In dogs, radical mastectomy (ie, surgical excision of all mammary glands on one or both sides of the body) is most often performed as a surgical treatment for mammary neoplastic processes. This surgery is usually associated with high levels of pain and stress, and additional techniques to mitigate pain during and after surgery would be clinically useful. A thoracic paravertebral block (TPVB) consists of injection of a local anesthetic within the so-called thoracic paravertebral space (TPVS), where the spinal nerve roots and the sympathetic chain with its communicating branches lie. In people, this locoregional technique is mainly used to provide unilateral somatic anesthesia of the thoracic wall. Several techniques have been described for performing a TPVB in humans and small animals but not all of them consistently resulted in a multisegmental nerve blockade after a single injection. In a recent cadaveric study, use of a loss-of-resistance to air injection technique resulted in effective localization of the TPVS and multisegmental dye spread in all subjects.

The innervation of the mammary glands in dogs is provided by the cutaneous branches of the ipsilateral thoracic spinal nerves from T4 to T13 and by the first three lumbar spinal nerves. In a recently published case series, a combination of multiple locoregional techniques showed the potential to reduce pain and
discomfort associated with radical mastectomy. With its multisegmental spread and the potential to block the sympathetic chain, a single-injection caudal TPVB represents an intriguing alternative to provide analgesia during and after this surgical procedure.

The objective of the study reported here was to test the clinical and analgesic effects of a single-injection caudal TPVB after localization of the TPS with a loss-of-resistance-to-air injection technique in female dogs undergoing unilateral radical mastectomy. Our hypothesis was that there would be a reduction in intraoperative nociception, superior recovery quality, and better postoperative pain control in dogs receiving the TPVB, compared with dogs in a control group.

Materials and Methods

The study was designed as a randomized, controlled clinical trial. The study design was approved by the Ethical Committee of the Veterinary Teaching Hospital of the University of Turin (protocol No. 1516/2020). Written informed consent was obtained from the owners of all dogs included in the study.

Study population

Client-owned, mixed-breed or purebred dogs admitted to a veterinary general practice (Ambulatorio Veterinario, Iglesias, Italy) between August and November 2020 because of a mammary gland tumor were eligible for inclusion in the study. Dogs enrolled in the study were scheduled for tumor staging and unilateral radical mastectomy. All dogs underwent a physical examination, CBC, serum biochemical analyses, 3-view thoracic radiography, and abdominal ultrasonography. Dogs with evidence of clinical abnormalities other than the neoplastic process or with lesions compatible with mammary gland tumor metastasis were excluded from the study.

Study protocol

Enrolled dogs were randomly allocated to 2 groups with an intended allocation ratio of 1:1 through the use of standard software (www.randomization.com). After catheterization of a cephalic vein, methadone (0.2 mg/kg) was administered IV, and 15 minutes later; anesthesia was induced with propofol administered IV to effect. An orotracheal tube was placed, and anesthesia was maintained with sevoflurane in oxygen. Vital parameters (ECG, oxygen saturation as measured with pulse oximetry, end-tidal partial pressure of carbon dioxide, end-tidal fractional concentration of sevoflurane, inspired fraction of oxygen, blood pressure [measured noninvasively], and esophageal temperature) were monitored with a multiparametric monitor (Carescape B450; GE Healthcare). Once the plane of anesthesia was deemed adequate and stable (approximately 10 minutes after anesthetic induction), the dorsal thoracolumbar parasagittal area ipsilateral to the affected mammary glands was clipped and surgically scrubbed. Dogs then received the assigned treatment for their group.

TPVB group

The procedure for administering a TPVB was similar to that described recently.25 A cutaneous mini-cutdown was performed, and a 20- or 22-gauge Tuohy needle was inserted 2 to 2.5 cm lateral to the spinous process of T13, parallel to the median plane, and advanced toward the head of the last rib. Once the bony structure was encountered, an 8-mL loss-of-resistance syringe (Periflex LOR syringe; B. Braun) primed with 6 to 8 mL of air was connected to the needle. Then, while intermittent pulsations were applied to the syringe plunger, the tip of the needle was walked off the head of the rib and advanced in a cranioventral direction until a substantial change in resistance to air injection was detected (Figure 1). Aspiration was performed, and if no blood or air was observed in the needle hub or syringe, ropivacaine (0.6 mL/kg of a 1% solution diluted with sterile saline [0.9% NaCl] solution to a concentration of 0.4%) was injected within 1 minute. The needle was then withdrawn, and a 5 X 5-cm patch (Fixomull stretch; BSN Medical) was applied to the paravertebral skin to hide and protect the small skin incision. All TPVBs were performed by a single individual (PD); performing each block required < 10 minutes.

Control group

No paravertebral injection was performed in dogs in the control group. However, for blinding purposes, the same protective patch used in the TPVB group was applied on the paravertebral skin, and the dogs were maintained in lateral recumbency for 10 minutes.

Surgical procedure and anesthetic monitoring

After the group-specific intervention, dogs were positioned in dorsal recumbency for surgical site preparation (approximately 15 minutes) and transferred to the operating room, where anesthetic monitoring was performed by an individual blinded to the group allocation. An elliptical skin incision extending from 2 to 3 cm cranial to the first nipple to 2 to 3 cm caudal to the last nipple was performed. Medially, the incision extended to the midline; laterally, the incision extended the same distance as used to calculate the medial extent.

During the intraoperative period, patients were mechanically ventilated (Carestation 620; GE Healthcare) with 40% O₂ at a tidal volume of 10 to 15 mL/kg and respiratory rate of 8 to 20 breaths/min to maintain normocapnia. Lactated Ringer solution was administered at a rate of 5 mL/kg/h. The aforementioned vital parameters and ventilation parameters (tidal volume, peak inspiratory pressure, and end-expiratory pressure) were recorded every 5 minutes from the induction of anesthesia until extubation. Values recorded

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5 minutes before the initial skin incision were defined as preincisional values. If cardiovascular parameters (heart rate [HR] and noninvasively measured blood pressure) increased by more than 30% of the preincisional values, fentanyl (2 μg/kg) was administered IV over 1 minute. During the preoperative and intraoperative periods, if mean arterial pressure was < 60 mm Hg for more than 5 minutes, hypotension was considered to be present, and the anesthetic plane was evaluated. If the anesthetic plane was deemed adequate, a bolus of lactated Ringer solution (5 mL/kg) was administered IV over 5 minutes. If this intervention failed to reduce the HR or increase the mean arterial pressure, the hypotension was deemed unlikely to be related to a preload deficit, and ephedrine (50 μg/kg) was administered IV. If the HR was < 45 beats/min for more than 5 minutes, bradycardia was deemed to be present, and atropine (20 μg/kg) was injected IV. In all dogs, meloxicam (0.2 mg/kg, IV) was administered 30 minutes before the end of surgery.

Postoperative procedures

Quality of recovery from anesthesia was scored in all patients on a scale from 1 to 6 with a previously published simple descriptive scale14 (Appendix). Severity of postoperative pain was assessed with the short form of the Glasgow Composite Pain Scale; all scores were assigned by a single trained individual who was unaware of group allocation. The first score was assigned as soon as dogs were considered conscious and fully recovered from anesthesia (ie, capable of lifting the head, able to regain sternal recumbency, aware of surroundings, and responsive to stimuli). For all time points, no treatment was administered if the score was < 6 on a scale from 0 to 24 or < 5 on a scale from 0 to 20, and the pain assessment was repeated after 1 hour. If a score ≥ 6/24 or ≥ 5/20 was assigned, methadone (0.2 mg/kg, IV) was administered over 1 minute, and the pain assessment was repeated after 30 minutes. In patients that still had pain scores ≥ 6/24 or ≥ 5/20 after 3 boluses of methadone had been administered within 4 consecutive hours, rescue analgesia was provided. This consisted of IV constant rate infusions of fentanyl (2 μg/kg bolus followed by 2 to 5 μg/kg/h, titrated to effect) and ketamine (0.5 mg/kg bolus followed by 0.5 mg/kg/h). For all dogs requiring this rescue analgesic protocol, the study was considered concluded. These dogs were kept hospitalized overnight and slowly weaned off the infusions according to their pain scores. In dogs not requiring a rescue analgesic infusion, the study was considered concluded 5 hours after the first postoperative pain assessment.

Outcome measures

Intraoperative antinociceptive efficacy of the studied treatment was evaluated with an intervention-based approach. For this purpose, the intraoperative
The fentanyl dose administered was chosen as the outcome variable. When considering postoperative analgesic effects, both the dose of methadone and pain scores were considered. The quality of recovery from general anesthesia was also used as an outcome measure. Differences between groups in terms of adverse events such as bradycardia and hypotension that required intervention were also analyzed.

**Statistical analysis**

A minimum required sample size of 20 dogs was calculated with commercial software (StatMate, version 2.0; GraphPad), assuming an \( \alpha \) error probability of 5% and statistical power of 80%. However, during the study, differences between groups were greater than initially estimated, and after a post hoc power calculation was performed, the total number of animals enrolled in the study was reduced for ethical reasons.

Owing to the small sample size, all variables were considered to not be normally distributed.\(^{15}\) The Mann-Whitney \( U \) test was used to assess differences between groups for the following variables: age, body weight, dose of propofol used for anesthetic induction, surgical time, mean intraoperative end-tidal fractional concentration of sevoflurane, intraoperative fentanyl dose, postoperative methadone dose, recovery score, and pain scores at the time of and 1 hour after extubation. Data are expressed as median and range. Values of \( P < 0.05 \) were considered significant. All statistical analyses were performed with standard software (Prism, version 8.0; GraphPad).

**Results**

Sixteen dogs were considered for inclusion in the study, but 2 were excluded because of comorbidities. The remaining 14 dogs were enrolled in the study, with 8 randomly assigned to the TPVB group and 6 assigned to the control group.

Eleven of the 14 dogs included in the study were of mixed breed; all dogs were assigned an American Society of Anesthesiologist physical status score of 2.

Table 1—Findings for 14 dogs undergoing unilateral radical mastectomy that, preoperatively, received a single-injection caudal thoracic paravertebral block (TPVB) after localization of the thoracic paravertebral space with a loss-of-resistance to air injection technique (\( n = 8 \)) or did not receive a paravertebral block (control; 6).

<table>
<thead>
<tr>
<th>Variable</th>
<th>TPVB group</th>
<th>Control group</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mon)</td>
<td>144 (132–204)</td>
<td>168 (156–180)</td>
<td>0.217</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>10.5 (5.3–20.1)</td>
<td>6.7 (2.9–8.9)</td>
<td>0.081</td>
</tr>
<tr>
<td>Propofol (mg/kg)(^a)</td>
<td>2.50 (2.00–3.78)</td>
<td>2.35 (1.70–2.60)</td>
<td>0.437</td>
</tr>
<tr>
<td>Surgical time (min)</td>
<td>50.5 (43–53)</td>
<td>53.0 (35–64)</td>
<td>0.596</td>
</tr>
<tr>
<td>End-tidal sevoflurane (%)</td>
<td>2.3 (2.2–2.5)</td>
<td>2.3 (2.2–2.4)</td>
<td>0.674</td>
</tr>
<tr>
<td>Intraoperative fentanyl (( \mu )g/kg)</td>
<td>0 (0–2)</td>
<td>4 (2–6)</td>
<td>0.005</td>
</tr>
<tr>
<td>Recovery score(^c)</td>
<td>1.5 (1–2)</td>
<td>4.5 (3–5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Postoperative methadone (mg/kg)</td>
<td>0 (0–0.2)</td>
<td>0.6 (0.4–0.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Pain score(^d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At extubation</td>
<td>1.5 (1–3)</td>
<td>9.5 (2–11)</td>
<td>0.003</td>
</tr>
<tr>
<td>1 h after extubation</td>
<td>3 (1–8)</td>
<td>7 (3–9)</td>
<td>0.038</td>
</tr>
</tbody>
</table>

Data are given as median (range).

\(^a\)Dose of propofol needed for anesthetic induction. \(^b\)Mean intraoperative end-tidal fractional concentration of sevoflurane. \(^c\)Assigned on a scale from 1 to 6. \(^d\)Assigned by use of the short form of the Glasgow Composite Pain Scale on a scale from 0 to 24.

Figure 2—Mixed box-and-whisker plots and scatterplots depicting postoperative pain scores (assigned with the short form of the Glasgow Composite Pain Scale [GCPS-SF]; potential range, 0 to 24) for 14 dogs undergoing unilateral radical mastectomy that, preoperatively, received a single-injection caudal TPVB after localization of the thoracic paravertebral space with a loss-of-resistance to air injection technique (\( n = 8 \)) or did not receive a paravertebral block (control; 6). The first score was assigned as soon as dogs were considered conscious and fully recovered from anesthesia (t\(_0\)), with additional scores assigned every hour thereafter (t\(_1\) through t\(_5\)). At t\(_2\) and t\(_3\), 3 and 1 dogs, respectively, in the control group required rescue analgesia and were excluded from the study. The horizontal dotted line represents the threshold for administration of methadone (0.2 mg/kg, IV) to provide additional analgesia. *Pain scores differed significantly (\( P < 0.05 \)) between groups.
not receive fentanyl intraoperatively, and the remaining 3 received a single bolus. Two dogs in the control group received a single bolus of fentanyl intraoperatively, 2 received 2 boluses, and the remaining 2 received 3 boluses. None of the dogs in either group received atropine intraoperatively, and only 1 dog (control group) received ephedrine intraoperatively.

Five of the 8 dogs in the TPVB group did not receive methadone postoperatively, and the remaining 3 received a single bolus. In contrast, 1 dog in the control group received 2 boluses of methadone, and the remaining 5 received 3 boluses. None of the dogs in the TPVB group required rescue analgesia. Three dogs in the control group required rescue analgesia between 1 and 2 hours postoperatively, and 1 additional control dog required rescue analgesia between 3 and 4 hours postoperatively. Following the exclusion of these dogs from the study, statistical analysis of the difference in post-operative pain scores was concluded.

Discussion

Results of the present study indicated that the single-injection caudal TPVB improved pain control and recovery quality in female dogs undergoing unilateral radical mastectomy. The size of the observed effect in the TPVB group was sufficiently large to allow us to reduce the number of patients enrolled in the study from our initial goal of 20 dogs. The resulting small sample size could be considered a limitation of the study. However, reducing the number of dogs in the study was in line with standard ethical principles. Although we did identify significant differences between groups, our results may not apply to different populations. Therefore, further studies are required to confirm our findings.

The exact mechanism of action of the TPVB is still not fully understood. Previous cadaveric studies investigating the spread of various injectates within the TPVS showed consistent findings in terms of longitudinal staining of the sympathetic trunk and different findings in terms of staining of contiguous intercostal nerves. When dissecting the TPVS from a dorsal approach after injection of a dense medium, only a single intercostal nerve appeared stained. On the basis of this finding, the most plausible mechanism of action for the TPVB is blockage of the sympathetic trunk. However, results of our study seem difficult to interpret in light of this hypothesis. On the one hand, blockage of the sympathetic trunk would likely explain the higher intraoperative stability of dogs in the TPVB group, but on the other hand, this blockade would not completely explain the lower postoperative pain scores. Similarly, in several human studies, a single injection in the extrapleural compartment of the TPVS resulted in a multisegmental somatic block. The role of the sympathetic nervous system in acute pain modulation is controversial and still not completely understood.

However, intraoperative inhibition of the sympathetic response has been associated with a reduction in the dose of postoperatively administered opioids in humans. Because the TPVB involves only a single injection, does not take long to perform, and requires only readily available low-cost equipment, the technique may be a valuable option in both referral and first-opinion practice for dogs undergoing radical mastectomy. The advantages of ultrasound-guided locoregional analgesic techniques are well known, and the choice of a blind approach could be considered a limitation of this technique. Although data in dogs concerning the incidence of TPVB-related complications, such as inadvertent intravascular or interpleural injection, pneumothorax, and nerve injury, are currently lacking, complications could potentially be minimized through the use of ultrasound guidance. However, ultrasound-guided approaches described to date for the TPVB in dogs rely on visualization of the parietal pleura as the ventral anatomical limit of the TPVS. At the most caudal thoracic paravertebral level, the proximal insertions of the quadratus lumborum muscles become part of the normal sonoanatomy of the area, making correct identification of the TPVS more challenging. Moreover, to date, no study has described the ultrasonographic approach for the TPVB at this caudal level. Results of the present study suggest that the loss-of-resistance-to-air injection technique might be a valid alternative technique to ultrasound guidance for the TPVB.

Pain scoring was discontinued 5 hours after the first postoperative pain assessment in the present study for practical clinical reasons. As a standard procedure of the practice where the study was conducted, patients not showing any signs of moderate or severe pain were typically discharged at that time. On the basis of this criterion, all dogs in the TPVB group were deemed eligible for discharge at the end of the study. However, this relatively short postoperative hospitalization time represented another important limitation of our study. In particular, it was not possible to determine the clinical duration of the TPVB, which to our knowledge has never been investigated in dogs.

In the present study, 3 dogs in the TPVB group required a single intraoperative fentanyl bolus, and 3 dogs received a single postoperative dose of methadone. A possible explanation for these findings could be dilution of the local anesthetic that was used. A total injection volume of 0.6 mL/kg was chosen to achieve longitudinal spread of the solution. As a consequence, reducing the concentration of the local anesthetic was deemed necessary to maintain a subtoxic dose. Data about the effective concentration of ropivacaine used for this purpose in dogs are lacking, and the dilution used in this study might be inadequate for some surgical nociceptive stimuli. Other factors that could explain the need for additional analgesia in some dogs in the TPVB group are a failure of the block or partial blockade owing to variability of
the local anesthetic spread pattern among dogs\textsuperscript{9,11,16} and the high number of dermatomes requiring blockade for this procedure.

In conclusion, a single-injection caudal TPVB performed with a loss-of-resistance to air injection technique resulted in lower perioperative opioid requirements, better recovery quality, and lower postoperative pain scores in female dogs undergoing unilateral radical mastectomy.

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References


Appendix

Descriptive scoring system used to evaluate the quality of recovery from anesthesia in dogs.\textsuperscript{14}

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Early: extubated; easy transition to alertness; coordinated movement.</td>
</tr>
<tr>
<td>2</td>
<td>Early: fairly easy transition; holds head up; no body movements attempted.</td>
</tr>
<tr>
<td>3</td>
<td>Late: holds head up; no body movements.</td>
</tr>
<tr>
<td>4</td>
<td>Late: alert; coordinated movement.</td>
</tr>
<tr>
<td>5</td>
<td>Some incoordination; does not startle; generally quiet.</td>
</tr>
<tr>
<td>6</td>
<td>Late: holds head up; no body movements.</td>
</tr>
<tr>
<td>7</td>
<td>Limited muscle control; startles; may paddle or whine.</td>
</tr>
<tr>
<td>8</td>
<td>Uncoordinated whole-body movements; startles; vocalizes.</td>
</tr>
<tr>
<td>9</td>
<td>Emergence delirium; thrashing; cannot easily restrain.</td>
</tr>
</tbody>
</table>

Early refers to the time of extubation and the time immediately after. Late refers to the time after the dog has been moved to the recovery area.