ORIGINAL

Intestinal hypomotility due to longitudinal enterotomy can be alleviated by transverse closure

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Abstract : Background : Heineke-Mikulicz (HM) strictureplasty is commonly used to treat short stenoses in Crohn's disease. However, the degree to which intestinal motility is maintained remains unclear. We compared the peristalsis and transport capacity of the sutured intestines with HM configuration and transverse (TS) and longitudinal (LS) incisions. Methods : The intestinal diameter, intraluminal pressure, and bead transit time of each sutured group were compared with that of the non-treatment (NT) group in the isolated proximal colon of rats. Propulsive contractions were induced using hydroxy-α-sanshool (HAS), a constituent of Japanese pepper. Results : There was no change in the intestinal diameter between HM, TS, and NT groups ; however, it was significantly narrowed at the suture site and its distal side in the LS group. After HAS administration, the intestinal diameter at the suture site in the HM group was higher than that in the LS group. The intraluminal pressure was higher and the transit time was shorter in the HM group compared to those in the LS group. Conclusions : The HM configuration, which widens the incision site and distal diameter and shortens the cut surface of the circular muscle in the longitudinal direction, may help maintain basal and HAS-induced intestinal peristalsis and motility. J. Med. Invest. 70 : 180-188, February, 2023

Keywords **:** *Crohn's disease, Heineke-Mikulicz strictureplasty, intestinal motility, Kono-S anastomosis*

INTRODUCTION

Crohn's disease (CD) is an inflammatory bowel disease that is medically managed in the early, uncomplicated stages and surgically when there are complications (abscess, perforation, fistula, or obstruction). For bowel obstruction, strictureplasty is the procedure of choice. Strictureplasty is a bowel-sparing procedure used to avoid short bowel syndrome caused by extensive small bowel resection in patients with Crohn's. Several types of stenoplasties have been used, including Heineke-Mikulicz (HM, Fig. 1), Finney, and side-to-side isoperistaltic strictureplasty, with HM and Finney being the most common methods.

The HM technique was reported separately by Heineke in 1886 and Von Mikulicz in 1887 as pyloroplasty by longitudinal incision and transverse closure, respectively (1). The HM strictureplasty (HMS) was first performed for stenotic lesions of CD and was reported to be promising and safe by Lee *et al*. in 1982 (2). Since then, HMS has been used for short-segment stenoses of approximately 10 cm or less. A systematic review and meta-analysis of conventional (HM and Finney) and non-conventional strictureplasties in CD was conducted by Campbell *et al*. in 2012 (3). Comparing the number of conventional and non-conventional strictureplasties, the rate of conventional strictureplasty was 88% (n = 4001 / 4583 [total]). Furthermore, HMS accounted for 89% (n = 3566 / 4001) of conventional strictureplasty cases, indicating that HMS is a major strictureplasty in CD.

However, in HMS, care must be taken to avoid tension during closure, which is commonly observed at the center point of the suture site, as shown in computerized three-dimensional geometry analysis (4, 5). HMS dilates the intestinal lumen at the incision site, but narrowing of the lumen adjacent to the suture site affects the local perfusion of the intestinal contents (4, 5). Whether this narrowing affects the maintenance of intestinal motility (contractility and transport capacity in the direction of the circular muscle) remains unknown. To verify the extent to which HM configuration suturing maintains intestinal motility,

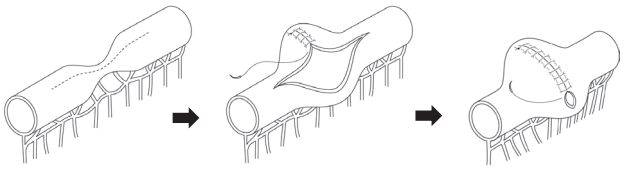

Fig. 1. Procedure of Heineke-Mikulicz strictureplasty.

Abbreviations :
HM, Heineke-Mikulicz ; TS, transverse suture ; LS, longitudinal suture ; NT, non-treatment ; HAS, hydroxy-α-sanshool ; CD, Crohn's disease ; HMS, Heineke-Mikulicz strictureplasty ; DMap, spatiotemporal map of colonic diameter ; AUC, area under the curve ; SSA, stapled side-to-side anastomosis.

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we compared intestinal peristalsis and motility after different enterotomies and repairs, including transverse (TS) and longitudinal (LS) configuration suturing, as shown in Fig. 2A, using the isolated rat proximal colon. In this study, intestinal motility was evaluated based on changes in intraluminal pressure, transit time, and a spatiotemporal map developed from a video image of the repaired intestinal segments.

We also investigated the effect on intestinal peristalsis and motility, not only at baseline, but also under propulsive contraction. Propulsive contraction was induced by hydroxy-a-sanshool (HAS)(6). HAS, a typical component of Japanese pepper, was used to induce peristalsis. When HAS is administered to a rat intestinal specimen, rhythmic propulsive contraction occurs, which propagates from the oral to anal side (7, 8). This reflects neural peristalsis (long-distance contraction) in the rat colon (9), which is an antegrade propulsion caused by the expansion of the intestinal tract by a liquid or solid that repeats when the stimulus is sustained. HAS is also considered one of the main active ingredients of medical-grade daikenchuto, a traditional Japanese herbal medicine that is prescribed as a prokinetic agent for abdominal distension and postoperative paralytic ileus (10, 11).

MATERIALS AND METHODS

Animals

Male Sprague-Dawley (SD) rats, aged 8-11 weeks (Charles River Laboratories, Kanagawa, Japan), were used for this study. Male rats were selected based on previous reports (7). The rats were housed in a room with controlled temperature and humidity under a 12-h (07 : 00–19 : 00 h) light/dark cycle with free access to food and water. All experimental procedures were approved by the Experimental Animal Ethics Committee of Tokushima University and Tsumura & Co. and performed according to the institutional guidelines for the care and use of laboratory animals, which is in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and the ARRIVE guidelines.

Chemicals and drugs

HAS, a constituent of Japanese pepper used as a spice and a Japanese herbal medicine, was supplied by Tsumura & Co. (Tokyo, Japan). The chemicals for Krebs solution were purchased from FUJIFILM Wako Pure Chemical Corporation (Osaka, Japan).

Isolation of proximal colon and surgical procedure

The proximal colons of rats were isolated for colonic diameter and motor function analyses and set up according to the method described by Kubota *et al*. (7). Overnight food-deprived rats were euthanized and their entire colon was isolated. Natural luminal fecal contents in the colon preparations were removed by gentle flushing with warmed Krebs solution from the oral end. A proximal colon segment (approximately 3-4 cm) was placed in an organ bath (100-mL), which was continuously perfused with Krebs solution [5% CO_2 and 95% O_2 (v/v) ; pH 7.3-7.4 ; 3.5 mL/min] at 34-37°C (Fig. 2B). Both the oral and anal ends of the proximal colon were cannulated using a saline-filled flow tube. To initiate contractions, the colon was infused with saline from the oral side at a rate of 0.15 mL/min and exposed to an intraluminal pressure load of approximately 4 cmH_2O by elevating the drain tube on the anal side.

Surgical treatments were performed in a bath before saline infusion in the isolated proximal colon of the rats. The specimens were divided into non-treatment (NT), HM configuration suture, transverse suture (TS), and longitudinal suture (LS) groups. For surgical treatment, short transverse and longitudinal enterotomies of approximately 0.5 cm and 1.0 cm, respectively, were made on the anti-mesenteric side in the middle of the proximal colon. HM, TS, or LS were applied for single-layer closure using 3-4 sutures with 7-0 nylon (Fig. 2A).

The proximal colon was left to equilibrate for 120-240 min after the surgical treatment before starting the experiment.

Construction of spatiotemporal maps of proximal colonic motion and analysis

To create images representing the motor activity of the proximal colon, spatiotemporal maps of colonic diameter (DMaps) were generated according to the method described by Hennig *et al*. and Kubota *et al*. (7, 8, 12). Images of the colons were sampled every 1 s from a video movie (DCR-SR87 and HDR-PJ670, SONY, Tokyo, Japan) (Fig. 2B). The diameter of the colon (in pixels) was coded by image intensity using ImageJ software (NIH, Bethesda, MD, USA), and the number of pixels in the colonic region at each point from the oral side to the aboral side of the proximal colon was counted using measurement software (Physio-Tech, Tokyo, Japan). The diameter data (in pixels) for each point were copied to an Excel (Microsoft, Redmond, WA, USA) sheet in the time order. The diameter of the colon was calibrated using the length scale (in pixels) of the video image. The cells at each data point were represented by color intensity between red (1 mm), white (5.5 mm), and blue (10 mm) on an Excel sheet (Fig. 2C). Data for the entire length of the proximal colon, surgical treatment segment (suture site), ascending side of the suture site (5 mm proximal), and descending side of the suture site (5 mm distal) were calculated for each group (Fig. 2C).

The following analyses were performed on the Dmap : the percentage of area below 5.5 mm in diameter and the average diameter before and after HAS addition ; the contraction amplitude (difference between the minimum and maximum diameters for 30 min) before HAS addition ; and the contraction amplitude (difference between the minimum and maximum diameters at neural peristalsis) after HAS addition. The diameter data within 30 min before (baseline condition) and immediately after the administration of HAS were calculated separately.

Intraluminal pressure of the proximal colon

The intraluminal pressure of the proximal colon was measured according to the method described by Kubota *et al*. (7). To monitor the intraluminal pressure in mmHg, a single pressure sensor (Mikro-Tip catheter transducer SPR-524, Millar Instruments Inc., Houston, TX, USA) was placed on the descending side of the suture or non-treatment site in the proximal colonic lumen (Fig. 2B). Intraluminal pressure curves were evaluated using a data acquisition and analysis system (Lab-Trax-4, World Precision Instruments, Sarasota, FL, USA). The peak pressure amplitude was calculated from the mean pressure of the peaks for 30 min after HAS (10 μmol/L) addition (Fig. 2D). The peak frequency was calculated from the number of pressure peaks over a 30-min period. The area under the curve (AUC) of the pressure waves during the allotted period was also calculated.

Transport of intraluminal contents in the proximal colon

Transport time of intraluminal contents in the proximal colon were measured according to the method described by Kubota *et al*. (7, 8). In the transport study, a plastic bead (5.9-mm diameter) was placed into the lumen before surgical treatment (Fig. 2B). The transit time of the plastic beads from the oral side to the anal side of the proximal colon was measured after HAS administration.

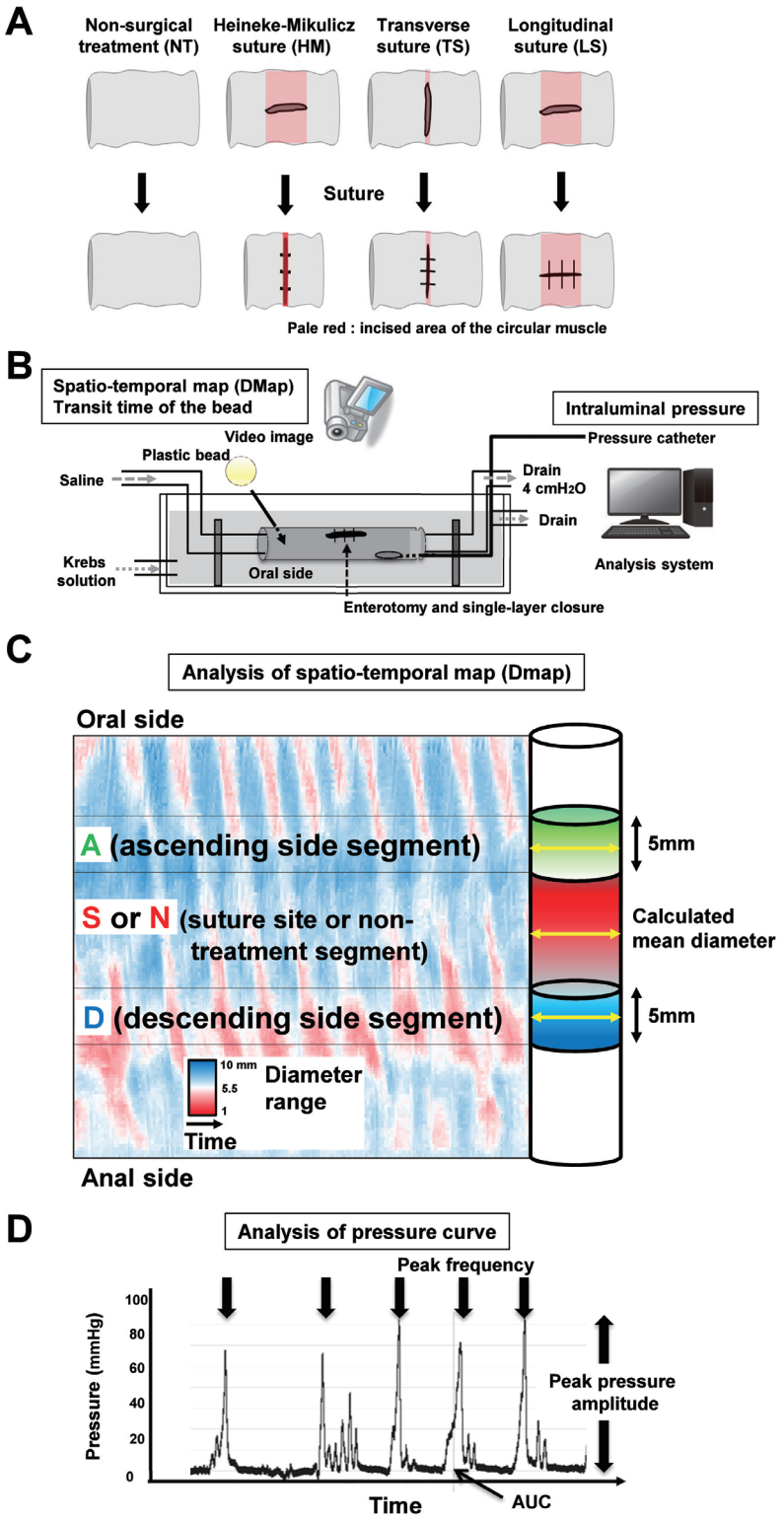

Fig 2. Experimental setup and analysis procedures. A : Three surgical models were created from the rat proximal colon. A longitudinal enterotomy incision or short transverse enterotomy incision was made, and Heineke-Mikulicz suture (HM) configurations, transverse suture (TS), or longitudinal suture (LS) were used to close the incision. B : A proximal colonic specimen was placed in the bath, and the motility and intraluminal pressure were recorded in the proximal colon of rats. The transit time of the plastic bead was evaluated using video images. C : The spatiotemporal maps of the colonic diameter (DMaps) represent the long axis of the proximal colon in the vertical direction and time in the horizontal direction. The upper and lower sides of the DMap were the oral and anal sides, respectively. The diameter of the proximal colon is represented by a color gradient, with red (1.0 mm), white (5.5 mm), and blue (10.0 mm). The red and blue colors indicate contraction and expansion, respectively. The diameter value along the length of the proximal colon was calculated from the DMap, which was divided into the entire proximal colon, surgical area (suture site), ascending side of surgical area (5 mm proximal), and descending side of surgical area (5 mm distal). The length of the non-treatment segment was 5 mm. D : Method for analyzing the intraluminal pressure curve. The peak pressure amplitude during each neural peristalsis, the area under the curve (AUC), and the peak frequency (counts per 30 mins) were analyzed from the intraluminal pressure curve after hydroxy-α-sanshool (HAS) administration.

Data analysis

All values were calculated using Excel and are expressed as mean ± SEs. Significant differences before and after HAS administration were evaluated using paired t tests. Significant differences between each group were evaluated using the Tukey-Kramer test. Statistical significance was set at $P < 0.05$. StatLight software (Yukms Co., Ltd., Japan) was used for the statistical analysis.

RESULTS

DMap analysis in rat proximal colons

In this experiment, NT and surgical treatment with HM, TS, or LS were performed on the proximal colons of seven rats each, and DMap analysis was performed for 30 min before and after the addition of HAS. A representative DMap image is shown in Fig. 3.

In the NT group, peristaltic contractions (reddish area on the DMap) occurred repeatedly from the oral to the anal side at baseline (before HAS administration). The addition of HAS induced neural peristalsis (a propulsive contractile movement with strong contractions) that continued from the oral to anal side, and a reddish area on the DMap expanded in the NT group.

In the surgical treatment groups, the reddish area on the DMap in the LS group was more extensive than that in the HM and TS groups at baseline. After the addition of HAS, neurogenic peristalsis, a propulsive contractile movement with strong contractions that continued from the oral to anal side, was induced in all surgical treatment groups. In the HM and TS groups, the reddish area on the DMap was more extensive than that before HAS addition, although the suture site retained a bluish color. However, no such changes were observed in the LS group.

Percentage of diameters below 5.5 mm (middle point) on DMap

The percentage of the area that contracted in the diameter range of 1.0-5.5 mm (reddish area) on the DMap of each group was determined and compared among the groups (Fig. 4A).

According to the analysis of the entire proximal colon, the percentage of area in the NT group was 32.6 ± 4.7% before the addition of HAS. It increased to 64.2 ± 8.8% after addition of HAS ($P = 0.0066$, paired t-test). There was no significant difference in percentage within the range between the HM, TS, and NT groups before the addition of HAS [TS : 36.0 ± 3.7% and HM : 37.6 ± 5.0%, Tukey-Kramer test]. However, the percentage of patients in the LS group within the range was significantly higher than that in the NT group [LS : 59.1 ± 8.2%, $P = 0.015$, Tukey-Kramer test]. After stimulation with HAS, the percentage in the HM and TS groups increased compared with each baseline value in the NT group, although no significant differences were observed in the LS group [HM : 63.3 ± 7.4% ($P = 0.019$), TS : 66.0 ± 4.2% ($P = 0.0050$), and LS : 72.8 ± 5.5% ($P = 0.088$), paired t-test].

When the analysis was performed in each colonic segment, the LS group had a significantly high proportion of contractile areas at the suture site compared with that in the NT and other surgical treatment (HM and TS) groups at baseline [NT : 34.2 ± 6.8% ($P = 0.0013$), HM : 28.3 ± 3.4% ($P = 0.00024$), TS : 36.3 ± 5.2% ($P = 0.0023$), and LS : 72.4 ± 8.5%, Tukey-Kramer test], and the

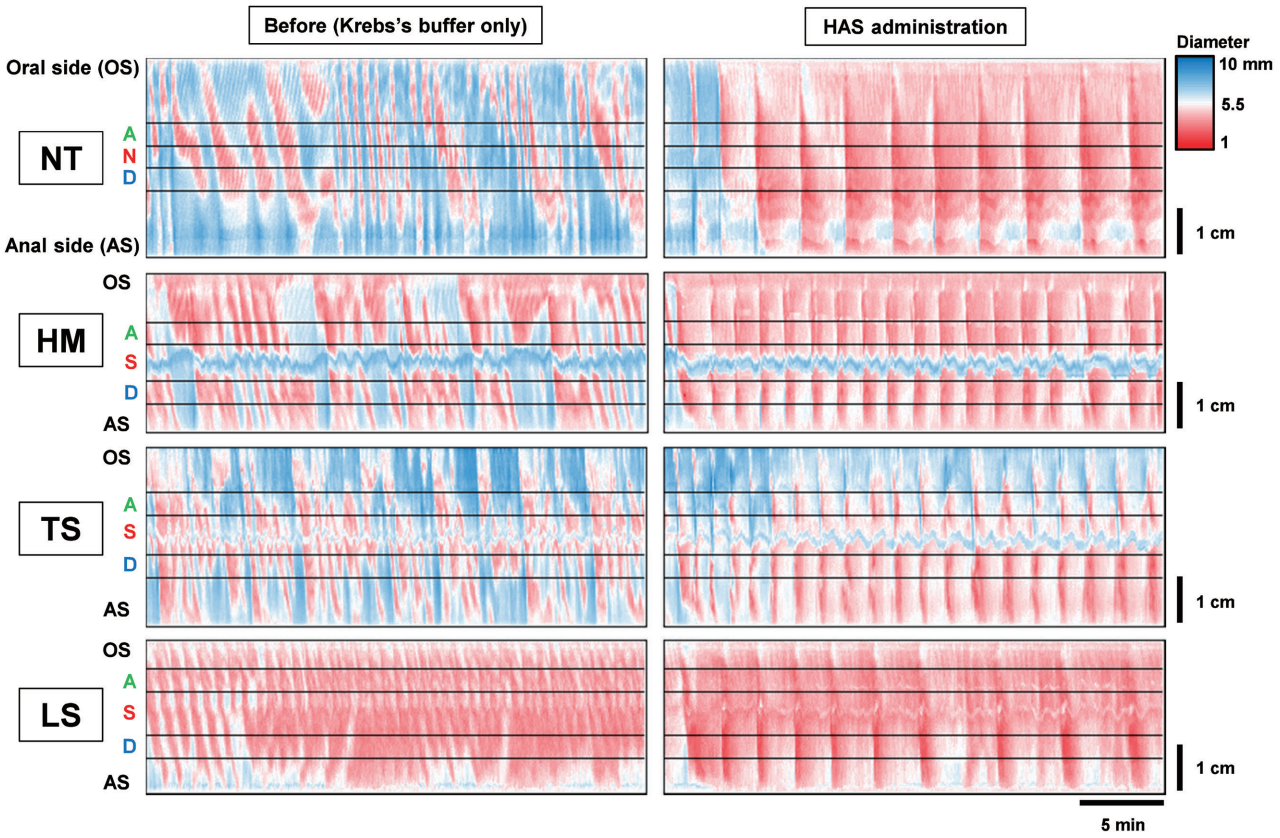

Fig 3. Typical spatiotemporal maps of the colonic diameter (DMaps) of the surgical models and the nontreated group in the rat proximal colons. NT, nonsurgical treatment ; HM, Heineke-Mikulicz suture ; TS, transverse suture ; LS, longitudinal suture ; HAS, hydroxy-α-sanshool.

significant difference between HM and LS was also observed after HAS administration. In the descending side segment, only the LS group among the surgical treatment groups had significantly higher values than those in the NT group at baseline [NT : 32.6 ± 4.7% ($P = 0.014$) and LS : 64.5 ± 9.0%, Tukey-Kramer test] ; however, no change was observed in the LS group by HAS administration (paired t-test).

Mean diameter on DMap

The mean diameter in the proximal colon was calculated using the DMap for each group and compared between groups (Fig. 4B).

In the analysis of the entire proximal colon in the NT group, the mean diameter before HAS was 6.26 ± 0.21 mm. After the addition of HAS, the mean diameter significantly decreased to 5.24 ± 0.21 mm ($P = 0.0014$, paired t-test). In all colonic segments, the mean diameters in the NT group significantly decreased after the addition of HAS.

In the HM and TS groups, the mean diameter of the entire proximal colon before the addition of HAS was not significantly different compared with the NT group [HM : 5.86 ± 0.23 mm and TS : 5.98 ± 0.11 mm, Tukey-Kramer test]. After HAS addition, the mean diameter of the entire proximal colon in the HM and TS groups decreased significantly, similar to the NT group [HM : 5.13 ± 0.11 mm ($P = 0.013$ vs before the addition of HAS) and TS : 5.25 ± 0.07 mm ($P = 0.0043$ vs before the addition of HAS), paired t-test]. Furthermore, in the HM and TS groups, the changes in the diameter of the ascending side, suture site, and descending side of the proximal colon were similar to that of the entire proximal colon.

In contrast, in the LS group, the mean diameter of the entire proximal colon before HAS administration was significantly lower than that in the NT group [LS : 5.32 ± 0.23 mm ($P = 0.015$ vs. NT group), Tukey-Kramer test]. Furthermore, no significant change was observed with HAS addition in the LS group unlike the NT group [LS : 4.73 ± 0.31 mm ($P = 0.13$ vs before the addition of HAS), paired t-test]. In the LS group, the mean diameters of the suture site and descending side of the proximal colon before HAS addition were significantly lower than that of the NT group, similar to the entire proximal colon [suture site : NT, 6.19 ± 0.27 mm ; LS, 4.91 ± 0.26 mm ($P = 0.0025$), descending side segment : NT, 6.31 ± 0.26 mm ; LS, 5.19 ± 0.28 mm ($P = 0.028$), Tukey-Kramer test]. Additionally, the differences of mean diameter at the suture site between the LS group and other surgical treatment groups were significant [HM : 6.15 ± 0.18 mm ($P = 0.0034$), TS : 5.97 ± 0.16 mm ($P = 0.013$), Tukey-Kramer test]. No significant change was observed with the addition of HAS at the suture and descending sides in the LS group.

Contraction amplitude on DMap

The contraction amplitude at baseline, 30 min before HAS addition, was calculated as the difference between the maximum and minimum diameters (Fig. 4C). There was no significant difference between the NT and surgical treatment groups (HM, TS, and LS) in the entire proximal colon and the ascending and descending sides. However, at the suture site, the contraction amplitudes in the surgical treatment groups (HM, TS and LS) were significantly lower than that in the NT group [NT : 5.10 ± 0.46 mm, HM : 3.43 ± 0.24 mm ($P = 0.0093$), TS : 3.30 ± 0.22 ($P = 0.0049$), and LS : 2.74 ± 0.37 mm ($P = 0.00026$), Tukey-Kramer test]. In addition, no differences were observed between the surgical treatment groups.

The contraction amplitude after HAS addition was calculated as the difference in diameter immediately before and during the occurrence of neural peristalsis (long-distance contraction) (Fig. 4D). There was no significant difference between the NT and surgical treatment groups (HM, TS, and LS) in the entire proximal colon and the ascending and descending sides of the suture site. However, at the suture site, the contraction amplitudes in the surgical treatment groups (HM, TS and LS) were significantly lower than that in the NT group [NT : 2.65 ± 0.20 mm, HM : 1.91 ± 0.13 mm ($P = 0.011$), TS : 1.80 ± 0.06 ($P = 0.0029$), and LS : 1.58 ± 0.18 mm ($P = 0.00024$), Tukey-Kramer test]. In addition, no differences were observed between the surgical treatment groups.

Analysis of intraluminal pressure

In this experiment, NT and surgical treatment with HM, TS, or LS were performed on the proximal colons of three rats each, and the intraluminal pressure following HAS administration was analyzed (Fig. 5). HAS increased intraluminal pressure with the development of neural peristalsis in all the groups.

In the NT group, the peak pressure amplitude was 80.9 ± 4.0 mmHg (Fig. 5A). In the HM and TS groups, no significant difference was observed between NT group [HM : 66.9 ± 5.5 mmHg, TS : 65.2 ± 4.5 mmHg, Tukey-Kramer test]. It was lower in the LS group and significantly different from that in the NT, HM, and TS groups [NT, $P = 0.0024$; HM, $P = 0.027$; TS, $P = 0.038$; and LS : 40.7 ± 6.1 mmHg, Tukey-Kramer test].

In the NT group, the AUC was 9402 ± 1069 (Fig. 5B). No significant differences were observed between the HM and TS groups and the NT group [HM : 6928 ± 613, TS : 6283 ± 566, Tukey-Kramer test]. It was lower in the LS group and significantly different from that in the NT, HM, and TS groups [NT, $P = 0.0008$; HM, $P = 0.015$; TS, $P = 0.037$; and LS, 2853 ± 413 ; Tukey-Kramer test].

In the NT group, the peak frequency was 23.3 ± 3.4 peaks/30 mins (Fig. 5C). The difference in the peak frequency among the groups was not significant (HM : 22.7 ± 2.3 peaks/30 mins, TS : 19.0 ± 1.2 peaks/30 mins, and LS : 21.0 ± 2.1 peaks/30 mins, Tukey-Kramer test), suggesting that the incision and suture had no impact on the intestinal pacemaker.

Transit time of intraluminal plastic beads

In this experiment, NT and surgical treatment of HM, TS, or LS were performed on the proximal colons of three rats each, and the time required by the plastic beads in the lumen to travel from the oral side to the anal side after HAS administration was measured (Fig. 6). The transit time in the NT group was 20.0 ± 1.5 min. In the HM and LS groups, they were significantly longer than that of the NT group [HM : 34.3 ± 2.7 min ($P = 0.029$) and LS : 47.3 ± 3.7 min ($P = 0.0006$), Tukey-Kramer test]. Moreover, the transit time in the LS group was significantly longer than that in the HM and TS groups [TS : 30.7 ± 2.9 min ($P = 0.013$) and HM : ($P = 0.047$), Tukey-Kramer test]. In contrast, there was no significant difference between the HM and TS groups (Tukey-Kramer test).

DISCUSSION

Lumen strictureplasty, such as HMS, is effective in preventing stricture recurrence in CD patients. However, it is unclear whether motor function of the intestinal tract is maintained after lumen strictureplasty. This study highlights that longitudinal closure after longitudinal enterotomy (LS) significantly reduces intestinal motor function. However, by suturing it perpendicularly in the transverse direction (HM), intestinal motility impairment is reduced.

HMS involves transversely closed longitudinal enterotomy, as shown in Fig. 1A (13). This study suggests that HMS may alleviate the decline in intestinal motility at the incision and

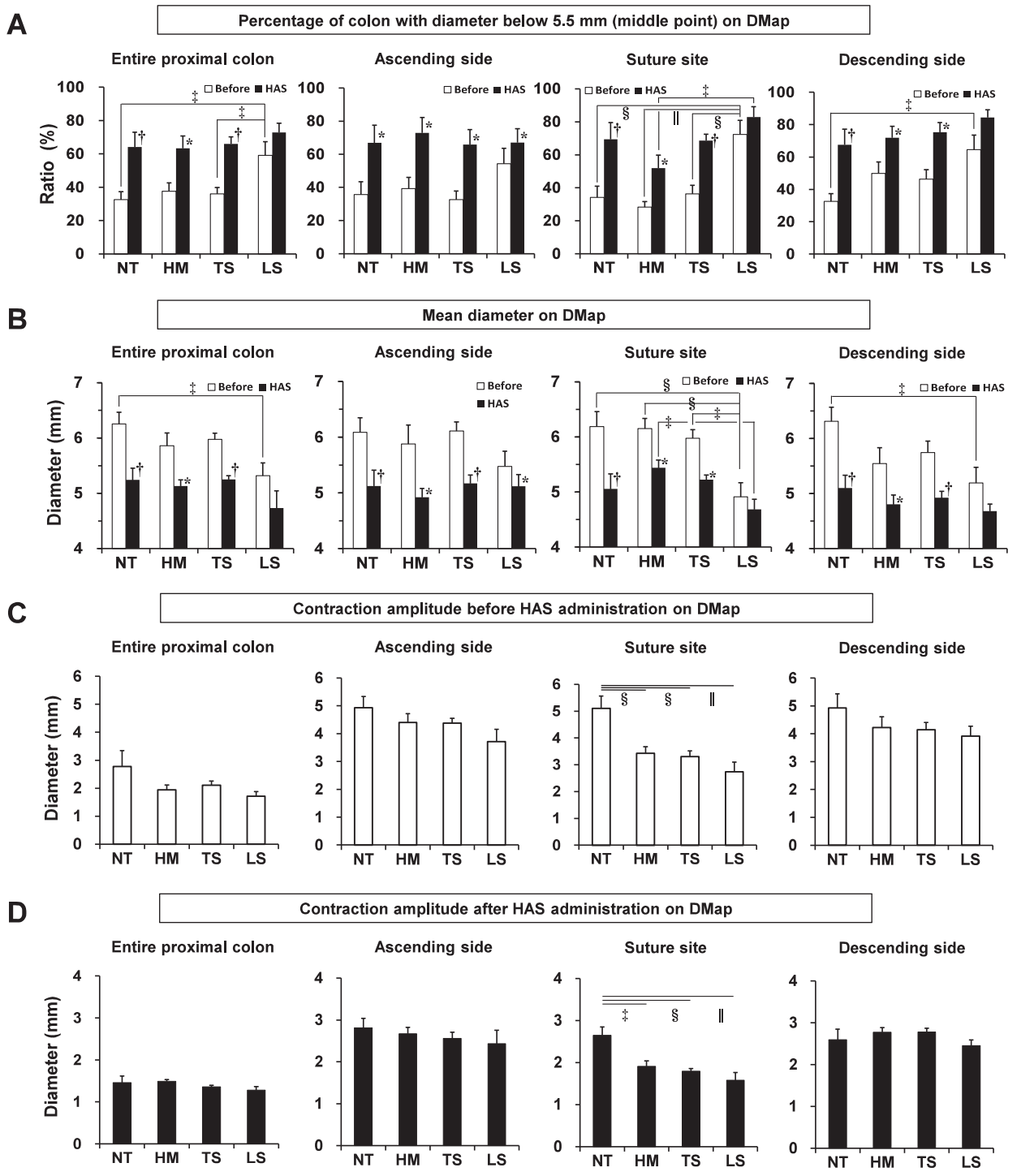

Fig 4. Diameter analysis of the entire proximal colon and of each segment on the DMap in the proximal colon of rats. A, B : Percentage of colons with diameters below 5.5 mm, which is the middle point (A), and the mean diameter (B). Each column represents the mean ± SE (n = 7). Open and closed columns represent before and after administration of HAS, respectively. *, † : $P < 0.05$, and 0.01, respectively, before vs. after HAS administration, according to the paired t-test. ‡, §, ‖ : $P < 0.05$, 0.01, and 0.001 between each group before or after administration of HAS according to the Tukey-Kramer test. C, D : Contraction amplitude before (C) and after (D) administration of HAS. Each column represents the mean ± SE (n = 7). ‡, §, ‖ : $P < 0.05$, 0.01, and 0.001, respectively, for NT vs. TS, LS, and HM, respectively, according to the Tukey-Kramer test. DMap, spatiotemporal map of the colonic diameter ; NT, nonsurgical treatment ; HM, Heineke-Mikulicz suture ; TS, transverse suture ; LS, longitudinal suture ; HAS, hydroxy-α-sanshool.

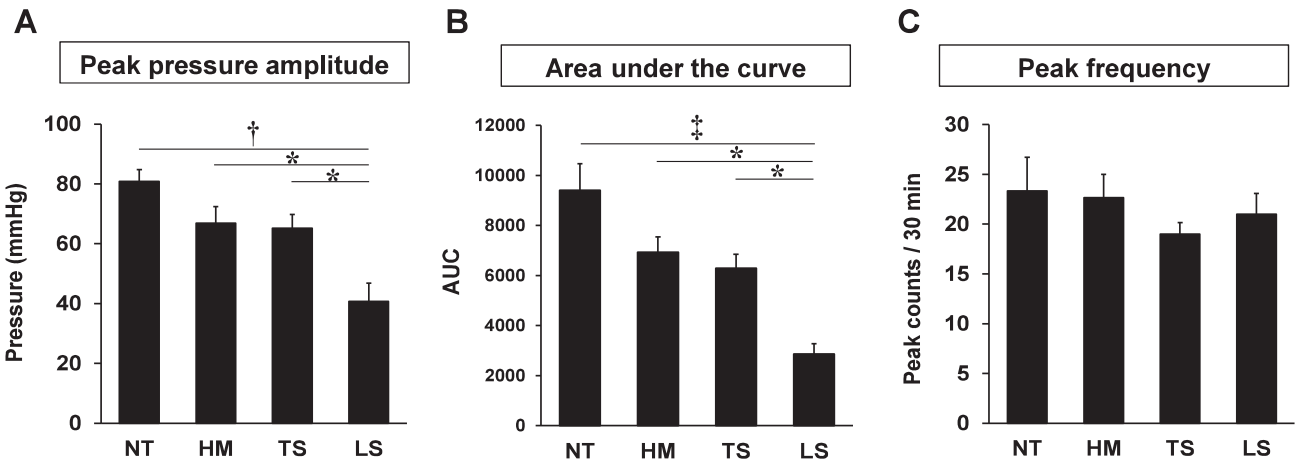

Fig 5. Peak pressure amplitude, AUC, and peak frequency of the intraluminal pressure curve after treatment of the isolated proximal colon of rats with HAS. Each column represents the mean ± SE (n = 3). *, †, ‡ : $P < 0.05$, 0.01, and 0.001, respectively, between each group according to the Tukey-Kramer test. NT, nonsurgical treatment ; HM, Heineke-Mikulicz suture ; TS, transverse suture ; LS longitudinal suture ; AUC, area under the curve ; HAS, hydroxy-α-sanshool.

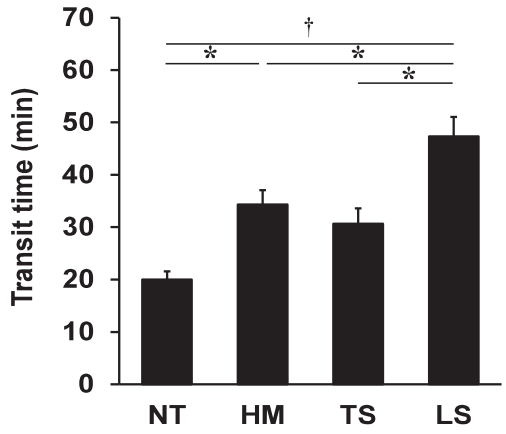

Fig 6. Intraluminal bead transit time after treatment of the isolated proximal colon of rats with HAS. Each column represents the mean ± SE (n = 3). *, † : $P < 0.05$, and 0.001, respectively, between each group according to the Tukey-Kramer test. NT, nonsurgical treatment ; HM, Heineke-Mikulicz suture ; TS, transverse suture ; LS, longitudinal suture ; HAS, hydroxy-α-sanshool.

suture sites, preventing stasis of intestinal contents, resulting in microbiome changes and bacterial overgrowth (14).

Computerized three-dimensional geometry analysis demonstrated that HMS preserved the intestinal lumen at the incision site, but narrowing of the lumen was noted at the proximal and distal sides of the suture site. At the same time, tension has been reported at the central point of the suture site (4, 5). These reports suggest that HMS affects the local perfusion of intestinal contents. In our study, the difference in the intestinal diameter of the suture site between the HM and NT groups was not significant, suggesting the preservation of the luminal diameter in the HM group. Additionally, the luminal diameter in the HM group was not significantly different from that in the NT group at 5 mm on either side of the suturing site. Similar results were observed in the TS group. In contrast, in the LS group, the intestinal diameter was significantly smaller, not only at the suture site, but also at 5 mm on the distal side, than the corresponding diameter in the NT and/or HM groups. The mechanism underlying narrowing of the intestinal tract in the LS group is unknown. We hope to investigate this in the future. The contraction amplitude on the DMap was significantly reduced at the suture site in all surgically treated groups compared to the NT group, suggesting that the effect of an incision and/or suture impairs intestinal contraction.

In the intraluminal pressure analysis, HAS-induced neural peristalsis with increased peak pressure amplitude and AUC in the HM group was similar to that in the NT and TS groups and was maintained, unlike in the LS group, in which the intraluminal pressure was attenuated. The transit times in the HM and TS groups were longer than that in the NT group. However, the LS group had the longest transit time of intraluminal plastic beads compared to the other groups, including the HM group, suggesting that it may be associated with incision-induced stenosis and intraluminal pressure changes. A recent study

examining the role of circular muscle in intestinal motility showed that injury to the smooth muscle layer of the intestinal wall of guinea pig ileal and colonic specimens caused a transient decrease in smooth muscle motility (15). This hypomotility is more pronounced in circular smooth muscles than in longitudinal smooth muscles (15, 16). The mechanism of its development is related to decreased reactivity of intestinal motor neurons (15, 16).

Intestinal motility did not differ between the HM group, incised longitudinally (circular myotomy) and sutured transversely, and the TS group, incised transversely (longitudinal myotomy), and sutured transversely. Considering the commonalities between these two approaches in terms of motility, the HM group had two vertices of the incision and sutures connected in the same transverse direction as the TS group. In the HM group, the cut surface of the circular myotomy was shortened in the longitudinal direction. Therefore, the normal circular muscle appeared to be continuous in the longitudinal direction, as in the TS group. Given that the length of circular myotomy is shortened, the influence of circular myotomy on intestinal motility may be diminished. However, the mechanism underlying this finding remains unknown. We hope to investigate this in the future.

This study offers new insights into intestinal hypomotility at the anastomotic site. Kono-S, which was developed in 2003, is an anastomosis technique that uses HMS (17-20). Recently, a prospective randomized controlled trial comparing different anastomotic configurations after intestinal resection in patients with CD has been reported. Compared with conventional stapled side-to-side anastomosis (SSA), the Kono-S procedure significantly reduced postoperative endoscopy at 6 months and clinical recurrence rates at 24 months after surgery (21). Both anastomoses start with the same longitudinal enterotomy, but in SSA, the suture is performed in the longitudinal direction, whereas in Kono-S anastomosis, the suture is made in the transverse direction, similar to HMS. The prevention of anastomotic recurrence using the Kono-S approach in CD has been previously reported. The reoperation rate for anastomotic recurrence of Kono-S is < 2% at 5 and 10 years of follow-up (18), which is 90% lower than that of conventional anastomosis at 5 years (22). Histologically, recurrence at the anastomotic site in CD begins within one week (23). Immediately after surgery, changes in the intestinal microbiome owing to stasis of the intestinal contents and/or bacterial overgrowth may lead to recurrence and exacerbation (14, 24, 25). HM-type sutures, as characterized in our study, may be beneficial in reducing stasis of intestinal contents and the recurrence rate at the anastomotic site.

This study has some limitations, as the examination of intestinal smooth muscle movement used specimens from isolated animal tissues. Considering the influence of immune inflammation and/or intestinal bacterial flora, future animal studies are required to assess intestinal motor function after HMS.

CONCLUSIONS

The HM configuration, which shortens the cut surface of the circular muscle in the longitudinal direction of the intestinal tract and widens the suture site and the descending side tract diameter, may help maintain intestinal motor function (peristalsis and transport function).

CONFLICT OF INTEREST

This work was supported by a grant from Tsumura & Co. K.K. and N.F. are employed by Tsumura & Co. T.K. and M.S. have a financial interest in Tsumura & Co. that is relevant to this research.

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