Original Article

Efficacy of epidural anesthesia in minimally invasive cardiac surgery

ABSTRACT

Introduction: The most commonly performed minimally invasive cardiac surgery (MICS) is lateral minithoracotomy, which requires one of the most painful incisions. Adequate postoperative pain management is essential for cardiac surgery to prevent perioperative complications. Thoracic epidural analgesia (TEA) is the gold standard for thoracotomy; however, it is still controversial because of the risk of epidural hematoma following systematic heparinization. The objective of our study was to investigate the safety and efficacy of TEA following MICS.

Methods: The clinical data of patients aged over 18 years who underwent elective MICS and received epidural analgesia along with general anesthesia between January 2014 and March 2019 were reviewed. Data were collected, including patient demographics, operative data, postoperative pain, postoperative course, and complications. Chronic pain was evaluated 6 months after discharge, and we defined it as a NRS score ≧3. Postoperative complications included epidural-related complications.

Results: Seventy patients were included in the analysis. The mean NRS score was below 2. We collected chronic pain data from 52 patients and found that 11 patients had chronic pain. TEA-related complications were not observed.

Conclusion: The current observational study revealed that TEA following lateral thoracotomy was effective for acute pain as well as chronic pain without causing any severe epidural-related complications. Protocols to prevent potential devastating complications, including epidural hematoma, should follow the American Society of Regional Anesthesia and Pain Medicine recommendation. If the rules are strictly followed, TEA can be a safe and effective pain management method for patients who undergo MICS.

Key words: Epidural analgesia, minimally invasive cardiac surgery, postoperative pain

Introduction

Lateral minithoracotomy is the most commonly performed minimally invasive cardiac surgery (MICS). Lateral thoracotomy requires one of the most painful incisions and involves the ribs, multiple thoracic muscle layers, costovertebral joints, and potential lesions to intercostal nerves. In addition, patients undergoing MICS tend to be younger than patients undergoing median sternotomy, and younger patients are known to have a lower pain threshold than older patients.[1] Therefore, it is being said that the management

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of postoperative pain following thoracotomy is more challenging than median sternotomy for both patients and anesthesiologists.[2]

Adequate postoperative pain management is essential for cardiac surgery because it provides patient comfort and reduces undesirable complications, such as cardiovascular, pulmonary, and sympathetic responses.[3] Patients with insufficient acute pain control and of a younger age have been found to have a high risk of chronic post-thoracotomy pain syndrome (CPSP).[4,5] To provide adequate pain control after MICS, a wide variety of analgesia techniques have been investigated; however, the most suitable technique has not been established.

Thoracic epidural analgesia (TEA) is the gold standard for thoracotomy. It has been shown to provide significant pain control and improved clinical outcomes after cardiac surgery, such as a reduction in the incidence of new onset atrial fibrillation (NOAF), a significant improvement in postoperative pulmonary function, a shorter time to extubation, and a lower rate of pulmonary complications.[6,7] Given that epidural analgesia is effective for pain control after cardiac surgery, it is still unknown whether there is a concern that it may increase the risk of epidural hematoma following systematic heparinization for cardiopulmonary bypass.[7] According to the American Society of Regional Anesthesia and Pain Medicine (ASRA), some special precautions should be taken to minimize the risk of epidural hematoma if an epidural block is performed in cardiac patients,[8] which requires a delay of surgery of 24 hours in the event of a traumatic tap, a delay of 60 minutes after heparinization for catheter insertion, and tight perioperative control of anticoagulation.[9]

The objective of our study was to investigate the safety and efficacy of TEA in reducing postoperative pain and complications following MICS.

Method

This was a single-center, retrospective observational study that was conducted at Osaka Police Hospital, Osaka, Japan. We evaluated NRS scores and nonsteroidal anti-inflammatory agent (NSAID) consumption as well as the incidence of postoperative complications, including those associated with epidural analgesia.

This study was approved by the local ethical committee (approval number: 850). The clinical data of patients aged over 18 years who underwent lateral thoracotomy as an elective MICS and received epidural analgesia along with general anesthesia between January 2014 and March 2019 were reviewed. The exclusion criteria included conversion to median sternotomy, reoperation within 24 hours, and requiring extracorporeal membrane oxygenation or intra-aortic balloon counterpulsation after operations. Data were collected, including patient demographics such as age, sex, body mass index (BMI), medical history (including hypertension, diabetes mellitus, chronic obstructive pulmonary disease, atrial fibrillation, smoking history), ejection fraction and respiratory function test, operative data, postoperative pain, postoperative course, and complications.

After confirming normal coagulation status, a TEA catheter was placed at the thoracic region between the fourth and sixth interspaces 1 day before the surgery. The loss of resistance technique was used to guide a 17-gauge Tuohy needle. After reaching the epidural space, 3 ml of 1% lidocaine was administered to exclude intravascular or intrathecal positioning. If the patient underwent heparinization, the heparin infusion was discontinued at least 4 hours before the procedure and restarted a minimum of 2 hours after catheter insertion. On the day of the procedure, anesthesia was induced with propofol or midazolam along with rocuronium and the patients were intubated orally with a double-lumen tube (Shiley™ Endobronchial tube, Covidien Japan, Tokyo, Japan) for one-lung ventilation. A pulmonary artery catheter and central venous catheter were inserted via the right or left internal jugular vein. Other monitoring included continuous arterial, central venous, pulmonary artery pressure, pulse oximetry, five-lead electrocardiograph, rectal and pharyngeal temperature, end-tidal carbon dioxide concentration, and transesophageal echocardiography. Anesthesia was maintained with sevoflurane and continuous infusion of propofol, remifentanil, and fentanyl, which were manipulated according to clinical status and procedural requirement. The dose of intraoperative epidural analgesia was decided by the treating anesthesiologists. Sivelestat sodium hydrate (12 mg/h) was administered to all patients to prevent re-expansion pulmonary edema. For the initiation of cardiopulmonary bypass (CPB), 300 units/kg unfractionated heparin was administered to achieve an activated coagulation time (ACT) of more than 450 s. For off-pump cardiac surgery, an initial dose of 150 units/kg heparin was administered, aiming for a minimal ACT >300 s. The heparin was reversed with protamine 1.5 mg/kg for off-pump cases and 3 mg/kg for CPB cases. All patients were reintubated with a single-lumen tube after the completion of surgery and transferred to the intensive care unit under continuous infusion with propofol. A patient control analgesia infusion system was used to continuously infuse 2 or 3 ml/h of 0.125 to 0.25% levobupivacaine postoperatively. A 3 or 4 ml bolus was

used on demand, and the lock-out time was 20 minutes. Fentanyl was added to levobupivacaine at the treating anesthesiologists' discretion. The position of the catheter was confirmed by postoperative X-rays. The catheter was removed by cardiac surgeons based on the coagulation status. Abnormal coagulation status was defined as a prothrombin time international normalized ratio (PT-INR) >1.5, an activated partial thromboplastin time (APTT) >50 seconds, and a platelet count <100,000/μl.

The NRS score was obtained every 6 hours until catheter removal. The NRS is an 11-point scale to measure pain intensity, ranging from 0 (no pain) to 10 (worst imaginable pain). An NRS score of 0–2 was assessed as "mild pain", 3–5 as "moderate", and more than 6 as "severe pain".[10] As rescue analgesia drugs, loxoprofen sodium or acetaminophen was available, and the number of doses per day was measured while TEA was applied. Chronic pain was evaluated 6 months after discharge, and we defined it as an NRS score ≧3.[11]

The postoperative complications included pulmonary complications, a new onset of atrial fibrillation, myocardial infarction, and epidural-related complications. Pulmonary complications were defined as reintubation, tracheotomy, pneumonia, pulmonary edema, and serious atelectasis. Pneumonia was defined as the presence of clinical symptoms requiring antibiotic treatment. Pulmonary edema included re-expansion pulmonary edema. Serious atelectasis was defined as requiring bronchoscopy treatment. Atrial fibrillation was defined as requiring treatment with antiarrhythmic medication with or without electrical cardioversion during TEA. Myocardial infarction was defined as the need for percutaneous coronary intervention. Epidural-related complications were defined as epidural hematoma, epidural abscess, retained fragment of epidural catheter, and inferior limb neurologic symptoms.

Data are summarized as the mean ± standard deviation (SD), medians with interquartile ranges for continuous variables, and counts with percentages for categorical variables.

Result

Seventy patients were included in the analysis. The baseline characteristics are shown in Table 1. The mean age of the patients was 64 ± 10 years. There were 19 patients who were previously diagnosed with atrial fibrillation (27.5%). Three patients (4.2%) had a history of COPD, and 17 patients (24.3%) had a history of smoking, whereas none of them showed any abnormal respiratory function.

The intraoperative data are summarized in Table 2. Of the 70 patients, 59 (84%) required cardiopulmonary bypass for the procedure, and 11 (16%) required off-pump CABG. Remifentanil and fentanyl were administered for all of the patients, and 12 patients received morphine via the TEA catheter.

Figure 1 illustrates the evaluation of postoperative pain. A TEA catheter indwelled for 3.3 ± 1.0 days. The mean NRS score was below 2 at any point after extubation. The mean number of rescue analgesia drugs from extubation to removal of TEA was 0.8 ± 1.2 times in a day. We collected chronic pain data from 52 patients 6 months after discharge. Eleven of 52 patients (21%) reported an NRS score ≧3 at 6 months after discharge.

Postoperative data are displayed in Table 3. Seventeen (24%) patients developed postoperative complications. Fifty-one (22%) patients who were not previously diagnosed with AF developed new-onset AF. When classified by the

Table 1: Patient characteristics (*n*=70)

Demographics	
Age (years)	64±10
Sex (male)	43 (61%)
Body mass index, kg/m^2	23.3±4.0
Comorbidities	
Hypertension	40 (57.1)
Diabetes mellitus	9 (12.8)
COPD	3 (4.2)
Atrial fibrillation	19 (27.5)
Smoking history	17 (24.3)
Preoperative examination	
LV ejection fraction (%)	65.2±10.8
FVC (L)	3.0±0.6
FEV1.0 (L)	2.2±0.5

The values are presented as the mean ± SD or number of patients (%). COPD = chronic obstructive pulmonary disease; LVEF = left-ventricular ejection fraction; FVC = forced vital capacity; FEV1.0 = forced expiratory volume 1.0 (sec)

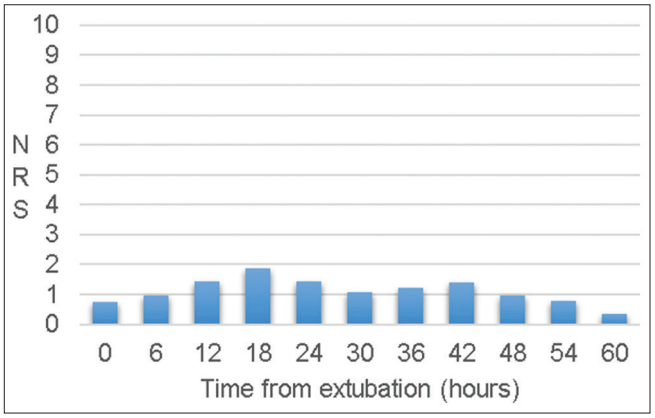

Figure 1: NRS score from 0 to 60 hours after extubation. The vertical axis shows the mean NRS score of all patients, and the horizontal axis shows the time from extubation

Table 2: Intraoperative data

Operative procedure	
MVP	36 (51)
AVR	10 (14)
ASD or PFO closure	7 (10)
LA tumor resection	6 (9)
Off-pump CABG	11 (16)
Narcotic drug consumption	
Remifentanil (mg)	1.29±1.19
Fentanyl (μg)	612±248
Morphine (mg)	0.38±0.89
Surgery time, min	375±98

The values are presented as the mean ± SD or number of patients (%).
MVP = mitral valve plasty; AVR = aortic valve replacement; ASD = atrial septum defect; PFO = patent foramen ovale; CABG = coronary artery bypass grafting; LA = left atrium

Table 3: Postoperative data

Postoperative course	
Mechanical ventilation time (hour)	18.1±16.4
Epidural catheter removal (day)	3.3±1.0
Ambulation (POD)	1.9±1.1
Length of hospital stay (POD)	21.7±20.5
Postoperative complications	
Pulmonary complication	6 (8.5)
New onset of atrial fibrillation	11 (21.5)
Myocardial infarction	0 (0)
Epidural related complications	0 (0)

The values are presented as the mean ± SD or number of patients (%).
POD = Postoperative day

surgical technique, the percentage of new-onset AF was 38% (8/21) in patients who underwent MVP, 50% (4/8) in patients with AVR, 50% (3/6) in patients who underwent tumor resection, 42% (3/7) in patients who underwent ASD or PFO closure, and 0% (0/9) in those who underwent off-pump CABG. In spite of robust department protocols with coagulation status, there were violations related to catheter removal. Abnormal coagulation status was detected in 16 patients (22.8%), and 67 patients (95.7%) took aspirin on the morning of catheter removal; however, TEA-related complications, including epidural hematoma or abscess, were not observed.

Discussion

The current observational study revealed that TEA following lateral thoracotomy was effective for acute pain as well as chronic pain without causing any severe epidural-related complications. We did not find a reduced incidence of NOAF or any respiratory complication.

Introducing minimally invasive surgery was revolutionary for the medical field. Since Cosgrove attempted the first minimally invasive valve operation[12] in 1996, the demand has increased; the technique has been applied in approximately 50% of isolated mitral cases in Germany and in approximately 25% in U.S.A.[13]

Patients who underwent MICS were initially believed to have less pain; however, it gradually became evident that lateral thoracotomy causes more pain than median sternotomy and that poor pain control causes undesirable outcomes such as pulmonary complications, NOAF or chronic pain, which significantly impair patients' quality of life.[14-16] Numerous studies on intravenous analgesia, nerve block techniques, and TEA have been performed to identify the most adequate pain management strategy that causes the fewest complications associated with MICS procedures.

TEA plays an important role in analgesic management following MICS procedures. An observational study to determine the impact of TEA on MICS patients revealed that TEA provided a superior analgesic effect and contributed to a dramatic reduction in the incidences of perioperative respiratory complications and mortality.[17,18] A recent RCT of patients who underwent robotic coronary artery bypass with a lateral thoracotomy indicated that the comparison group that received intrathecal saline showed severe postoperative pain with a median pain score of 8 (VAS) at rest. Another study showed that patients who underwent lateral thoracotomy as an MICS suffered more pain for the first 2 postoperative days than the conventional approach group.[19] It has been said that insufficient pain control in the acute stage is related to the incidence of chronic pain, which affects 10–50% of individuals after common operations.[20] A recent RCT that evaluated the efficacies of thoracic paravertebral block (TPVB) and intrathoracic intercostal nerve block (INB) or video-assisted thoracoscopic surgery (VATS) revealed that a significant number of patients suffered chronic pain after surgery. Fifty-eight percent of patients in the TPVB group, 46% of patients in the INB group, and 76% in the control group suffered chronic pain 3 months after the surgery. Furthermore, 56% of all patients still suffered chronic pain 6 months after the surgery, and among them, 44% reported moderate and severe pain.[21] Another observational study that investigated the incidence of chronic pain after VATS with intravenous pain control reported that 25% of patients expressed mild pain.[22] Chronic pain may also impact individual quality of life, employment, and mental health[23]; therefore, early intervention is the key to preventing the transition to chronic pain, which subsequently conveys significant health and economic benefits. In the current study, the NRS score remained under 2 at any time point after extubation, and only 21% of the patients had chronic pain, which indicated that TEA was effective for providing

sufficient acute pain control after a lateral thoracotomy and consequently preventing persistent pain.

Postoperative atrial fibrillation (POAF) is the most common complication encountered after cardiac surgery, and incidents reportedly vary depending on the type of surgery, definition, and methods of detection. The etiology of POAF is not accurately elucidated; however, various risk factors have been determined, including age, hypertension, and a history of AF, COPD, or vascular heart disease.[24] Potential advantages of TEA have been suggested, including sympathicolysis with subsequent improvement of coronary perfusion, a decreased heart rate, and decreased endogenous stress response.[25] According to a Cochrane review that evaluated the efficacy of TEA for adult patients undergoing cardiac surgery, TEA helped to reduce the incidence of POAF.[26] In the current study, the incidence of new-onset POAF was 22%, which was comparable with previous reports.[27] They reported that the incidence of POAF was 26% in MICS-AVR and 22% in MICS-MVP.

In the current study, no TEA-related epidural hematoma was observed. TEA for cardiac surgery is controversial due to a theoretical increased risk of epidural hematoma associated with systematic heparinization, which consequently results in neurological damage, including paraplegia. Epidural hematoma is caused by repetitive punctures, bloody taps, abnormal anticoagulation status, or excessive antiplatelet drug administration during catheter positioning or removal. Based on the fact that TEA may contribute to an increased risk of hematoma and according to the ASRA guidelines, certain precautions should be taken to minimize the risk of hematoma: 1) Surgery should be delayed for 24 hours in the event of a traumatic tap. 2) The time from instrumentation to systematic heparinization should exceed 60 minutes.[8] Despite these concerns, a previous systematic review of 88,820 cardiac cases found only 25 cases of epidural hematoma, with an estimated risk of catheter-related epidural hematoma of 3 per 10,000 procedures. The other systematic review also reported that no epidural hematoma was found in 66 RCT trials, which involved 3320 epidural procedures.[28] Until 2004, epidural hematoma patients were not reported,[29] and only estimated mathematical modeling of an event was applied with large confidence intervals ranging from 1:1500 to 1:150,000 patients.[30] As more cases have been reported over time, the most recent risk assessment was an estimated incidence of 1:12,000 patients, which was comparable with the risk assessment for noncardiac surgery.[28] In our institution, anesthesiologists followed the ASRA guidelines when the TEA catheter was inserted on the day before surgery, and the puncture site, lower limb symptoms, and sudden back pain were assessed perioperatively. However, there were a few issues with catheter removal.

Given that CPB has been associated with epidural hematomas, a thoracic paravertebral block (TPVB) has become another choice for analgesic management in MICS patients. TPVB has become popular for controlling acute pain in thoracotomy patients.[31] When compared with TEA after MICS, a PVB was suggested to be as effective, potentially conferring less risk of neuroaxial hematoma formation based on the fact that the procedure was performed under ultrasound.[32] Despite it being a convenient technique, a TPVB has been classified by the ASRA as an intermediate- or high-risk procedure for cardiovascular patients due to the concern of bleeding[8]; therefore, a TPVB should be treated as a high-risk procedure similar to TEA, and it is recommended that catheters be placed on the day before cardiac surgery.

A few limitations should be acknowledged in our study. First, this was a retrospective observational study that was conducted in a single center; therefore, the generalizability of our results may be limited, and the NRS scores in the acute or chronic period may not have been evaluated properly as there was no comparison group. In particular, the incidence of postoperative complications may be underrated. Second, the NRS score was not taken "at rest" and "at movement" separately, which may have influenced the evaluation of pain. However, even with measuring pain under movement, all patients had NRS scores that remained under 2 in our institution, which suggested that patients had sufficient pain relief with TEA, as patients are more likely to express pain at movement than at rest. Third, the duration of TEA use was not unified and depended on the surgeon's judgment. This may have affected the evaluation of chronic pain as the period of acute pain control was not unified.

The current study indicated that TEA provided excellent postoperative analgesia in MICS patients without causing any major neurological complications. It also suggests that TEA has the potential benefit to prevent the transition to chronic pain because of its effective pain relief. Protocols to prevent potential devastating complications, including epidural hematoma, should follow the ASRA recommendation. If the rules are strictly followed, TEA can be a safe and effective pain management method for patients who undergo MICS.

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Conflicts of interest
There are no conflicts of interest.

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