

# Lactate Levels in Bowel Strangulation With Experimental Animal Model

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Bowel strangulation is a common disease and often requires an urgent operation. Our previous report showed that lactate concentration in the blood is a good predictive marker for emergency. However, the alteration in lactate levels during the course of bowel strangulation remains unclear. We have investigated the progressive increase of lactate after induction of bowel strangulation with animal experiments. Thirty-six mice were randomly divided into 6 groups: 0, 8, 16, 24, 48, and 72 hours after operation. Under anesthesia, laparotomy was performed and a 5-cm segment of terminal ileum with the mesenteric artery and veins was ligated to create a strangulation obstruction. After operation, the arterial blood was collected and lactate concentration and pH were measured using a blood gas analyzer. Lactate concentration in the 8-hour group was markedly increased, while pH decreased significantly ( $P < 0.05$ ). Lactate concentrations were kept at a high level from 8 to 72 hours after operation. The time lag between strangulation and an increase of lactate is 8 hours. Our study is the first report of a bowel strangulation mouse model. Therefore, it would be possible to find a more specific marker of bowel strangulation using our experimental model.

*Key words:* Bowel strangulation – Lactate – Blood gas analyzer – Animal model

Bowel strangulation is a common but very serious condition. Although some patients of it can be cured with a safe nonoperative management, others require an emergent operation. Therefore, an accurate and prompt diagnosis is important to consider an effective therapeutic

strategy. Several studies have proposed predictive factors including acidosis and serum concentrations of creatine phosphokinase, lactic dehydrogenase, and amylase.<sup>1–3</sup> Nonetheless, the early detection of bowel strangulation is often difficult, and reliable diagnostic information that may

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suggest its presence is required in clinical practice.

Lactate is a product of anaerobic metabolism of glucose, and its concentration in the arterial blood is a good indicator of the severity of metabolic acidosis secondary to tissue hypoperfusion. The time needed to normalize the serum lactate levels is an important prognostic factor for survival.<sup>4-7</sup> In ischemia associated with bowel strangulation, anaerobic metabolism causes an increase in the concentrations of lactate. We previously reported that lactate concentration is a good predictive factor for strangulation obstruction.<sup>8</sup>

However, the alterations of lactate concentration during the course of bowel strangulation remain unclear. In order to reveal various pathophysiological changes, including the alterations of lactate concentration after bowel strangulation, it is very profitable to develop a novel animal model, especially with a genetically controlled mouse. In the present study, the arterial blood was obtained from mice at designated times after they had undergone a procedure to cause the closed loop obstruction, and pH and lactate concentrations in it were measured by using a blood gas analyzer. We focused on the progressive increase of lactate during first 72 hours after induction of bowel strangulation.

## Materials and Methods

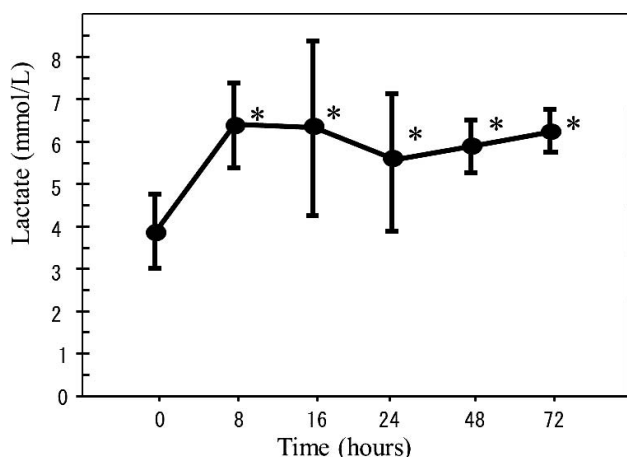
Twelve-week-old female C57BL/6J mice were used in this study. The present animal experiment was admitted by the animal experiment committee and was carried out in accordance with their guidelines. Thirty-six mice were randomly divided into 6 groups: 8, 16, 24, 48, and 72 hours after operation, and 0 hours (without operation) for control. Under ether anesthesia, laparotomy was performed and a 5-cm segment of the terminal ileum with mesenteric artery and veins was ligated to create a strangulation obstruction (Fig. 1). And then, the peritoneum and skin were sutured. At 8, 16, 24, 48, and 72 hours after operation, the arterial blood was collected from the tail artery, and the lactate concentration and pH of the blood sample were immediately measured by using a blood gas analyzer (ABL 800 FLEX; Radiometer Medical ApS, Brnshj, Denmark). Thereafter, during laparotomy under ether anesthesia, the strangulation was released and the strangulated bowel was examined for blood flow. Finally, the animals were sacrificed using CO<sub>2</sub>.



**Fig. 1** Creating bowel strangulation. Laparotomy was performed and a 5-cm segment of terminal ileum with mesenteric artery and veins was ligated to create a strangulation obstruction (arrow).

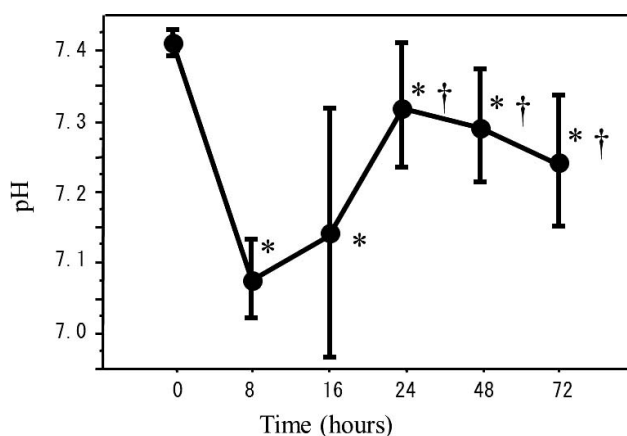
## Results

In the control group (0 hours), the mean value and standard deviation of lactate concentration in the arterial blood were  $3.850 \pm 0.357$  mmol/L and those of pH were  $7.414 \pm 0.005$ . Lactate concentration in the arterial blood was markedly increased in the 8-hour group, while pH decreased significantly (both,  $P < 0.05$ ,  $t$  test) (Figs. 2, 3). Lactate concentrations were kept at a high level from 8 to 72 hours after operation and no significant difference was found among them. The pH of the blood samples of 8 hours after operation group was decreased to  $7.076 \pm 0.021$ , indicating acidosis. Interestingly, the pH

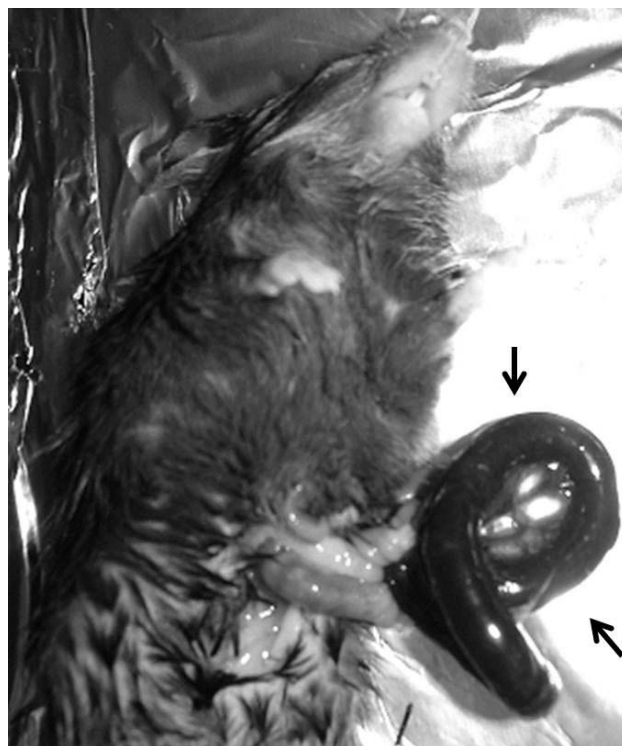


**Fig. 2** Lactate concentration in the arterial blood after bowel strangulation. In the control group, lactate level averages ( $\pm$  SD)  $3.850 \pm 0.357$  mmol/L. At 8 hours after operation, lactate level increases significantly. Lactate levels from 8 to 72 hours were not different significantly. \*  $P < 0.05$  versus 0 hours.

was elevated to  $7.325 \pm 0.035$  in the blood samples of the 24-hour group, and the mice recovered from acidosis ( $P < 0.05$  against that of 8 hours,  $t$  test). Then, the pH of arterial blood was gradually decreased from 24 to 72 hours after operation. The strangulated bowels were never recovered from ischemia, in spite of the release of strangulation (Fig. 4).



**Fig. 3** Alteration of the pH values of the arterial blood after bowel strangulation. In the control group, pH averages ( $\pm$ SD)  $7.414 \pm 0.005$ . After strangulation, pH is decreased to  $7.076 \pm 0.021$  at 8 hours, significantly recovers at 24 hours, and then gradually drops again. \*  $P < 0.05$  versus 0 hours. †  $P < 0.05$  versus 8 hours.



**Fig. 4** Strangulated bowel 8 hours after operation. The strangulated bowel already shows necrosis (arrows).

## Discussion

Lactate is the product of anaerobic metabolism in the cell under hypoxia, and its concentration in the blood has been well correlated to survival from various forms of acute circulatory failures. First, blood lactate levels reflect not only the production but also the elimination of the molecule, and the lactate clearance can sometimes be protracted, especially in the presence of liver impairment. Second, sepsis can increase lactate production by increasing cell glycolysis. Third, increased lactate production in sepsis may result from other cellular alterations than hypoxia, in particular, the inhibition of pyruvate metabolism. Finally, lactate levels reflect only global changes but give no indication about the regional distribution of blood flow.<sup>7</sup>

It is conceivable that a progressive increase in lactate would result from strangulation. De Laurier et al.<sup>9</sup> reported that plasma lactate levels increased after 8 hours of experimental bowel strangulation in dogs, and several studies and experimental models have shown serum lactate levels to be useful in the accurate preoperative diagnosis of bowel strangulation.<sup>9–15</sup> In our studies, the time lag between

strangulation and increase of lactate is 8 hours. Lactate concentration was increased 2-fold at 8 hours and remained at a high level for 3 days. In contrast, pH decreased at 8 hours and recovered at 24 hours. We had no reports on bowel strangulation with mouse model,<sup>9,10</sup> but could demonstrate that our mouse model reproduced pathophysiological changes after bowel strangulation. This is the first report of bowel strangulation with mouse model.

Because the above findings are consistent with those from previous experimental models, it is possible to find a new specific marker of bowel strangulation by using our experimental model.<sup>9,10</sup>

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