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Protective effect of remifentanil on blood loss in endoscopic subcutaneous mastectomy: a retrospective study

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Abstract

Background: Remifentanil decreases blood loss during spinal surgery, rhinoplasty, and endoscopic sinus surgery. However, there are no reports regarding its effect on intraoperative blood loss during endoscopic body surface surgery. The present study aimed to investigate the effect of intraoperative remifentanil on blood loss during endoscopic subcutaneous mastectomy.

Methods: In this single-center, retrospective observational study conducted from August 2005 to June 2010, 443 patients who underwent either endoscopic subcutaneous partial mastectomy or quadrantectomy were included ($n = 231$ and 212, respectively). Patients were categorized into the remifentanil and non-remifentanil groups ($n = 154$ and 289, respectively) based on intraoperative use of remifentanil. We compared the amount of blood loss between the remifentanil and non-remifentanil groups.

Results: Blood loss was significantly smaller in the remifentanil group than in the non-remifentanil group in patients undergoing partial mastectomy (median [25%, 75%], 60 [30, 94] vs. 90 [50, 165] ml, $P < 0.001$) and quadrantectomy (90 [30, 163] vs. 140 [74, 220] ml, $P = 0.001$).

Conclusions: Intraoperative bleeding was significantly smaller in patients receiving remifentanil than that in those not receiving remifentanil during endoscopic subcutaneous mastectomies.

Keywords: Anesthesiology, Blood pressure, Remifentanil, Mastectomy, Blood loss, Endoscopy

Background

Remifentanil is a potent opioid, which has analgesic effects and suppresses the sympathetic nerves (Komatsu et al. 2007), leading to intraoperative hemodynamic stability (Joshi et al. 2002). The hemodynamic stability provided by intraoperative remifentanil may reduce blood loss (Degoute et al. 2001). Several studies have reported reduced blood loss in spinal surgery, rhinoplasty, and endoscopic sinus surgery (Komatsu et al. 2007; Kawano et al. 2013; Ha et al. 2014; Kosucu et al. 2014; Cardesin et al. 2015). Those studies indicated that hemodynamic stability derived from intraoperative remifentanil use contributed to reduced blood loss.

In endoscopic surgery, even a small amount of bleeding interferes with the visual field; therefore, a reduction in bleeding is essential to facilitate a smooth and successful procedure. However, the reduced blood loss provided by remifentanil in endoscopic surgery has only been reported for otolaryngology procedures such as rhinoplasty and sinus surgery (Ha et al. 2014; Kosucu et al. 2014; Cardesin et al. 2015; Rodriguez Valiente et al. 2013). It is unknown whether there is a relationship between the use of intraoperative remifentanil and blood loss in other types of endoscopic surgery such as endoscopic body surface surgery.

The present study aimed to examine the effect of remifentanil on the level of bleeding during endoscopic body surface surgery. We evaluated patients undergoing

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two types of endoscopic subcutaneous mastectomy (ESM)—partial mastectomy and quadrantectomy—and compared blood loss between those who received intraoperative remifentanil and those who did not.

Methods

Participants

The ethics committee of Kameda Medical Center approved this retrospective study, which conformed to the tenets of the Declaration of Helsinki on March 2011. The requirement for informed consent was waived, because of the retrospective nature of the study.

One thousand two patients with breast cancer, who underwent ESM at Kameda Medical Center between August 2005 and June 2010, were enrolled. The ESM procedure varies among patients, but generally comprises a series of standardized procedures (Sakamoto et al. 2009; Patani and Mokbel 2008). To eliminate factors influencing intraoperative blood loss, patients with the following factors were excluded: bilateral mastectomies ($n = 12$), total mastectomy ($n = 359$), axillary lymphadenectomy ($n = 61$), total intravenous anesthesia ($n = 37$), American Society of Anesthesiologists physical status (ASA-PS) 3 or 4 ($n = 14$), and coagulopathy disorder, antiplatelet therapy, or anticoagulation therapy documented by preoperative anesthesiologists' evaluation ($n = 47$) (Hackett et al. 2015; Miłoński et al. 2013).

Thus, primary screening automatically excluded 530 patients based on the exclusion criteria. We investigated each of the remaining patients for availability and reliability for analysis in a secondary screening, by reviewing each anesthesia record. In 22 of the remaining 472 patients, the data regarding remifentanil use could not be accessed because of issues relating to computer system maintenance. In addition, we excluded patients who had a remifentanil infusion rate of less than 0.05 μg/kg/min ($n = 5$), duration of remifentanil administration of less than 1 h ($n = 1$), and intraoperative landiolol use ($n = 1$) (Fig. 1).

Finally, 443 patients who underwent partial mastectomy ($n = 231$) and quadrantectomy ($n = 212$) were available for data analysis. We allocated patients who received remifentanil to the remifentanil group, and those who did not receive remifentanil to the non-remifentanil group. In the remifentanil group, partial mastectomy was performed in 98 patients, and in the non-remifentanil group, in 133 patients. Quadrantectomy was performed in 56 patients of the remifentanil group and in 156 patients of the non-remifentanil group.

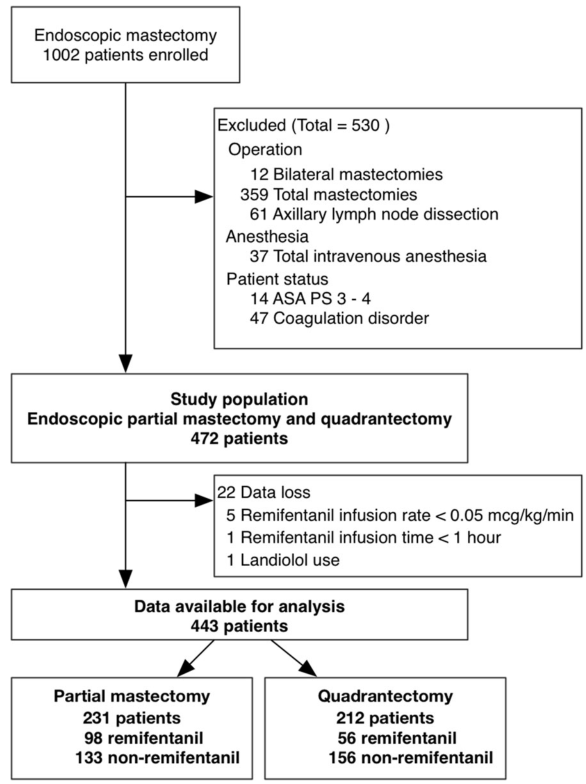

Fig. 1 Flowchart of enrolment. A total of 1002 patients underwent mastectomies between August 2005 and June 2010. Initial screening excluded 530 patients by evaluating suitability for operation, anesthesia, and patient-related factors. Secondary screening excluded additional patients because of unreliable data

Anesthesia

General anesthesia was induced with thiopental 3–4 mg/kg or propofol 2–3 mg/kg, and vecuronium 0.1–0.15 mg/kg was used for tracheal intubation. Anesthesia was maintained with nitrous oxide–oxygen–sevoflurane or oxygen–sevoflurane. In the remifentanil group, remifentanil was started at 0.1 μg/kg/min and adjusted by 0.05 μg/kg/min to provide sufficient analgesia, intraoperatively (Chelliah 2003). In both groups, fentanyl and non-steroidal anti-inflammatory drugs were given based on the anesthesiologist's decision.

Subcutaneous endoscopic mastectomies

Resection size is thought to affect blood loss during mastectomy (Clegg-Lamptey and Dakubo 2014). Therefore, mastectomies were classified in accordance with the resection size: partial mastectomy and quadrantectomy. ESM involves two steps: an operator detaches the lacteal gland from the pectoralis major muscle under endoscopic vision through a small axillary incision. In the second step, under direct vision, the surgeon removes the lacteal gland containing the breast cancer tissue (Sakamoto et al. 2009).

The Department of Breast Oncology at Kameda Medical Center, where the operations took place, has received accreditation by the Japanese Breast Cancer Society. Sixteen surgeons performed ESM on patients participating in the present study. All of the operations were observed and supervised by the Chief of the Department of Breast Oncology—a Councilor of the Japanese Breast Cancer Society.

Data collection

Data were obtained retrospectively after review of the automated and computerized anesthesia records and medical charts. The primary outcome was the volume of blood loss during the procedures. This was defined by the volume of blood loss determined by suctioning and gauze absorption during surgery.

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by cuff on the arm opposite the surgical site every 5 min. Mean blood pressure (MBP) was calculated using the following equation: MBP = (pulse pressure)/3 + DBP. The six measurement points were defined as follows: on admission to the operation room = T0 as the baseline measurement, immediately after skin incision = T1, 10 min = T2, 30 min = T3, and 60 min into the surgery = T4, and after surgery had finished = T5. The mean SBP and MBP were the average of these five time points (T1–T5). Heart rate was evaluated at T0, T1, T3, T4, and T5. The heart rate at T2 was not suitable for evaluation, due to fluctuations following the skin incision.

Anesthesia time and operative time were defined as the time from the administration of the induction drug to discharge from the operating room, and from the skin incision to skin closure, respectively. None of the enrolled patients was administered colloid or a blood transfusion.

We analyzed the use of intraoperative drugs, other than atropine and neostigmine, which were used as reversal drugs for the muscle relaxant. The rate of remifentanil was calculated as microgram per kilogram per minute by dividing the amount of remifentanil administered by the total time during which it was administered.

Statistical analysis

Continuous variables with normal and skewed distribution were expressed as mean ± SD and median [25%, 75%], and categorical variables were expressed as number (%).

We analyzed data for partial mastectomy and quadrantectomy separately. Continuous variables were analyzed using Student's t test for normal distribution or the Mann–Whitney U test for skewed distribution as appropriate. Categorical variables were analyzed using Fisher exact test. The relations between the mean SBP and MBP, and blood loss were plotted and examined using a univariate linear regression model, stratified by the remifentanil and non-remifentanil groups.

Univariate and multivariate linear regression models were used to identify the factors influencing blood loss during mastectomies. The factors included were as follows: vasopressor use such as ephedrine, phenylephrine, and atropine; age; diclofenac suppository; and remifentanil use. We presumed that hemodynamic stability contributed to decreasing blood loss. Thus, we included the drug, ephedrine, phenylephrine, and atropine. A previous report demonstrated that age and non-steroidal anti-inflammatory drug were potential factors for increased blood loss (Winther Lietzen et al. 2012; Ong et al. 2007). All of the above factors were entered into a multivariate linear regression model.

All analyses were performed using R 3.3.1 (The R Foundation for Statistical Computing, Vienna, Austria) and EZR 1.3.2 (Saitama Medical Center, Jichi Medical University, Saitama, Japan) (Kanda 2013).

Results

Patient criteria, operative time, and hemodynamic parameters

There were no differences between the remifentanil and non-remifentanil groups in terms of age, body weight, height, body mass index, and American Society of Anesthesiologists physical status in patients undergoing either partial mastectomy or quadrantectomy (Table 1).

Operative time in the remifentanil group was shorter than that in the non-remifentanil group in each mastectomy (partial mastectomy, remifentanil group, 138 [115, 162] min vs. non-remifentanil group, 167 [139, 190], $P < 0.001$; quadrantectomy 138 [115, 162] min vs. non-remifentanil group, 179 [150, 211], $P = 0.056$; Table 2).

SBP and DBP were significantly lower, and heart rate was significantly slower in the remifentanil group than in the non-remifentanil group at all time points (T1–5) except baseline in patients undergoing partial mastectomy and quadrantectomy (see Additional files 1 and 2).

Intraoperative drug use in partial mastectomy

Anesthesiologists administered a lower amount of crystalloid infusion in the remifentanil group than in the non-remifentanil group, significantly. Some patients in the non-remifentanil group required an additional operation due to postoperative bleeding; however, this was not statistically different as compared to the remifentanil group. For intraoperative drug use, anesthesiologists administered ephedrine, atropine, and flurbiprofen axetil more frequently in the remifentanil group than in the non-remifentanil group, significantly. There was no difference in phenylephrine, fentanyl, pentazocine, and diclofenac

Table 1 Baseline characteristics of patients undergoing partial mastectomy

	Partial mastectomy				Quadrantectomy			
	Total	Remifentanil	Non-remifentanil	*P* value	Total	Remifentanil	Non-remifentanil	*P* value
	n = 231	*n* = 98	*n* = 133		*n* = 212	*n* = 56	*n* = 156	
Age, years	51 ± 12	51 ± 5	53 ± 7	0.43	52 ± 11	51 ± 11	52 ± 12	0.36
Body weight, kg	55 [50, 62]	55 [50, 60]	55 [50, 63]	0.51	55 [50, 62]	55 [50, 62]	56 [51, 61]	0.85
Height, cm	157 ± 6	157 ± 5	157 ± 7	0.85	156 ± 6	157 ± 7	156 ± 6	0.35
BMI, kg/m^2	22.4 [20.3, 25.0]	22.4 [20.0, 25.4]	22.3 [20.4, 24.7]	0.72	22.4 [20.3, 25.0]	22.4 [20.3, 25.0]	22.7 [20.7, 25.3]	0.43
ASA-PS 1, *n* (%)	108/231 (47)	45/98 (46)	63/133 (47)	0.93	85/212 (40)	24/56 (43)	61/156 (39)	0.74

BMI body mass index, *ASA-PS* American Society of Anesthesiologists physical status
Continuous variables with normal distribution and with skewed distribution were expressed as mean ± SD and median [25%, 75%]. Categorical variable (ASA-PS) was expressed as number (%). Continuous variables were analyzed using Student's *t* test or the Mann–Whitney *U* test along with the distribution of each variable as appropriate. Categorical variables were analyzed using Fisher exact test. Apart from ASA-PS 1, it was ASA-PS 2

suppository use between the two groups. Nitrous oxide–oxygen–sevoflurane was used more in the remifentanil group, and oxygen–sevoflurane was used more in the non-remifentanil group, significantly (Table 2).

Blood loss in partial mastectomy

Blood loss was significantly lower in the remifentanil group than in the non-remifentanil group (60 ml vs. 90 ml; $P < 0.001$; Fig. 2).

Relation between blood pressure and blood loss in partial mastectomy

The univariate linear regression model showed a positive correlation between the mean SBP and the amount of blood loss in the non-remifentanil group (slope 1.45, intercept −45.13, $P = 0.024$; Fig. 3a). In contrast, the correlation was not significant in the remifentanil group.

There was no correlation between the mean MBP and blood loss in either of the two groups.

Table 2 Operative profile of mastectomies

	Partial mastectomy			Quadrantectomy		
	Remifentanil	Non-remifentanil	*P* value	Remifentanil	Non-remifentanil	*P* value
	n = 98	*n* = 133		*n* = 56	*n* = 156	
Blood loss, ml	60 [30, 94]	90 [50, 165]	< 0.001	90 [30,163]	140 [74, 220]	0.001
Mean SBP, mmHg	98 ± 11	115 ± 14	< 0.001	100 ± 11	115 ± 14	
Mean MBP, mmHg	74 ± 9	86 ± 11	< 0.001	74 ± 9	86 ± 11	< 0.001
Mean HR, bpm	71 ± 12	79 ± 12	< 0.001	71 ± 11	80 ± 13	< 0.001
Anesthesia time, min	188 ± 38	206 ± 43	< 0.001	220 ± 47	238 ± 42	0.006
Operative time, min	138 [115, 163]	147 [126, 182]	< 0.001	167 [139, 190]	179 [150, 211]	0.056
Infusion volume, ml	1300 [962, 1500]	1500 [1200, 1800]	< 0.001	1500 [1088, 1863]	177 [1300, 2000]	0.031
Re-operation for bleeding, *n* (%)	0/98 (0)	1/133 (0.8)	1	0/56 (0)	1/ 156 (0.6)	1
Intraoperative drug using, *n* (%)						
Ephedrine	40/98 (41)	22/133 (17)	< 0.001	17/56 (30)	21/156 (13.5)	0.008
Phenylephrine	1/98 (1.0)	0/133 (0)	0.42	0/56 (0)	1/156 (0.6)	1
Atropine	41/98 (42)	11/133 (8.3)	< 0.001	21/56 (38)	34/156 (22)	0.032
Fentanyl	1/98 (1.0)	2/133 (1.5)	1	2/56 (3.6)	2/156 (1.3)	0.29
Pentazocine	0/98 (0)	4/133 (3.0)	0.14	0/56 (0)	2/156 (1.3)	1
Flurbiprofen axetil	59/98 (60)	52/133 (39)	0.002	38/56 (68)	42/156 (27)	< 0.001
Diclofenac suppository	5/98 (5.1)	7/133 (5.3)	1	4/56 (7.1)	30/156 (19)	0.035
Remifentanil infusion speed, mcg/kg/min	0.16 [0.11, 0.25]			0.21 [0.13, 0.29]		
Inhaled anesthetics						
Nitrous oxide–oxygen–sevoflurane*	3/98 (3.1)	107/133 (80)	< 0.001	1/56 (1.8)	138/156 (89)	< 0.001

SBP intraoperative systolic blood pressure; *MBP* intraoperative mean blood pressure; *HR* intraoperative heart rate
Continuous variables with normal distribution and with skewed distribution were expressed as mean ± SD and median [25%, 75%]. Categorical variable (ASA-PS) was expressed as number (%). Continuous variables were analyzed using Student's *t* test or the Mann–Whitney *U* test as long as appropriate. Categorical variables were analyzed using Fisher exact test
*One inhaled anesthetic other than nitrous oxide–oxygen–sevoflurane was oxygen–sevoflurane

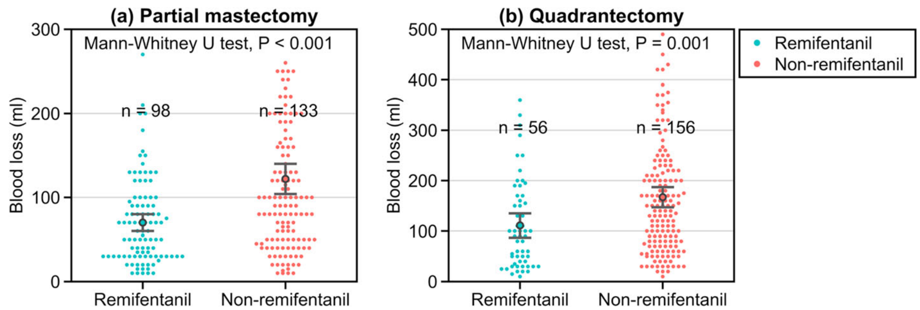

Fig. 2 Blood loss in mastectomies. Two types of mastectomies—partial mastectomy (**a**) and quadrantectomy (**b**)—were associated with a significant reduction in blood loss (partial mastectomy: 60 ml vs. 90 ml, $P < 0.001$; quadrantectomy: 90 ml vs. 140 ml, $P = 0.001$, Mann–Whitney *U* test). Error bar represents mean ± 95%CI

Linear regression analysis for blood loss in partial mastectomy

The univariate linear regression model demonstrated that operative time and atropine and remifentanil use were the determinants for blood loss (Table 3). The multivariate linear regression model found two major factors that influenced blood loss. These were operative time and remifentanil use (coefficient − 38.74, $P = 0.002$; Table 3).

Intraoperative drug use in quadrantectomy

The remifentanil group also had a shorter operative time; however, this was not statistically significant. Anesthesiologists administered less crystalloid infusion in the remifentanil group than in the non-remifentanil group, significantly. Some patients in the non-remifentanil group required an additional operation due to postoperative bleeding; however, this factor was not statistically significantly different between the two

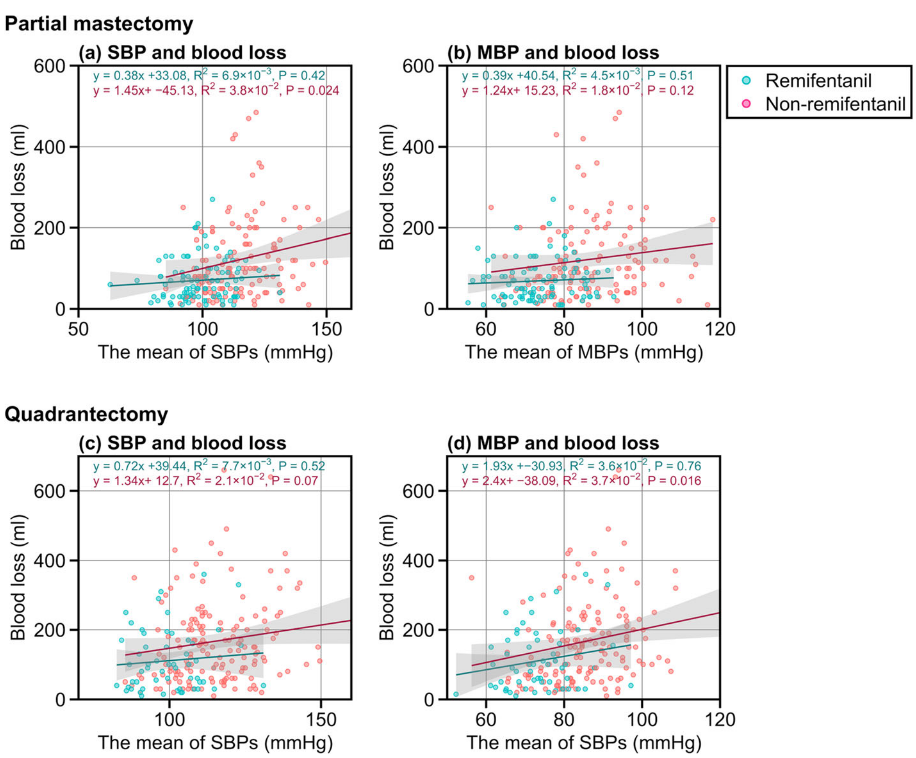

Fig. 3 Linear regression of blood pressure to blood loss in mastectomies. MBP mean blood pressure, SBP systolic blood pressure. **a** In partial mastectomy, systolic blood pressure (SBP) was positively correlated with blood loss in the non-remifentanil group. **b** Mean blood pressure (MBP) was not correlated with blood loss. **c** In quadrantectomy, SBP tended to be positively correlated with blood loss in the non-remifentanil group. **d** MBP was positively correlated with blood loss in the non-remifentanil group

Table 3 Univariate and multivariate linear regression analyses to identify the factors associated with blood loss during partial mastectomy

	Univariate			Multivariate		
Factor	Coefficient	Standard error	*P* value	Coefficient	Standard error	*P* value
Age, years	0.11	0.59	0.86	0.24	0.54	0.65
Operative time	1.11	0.14	< 0.001	1.03	0.14	< 0.001
Ephedrine use	− 9.41	13.34	0.48	7.84	12.53	0.53
Phenylephrine use	− 80.3	89.97	0.37	− 65.08	79.56	0.41
Atropine use	− 27.85	14.05	0.049	2.8	13.63	0.84
Diclofenac suppository use	− 11.55	26.65	0.67	− 15.53	24.01	0.52
Flurbiprofen axetil use	− 2.07	11.84	0.86	3.07	10.96	0.78
Remifentanil use	− 51.57	11.48	< 0.001	− 38.74	12.26	0.002
				$n = 231$		
				R^2/adj. R^2 = 0.269/0.243		
				$P < 0.001$		

R^2/adj. R^2 determination coefficient/adjusted determination coefficient

groups. In terms of intraoperative drug use, anesthesiologists administered ephedrine, atropine, flurbiprofen axetil, and diclofenac suppository more frequently in the remifentanil group than in the non-remifentanil group, significantly. There was no difference in phenylephrine, fentanyl, or pentazocine use between the two groups. Nitrous oxide −oxygen–sevoflurane was used more in the remifentanil group, and oxygen–sevoflurane was used more in the non-remifentanil group, significantly (Table 2).

Blood loss in quadrantectomy

Blood loss was significantly lower in the remifentanil group than in the non-remifentanil group (90 ml vs. 140 ml; $P = 0.001$; Fig. 2).

Relation between blood pressure and blood loss in quadrantectomy

The univariate linear regression model demonstrated a trend for a positive correlation between the mean SBP and the amount of blood loss in the non-remifentanil group (slope 1.34, intercept 12.7, adjusted $R^2 = 0.021$, $P = 0.07$; Fig. 3c). However, this correlation was not statistically significant. There was no significant correlation between SBP and blood loss in the remifentanil group. There was a positive correlation between the mean MBP and the amount of blood loss in the non-remifentanil group (slope 2.4, intercept − 38.09, $P = 0.016$; Fig. 3d). There was no significant correlation of MBP with the amount of blood loss in the remifentanil group.

Linear regression analysis for blood loss in quadrantectomy

The univariate linear regression model demonstrated that operative time and atropine and remifentanil use were the determinants for blood loss (Table 4). The multilinear regression model found two major factors influencing blood loss. These were operative time and remifentanil use (coefficient − 39.12, $P = 0.048$; Table 4).

Discussion

This study investigated the effect of remifentanil on blood loss in ESM and yielded two major findings. First, patients who received remifentanil for both partial mastectomy and quadrantectomy by means of ESM suffered less blood loss; this effect of remifentanil on reducing blood loss via ESM has not been reported previously. Second, the remifentanil group had lower blood pressure at five intraoperative measurement points.

Remifentanil use has been reported to be associated with lower blood loss in spinal surgery and rhinoplasty (Kawano et al. 2013; Kosucu et al. 2014). However, there have been no reports on the effect of remifentanil in any other type of endoscopic surgery with the exception of otolaryngology endoscopic surgery. To investigate the effect of remifentanil on blood loss during ESM, we examined patients undergoing two types of ESM: partial mastectomy and quadrantectomy. Both patients who underwent partial mastectomy and those who underwent quadrantectomy in the remifentanil group had lower volumes of blood loss than those in the non-remifentanil group (Fig. 2). These operations were associated with different amounts of lacteal gland resection. However, we have shown that there were lower levels of blood loss associated with both procedures in patients allocated to the remifentanil group regardless of the resection size.

Previous studies have shown that blood loss during mastectomy was associated with the size of resection (Yamaguchi et al. 2008; Lai et al. 2016). Therefore, in

Table 4 Univariate and multivariate linear regression analyses to identify the factors associated with blood loss during quadrantectomy

Factor	Univariate			Multivariate		
	Coefficient	Standard error	*P* value	Coefficient	Standard error	*P* value
Age, years	− 0.96	9.74	0.2	− 0.33	0.71	0.65
Operative time	1.18	0.18	< 0.001	1.08	0.18	< 0.001
Ephedrine use	− 22.33	21.9	0.31	− 7.4	20.79	0.72
Phenylephrine use	− 82.66	122.77	0.5	− 77.67	113.72	0.5
Atropine use	− 39.28	19.02	0.04	− 15.21	18.36	0.41
Diclofenac suppository use	5.7	22.95	0.8	− 7.08	22.27	0.75
Flurbiprofen axetil use	− 13.79	17.35	0.43	− 0.25	18.18	0.99
Remifentanil use	− 56.11	18.7	0.003	− 39.12	19.68	0.048
				$n = 212$		
				R^2/adj. $R^2 = 0.199/0.167$		
				$P < 0.001$		

R^2/adj. R^2 determination coefficient/adjusted determination coefficient

order to address this matter, the present study analyzed both partial mastectomy and quadrantectomy, separately. Factors previously shown to influence blood loss in mastectomy have included the size of resection, age > 80 years, steroid use, and congestive heart failure (Winther Lietzen et al. 2012; Nwaogu et al. 2015). In high-risk patients, the appropriate methods should be chosen in order to reduce blood loss. These include local injection of adrenaline (Chelliah 2003), use of a harmonic scalpel (Deo et al. 2002), and deliberate hypotensive anesthesia (Moersch et al. 1960). A local injection of adrenaline does not cover the whole surgical field if the resection area is large, and it is unable to reach deep surgical sites. Additionally, the harmonic scalpel is limited to facilities that approve its use. Furthermore, a harmonic scalpel is not readily available worldwide. Unlike adrenaline administration and the use of a harmonic scalpel, remifentanil is performed not by an operator, but by an anesthesiologist, and the effects of remifentanil are well known. The reduction in blood loss associated with remifentanil use in the present study was found to be independent of the techniques used by the anesthesiologists and surgeons.

The reduced amount of bleeding associated with remifentanil use may be related to hemodynamic stabilization during the operation. Remifentanil use was associated with significantly lower blood loss and lower intraoperative SBP than observed in the non-remifentanil group. Linear regression analysis of intraoperative SBP and bleeding volume revealed a significant positive correlation in the non-remifentanil group, but no correlation was found in the remifentanil group. There was no significant positive correlation between MBP and bleeding volume in either group. Based on these findings, the increase in blood loss proportional to the SBP may have contributed to the increase in intraoperative blood loss in the non-remifentanil group.

Injury to the vascular supply evokes bleeding when the surgeon detaches the lacteal gland from the greater pectoral muscle during ESM. The internal and lateral thoracic arteries and posterior intercostal arteries from the arterial plexus provide blood to the lacteal gland (Cunningham 1977). It is conceivable that the blood flow to this area was increased in the non-remifentanil group and that insufficient analgesia raised the blood pressure. In contrast, a low perfusion pressure and low cardiac output were thought to be the reasons for the decreased blood loss in the remifentanil group. Retaining reactive hypertension should result in a lower perfusion pressure. This should secure the endoscopic field of vision, even during bleeding, because at a low perfusion pressure, the force of the bleeding is much lower. Remifentanil also decreases the heart rate, and consequently cardiac output, by blockade of the sympathetic nerves. At a certain threshold, a lower cardiac output leads to lower amounts of blood in the plexus. Thus, despite the occurrence of bleeding, there should be less blood loss per unit of time (Degoute et al. 2001; Ha et al. 2014; Koshika et al. 2011; Kemmochi et al. 2009; Nishizawa et al. 2012). In the linear regression model of SBP to blood loss, there seemed to be a threshold for blood pressure (100 mmHg) beyond which blood loss increased. Exceeding this limit may be associated with an increase in blood loss. In this study, the anesthesiologists were not aware of the effect of remifentanil on blood loss. If remifentanil alone is administered, the threshold of 100 mmHg would not be exceeded and bleeding may be kept stable.

Limitations

The present study has a few limitations. Firstly, a shorter operative time in the remifentanil group may have contributed to decreased blood loss. Secondly, a cuff method, rather than invasive monitoring, was used to measure blood pressure. Thirdly, suction and absorption of blood on the gauze were used to quantify the volume of blood lost. The gauze may have dried before the volume was measured, increasing the error of this method. However, most of the lost blood was measured by using a suction bottle clinically. Fourthly, preoperative chemotherapy and steroid use in some patients could have affected blood loss, as patients on steroids tend to bleed more (Lai et al. 2016). We could not address the information on preoperative chemotherapy and steroid use. Lastly, the rate at which remifentanil was administered was controlled by the anesthesiologists in order to obtain appropriate anesthesia levels. Each anesthesiologist had an ideal target blood pressure for each patient. Therefore, there may have been differences in the rate of remifentanil administration among anesthesiologists.

Conclusions

Remifentanil was associated with lower volumes of blood loss during ESM. The potent analgesic effect should contribute to controlling intraoperative reactive hypertension. Therefore, remifentanil should be considered as an agent that offers a protective effect against blood loss in body surface endoscopic surgeries, including ESM.

Additional files

Additional file 1: Table S1. Hemodynamics in the operating room (DOCX 18 kb)

Additional file 2: Figure S1. Time course of blood pressure. (a, b) In partial mastectomy, the remifentanil group had lower systolic blood pressure (SBP) (a) and mean blood pressure (MBP) (b) than the non-remifentanil group at all five intraoperative measurements. (c, d) In quadrantectomy, the remifentanil group had lower SBP (c) and MBP (d) at all five intraoperative measurements. $^{**}P < 0.001$, $^{***}P < 0.001$ between the two groups, Student's *t* test. (PNG 147 kb)

Abbreviations

BMI: Body mass index; DBP: Diastolic blood pressure; ESM: Endoscopic subcutaneous mastectomy; MBP: Mean blood pressure; SBP: Systolic blood pressure

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Availability of data and materials

The dataset generated and/or analyzed during the current study is not publicly available due to ethical issues.

Authors' contributions

SY created the idea of this study. SY corrected the data and wrote the manuscript. KN, OK, and YT deeply discussed the concept of this study. KS supervised the analyzing of the data. MS supervised the writing of this manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the local ethical committee at Kameda Medical Center. The informed consent was waived, because of the nature of the study.

Consent for publication

The local ethical committee approved the publication of data from this study. The documented informed consent was waived.

Competing interests

The authors declare that they have no competing interests.

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