Thoracic paravertebral block *vs.* mid-point transverse process to pleura block in thoracic surgery. Preliminary evaluation of effectiveness and safety

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Abstract

Mid-point transverse process to pleura block (MTPB) is an alternative approach to paravertebral block. We retrospectively assessed hemodynamic stability, inadvertent pleural puncture and antalgic effectiveness of this approach compared with traditional paravertebral block. Moreover, being used to add methylene bleu to local anesthetic solution as a tracer, we compared the diffusion pattern in paravertebral space of the two techniques. We reported retrospectively 40 patients underwent lung lobectomy from July to October 2021 in Monaldi Hospital (Naples, Italy) receiving thoracic paravertebral block (n=20) or mid-point transverse process to pleura block (n=20). The primary outcomes were a 20% mean arterial pressure variation from the base line, chest wall or pleural hematoma and technique failure. Analgesic effectiveness was assessed comparing remifentanil consumption to keep nociception index level <25 and patient's visual analog scale (VAS) in post anesthesia care unit or daycare surgical unit at 60'. Also the methylene blue spread was assessed by a surgeon, blinded to patient's name, reviewing surgery videorecord of every cases. MAP decrease >20% was greater in the thoracic paravertebral block (TPVB). No significative differences were reported for pleural punctures, chest wall hematomas or failure of the technique in the two groups. Methylene blue was evident in all patients of the TPVB, while it was not visible in any of the patients of the MTPB group. Remifentanil consumption, nociception index level and postoperative 60' VAS were greater in the MTPB. Antalgic power and local anesthetic spread of TPVB seems to be superior to the MTPB, even if the safety profile of the latter seems to be better. Due to the retrospective nature of the study and the small number of cases in the sample, further studies are needed.

Introduction

Thoracic paravertebral block (TPVB) is the recommended technique for analgesia in video assisted thoracic surgery (VATS) according to the Italian intersociety consensus on Perioperative Anesthesia Care in Thoracic Surgery (PACTS), thanks to the effective analgesia and its technical simplicity and safety profile.[1] This block produces ipsilateral somatic and sympathetic nerve blockade due to a direct effect of the local anesthetic on the somatic and sympathetic nerves in the thoracic paravertebral space (TPVS, Figure 1A),[1-6] extended into the intercostal space laterally, and the epidural space medially.[7] Despite the low rate of technical failure in TPVB execution (6.1%),[2] pulmonary complications, such as inadvertent pleural puncture (0.8%) and pneumothorax (0.5%),[2] are still a recognized risk although the ultrasound guided approach. Some other complications are inadvertent vascular puncture (6.8%), hematoma (2.4%), pain at site of skin puncture (1.3%), signs of epidural or intrathecal spread (1.0%).[2] Compared with epidural analgesia, patients treated with TPVB (Figure 1B) benefit of less hemodynamic adverse effects[8] falling into hypotensive events only in the 4% of cases,[3] probably due to local anesthetic spread in the epidural space. Mid-point Transverse process to Pleura Block (MTPB) provides the local anesthetic injection point within the thoracic intertransverse tissue complex and posterior to the superior costotransverse ligament instead of directly into the paravertebral space (Figure 1C).[9] Compared to traditional TPVB (Figure 1B), this technique is considered safer in preventing inadvertent pleural puncture,[9] (especially in difficult ultrasound imaging), and we believe that it could reduce hypotensive events, because of minor spread of local anesthetic in the TPVS (Figure 1A).

An injection at the mid-point between the transverse process and pleura is reported to result in a spread to the paravertebral space ensuring effective analgesia just like the traditional paravertebral block approach.[9,10] The costotransverse ligament flattening confirms the correct execution of the MTPB (Figure 1C). In light of the fact that the TPVS is not a true anatomical compartment (paravertebral spread, in fact, can be achieved with an injection outside this space for the characteristics of the posterior boundary and connectivity of the TPVS),[10] more superficial needle placement options could provide an effective block without the necessity to approach the pleura and the attendant risks of pleural puncture and pneumothorax,[9,10] as illustrated by several recently described thoracic paravertebral block variants,[11] such as the erector spinae plane (ESP) block[12,13] and the retrolaminar block.[14] MTPB could be safer than TPVB in some clinical applications like thoracic surgery, breast surgery and analgesic treatment of rib fractures, if its effectiveness was confirmed. In this preliminary study, we retrospectively assess the hemodynamic stability of MTPB compared with TPVB also monitoring for possible inadvertent pleural puncture in 40 patients undergoing VATS. We also aimed to compare the block effectiveness in patients receiving MTPB *vs* TPVB measuring the intraoperative nociception level (NOL), the intraoperative remifentanil consumption and 60' after surgery VAS in patients undergoing lung resection surgery. NOL index was monitored during all time of VATS. It was constantly maintained between the values of adequate analgesia (10 <NOL <25). As NOL index was >25 for more than 1 minute, we increased the remifentanil infusion until the NOL was again in the range of 10-25, to prevent any hemodynamic reaction caused by pain. Moreover, a low dose of methylene bleu was added in the anesthetic solution, to evaluate the anesthetic spread in the TPVS after MTPB and TPVB.

Materials and Methods

In Monaldi Hospital (Naples, Italy) both TPVB and MTPB are usually performed in patients undergoing VATS. Therefore, we reported retrospectively 40 patients underwent VATS for lobectomy from July to October 2021 receiving TPVB (Group TPVB n=20) or MTPB (Group MTPB n=20). The primary outcomes were the intraoperative hemodynamic assessment (considering as hypotension a MAP variation of more than 20% from the base line), the safety of the two types of chest wall block (reporting inadvertent pleural puncture, chest wall hematoma or bleeding) and the failure of the technique (no pleural displacement for the TPVB or no costotransverse ligament flattening for MTPB). Sample size of 40 was calculated considering data from literature reporting hypotension (20% MAP decrease from baseline) in 30% of patients receiving TPVB and expecting no hypotension in the MTPB group with an alpha level 0.05 and power of 0.8. The possible spread of MB from the TPVS during VATS was examined from the start to the end of surgery. We also evaluated the analgesic effectiveness, analyzing the

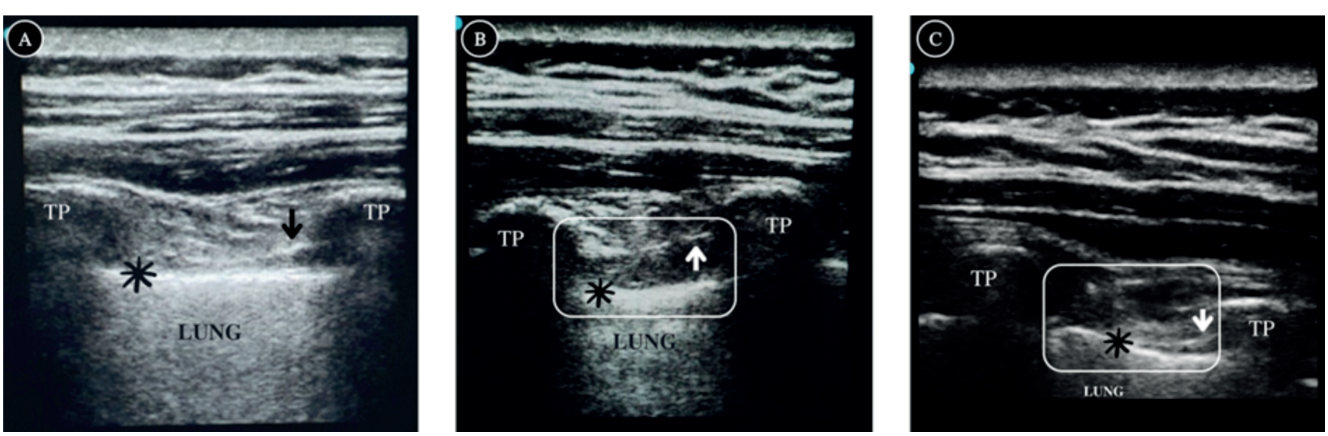

Figure 1. A) Ultrasound vision of the thoracic paravertebral space (TPVS), parasagittal scan. Transverse processes (TP), pleura (*) and superior costotransverse ligament (↓) are clearly visible; B) TPVB, needle insertion, out of plane approach. The needle tip crossed the costotransverse ligament (↑) without passing the pleura (*). The injection of the local anesthetic solution in the PVS causes the anterior pleural displacement. In the square, the local anesthetic solution spread and pleural displacement are highlighted; C) MTPB, needle insertion, out of plane approach. The needle tip is placed at the mid-point between the transverse process (TP) and pleura (*). The injection of the local anesthetic is reported to result in a spread to the paravertebral space ensuring effective analgesia just like the traditional paravertebral block approach. The costotransverse ligament (↓) flattening confirms the correct execution of the MTP block. In the square, the local anesthetic solution spread and the costotransverse ligament flattening are highlighted.

intraoperative consumption of remifentanil to maintain the NOL between 10 and 25 and the percentage of time that NOL was >25. For both groups of patients, then, we described the patient's post-procedural VAS in PACU or daycare surgical unit at 60'. The data were analyzed with t-test and a significant value was $p<0.05$. General anesthesia was induced with propofol and remifentanil in total IV anesthesia target-controlled infusion, using rocuronium as neuromuscular blockade and sugammadex if reversal was needed. Monitoring procedures in the operating room included standard monitoring: ECG, IBP or NIBP (depending by indications of surgery), SpO_2, temperature, diuresis, Train-Of-Four (TOF) for neuromuscular block monitoring, Bispectral Index (BIS) for the depth of anesthesia monitoring (Covidien, Dublin, Ireland), Medasense PMD200 (Medasense, Ramat Gan, Israel) and its NOL index to nociception monitoring. Before surgery, the block was performed in two lung ventilation, with patient lying on the side and the site of surgical interest uppermost. All the TPVB and MTPB were performed in a sterile manner, by the side of surgery interest, using dynamic ultrasound, high frequency 5-15 MHz linear transducer (Fujifilm SonoSite Edge II Total, Fujifilm Sonosite, Bothell, Washington, USA), in parasagittal scan and out-of-plane approach. We used Temena UPB 50 (Temena group, Bonn, Germany), 22 G, 50 mm needle. Injection was performed in single shot at the levels T3-T4 and T5-T6. We administered ropivacaine 0.75%, 6 mL, 90 mg, for each level. Hydrolocation technique was used to reach the target. Successful TPVB feedback was pleural displacement and costotransverse ligament flattening for successful MTPB. Postoperative analgesic regiment was standardized, so each patient received in 48 h: morphine 6 µg/kg/h, ketorolac 150 mg, ondansetron 16 mg, dexamethasone 16 mg, clonidine 300 µg, provided by continuous IV elastomeric pump 2 mL/h (100 mL); acetaminophen 1 g IV was also administered each 8 hours. We use to record and to screenshot the local anesthetic (LA) injection every time performing a block, so an ultrasound experienced anesthetist blinded to patient's name reviewed all the cases checking the correct placement of the needle tip in TPVB Group and in MTPB Group. To assess the possible secondary failure of the block (total intercostal LA spread, "cloud pattern" or insufficient LA spread) we are used to inject 1 mL of methylene bleu 1% with the anesthetic solution so during surgery the direct vision of the dye can reveal the spread pattern (Figure 2) or the technique complications (bleeding, hematoma etc.). The proper methylene blue diffusion in the PVS and possible complications were assessed by a surgeon, blinded to patient's name, reviewing surgery videorecord of every cases. NOL was maintained in the range of 10-25 by regulating the remifentanil infusion. As the NOL was >25 for more than 1 minute, the remifentanil infusion was increased of 1 ng/ml until the NOL was again in the range of 10-25.

Results

Patients' characteristics are reported in Table 1 and resulted not having significant differences. We had a MAP decrease >20% in 5 patients in TPVB Group and in 1 patient in MTPB Group, with a sig-

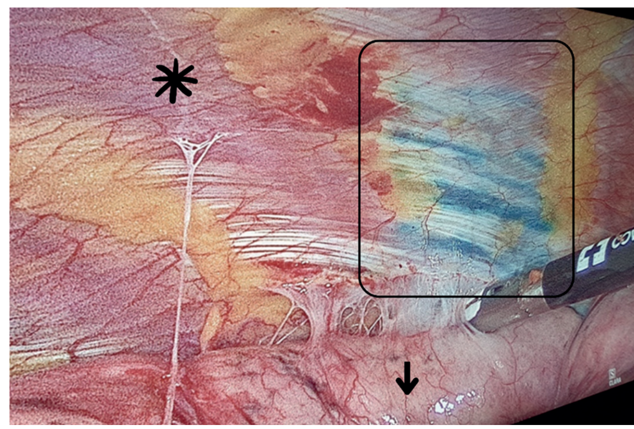

Figure 2. Methylene bleu in the local anesthetic solution was visible in the PVS and in the intercostal spaces after the injection in TPVB. In the square: methylene blue and local anesthetic solution spread. The arrow (↓) indicates the lung. The asterisk (*) indicates the chest wall.

Table 1. Patient characteristics; TPVB Group *vs* MTPB Group.

	TPVB Group n=20	MTPB Group n=20	p (t-test)
Sex, M/F	9/11	12/8	0.38
Age, y	61.35 (40-74)	65.5 (56-76)	0.11
Height, cm	167.55 (153-177)	170.45 (158-181)	0.19
Weight, kg	71.1 (45-89)	71.95 (61-88)	0.81
BMI, kg/m_2	24.95 (19-29)	24.7 (22-30)	0.78
ASA, 2/3	16/4	17/3	0.71
Δt surgery, min	241 (135-390)	232 (100-350)	0.77

Table 2. Hemodynamic assessment and safety, TPVB Group *vs* MTPB Group.

	TPVB Group n=20	MTPB Group n=20	p (t-test)
ΔMAP>20%, %	25	5	0.042
Methylene bleu (MB) visible, %	100	0	-
Pleural puncture, %	10	0	0.162
Chest wall hematoma, %	0	0	

nificant statistical difference, p=0.042 (Table 2). Two inadvertent pleural punctures were detected in patients in TPVB Group while no puncture was detected in patients in MTPB Group (Table 2). No chest wall hematomas were detected in the two groups. No failure of the technique was described in the two groups. MB was evident in all patients of the TPVB Group, albeit with different spreading patterns, in contrast no MB was visible in any patient in MTPB Group. The average intraoperative consumption of remifentanil was 2.6 µg/kg/h in TPVB Group, while it was 5.2 µg/kg/h in MTPB Group, with a significant difference, p=0.00007 (Table 3). The percentage of NOL time over 25 during surgery was 15.8% in TPVB Group and 23,6% in MTPB Group, with a significant statistical difference, p=0.011 (Table 3). 60' VAS after surgery was 2.2 in TPVB Group and 4.4 in MTPB Group, with a significant higher rate of rescue therapy in MTPB Group, p=0.005 (Table 3).

Discussion

In this study we compared the hemodynamic impact of TPVB *vs* MTPB in mini-invasive lung resection surgery. Our hypothesis was that MTPB had a minor hemodynamic impact than TPVB, due to a minor and slower anesthetic spread in the TPVS[15] with a consequent sparing of sympathetic block, just like TPVB keeps hemodynamic more stable compared to TEA.[8] Our secondary outcome so was to evaluate if this minor and slower spread of the anesthetic solution in the TPVS in MTPB, and its consequent sympathetic block sparing, could determine a sufficient analgesic effect in the patient.[16] Neuraxial blocks, (like spinal anesthesia, TEA, TPVB), are frequently associated with hypotension[8] causing an imbalance between sympathetic and parasympathetic systems in favor of the parasympathetic tone.[17] The consequences are bradycardia and hypotension.[17-25] Drop in blood pressure is a consequence of arterial and arteriolar vasodilation in the regions concerned by the block, compensatory augmentation of sympathetic arterial vascular tone in the regions not subject to the block through a baroreflex (usually more effective in younger patients)[17,26] and the interest of the venous reservoir, pooling blood in the capacitance vessels in the lowermost regions.[17,26-28] All of this, in addition to the restrictive fluid management usually employed in thoracic surgery[8,17,29] can lead to severe hemodynamic instability, therefore PACTS recommends the use of TPVB in preference to TEA in locoregional anesthesia for VATS,[1] considering their comparable efficacy for the management of intraoperative and postoperative pain in thoracotomy patients[1,30-36] and fewer intraoperative complications than TEA.[1]

Costache *et al.* described that MTPB mimics TPVB, but with injection point within the thoracic intertransverse tissue complex and posterior to the superior costotransverse ligament (SCTL)[9] defining MTPB as a chest wall block with the same effects of TPVB, in consideration of the anesthetic solution spread in the TPVS[9,10] so we focused on the hemodynamic impact of MTPB *vs* TPVB, hypothesizing that the anesthetic spread in the TPVS could be less important in MTPB causing a better hemodynamic stability than TPVB. To check if the chest wall block was successful, we add a low dose of MB to the anesthetic solution during the performance of the blocks. When the TPVB is successful, MB is visible in PVS and in the intercostal spaces during VATS (Figure 2), consequently to the anesthetic solution spread in these spaces. MB is a cationic thiazine dye, widely used as a biological stain and chemical indicator; it is applied as a dye to mark and visualize a certain tissue or region in the clinical and experimental settings.[37] MB has been and is used with beneficial effects to lessen pain in some pathologic conditions such as chronic discogenic low back pain (CDLBP),[37,38] oral mucositis-related intractable pain[37,39] and intractable and idiopathic *Pruritus Ani*.[37,40] The beneficial analgesic result of MB is mediated by anti-inflammation effect, sodium current reduction and denervation.[37]

In consideration of the limits of the fluid management optimization imposed by this kind of surgery and the specifics of patients (sometimes characterized by various elements of frailty), we decided to consider as clinically significant a restrictive cut-off for MAP decrease after the chest wall block, so we fixed it to 20% of MAP decrease. In our experience we obtained a relevant MAP decrease in 25% of patients of the TPVB group, despite 5% of patients of the MTPB group, so patient's hemodynamic impact is lower in MTPB than TPVB. The MTPB is performed staying with the needle tip to a greater distance to pleura, reducing the risk of pneumothorax. In our experience, no pneumothorax, nor chest wall hematomas were detected in both the two groups of patients and, although two accidental pleural punctures were reported in TPVB group, no significant reduction of incidental pleural puncture was reported in MTPB group. Both approach to the TPVS seems to have comparable security profiles in term of pneumothorax, pleural puncture and chest wall hematoma, as exposed in our results.

Nociception was intraoperatively continuously monitored with PMD200 (Medasense, Ramat Gan, Israel). NOL index allows us to titrate precisely the opioid needing of the patient in the different times of surgery,[41] avoiding undertreatment and overtreatment of analgesia. Having feedback by the trend and the value of NOL index allowed us to test if our chest wall block was successful or not and to anticipate hemodynamic reactions caused by pain. As NOL index was >25 for more than 1 minute, we increased the remifentanil infusion of 1 ng/mL until the NOL was again in the range of 10-25. In the other hand, the intraoperative use of NOL index as our nociception monitor allowed us to consider hypotension events for opioid overdosing as a negligible confounding factor in the analysis of hemodynamic response in the two types of chest wall block.

We found that in TPVB group NOL index was noticeably lower than in MTPB group, consequently remifentanil consumption to get 10 ≤NOL index ≤25 was noticeably higher in MTPB group than TPVB. VAS values registered at 1 hour after the end of surgery also were higher in MTPB group than TPVB. Despite these data, the consumption of morphine in the postoperative period was comparable. According to our data, antalgic power of TPVB is superior to MTPB while MTPB has a better hemodynamic stability and safety profile than TPVB, ultimately proving to be a less effective blockade but with greater safety margins. This could be explained by a slower reaching of the target in the

Table 3. Evaluation of analgesic effectiveness, TPVB Group *vs* MTPB Group.

	TPVB Group n=20	MTPB Group n=20	p (t-test)
Remifentanil (µg/kg/h)	2.6 (2-4)	5.2 (2-9)	0.00007
Δt% NOL>25 (%)	15.8 (9-27)	23.6 (9-38)	0.011
VAS (t=1 h)	2.2 (0-5)	4.4 (2-6)	0.005

paravertebral space by the anesthetic solution, that in MTPB is probably caused by a double passage of the anesthetic solution firstly across the SCTL and its gaps and fenestrations, and then in the TPVS, that maybe could not produce a bulk flow and a useful spread of the anesthetic solution.[15] In our study this double passage could not happen at all: for any MTPB performed, in fact, our intraoperative check during VATS showed no methylene blue in the TPVS or in the intercostal spaces across the pleura, so it didn't spread in these spaces. The interindividual anatomical variability of the TPVS with his consistency of the tissue and the SCTL's gaps and fenestrations could play a significant role by influencing the spread of the anesthetic solution after injection behind it. In the postoperative time the comparable consumption of morphine indicates a good analgesic long term coverage. Maybe the double passage to the TPVS and the slow spread of the anesthetic solution across the SCTL determine an insufficient level of analgesia during the time of surgery, but a sufficient antalgic cover in the postoperative time, because of the longer time that the anesthetic solution needs to reach the target of the TPVS and the consequent longer onset time of the block, despite the fact that the dye never appeared in the TPVS even hours after the start of surgery. We also hypothesize that MTPB doesn't produce a useful block of somatic intercostal nerves for the time of surgery and that it produces a negligible sympathetic block than TPVB for a minor and slower anesthetic spread in the TPVS. The minor sympathetic block in MTPB and its slower onset time could also explain because patient's hemodynamic assessment was better in MTPB group than TPVB one. The minor sympathetic block could also be one of the reasons of the lower antalgic power of MTPB than TPVB during surgery.

In conclusion, evaluating benefits and risks in thoracic surgery of the two types of chest wall blocks studied, we conclude that MTPB offers more hemodynamic stability and a higher safety profile in preventing pneumothorax, inadvertent pleural puncture and chest wall hematoma, despite a noticeable lower intraoperative antalgic efficacy than TPVB. Analgesia plays a significant role in thoracic surgery, by influencing the patient's postoperative ability of breathing, coughing, and expectorating. Furthermore, chronic pain is an important complication of patients undergoing to thoracic surgery, occurring in up then 20% of patients.[42] In thoracic surgery, finally, the clinical risks and complications of pleural puncture and pneumothorax are shot down by the routinely creation of iatrogenic pneumothorax and the consequent placement of a chest drainage at the end of the surgery. For these reasons, according to our data, our analysis and our clinical experience, TPVB is more useful than MTPB in patients undergoing to mini-invasive thoracic surgery. Maybe, for its higher safety profile, MTPB could be useful in breast surgery, but according to our opinion it is necessary to anticipate the time of the block before the surgery, considering the slower onset time, and it is necessary to perform multiple injections at the level of different metamers to promote the spread of the anesthetic solution. Finally, further studies are needed to clarify the mechanism of action of the MTPB.

Limits

The limits of this study were the retrospective nature, the operator depending execution of the chest-wall block, the restrictive cut-off chosen for the range of hypotension (although we have managed to eliminate several confounding factors) and the small sample analyzed.

To reduce the influence of the operator depending execution in our study, all the blocks were performed by an experienced anesthetist and then the performances were reviewed, after the local anesthetic injection was recorded, by a second ultrasound experienced anesthetist blinded to patient's name, who checked the correct placement of the needle tip in TPVB Group and in MTPB Group.

By monitoring nociception intraoperatively and continuously with PMD200 (Medasense, Ramat Gan, Israel) and analyzing the NOL index, in fact, we were able: to titrate the opioid needing of the patient in the different times of surgery[41] (avoiding undertreatment and overtreatment of analgesia), to test if our chest wall block was successful or not, to anticipate hemodynamic reactions caused by pain, to consider hypotension events for opioid overdosing as a negligible confounding factor and finally to discriminate if an hemodynamic reaction was caused by pain or not.

Our results must consider the small sample used and further studies are needed to better understand the issue treated.

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