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Effects of Timing of Paravertebral Block on Recovery after Robotic Mitral Valve Repair: A Retrospective Chart Review

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1. Abstract

1.1. Introduction: To evaluate the analgesic efficacy of ultrasound-guided Paravertebral Block (PVB) when administered before versus after robotic Mitral Valve Repair (MVR) surgery.

1.2. Materials and Methods: Eighty-eight ASA physical status III and IV adult inpatients underwent elective robotic MVR surgery were enrolled in this retrospective medical chart reviewed study. PVB was performed either before (Pre-, n = 43) or immediately after (Post-, n = 45) MVR surgery. Perioperative opioid dosages as oral Morphine Milligram Equivalents (MME) and VAS pain score were recorded. The recovery time such as the duration of ICU and hospital Length of Stay (LOS) were recorded.

1.3. Results: Preoperative PVB significantly decreased the intraoperative requirements for Midazolam And Opioid Analgesics (MME). A second PVB was required in 63% and 71% of the patients in the Pre- and Post-PVB groups, respectively ($p > 0.05$). The time interval from 1st to 2nd PVB was significantly prolonged in the Pre- (23.6 ± 9.0 hrs) vs. Post-PVB (19.6 ± 3.9 hrs) group ($p = 0.04$). The Pre-PVB group also required significantly less antiemetic rescue medications (35% vs. 60%) and had lower initial WBC count postoperatively. The postoperative VAS pain scores, opioid dosages, and hospital LOS were similar between two study groups.

1.4. Conclusion: These findings suggested that PVB administered either before or after robotic MVR surgery produced similar effects on postoperative analgesia and hospital LOS. However, preoperative PVB appeared to be associated with intraoperative opioid-sparing effects, reduced postoperative emesis and an anti-inflammatory effect after surgery.

2. Introduction

Robotic Mitral Valve Repair (MVR) is a minimally invasive cardiac surgery procedure for treating select patients with mitral regurgitation. Studies suggest that minimally invasive mitral valve procedure via right thoracotomy results in reduced durations of postoperative ventilation, Intensive Care Unit (ICU) and hospital Length of Stay (LOS), as well as decreased postoperative mortality when compared with patients who undergo traditional open mitral valve surgery via median sternotomy [1-4]. However, postoperative pain remains a problem even after this minimally invasive thoracotomy procedure [5-7]. Inadequate pain control after cardiac surgery can impede the recovery process [8-10] and may result in chronic postsurgical pain and opioid dependency [11,12].

Even though opioid analgesics are still considered the mainstay for perioperative pain management, frequent opioid related side effects and addiction liability has led to the development of opioid-sparing multimodal analgesic regimens [13]. Local anesthetic-based techniques like Paravertebral Block (PVB) are becoming increasingly popular for pain management after minimally invasive cardiac surgery [10,14-16]. Prospective, randomized studies have demonstrated that a preoperative PVB can provide effective

postoperative analgesia after minimally invasive coronary artery bypass surgery [10,14]. When used for robotic MVR, a preoperative PVB was found to produce intraoperative opioid-sparing effects, reduce postoperative pain score and opioid usage, as well as a reduced hospital LOS, in both retrospective [15] and prospective [16] studies.

The optimal time to perform a peripheral nerve block during the perioperative period is unclear. For example, when a preoperative adductor canal block was performed for arthroscopic knee surgery under general anesthesia [17], it produced similar postoperative pain control compared with a postoperative adductor canal block. On the other hand, preoperative Transversus Abdominis Plane (TAP) block resulted in a statistically-significant improvement in postoperative analgesia compared to postoperative TAP block in patients undergoing laparoscopic surgical procedures (i.e., laparoscopic cholecystectomy, laparoscopic hysterectomy) under general anesthesia [18]. For long robotic MVR procedure, the duration of analgesia provided with a single preoperative PVB may be inadequate [16,19,20]. Therefore, we designed this retrospective study to test the hypothesis that postoperative PVB would result in superior postoperative pain control compared to a preoperative PVB in patient undergoing robotic MVR. The secondary hypothesis was that postoperative PVB would facilitate the recovery processes with respect to the length of stay in the hospital.

3. Methods

Following institutional review board approval, including a waiver of written informed consent, a retrospective medical record review was conducted on patients aged ≥ 18 yrs old who underwent minimally invasive cardiac procedures at Cedars-Sinai Medical Center in Los Angeles, CA from 02/2019 to 05/2020. Patients who underwent robotic MVR with the da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA) assistance and received a perioperative PVB were identified and included in this retrospective study. Patients who met the study requirements were assigned to one of two treatment groups based on the timing of the PVB performed: Group 1 (PVB performed before surgery) and Group 2 (PVB performed after surgery). Patients were excluded from this study if they had a history of chronic pain, relevant allergies, alcohol or drug abuse, concomitant major procedure (such as coronary artery bypass graft, combined valve replacements), or required conversion to traditional open-heart surgery with a median sternotomy.

In the operating room, patients were monitored with standard monitoring devices, including radial arterial pressure monitor, central venous pressure monitoring via right internal jugular vein, transesophageal echocardiography, bispectral index monitor, and cerebral oximetry. General anesthesia was induced with a combination of propofol and fentanyl (or sufentanil). Rocuronium was used to facilitate tracheal intubation with one-lung ventilation. Lung isolation was achieved with either a left-sided double-lumen endotracheal tube, or endobronchial EZ-Blocker® through a single-lumen endotracheal tube. The tube position was confirmed by fiberoptic bronchoscopy. Sevoflurane, midazolam, fentanyl (or sufentanil), and rocuronium were used for maintenance of anesthesia.

All robotic MVR procedures included in this study were performed by two cardiac surgeons. The endoscope was placed in the right 4th infra-mammary intercostal space via a 12 mm access soft port. Two 12 mm instrument ports were placed above and below the access port and an atrial retractor was positioned in the 4th intercostal space at the right sternal border. Cardiopulmonary bypass was achieved by placement of a long femoral venous cannula and a femoral arterial cannula via cut down under transesophageal echocardiography guidance. Systemic hypothermia (30° C) was employed following direct ascending aorta cross-clamp. The heart was arrested by injecting 1 L of cardioplegia via the aortic root. After mitral valve repair, the patient was rewarmed, the cross-clamp removed, and weaned from cardiopulmonary bypass. At the end of surgery, a right pleural and two mediastinal chest tubes were placed. All patients were transported directly to the cardiac surgery ICU.

The standard practice at our institution was to performed a PVB either (1) after sedation with midazolam and fentanyl but prior to induction of anesthesia, or (2) immediately after surgery when the patient was hemodynamically stable and had laboratory evidence of international normalized ratio (INR) ≤ 1.4 and platelet ≥ 100 (x1000/uL). All blocks were performed by an anesthesiologist experienced in regional anesthesia. A right-sided PVB injection was administered with dynamic ultrasound guidance (SonoSite with a high-frequency linear ultrasound probe 15-6 MHz). A total of 30-40 mL of 0.25% bupivacaine with epinephrine (1:200,000) was injected through a 21G regional block needle (StimuQuik®) at 1 or 2 levels between T3 and T6.

Postoperative pain assessment was performed by the ICU nurse using the visual analog scale (VAS), with pain score ranging from 0 (no pain) to 10 (worst possible pain). Postoperative analgesia (a combination of "breakthrough" and scheduled medication) was prescribed by the primary surgical team and consisted of an opioid (e.g., fentanyl, hydromorphone, or oxycodone) and a combination of adjuncts (e.g., acetaminophen, ketorolac, gabapentin). A repeat PVB was requested by the surgical team when the previous PVB block had worn off and the patient complained about severe chest postoperative pain (VAS > 7) which was not adequately controlled with the standard analgesic regimen.

All data were extracted via our institutional electronic medical record database. Demographic information (including age, weight, height, alcohol or drug consumption, history of smoking, and concomitant medical disease) and the preoperative baseline VAS pain score were recorded. During the surgical procedure, data collec-

tion included anesthetic and analgesic requirements (e.g., midazolam, opioid analgesics expressed as oral morphine milligram equivalents [MME], end-tidal sevoflurane concentrations), as well as the durations of aortic cross-clamping, cardiopulmonary bypass time and duration of anesthesia. After surgery, the time to extubation, chest tube removal, urinary catheter removal, and 1st bowel movement, as well as the length of ICU and hospital LOS were recorded. The VAS pain scores, MME dosages during the first 72 hrs postoperatively, as well as the time and number of patients who required a 2nd PVB (i.e., "re-block") and rescue with adjunctive analgesic therapies in the ICU were also noted. In addition, preoperative and postoperative laboratory values, as well as the incidence of postoperative complications were recorded.

3.1. Statistical Analysis

Student's t test was used to compare the continuous variables between the two study groups (e.g., opioid MME, time interval to receive 2nd block, ICU and hospital LOS). Continuous data not normally distributed were analyzed using the Mann-Whitney U test. Chi-square test (or Fisher's exact test wherever applicable) was used to analyze the categorical variables including number of patients receiving a 2nd PVB block and the incidence of side effects. Data are presented as mean values ± SD, or median values (with inter-quartile ranges), numbers (n), and percentages (%). A p value < 0.05 was considered statistically significant.

4. Results

Medical records of 100 consecutive patients aged ≥ 18 yrs who underwent robotic MVR procedure and received a perioperative PVB from 02/2019 to 05/2020 at Cedars-Sinai Medical Center in Los Angeles, CA were reviewed. Twelve patients were excluded because 0.5% bupivacaine was used for PVB. Therefore, eighty-eight study patients were included for the final analysis (Group 1: 43 patients received PVB before surgery, and Group 2: 45 patients received PVB after surgery). The two treatment groups were similar with respect to demographic characteristics, including age, weight, height, gender, baseline left ventricular ejection fraction and other concomitant disease (Table 1).

All study patients underwent a successful robotic MVR procedure. A concomitant left atrial appendage occlusion was performed in 41 (95%) patients in Group 1 versus 42 (93%) patients in Group 2. There was no difference between groups in duration of anesthesia, cross-clamp, or cardiopulmonary bypass. However, patients in Group 1 (PVB before surgery) required significantly lower intraoperative dosages of both midazolam (4.6 ± 2.5 mg in Group 1 versus 6.6 ± 3.0 mg in Group 2) and opioid analgesics (MME) (81.3 ± 41.7 mg in Group 1 versus 171.9 ± 72.3 mg in Group 2). Recovery profiles were similar between the two groups with respect to time to extubation, chest tube removal, urinary catheter removal, 1st bowel movement, as well as duration of ICU and hospital LOS (Table 2).

During the first 72 hrs after surgery, postoperative VAS pain scores and opioid requirements (MME) at different time intervals were similar between groups. Interestingly, most patients in both groups required a repeat PVB (63% in Group 1 versus 71% in Group 2, $p > 0.05$), but the time interval from 1st PVB to 2nd PVB was significantly longer in Group 1 (PVB before surgery) (23.6 ± 9.0 hrs) compared to Group 2 (PVB after surgery) (19.6 ± 3.9 hrs) (Table 3).

Baseline laboratory values were similar between two treatment groups; however, the initial postoperative WBC count upon arrival in the ICU was significantly lower in Group 1 (Table 4). The incidence of postoperative complications (e.g., wound infection, neurologic events, and atrial fibrillation) did not differ between treatment groups. Finally, patients in Group 1 required significantly less antiemetic recue medication after surgery than patients in Group 2 (Table 5).

Table 1: Demographic characteristics between Pre-op PVB (Group 1) and Post-op PVB (Group 2).

	Group 1	Group 2	*P*
Number (n)	43	45	
Age (yrs)	62 ± 12	62 ± 11	0.83
Weight (kg)	82 ± 16	81 ± 15	0.8
Height (cm)	176 ± 9	174 ± 9	0.3
Gender (male/female) (n)	35/8	33/12	0.37
History of smoking (yes/no) (n)	15/28	17/28	0.78
History of arrhythmia (n)	10	12	0.71
History of chronic lung disease (n)	6	1	0.06
History of diabetes (n)	1	2	1
Baseline left ventricular ejection fraction (%)	62 ± 8	63 ± 6	0.45
Baseline VAS Pain scores (0-10) (n)	0.2 ± 0.9	0.1 ± 0.6	0.66

Note: Data are presented as Mean ± SD, number (n), and percentage (%).

VAS = visual analog scale.

Table 2: Profiles of anesthesia, surgery and recovery process between Pre-op PVB (Group 1) and Post-op PVB (Group 2).

	Group 1	Group 2	*P*
Intraoperative parameters			
Anesthesia time (min)	303 ± 34	307 ± 38	0.61
Intraoperative midazolam (mg)	4.6 ± 2.5	6.6 ± 3.0*	< 0.01
Intraoperative opioid MME (mg)	81.3 ± 41.7	171.9 ± 72.3*	< 0.01
Duration of cross-clamp (min)	74 ± 14	76 ± 20	0.6
Duration of cardiopulmonary bypass (min)	112 ± 18	119 ± 24	0.11
Postoperative parameters			
Extubation time (min)	280 ± 88	249 ± 107	0.14
Chest tubes removed (hrs)			
pleural	61 ± 49	55 ± 29	0.49
mediastinal	44 ± 32	37 ± 24	0.26
Chest tube output (mL)			
POD # 0	392 ± 274	392 ± 156	1
POD # 1	286 ± 142	266 ± 152	0.53
Urinary catheter removed (hrs)	62 ± 26	58 ± 20	0.46
Time to 1st bowel movement (hrs)	72 ± 26	78 ± 25	0.27
Duration of ICU (d)	2.3 ± 1.2	2.2 ± 1.0	0.63
Hospital length of stay (d)	5.4 ± 1.4	5.3 ± 1.1	0.89

Note: Data are presented as Mean ± SD.

* $p < 0.05$ compared with Group 1.

ICU = intensive care unit; MME = morphine milligram equivalent; POD = postoperative day.

Table 3: Postoperative pain management between Pre-op PVB (Group 1) and Post-op PVB (Group 2).

	Group 1	Group 2	*P*
Postoperative opioid MME (mg)			
0-4 hrs	3.9 ± 6.7	3.5 ± 7.3	0.78
4-8 hrs	7.5 ± 6.9	8.1 ± 13.3	0.79
8-12 hrs	6.8 ± 10.2	6.7 ± 7.1	0.93
12-24 hrs	16.4 ± 13.6	18.2 ± 21.8	0.64
0-24 hrs	34.6 ± 22.5	36.4 ± 42.0	0.8
24-48 hrs	23.8 ± 20.7	22.8 ± 23.3	0.84
48-72 hrs	18.6 ± 18.7	16.2 ± 24.4	0.6
Postoperative VAS pain scores (0-10) (n)			
4 hrs	5.6 ± 3.1	4.3 ± 3.2	0.06
8 hrs	4.3 ± 3.2	4.2 ± 3.1	0.93
12 hrs	5.3 ± 2.8	4.7 ± 3.0	0.36
24 hrs	3.1 ± 2.6	2.9 ± 2.5	0.74
36 hrs	3.5 ± 2.6	3.9 ± 2.6	0.55
48 hrs	2.8 ± 2.2	2.7 ± 2.1	0.71
72 hrs	2.2 ± 2.3	2.2 ± 2.4	0.99
Time to 2nd PVB block (hrs)	23.6 ± 9.0	19.6 ± 3.9*	0.04
Patient needed 2nd PVB block (n,%)	27,63	32,71	0.41
Analgesic adjuncts in the ICU (n,%)			
acetaminophen	42,98	42,93	0.62
gabapentin	31,72	11,24*	< 0.01
ketorolac	11,26	9,20	0.53

Note: Data are presented as Mean ± SD, number (n), and percentage (%).

* $p < 0.05$ compared with Group 1.

ICU = intensive care unit; MME = morphine milligram equivalent; PVB = paravertebral block;

Postop = postoperative; VAS = visual analog scale.

Table 4: Perioperative laboratory values between Pre-op PVB (Group 1) and Post-op PVB (Group 2).

	Group 1	Group 2	*P*
Preoperative			
Hemoglobin (g/dL)	14.7 ± 5.3	14.3 ± 3.4	0.71
White blood cell count (x1000/uL)	6.7 ± 2.4	7.0 ± 2.2	0.57
Platelet count (x1000/uL)	206 ± 60	212 ± 59	0.65
International normalized ratio (INR)	1.1 ± 0.2	1.1 ± 0.1	0.96
Creatinine (mg/dL)	0.9 ± 0.2	0.9 ± 0.2	0.73
Intraoperative			
Lowest hemoglobin (g/dL)	9.7 ± 3.9	9.7 ± 2.7	0.93
Postoperative white blood cell (x1000/uL)			
Upon arrival in ICU	12.9 ± 3.7	15.4 ± 4.0*	< 0.01
4 hrs after arrival in ICU	13.2 ± 2.7	14.9 ± 3.4*	0.02
Postoperative day # 1	13.1 ± 3.3	14.2 ± 3.6	0.15
Postoperative peak glucose (mg/dL)	162 ± 37	150 ± 27	0.09

Note: Data are presented as Mean ± SD.

* $p < 0.05$ compared with Group 1.

ICU = intensive care unit.

Table 5: Incidence of postoperative side effects between Pre-op PVB (Group 1) and Post-op PVB (Group 2)

	Group 1	Group 2	*P*
Incision site infection (n,%)	1,2	0,0	0.49
Neurologic complication (n,%)	0,0	0,0	1
Atrial fibrillation (n,%)	17,40	14,31	0.41
Postoperative vomiting (n,%)	5,12	10,22	0.26
Patients received antiemetics (n,%)	15,35	27,60*	0.02

Note: Data are presented as Number (n) and percentage (%).

* $p < 0.05$ compared with Group 1.

5. Discussion

This study is the first study to evaluate the effects of timing of PVB administration on the outcome of patients undergoing robotic MVR. The findings refuted our null hypotheses because they demonstrated that a PVB performed before (vs. after) surgery resulted in similar postoperative pain control (including VAS pain scores and opioid requirements within the first 72 hrs), and similar recovery times (e.g., ICU and hospital LOS). However, the dosages of intraoperative opioid and midazolam were significantly decreased, as well as the requirement for rescue antiemetic medication after surgery, in patients receiving a PVB before (vs. after) surgery. The intraoperative opioid-sparing effect associated with preoperative PVB are consistent with previous studies [15,16].

Surprisingly, the time interval from 1st PVB to 2nd PVB was significantly prolonged in patients receiving a preoperative PVB. These data are consistent with a preemptive analgesic effect when the PVB is performed prior to the surgical insult (namely, thoracotomy and cardiopulmonary bypass). Although the WBC count is a nonspecific marker of inflammation, the finding of a lower WBC count in the immediate postoperative period in patients in the pre-surgery PVB group is also consistent with a preemptive effect in blunting the inflammatory response to surgery. This observation suggests that a preoperative PVB may attenuate the release of inflammatory mediators and stress hormones caused by the noxious surgical stimulation which could contribute to increased postoperative morbidity [21]. This finding is also consistent with the study reporting that the use of a PVB in thoracic and cardiac surgery was associated with ablunted stress response to surgery and a decreased incidence of chronic post-thoracotomy pain [22].

Patients who experience severe acute post-thoracotomy pain after undergoing MVR via the minimally invasive thoracotomy approach, have a higher prevalence and severity of chronic pain compared to the traditional median sternotomy approach [4]. It is important to use more effective early postoperative analgesia interventions to facilitate rapid recovery and decrease the incidence and severity of chronic postoperative pain. Due to the variable duration of a single PVB (4-23 hrs) [16,19,20], it is not surprising to find that a high percentage of patients in both groups required a second PVB block (63% in pre-surgery PVB group, and 71% in the post-surgery PVB group, respectively). Given the requirement for chest tube(s) to remain in place for at least 24 hrs after surgery, the use of a paravertebral catheter with continuous local anesthetics administration could significantly benefit patients undergoing robotic MVR. As a result of these findings, our institution

has adopteda policy involving the use of continues paravertebral catheter for both robotic MVR and minimally invasive direct coronary artery bypass surgery. Finally, the decreased intraoperative opioid requirement in the pre-PVB group might account for lower requirement for postoperative antiemetics rescue medication. These data also suggest that preoperative PVB was associated with lower rates of postoperative nausea and vomiting.

There are several limitations to this retrospective chart review. Firstly, as this was a retrospective study there may be potentially confounding variables that were not accounted for in the data analysis. Secondly, as PVB has only recently gained wide-spread acceptance at our institution, we cannot rule-out the possibility of a type 2 error from an inadequate sample size. Thirdly, there is no standardized protocol at our institution for performing a PVB. As such, variable volumes of local anesthetics (30-40 mL) were injected at either 1 or 2 levels. Fourthly, an Enhanced Recovery After Surgery (ERAS) protocol was only recently implemented at our institution during this time period. As a result, the postoperative opioid and opioid-sparing analgesic adjuncts prescribed to patients was not standardized. Finally, as with any academic institution, our PVB was performed by trainees of varying skill levels. Although all trainees were directly supervised by an experienced attending anesthesiologist, the efficacy of the block may have varied among this patient population.

6. Conclusion

In conclusion, this retrospective study suggests that performing a PVB before or after robotic MVR results in comparable postoperative pain control and recovery profiles. However, the preoperative PVB is recommended because it was associated with lower intraoperative opioid and midazolam requirements, produced a longer duration of analgesia, required less postoperative antiemetic use, and had an apparent anti-inflammatory effect immediately after surgery. Finally, there remains the need for prospective randomized controlled trials to better elucidate the effects of timing of PVB on perioperative pain control and recovery profiles in patients undergoing minimally invasive cardiac surgery using a state-of-the-art ERAS protocol.

7. Disclosures

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