Increasing evidence implies the existence of a visceral pain pathway in the dorsal column of the spinal cord. Limited midline myelotomy has been used to treat intractable pelvic cancer pain. However, no obvious evidence has been provided that high cervical punctate midline myelotomy (CPMM) relieves visceral pain originating from the abdomen. This study was designed to examine the pain relief effect of CPMM in a mouse model of visceral pain. Thirty-six Institute of Cancer Research (ICR) mice were divided into three groups: Group 1, healthy controls; Group 2, treated with CPMM at C1 and C2; and Group 3, a sham group that underwent laminectomy at C1 and C2 without CPMM. All animals were tested for antinociception in the writhing test 24 hours after surgery. Visceral pain-related behaviors were counted from 5–20 minutes after intraperitoneal injection of 0.6% acetic acid. Writhing test scores were not significantly different between Groups 1 (56.7 ± 10.7) and 3 (50.7 ± 17.4). However, Group 2 (30.0 ± 14.3) showed more than 40% antinociception after treatment, and writhing test scores were significantly different from those of Groups 1 and 3 (p < 0.001). Our results confirm that midline punctate myelotomy can relieve visceral pain and imply that there is a pathway in the posterior funiculus that signals visceral pain. Punctate midline myelotomy at the cervical or high thoracic level may be an alternative strategy in the management of intractable visceral pain due to abdominal or pelvic cancers.

Key Words: midline myelotomy, visceral pain, writhing test

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of high cervical punctate midline myelotomy (CPMM) in the treatment of visceral pain originating from oncogenic pain in the abdomen and/or pelvis is still controversial. In order to evaluate the possibility of using CPMM in releasing intractable cancer-related visceral pain and to investigate the signaling pathways of visceral pain, it is necessary to develop an animal model. Our study was designed to develop a new animal model to examine the antinociceptive effect of CPMM in the treatment of visceral pain.

**Materials and Methods**

**Animals**
A total of 36 male Institute of Cancer Research (ICR) mice weighing 26–34 g were used in this study. Surgical and experimental protocols were approved by the Kaohsiung Medical University Animal Research Committee. Animals were divided into three groups: Group 1, healthy controls; Group 2, mice undergoing CPMM at C1 and C2; and Group 3, sham mice that underwent laminectomy at C1 and C2 without CPMM.

**Surgical Preparation**
Mice were anesthetized with chloral hydrate (350 mg/kg intraperitoneally) and xylazine (4 mg/kg intraperitoneally) in the right lower quadrant of the abdomen. Animals were subsequently placed in a prone position with the head flexed below the horizontal by approximately 30°. With the aid of a Zeiss OPM 212–7 operating microscope (Zeiss, Oberkochen, Germany), the C1 and C2 laminae were exposed after dissection of the muscle layers. After C1–C2 laminectomy and longitudinal opening of the dura, the arachnoid and septum posticum were incised using a 30-gauge needle. The exact midline of the spinal cord was determined by measuring midway between the two root entry zones. With the aid of the operating microscope and after deposition of the dorsal vein, CPMM was performed at C1–C2 using a 30-gauge needle with a mark 1 mm from the beveled tip. Midline punctate was performed in the sagittal plane of the median septum to a depth of 1 mm. The incision was closed with sutures once hemostasis was achieved. The entire procedure was completed within approximately 15–20 minutes. After surgery, animals were monitored closely for respiratory distress. Body temperature was maintained at 37 ± 1°C until the animals were fully awake from the anesthesia. In the sham group, animals underwent C1–C2 laminectomy without CPMM.

**Behavioral Tests**
Each mouse was placed in a 30 x 30 x 30 cm polypropylene box and initially allowed 30 minutes to get used to its surroundings. Behavioral investigators were blinded to the treatment groups. Twenty-four hours after surgery, animals were intraperitoneally injected with 0.6% acetic acid (0.1 ml/10 g) in the left lower quadrant of the abdomen. Visceral pain-related behaviors (licking abdomen, stretching, contraction of abdomen, and so on) were counted between 5 and 20 minutes after injection.

**Statistical Analysis**
Group data are expressed as mean ± standard deviation of the mean. For group comparisons, analysis of variance was performed with Bonferroni post-hoc tests. Differences were considered statistically significant at p values of less than 0.05.

**Results**
None of the 24 animals undergoing surgery died or had neurologic deficits. Writhing test scores were not significantly different between Groups 1 (56.7 ± 10.7) and 3 (50.7 ± 17.4). However, Group 2 showed more than 40% antinociception after treatment (30.0 ± 14.3), which was significantly different from the scores in the other two groups (p < 0.001).

**Discussion**
Visceral pain in patients with advanced cancer is difficult to control with either medication or surgery. Commissural myelotomy is relatively effective for midline pain of several spinal segments, but it has significant complications including a decrease in proprioception, dysesthesia, transient paresis, sphincter dysfunction, and even death [14]. The poor localization of spinal segments responsible for visceral pain and the increased surgical risk of extended commissurotomy of more than four segments also limit the use of midline commissural myelotomy. Limited midline myelotomy at C1, introduced by Hitchcock [8], is performed stereotactically and has surprisingly wide-
spread visceral pain relief. In order to reduce the risk of respiratory complications and upper limb sequelae, the spinal cord is placed under direct visual control [9, 10, 15]. CPMM at the thoracic cord also provides surprisingly widespread visceral pain relief while decreasing proprioceptive or other complications [9–13, 15]. In mice with experimental pancreatitis, dorsal column lesions at C1 could reverse the reduction in homecage activity [16]. This implies that dorsal column lesions are involved in transmitting nociceptive signals from the pancreas to the brain. Taking these findings together, the dorsal column may be the major pathway of visceral pain. Theoretically, a midline lesion would interrupt the visceral pathways that enter and ascend from the spinal cord below the lesion.

Our results showed satisfactory relief of visceral pain by CPMM. Mice undergoing CPMM had more than 40% antinociception after treatment, with significantly different writhing test scores compared with control and sham groups. CPMM is a simple, effective, and safe procedure. Although CPMM is a neuroablative procedure and adverse complications or sequelae may occur, our method did not result in any obvious neurologic complications. CPMM may enable cancer patients to tolerate severe cancer pain and provide them with a better quality of life. Our results also confirmed that there is a posterior column sensory pathway that mediates visceral pain.

REFERENCES