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Comparison of bupivacaine and levobupivacaine for treatment of post-thoracotomy pain through thoracic paravertebral block

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ABSTRACT

Objectives. The aim of this study was to compare postoperative pain and respiratory functions of lobectomy patients who were given bupivacaine or levobupivacaine with fentanyl through a paravertebral catheter. ***Methods.*** ASA I-II patients (n=40, 18-65 years old) randomized into two groups. While Group B was administered 0.25% bupivacaine with fentanyl, Group L was administered 0.25% levobupivacaine with fentanyl at a rate of 0.1 ml/kg/hr through paravertebral catheter for patient controlled analgesia. Visual analog scale (VAS), arterial blood gases and respiratory function tests were assessed. ***Results.*** There were no significant differences in terms of demographic characteristics and surgery durations between the groups ($p>0.05$). VAS scores recorded at the 1st postoperative hour were higher in both groups compared to the following hours ($p<0.001$), but there was no difference between the groups. FEV1 and FVC measured in the postoperative period were significantly lower than preoperative values in both groups ($p<0.001$); however, there was no significant difference between the groups. There was no significant difference between the two groups regarding side effects, mean values of PaO_2, $PaCO_2$ and SpO_2 ($p>0.05$). ***Conclusion.*** Bupivacaine and levobupivacaine had equivalent efficiency and could be safely used in treatment of post-thoracotomy pain through thoracic paravertebral block.

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Keywords: Bupivacaine; levobupivacaine hydrochloride; post-thoracotomy pain; thoracic paravertebral block

Introduction

Pulmonary lobectomy is a common surgical procedure that removes one lobe of the lung, is used to treat fungal infections, benign tumors, emphysema, lung abscesses, and tuberculosis. A thoracotomy involves an incision between two ribs on the one side of chest. Successful treatment of the thoracotomy pain

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is one of the most important aspects of optimal postoperative management of surgery and anesthesia. Severe pain contributes to postoperative pulmonary dysfunction [1, 2]. As it adversely affect coughing and deep breathing, such a pain may lead to hypoxia, atelectasis, lung infection or respiratory failure. Delay in the initiation of pain treatment may lead to life-threatening situations [3, 4]. There are many pain sources related with thoracostomy, such as location of surgery incision, damage on ribs and intercostal nerves, inflammation of the chest wall around the incision, incision or crushing of pulmonary parenchyma and pleura, placement/implantation of single or multiple drains [5]. Paravertebral block is the injection of local anesthetics on the spinal nerves located in the paravertebral space. Local anesthetics infused alongside the vertebral column enable ipsilateral analgesia. Although it is mainly used for unilateral surgeries, such as chest wall trauma, breast surgery, cholecystectomy, hernia repair and renal surgery, it can be performed for bilateral surgeries as well. Paravertebral block is also applied for chronic pain and treatment of benign or malignant neuralgia [6, 7].

In this study, we aim to compare the influence and side effects of continuous of bupivacaine-fentanyl and levobupivacaine-fentanyl infusion through a paravertebral catheter on postoperative pain, pulmonary functions and arterial blood gas values of patients who underwent thoracic surgery.

Methods

The study was carried out after the approval of the Local Research Ethics Committee and the provision of informed consents of the patients. The study included 40 ASA (American Society of Anesthesiologists) I-II patients, aged between 18 and 65 years, who were scheduled to have elective surgical lobectomy under general anesthesia. Exclusion criteria consisted of infection in the area where the catheter should be installed, allergy to local anesthetics and opioids, kidney failure or liver dysfunction, pregnancy or breast-feeding, using anticoagulant drugs, and unwillingness for the study. Additionally, the patients who could not be provided with an extrapleural pocket were not included in the study. The patients were randomized into two groups according to the sealed envelope method. Twenty milliliters of 0.5% bupivacaine (Marcaine®, AstraZeneca, Istanbul, Turkey) was gived to Group B and 20 ml of 0.5% levobupivacaine hydrochloride (Chirocaine®, Abbott, Istanbul, Turkey) was gived to Group L through an epidural catheter placed in the paravertebral area.

PaO_2, $PaCO_2$ and SpO_2 values were recorded on the day before the surgery. FEV1 and FVC values were recorded preoperatively while the patient in the room air by the pulmonary function test performed with a portable spirometer (ContecTM SP10, China). None of the patients received premedication. Patients taken to the operating theater were monitored for non-invasive arterial blood pressure, heart rate, DII lead electrocardiogram, and SpO_2. After 3 minutes preoxygenization with 3 mL/minute 100% O2, 0.03-0.05 mg/kg iv midazolam, 2 mcg/kg fentanyl, 1 mg/kg 2% lidocaine, 2-3 mg/kg propofol and 0.6 mg/kg rocuronium were administered to induce general anesthesia. 50% oxygen/air and 2% sevoflurane were used for the maintenance of anesthesia. Patients were intubated with a double-lumen endobronchial tube, and the position of the tube was checked with fiberoptic bronchoscopy. At the end of the operation, the surgeon placed an epidural catheter (Perifix®, Braun, Germany) by inserting an 18-G Tuohy needle percutaneously 2.5-3 cm lateral to the incision and advancing it perpendicularly to the skin by spinous process towards the paravertebral area. After the pleural space was closed, Group B was given 20 ml of 0.5% bupivacaine and Group L was given 20 ml of 0.5% levobupivacaine through the catheter. For patient controlled analgesia, solutions of 425 mg of 0.25% bupivacaine+350 mcg fentanyl, and of 425 mg of 0.25% levobupivacaine+350 mcg fentanyl were used for Group B and Group L, respectively. Both groups received a continuous 48 hour infusion at a rate of 0.1 ml/kg/hr for patient controlled analgesia.

Patients' pain levels during rest, movement and coughing were measured at the 1st, 6th, 24th and 48th postoperative hours using the Visual Analog Scale (VAS) (0=No pain, 10=Severe pain). Patients with a VAS score of >3 were administered 1 mg/kg im pethidine (Aldolan-Gerot ®, LibaLab, Istanbul, Turkey). Application times and doses were recorded. PaO_2, $PaCO_2$, SpO_2, FEV1 and FVC values were recorded at the 24^{th} and 48^{th} postoperative hours. Side effects, such as hypotension, bradycardia nausea, vomiting and pain, were recorded postoperatively.

Statistical Analysis

Statistical analysis of the study was carried out using Statistical Package 13.0 for Windows (SPSS Inc., Chicago, USA). Shapiro-Wilk test was used as

normallity test. Continuous variables were compared using Mann-Whitney U test when the data were not normally distributed. Wilcoxon Signed rank test was used for dependent groups. Categorical variables were compared using Pearson's chi-squared test and Fisher's exact test. The *p* value of <0.05 was considered statistically significant and the values were expressed as "median" or as a number. Results were given as median values.

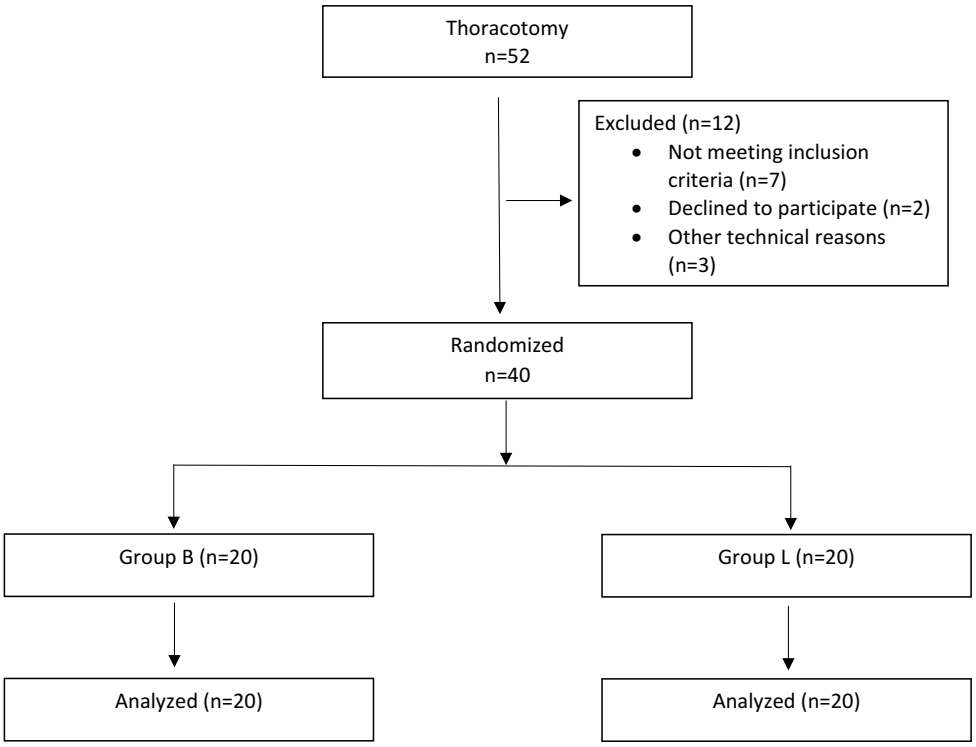

Figure 1. Flow chart of patient enrollment and analysis

Results

Out of 52 patients undergoing elective lobectomy, 40 patients were included in the study. Twelve patients were excluded (not meeting inclusion criteria, declined to participate, etc). A total of 40 patients were assessed statistically (Figure 1). There was no statistically significant difference between the groups in terms of their demographic characteristics (p>0.05) (Table 1).

When the VAS scores during rest, movement and coughing were compared, the scores obtained at the 1st postoperative hour were significantly lower than the scores measured at the 6th, 24th and 48th hours in both groups (p<0.001) (Figures 2, 3 and 4). Rest, movement, and coughing VAS scores did not show significant difference between the two groups at any time (p>0.05).

The average pethidine use was 155±117.9 mg in Group B and 142.5±144.4 mg in Group L. There was no significant difference between the two groups regarding the use of pethidine (p>0.05).

Table 1. Distribution of demographic characteristics, operation time

	Group B (n=20)	Group L (n=20)	*p*
Age (year)	51.1±10.88	50.9±11.96	0.956
Male/Female	13/7	15/5	0.490
Height (cm)	167.45±7.9	168.2±8.9	0.780
Weight (kg)	74.65±11.7	75.4±10.7	0.835
ASA I/II (n)	6/14	7/13	0.600
Operation time (minute)	139±56.6	150±61.5	0.640

Data are shown as mean ± standard deviation or number. ASA=American society of anesthesiologists

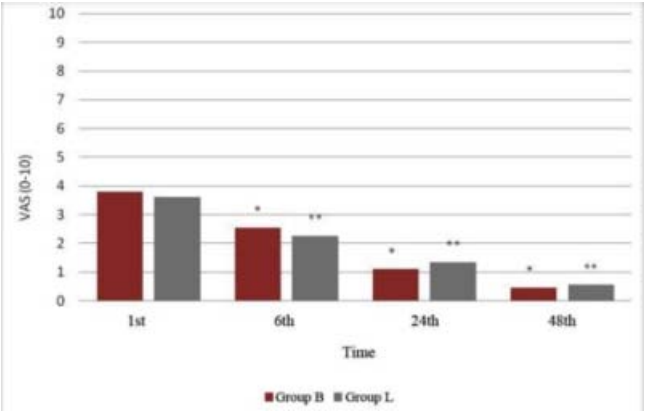

Figure 2. Mean values of VAS according to groups at the rest. VAS=Visual analogue scale, *p<0.001 (difference between 1st, 6th, 24th and 48th hours in Group B), **p<0.001 (difference between 1st, 6th, 24th and 48th hours in Group L)

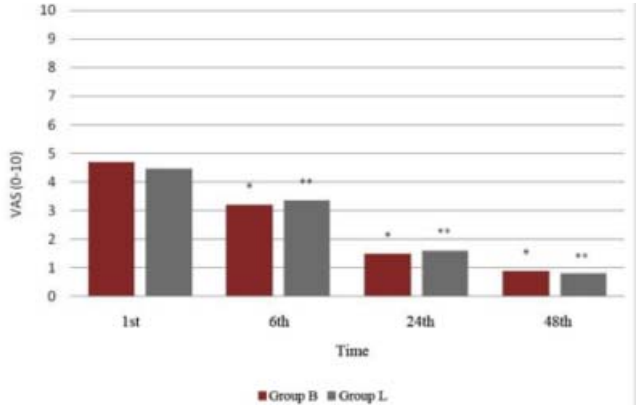

Figure 3. Mean values of VAS according to groups at the movement. VAS=Visual analogue scale, *p<0.001 (difference between 1st, 6th, 24th and 48th hours in Group B), **p<0.001 (difference between 1st, 6th, 24th and 48th hours in Group L)

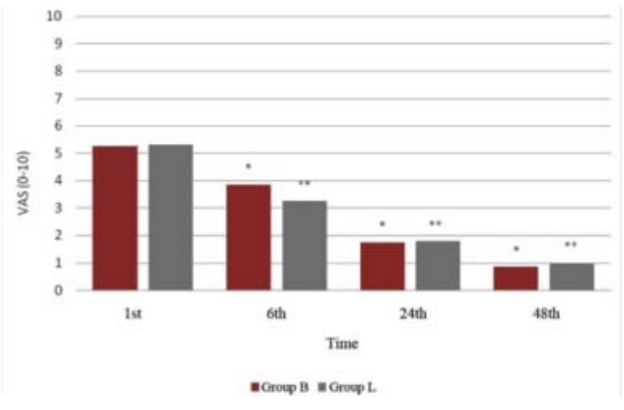

Figure 4. Mean values of VAS according to groups during the cough. VAS=Visual analogue scale, *p<0.001 (difference between 1st, 6th, 24th and 48th hours in Group B), **p<0.001 (difference between 1st, 6th, 24th and 48th hours in Group L)

The preoperative FEV1 values did not show any significant difference between Group B and Group L (p>0.05). However, in both groups, the FEV1 values measured at the 24th and 48th postoperative hours were found to be significantly lower than the preoperative FEV1 values (p<0.001) (Figure 5). The FEV1 value of both groups decreased approximately to 68% and 83% of the preoperative FEV1 value at the 24th and 48th postoperative hours, respectively. The FEV1 values measured at the 24th and 48th postoperative hours were no significant difference in both groups (p>0.05).

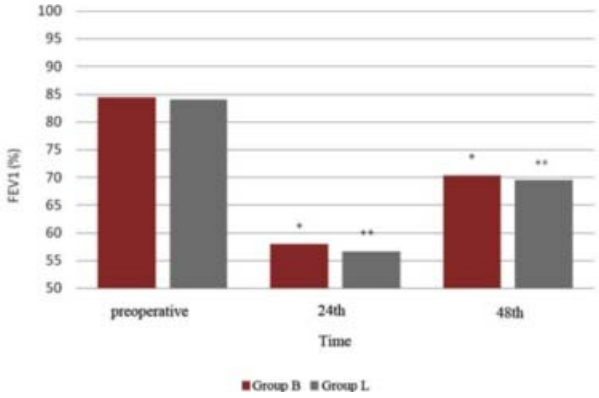

Figure 5. Mean values of FEV1 according to groups. FEV1=forced expiratory volume 1 second. VAS=Visual analogue scale, *p<0.001 (difference between preoperative, 24th and 48th hours in Group B), **p<0.001 (difference between preoperative, 24th and 48th hours in Group L)

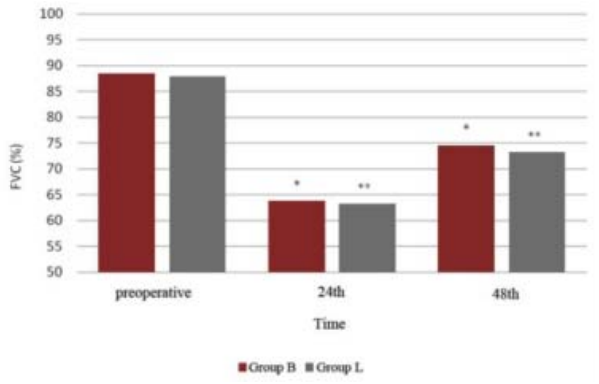

Figure 6. Mean values of FVC according to groups. FVC=forced vital capacity. VAS=Visual analogue scale, *p<0.001 (difference between preoperative, 24th and 48th hours in Group B), **p<0.001 (difference between preoperative, 24th and 48th hours in Group L)

We did not find any difference between the groups regarding the preoperative FVC values (p>0.05). In both groups, the FVC values obtained at the 24th and 48th postoperative hours were statistically significantly lower than the preoperative FVC values (p<0.001) (Figure 6). While the FVC value measured at the postoperative 24th hour was almost equal to

Table 2. PaO_2, $PaCO_2$, SpO_2 values according to groups

	Group B (n=20)	Group L (n=20)	*p*
Preoperative PaO_2 (mmHg)	91.29±6.20	91.28±5.1	0.998
Preoperative $PaCO_2$ (mmHg)	43.05±4.12	42.23±4.55	0.557
Preoperative SpO_2 (%)	79.03±3.56	83.25±3.17	0.695
Postoperative 24th hour PaO_2 (mmHg)	82.75±4.3	81.49±4.26	0.926
Postoperative 24th hour $PaCO_2$ (mmHg)	37.3±1.32	36.67±1.24	0.877
Postoperative 24th hour SpO_2 (%)	93.01±1.97	97.1±1.82	0.362
Postoperative 48th hour PaO_2 (mmHg)	80±3.83	86.32±3.05	0.573
Postoperative 48th hour $PaCO_2$ (mmHg)	37.34 ± 1.23	40.57 ± 6.03	0.300
Postoperative 48th hour SpO_2 (%)	96.11±1.3	91.76±1.94	0.325

Data are shown as mean ± standard deviation or number. PaO_2=partial pressure of oxygen in arterial blood, $PaCO_2$= partial pressure of carbon dioxide in arterial blood, SpO_2=saturation of arterial blood with oxygen

71% of preoperative FVC value, the FVC at the 48th was nearly equal to 84% of preoperative FVC. Additionally, the FVC values measured at the 24th and 48th postoperative hours did not show any significant difference between the two groups (p>0.05).

In terms of PaO_2, $PaCO_2$, SpO_2 values measured respectively preoperative period, postoperative 24th and 48th hours, there were not any significant difference between Group B and Group L (p>0.05) (Table 2).

In both groups, two (10%) patients had nausea, two (10%) patients from Group B and one (5%) patient from Group L had hypotension, which did not require therapy, and there were no significant differences between the groups (p>0.05).

Discussion

In this study, we compared the effects of bupivacaine and levobupivacaine administered through a paravertebral catheter was placed at the end of surgery for the treatment of post-thoracotomy pain. We found that bupivacaine and levobupivacaine which were combined with fentanyl and administered in equivalent doses at a fixed rate provided similar analgesia. As the thoracic epidural block, which is considered as the golden standard in thoracic surgery for the treatment of postoperative pain, has some side effects, alternative methods instead of central blocks have come into use in recent years. As a result, paravertebral block applications are becoming increasingly common [8, 9]. Some earlier studies have already reported that bupivacaine and levobupivacaine can provide sufficient analgesia in paravertebral block applications [10, 11].

Novak-Jankovic *et al.* [12] compared the efficacy of 0.25% levobupivacaine and bupivacaine infused through a paravertebral catheter, which was installed percutaneously in the preoperative period on 40 patients undergoing thoracotomy. After a bolus of morphine and 0.5% bupivacaine or levobupivacaine were administered following the placement of the catheter, morphine, clonidine and 0.25% bupivacaine or levobupivacaine were used continuously. The researchers reported that the intraoperative fentanyl requirement was less, pain scores obtained during the first 3 days of postoperative rest and during the first 2 days of exercise were lower, and the dose of the rescue analgesic was lower in the group receiving levobupivacaine. Nevertheless, pulmonary function tests and hemodynamic parameters showed similar results. In our study, patients received similar concentrations of bupivacaine and levobupivacaine infusion, which were combined with fentanyl instead of clonidine and morphine, through the paravertebral catheter which was placed at the end of the operation. Unlike the study of Novak-Jankovic *et al.* [12], the infusion rate was two times faster, and the VAS scores and rescue analgesic requirement was similar in bupivacaine and levobupivacaine groups in our study. As in the aforementioned study, the pulmonary function tests and arterial blood gas values did not show any difference between the groups in our study. In the study comparing paravertebral block and thoracic epidural block in patients having thoracotomy, Gulbahar *et al.* [13] administered 0.25% bupivacaine at a dose of 0.1 ml/kg/h using both methods and indicated that paravertebral block could provide equal and sufficient analgesia as epidural block did. In our study, we want to compare type of local anesthetic drugs administered via a paravertebral catheter, not to compare technics like that paravertebral block and thoracic epidural block. Like

this study our groups received an infusion at a rate of 0.1 ml/kg/hr bupivacaine or levobupivacaine for patient controlled analgesia. There were not any significant differences between bupivacaine or levobupivacaine groups in our study.

Garutti *et al.* [14] made comparison of three different paravertebral block applications in their study. During the operation, each patient in the three groups was infused with 0.25% bupivacaine at a rate of 0.15 ml/kg/h through a paravertebral catheter, which was percutaneously placed by the anesthesiologists in the preoperative period. While the 1st group was infused using only the paravertebral catheter, the 2nd group received subcutaneous infusion through the surgical incision. On the other hand, in the 3rd group, the percutaneous catheter was removed at the end of the operation and a new catheter was placed in the T5-T6 paravertebral space through the surgical incision. While the researchers observed that analgesia was more effective in the 2nd group, the other two paravertebral blocks were reported to ensure similar analgesic efficacy. The VAS scores of the 3rd group measured during rest, movement and coughing did not show any change at the 4th, 8th, 12th, 24th, 48th, and 72th hours. The lack of change in the VAS scores may be attributed to the fact that there was enough time for development of the block because the 1st VAS measurement took place at the postoperative 4th hour, and that the infusion rate of bupivacaine (not combined with fentanyl) was higher compared to our study.

Pintaric *et al.* [11] compared the effects of preoperative bolus dose and postoperative infusion applications in the thoracic epidural and paravertebral block on the analgesia and hemodynamics in patients undergoing thoracotomy. After catheters were placed at the beginning of the operation, a bolus of 0.25% levobupivacaine and 30 mcg/ml morphine was given through the epidural catheter and 0.5% levobupivacaine and 30 mcg/ml morphine were administered by bolus through the paravertebral catheter. The infusion was started with 200 ml of 0.125% levobupivacaine and 20 mcg/ml morphine at a rate of 0.1 ml/kg. Piritramide was used as rescue analgesic. The authors reported that there was no difference between the two groups regarding the pain scores and use of additional analgesics. Perioperative hypotension was more common in the group receiving thoracic epidural analgesia. In both groups, two (10%) patients from Group B and one (5%) patient from Group L had hypotension, which did not require therapy in our study. We also found that bupivacaine and levobupivacaine which were combined with fentanyl and administered in equivalent doses at a fixed rate provided similar analgesia and no significant difference between the two groups regarding the use of additional analgesics in paravertebral block applications.

Gulbahar *et al.* [13] indicated in the study comparing epidural block and continuous paravertebral block regarding their effects on postoperative pain and pulmonary functions after thoracotomy that both methods were effective and safe for postoperative pain treatment and improvement of pulmonary functions. In that study, postoperative the FEV1, and PEFR (peak expiratory flow rate) values showed a significant decrease compared to the preoperative values. However, there was no difference between two groups in the pre- and postoperative FEV1, and PEFR values. In the present study, the FEV1 and FVC values also showed a significant decrease in both groups at the postoperative 24th and 48th hours compared to the preoperative measurements and there was no difference between the groups regarding that decrease. We obtained similar results with the studies [13, 15] reporting significant decrease in the pulmonary function tests after thoracotomy compared to preoperative values.

The Limitations of the Study

The limitation of this study is the absence of different doses of local anesthetics. Doses we used were safe and effective, but it is need to find the minimal doses in order to optimal effectivity for both local anesthetics. The other limitation is the small number of patients involved in this study. Hence, further studies are required with a greater number of patients.

Conclusions

We concluded that bupivacaine-fentanyl or levobupivacaine-fentanyl combination infused after a bolus dose through paravertebral catheter which was inserted at the end of the operation by surgeon provided effective analgesia in patients who underwent thoracotomy. Positive effects of the catheter on pulmoner functions began second postoperative day. In conclusion, we think that the efficacy of bupivacaine and levobupivacaine is

equivalent through paravertebral catheter, and they can be safely used for post-thoracotomy pain.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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