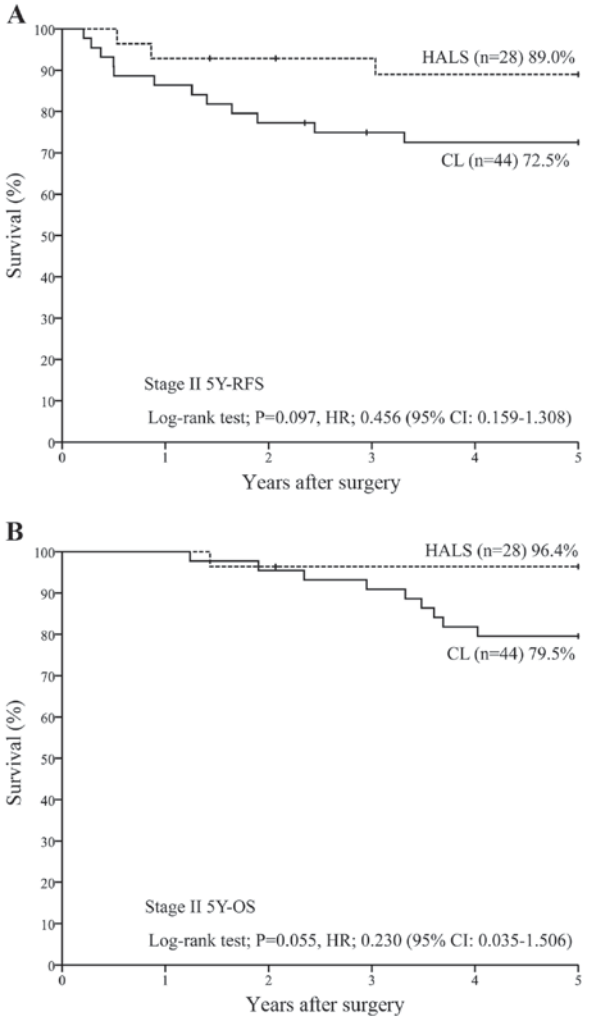

Figure 2. (A) 5-year relapse-free survival rate (5Y-RFS) and (B) 5-year overall survival rate (5Y-OS) of stage II patients in the hand-assisted laparoscopic surgery (HALS) and conventional laparotomy (CL) groups. The Kaplan-Meier method was employed, followed by comparison with the log-rank test and and hazard ratio (HR) [95% confidence interval (CI)].

this type of surgery has limitations. In the present study, 5-year data on the clinical outcomes of HALS and CL for colorectal cancer were analyzed at a single institution in Japan.

Patients and methods

Patients. In total, 850 patients underwent radical curative resection of primary colorectal cancer between April 2002 and December 2012. Aggressive introduction of HALS colorectal cancer surgery commenced in July 2007. Of the patients that were followed up over a period of 5 years, 114 patients (stage I, 27; stage II, 44; and stage III, 43) who received radical curative resection via CL prior to the introduction of HALS in July 2007, were carefully selected as historical controls (CL group), and were compared with 96 patients (stage I, 40; stage II, 28; and stage III, 28) who underwent resection by HALS (HALS group). The two groups were matched for stage and received the same postoperative adjuvant chemotherapy regimen and follow-up protocol. HALS and CL were performed in patients with a performance status of 0-2, and who exhibited no serious cardiopulmonary disease, no obvious preoperative lateral lymph node metastasis or multiple organ involvement, and no pelvic cavity disease (4,24-27).

In the CL group, standard midline laparotomy was performed with a ≥30 cm incision, while 2-port HALS (colon, 5 mm/5 mm) or 3-port HALS (rectum and sigmoid colon, 5 mm/12 mm/5 mm) was performed in conjunction with a 45-55 mm longitudinal midline upper umbilical (colon)/umbilical (rectum/sigmoid colon) incision (4,26,27). At least 12 lymph nodes were collected from patients in the two groups following D2 or D3 resection according to the Japanese classification (28-30). The postoperative adjuvant chemotherapy regimens were as follows: No chemotherapy in stage I, only oral anticancer agents (UFT/PSK) in stage II, and modified 5-fluorouracil (5-FU)/leucovorin (LV) or modified FOLFIRI (5-FU/LV+CPT-11) for ≥6 months in stage III (25,31-36). To detect metastasis/recurrence, ultrasound scan (US) and computed tomography (CT) were performed 3-4 times annually, and patients in whom US and CT simultaneously identified metastatic/recurrent disease were classified as positive for metastasis/recurrence (25,31-36). The 5-year relapse-free survival (5Y-RFS)

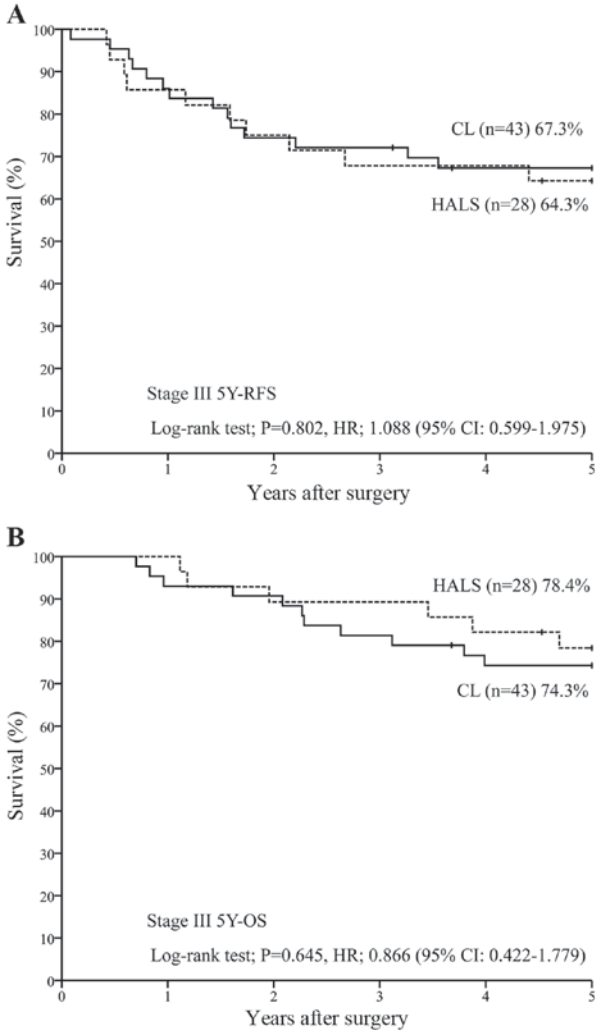

Figure 3. (A) The 5-year relapse-free survival rate (5Y-RFS) and (B) 5-year overall survival rate (5Y-OS) of stage III patients in the hand-assisted laparoscopic surgery (HALS) and conventional laparotomy (CL) groups. The Kaplan-Meier method was employed, followed by comparison with the log-rank test and hazard ratio (HR) [95% confidence interval (CI)].

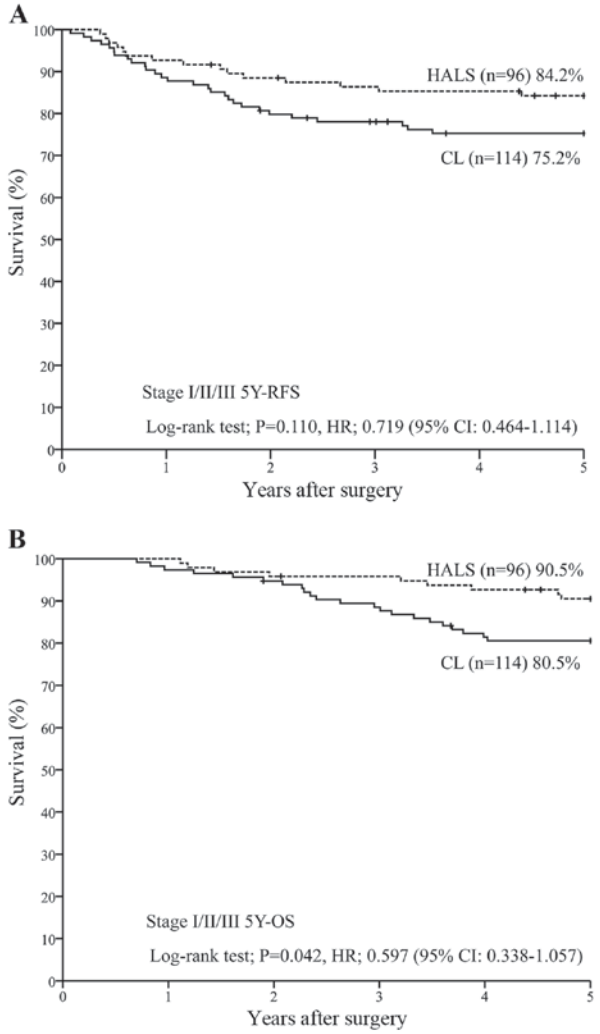

Figure 4. (A) The 5-year relapse-free survival rate (5Y-RFS) and (B) 5-year overall survival rate (5Y-OS) of all the patients (stages I/II/III) in the hand-assisted laparoscopic surgery (HALS) and conventional laparotomy (CL) groups. The Kaplan-Meier method was employed, followed by comparison with the log-rank test and hazard ratio (HR) [95% confidence interval (CI)].

and 5-year overall survival (5Y-OS) were calculated for each group and the results were compared.

Statistical analysis. The Kaplan-Meier method was used to estimate 5Y-RFS and 5Y-OS, while the log-rank test and hazard ratio [95% confidence interval (CI)] were used for comparison between the two groups. The χ^2 test and Mann-Whitney U test were employed for any other parameters. SPSS statistics 21.1 software (IBM Corp., Armonk, NY, USA) was used. $P<0.05$ was considered to indicate a significant difference in all the analyses.

Results

Prognosis. For patients in stage I (n=67), 5Y-RFS was 95.0% with HALS (n=40) vs. 92.4% with CL (n=27) [P=0.690; hazard ratio (HR), 0.829 (95% CI, 0.305-2.254)] (Fig. 1A), while 5Y-OS was 94.9% with HALS (n=40) vs. 92.3% with CL (n=27) [P=0.637; HR, 0.829 (95% CI, 0.305-2.254)] (Fig. 1B). For patients in stage II (n=72), 5Y-RFS was 89.0% with HALS (n=28) vs. 72.5% with CL (n=44) [P=0.097; HR, 0.456 (95% CI, 0.159-1.308)] (Fig. 2A), while 5Y-OS was 96.4% with HALS (n=28) vs. 79.5% with CL (n=44) [P=0.055; HR, 0.230 (95% CI, 0.035-1.506)] (Fig. 2B). For patients in stage III (n=71), 5Y-RFS was 64.3% with HALS (n=28) vs. 67.3% with CL (n=43) [P=0.802; HR, 1.088 (95% CI, 0.599-1.975)] (Fig. 3A), while 5Y-OS was 78.4% with HALS (n=28) vs. 74.3% with CL (n=43) [P=0.645; HR, 0.866 (95% CI, 0.422-1.779)] (Fig. 3B).

For all the patients in stages I-III (n=210), 5Y-RFS was 84.2% with HALS (n=96) vs. 75.2% with CL (n=114) [P=0.110; HR, 0.719 (95% CI, 0.464-1.114)] (Fig. 4A), while 5Y-OS was 90.5% with HALS (n=96) vs. 80.5% with CL (n=114) [P=0.042; HR, 0.597 (95% CI, 0.338-1.057)] (Fig. 4B).

Patient characteristics. There were 67 patients with stage I disease. Forty stage I patients underwent HALS, accounting for 41.7% of the HALS group, while 27 stage I patients underwent CL, accounting for only 23.7% of the CL group, indicating a significant difference (P=0.005). Of the 72 patients in stage II, 28 patients underwent HALS (29.2% of the HALS

Table I. Comparison of stage between the HALS group (n=96) and the CL group (n=114).

Stage	HALS	CL	P-value (χ^2)
1	41.7% (40/96)	23.7% (27/114)	0.005
2	29.2% (28/96)	38.6% (44/114)	0.152
3	29.1% (28/96)	37.7% (43/114)	0.192

HALS, hand-assisted laparoscopic surgery; CL, conventional laparotomy.

Table II. Tumor site and stage distribution of patients.

A, Comparison of tumor site between the HALS group (n=96) and the CL group (n=114)

Tumor site	HALS	CL	P-value (χ^2)
Colon	55.2% (53/96)	67.5% (77/114)	0.067
Rectum	44.8% (43/96)	32.5% (37/114)	

B, Stage distribution of patients with colon cancer (n=130) and rectal cancer (n=80)

Stage	Colon	Rectum	P-value (χ^2)
1	30.8% (40/130)	33.8% (27/80)	0.653
2	38.5% (50/130)	27.5% (22/80)	0.104
3	30.8% (40/130)	38.8% (31/80)	0.235

HALS, hand-assisted laparoscopic surgery; CL, conventional laparotomy.

Table III. Comparison of age between the HALS group (n=96) and the CL group (n=114).

A, All patients, n=210

Characteristics	HALS, n=96	CL, n=114	P-value, Mann-Whitney U test
Age, years			0.010
Average	62.4	65.6	
Median	62 (36-81)	66 (42-87)	

B, Stage I patients, n=67

Colon and rectum	HALS, n=40	CL, n=27	P-value, Mann-Whitney U test
Age, years			0.090
Average	64.5	68.3	
Median	64.5 (42-81)	71.0 (42-87)	

C, Stage II patients, n=72

Colon and rectum	HALS, n=28	CL, n=44	P-value, Mann-Whitney U test
Age, years			0.017
Average	60.7	66.1	
Median	61.0 (40-75)	66.5 (45-81)	

D, Stage III patients, n=71

Colon and rectum	HALS, n=28	CL, n=43	P-value, Mann-Whitney U test
Age, years			0.207
Average	60.9	63.5	
Median	60.0 (36-72)	64.0 (45-76)	

HALS, hand-assisted laparoscopic surgery; CL, conventional laparotomy.

group) and 44 patients were treated by CL (38.6% of the CL group), showing no significant difference (P=0.152). Of the 71 stage III patients, 28 patients underwent HALS (29.1% of the HALS group) and 43 patients received CL (37.7% of the CL group), also showing no significant difference (P=0.192; Table I). These results indicated that HALS was performed significantly more often than CL for stage I disease (Table I).

Regarding tumor site, the tumor was located in the colon in 53 patients undergoing HALS (55.2% of the HALS group) and 77 patients undergoing CL (67.5% of the CL group), while the tumor was located in the rectum in 43 patients undergoing HALS (44.8% of the HALS group) and 37 patients undergoing CL (32.5% of the CL group), and no significant difference was observed (P=0.067) (Table IIA).

Patients in stage I (n=40) accounted for 30.8% of all the colon cancer patients, while stage I rectal cancer patients (n=27) comprised 33.8% of all rectal cancer patients (P=0.653). There were 50 patients with stage II colon cancer, accounting for 38.5% of all colon cancer patients, and there were 22 patients with stage II rectal cancer, accounting for 27.5% of all rectal cancer patients (P=0.104). There were 40 patients with stage III colon cancer, accounting for 30.8% of all colon cancer patients, and there were 31 patients with stage III rectal cancer, accounting for 38.8% of all rectal cancer patients (P=0.235). There were no significant differences in stages I-III (Table IIB).

Regarding the age distribution, the mean age was 62.4 (median, 62) years in the HALS group and 65.6 (median, 66) years in the CL group (Table IIIA).

The mean age of the stage I patients was 64.5 years (median, 64.5) years and 68.3 (median, 71.0) years in the HALS and CL groups, respectively (P=0.090) (Table IIIB). In addition, the mean age of stage II patients was 60.7 (median, 61.0)

years and 66.1 (median, 66.5) years in the HALS and laparotomy groups, respectively (P=0.017) (Table IIIC), while that of stage III patients was 60.9 (median, 60.0) years and 63.5 (median, 64.0) years, respectively (P=0.207; Table IIID).

Discussion

Due to its rapid utilization in recent years, a number of studies have reported on pure LACS in comparison with CL and HALS (8,9,19-23). When surgical procedures are reviewed at a single center, CL is often selected as the control. However, it is difficult to exclude bias from the clinical background of the control group in relation to both pure LACS and HALS. In addition, problems with the standardization of subsequent treatment are likely to occur, such as the postoperative chemotherapy or radiotherapy regimens and the methods of handling recurrence. In the present study, we used historical controls treated prior to the utilization of HALS. The controls were matched for stage and for the postoperative adjuvant chemotherapy regimen, and were compared (4-10). The HALS and CL procedures were performed by Mukai *et al* (4,27); thus, the management of stage I/II/III colorectal cancer was standardized in the study population. Patients in stages II and III from the two groups received standardized chemotherapy and the ≥6-month completion rate was >80% in the two groups (data not shown) (25). The results of the 5-year follow up were also analyzed in the present study.

A comparison of pure LACS with CL has identified problems with human resources, surgical skill, a prolonged operating time, and higher cost in relation to LACS, although there have also been reports of a shorter hospital stay and a decrease in the total analgesic dose (7-10). Previous findings showed that the conversion rate of HALS was much lower than that of pure LACS (15). The rate for HALS in the present study was 4.2% (4/98 patients) in our study. There were significant differences of blood loss for stages I and II and in the length of hospital stay for stage III (25). However, stage III patients with multiple organ infiltration accounted for 18.6% (8/43 patients) in the CL group vs. 3.6% in the HALS group (1/28, P=0.063, data not shown) (25). There were no significant differences between the two groups with respect to complications.

Blood loss was obviously lower in stage I and II patients from the HALS group, suggesting that this method is safe when based on strict indications (25).

The present study also involved rectal cancer patients. Findings of studies conducted in Europe and America suggest that HALS does not show non-inferiority versus pure LACS and CL for the resection of rectal cancer (37,38). However, results of those studies, which included rectal cancer patients showed no significant difference between CL and HALS. Based on those findings, HALS is a safe and reliable technique for patients with colorectal cancer that achieves the same 5Y-RFS and 5Y-OS as CL, suggesting that it is a reasonable procedure to employ and is positioned between pure LACS and CL. Since HALS is easy to perform and is a cost-effective method, it is considered to be a superior technique that deserves to be reconsidered in the current medical environment where availability of surgeons and anesthesiologists is on the decrease at small and medium-sized hospitals in Japan.

Acknowledgements

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