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Angioarchitectural study of esophageal varices

With special reference to variceal rupture

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Summary. Pathomorphological and angioarchitectural characteristics of esophageal varices, mainly of ruptured varices, were studied in autopsy cases. Contrast medium was injected into the esophageal vein in 25 among 75 cases with varices, and in 4 cases without varices as a control. Out of the 75 cases with varices, rupture was confirmed in 8 cases. Ruptured points were recognized at the oral end of the longitudinal veins (these veins were called "sudare-like veins" in this study) in the lamina propria at the lower end of the esophagus in all of the 8 cases. This ruptured area was called the "critical area". By morphometric examination, dilatation of these sudare-like veins was the most obvious in severe varices, and these veins were observed to penetrate the muscularis mucosae to connect to the submucosal veins at the critical area. This area seemed to be of the greatest significance in the pathogenesis of spontaneous variceal rupture.

Key words: Portal hypertension – Esophageal varices – Pathogenesis of variceal rupture – Angioarchitecture

Introduction

Massive hemorrhage due to rupture of esophageal varices is a serious complication in portal hypertension, and it is important to understand the pathogenesis of variceal rupture in treatment and prevention of this fatal condition. Although there have been many pathological studies of esophageal varices, angioarchitectural changes have not been understood. The purpose of this study is to clarify the pathomorphological and angio-architectural characteristics of ruptured varices.

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Table 1. Histological findings

No.	Fibrinous thrombus	Irregular thickening of venous wall	Thinning of sq. epithelium	Inflamm. infiltration (PMN)	Diameter of ruptured vein (μ)
1	+	+	+	±	1450
2	+	+	+	−	1050
3	+	+	±	±	1050
4	+	+	+	−	850
5	±	+	+	−	800
6	−	±	+	−	200
7	+	+	+	−	1000
8	+	−	+	+	950

PMN: polymorphonuclear leukocyte

Materials and methods

This investigation was based on gross and histological studies of 75 cases with esophageal varices autopsied at the Pathology Department of the Kurume University Hospital during the two years from 1981 to 1983.

In each case, 5 sections were obtained routinely every 2 cm from the esophago-gastric junction and were studied with haematoxylin and eosin (H&E), and elastica Van Gieson (EVG) stains.

Gelatin solution containing contrast medium (7.5% of gelatin with 50% of barium) was injected into the esophageal vein through the left gastric vein in 25 cases with varices at autopsy. As a control, injection was also carried out in 4 normal esophaguses. Esophaguses after injection were cleared and were studied by stereoscopic microscope.

In 15 cases with adequate injection (normal esophagus: 4; mild varices: 5; severe varices: 6), the length, total numbers, size of total luminal area, and the mean luminal area of esophageal veins above and below the muscularis mucosa at the lower end of the esophagus were all examined using computer assisted image analysis system (NEC PC-8001), and were compared with each other. From the diameter of the most dilated submucosal vein, the cases with esophageal varices were divided into two groups: mild varices (veins ranging from 1.0 mm to 3.0 mm in diameter) and severe varices (veins over 3.0 mm in diameter). The size of the largest submucosal vein in the normal esophagus was up to 1.0 mm in diameter.

Histological findings

Out of the 75 cases with varices, blood clot and/or fresh blood in the stomach were observed in 37 at autopsy, and variceal rupture was confirmed in 8 cases (10.7%). In all of the 8 cases, ruptured veins which were approximately 1.0 mm in diameter, lay in the lamina propria. Fibrinous thrombus and irregular thickening of the venous wall were observed in almost all cases. Marked infiltration of neutrophils into the squamous epithelium was seen in one case (Table 1; Fig. 1).

Angioarchitectural findings

Fine longitudinal veins, which are normally seen in the lamina propria at the lower end of the esophagus (Kogure 1983), were called "sudare-like

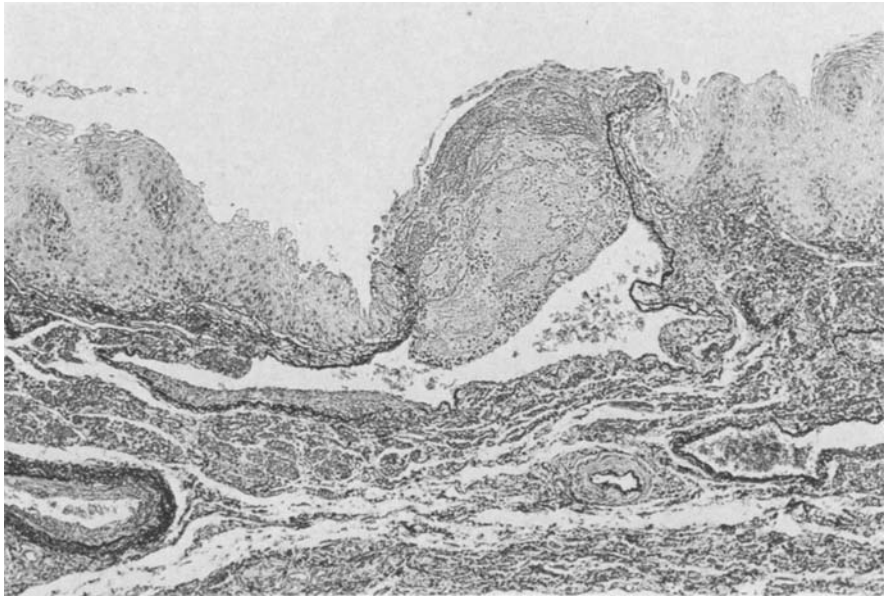

Fig. 1. Histological findings in ruptured varices. Ruptured vein is located in the lamina propria. Fibrinous thrombus and irregular thickening of venous wall are observed (EVG stain × 20)

veins" in this study, because of their resemblance to a traditional sun-shade made of bamboo ("sudare" in Japanese). These veins are clearly arranged in the lamina propria in normal esophagus (Fig. 2). They were observed in all cases with varices and showed varying degrees of dilatation and originated at the esophago-gastric junction and ran for approximately 3–4 cm upward. They were identified in groups and were seen to pierce the lamina muscularis mucosa and connected to the submucosal veins. In the more proximal region to this connecting zone the submucosal veins, after giving off anastomosing branches to each other, formed four main trunks. The individual trunks were tortuous in varying degree, uniformly dilated. In the more superficial layers there were also loop-like capillaries in the epidermal papillae which drained into the network of small veins just below the squamous epithelium (Fig. 3).

Rupture points were recognized at the oral end of the sudare-like veins in all of 8 cases (Fig. 4). Based on the reconstruction of serial sections of ruptured varices, all of the ruptured veins were situated in the lamina propria and ruptured points were located near the area where the varicosed sudare-like veins connected to the submucosal varices (Fig. 5). This transitional zone was named the "critical area" (cf. Fig. 10).

The distribution of dilated veins at each level in the esophagus is shown in Fig. 6. The sudare-like veins ran through the lamina propria and most of them finished draining to the submucosal veins at the critical area. On

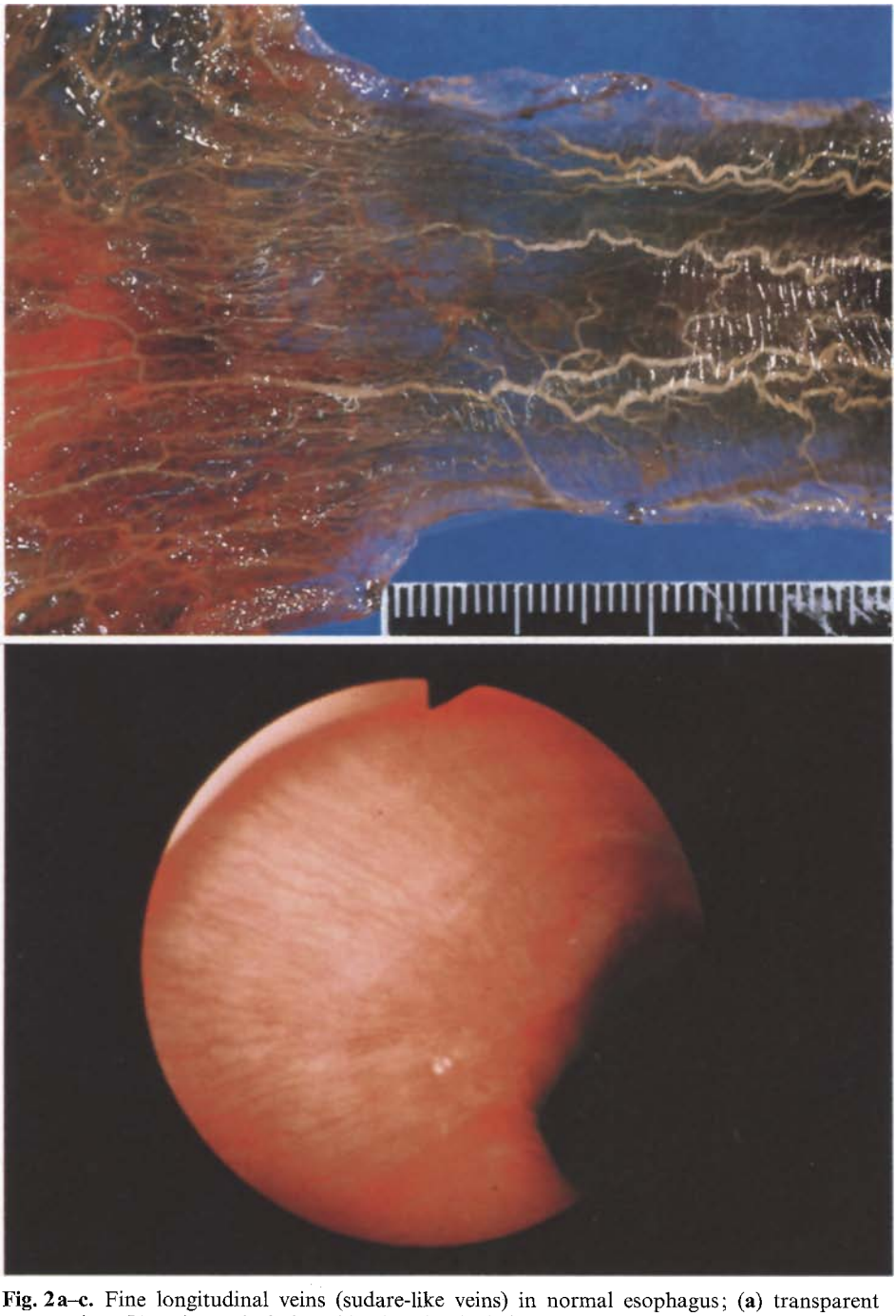

Fig. 2a–c. Fine longitudinal veins (sudare-like veins) in normal esophagus; (**a**) transparent preparation, (**b**) endoscopical view, (**c**) microscopical view (× 10)

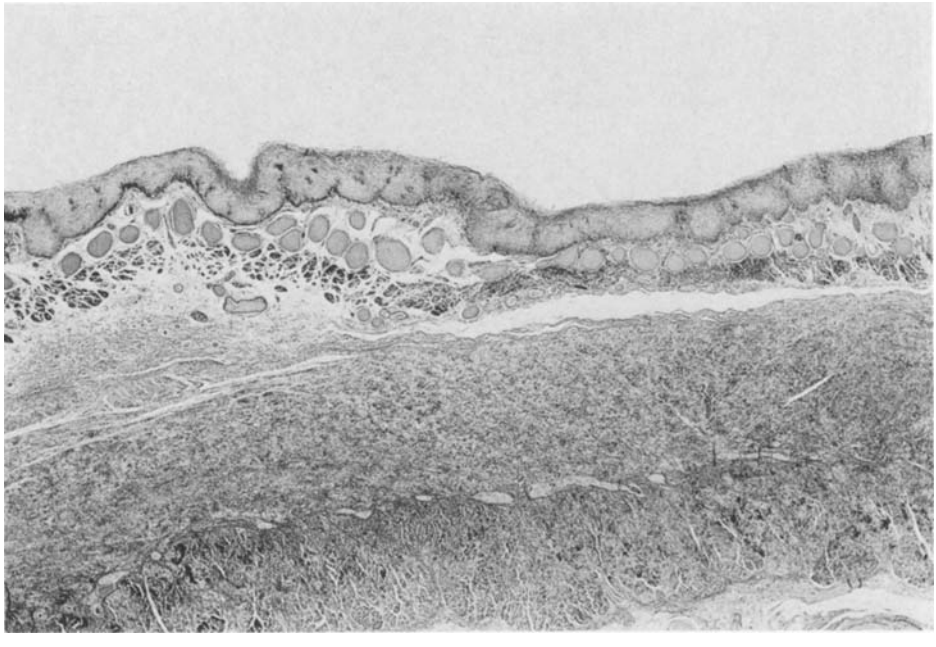

Fig. 2c

the "oral" side of the critical area, there were fewer veins in the lamina propria. Piling up and dilatation of the veins formed a mound-like evelation toward the lumen and gave a varicose appearance. The submucosal veins were the largest in diameter at the level of critical area, and a mound-like elevation was most marked in this area. Further, the thinning of the squamous epithelium was most common at this site.

Morphometric findings

As far as the area of sudare-like veins at the lower end of the esophagus are concerned (De Carvalho 1966), the following findings were obtained: (1) In the normal esophagus, the size of the mean venous luminal area above and below the muscularis mucosa was almost equal but the number of sudare-like veins was 3–4 times that of submucosal veins. (2) In mild varices, the size of the luminal area of submucosal veins increased and the ratio of the total luminal area of sudare-like veins to that of submucosal veins was almost 1:1. (3) In severe varices, dilatation of submucosal veins was prominent. Furthermore, dilatation of sudare-like veins was more dominant than in mild varices (Fig. 7). Varicosed sudare-like veins were observed to turn sharply to connect to the submucosal varices. Morphometric results of this area are represented in Fig. 8.

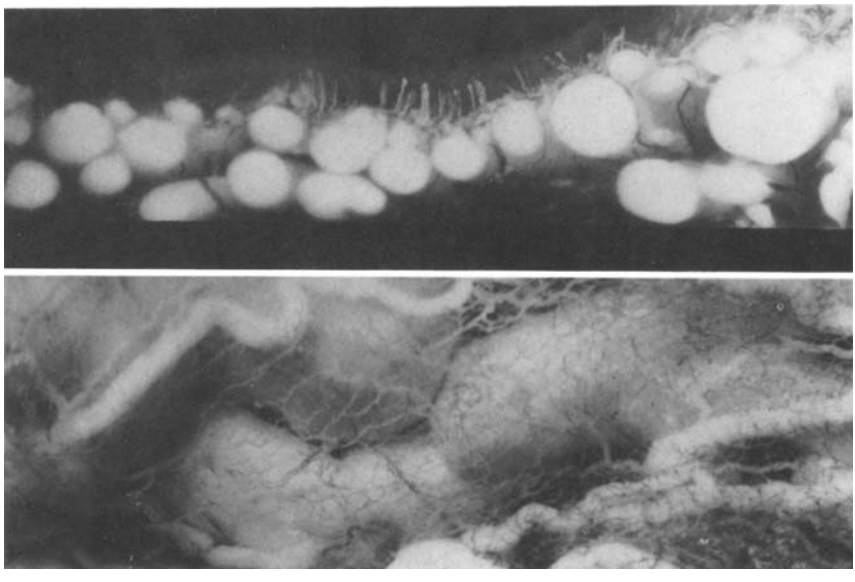

Fig. 3. Loop-like capillaries in the papilla (upper) and meshy small veins (lower). (transparent preparation)

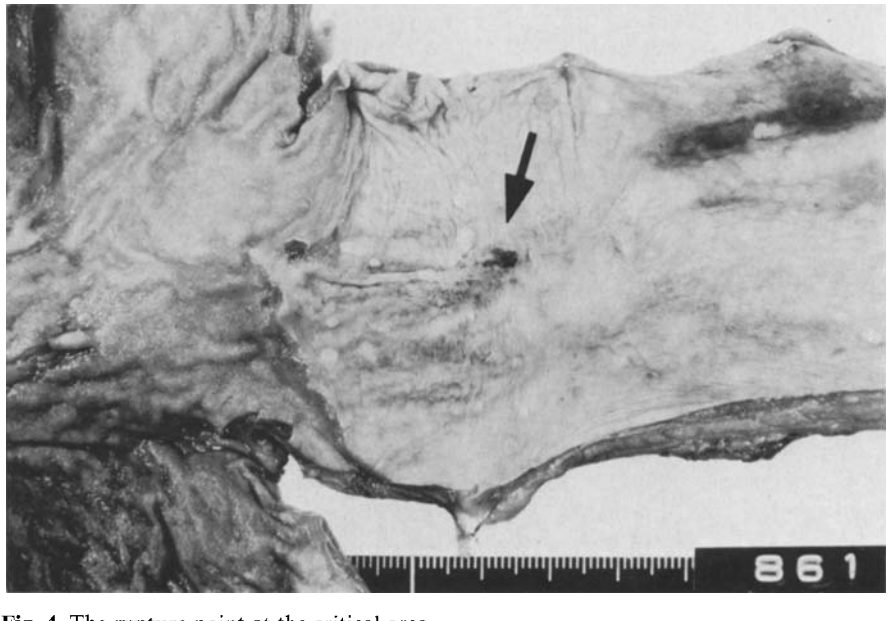

Fig. 4. The rupture point at the critical area

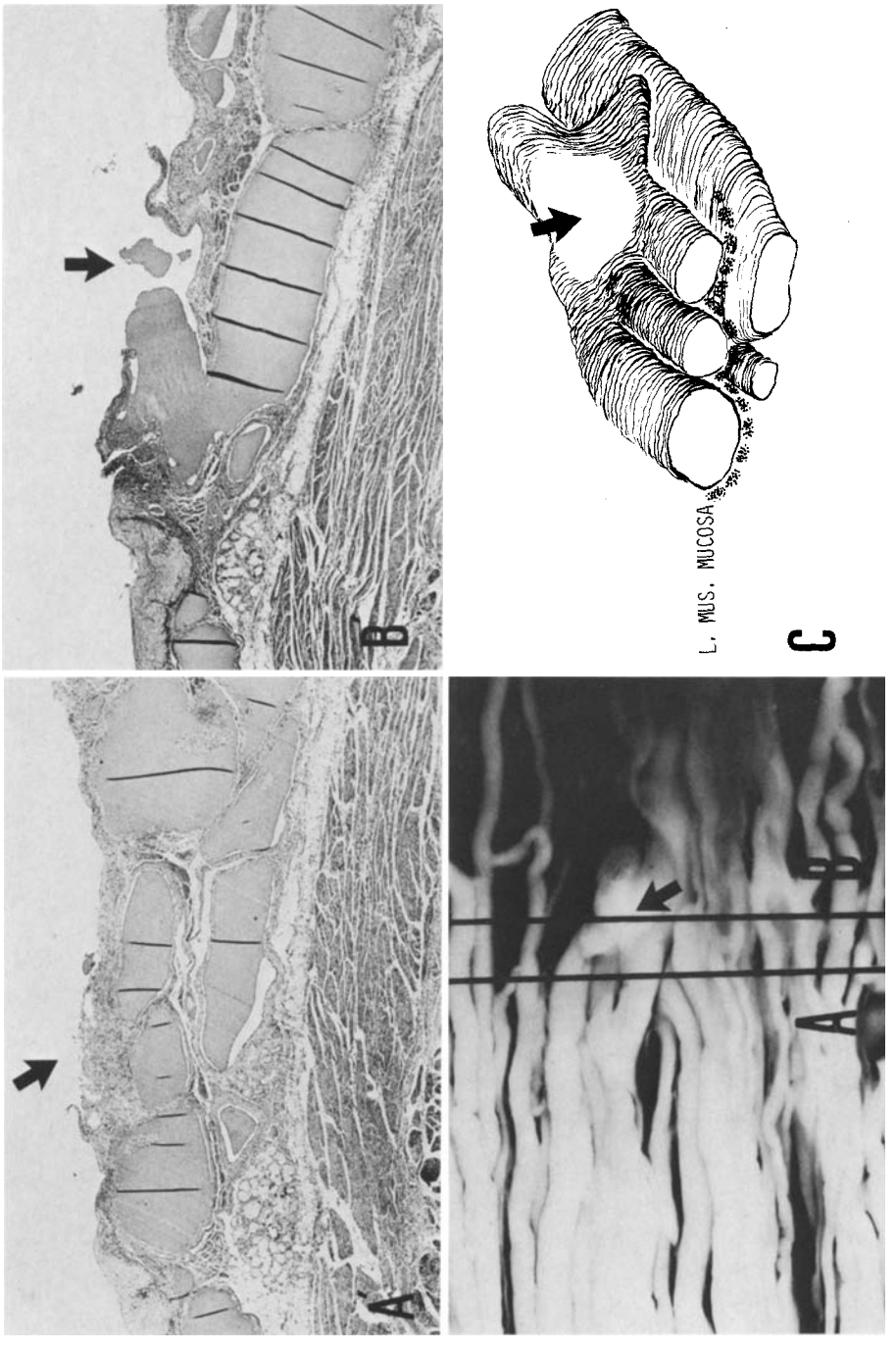

Fig. 5. A', B' the microscopical views of section **A** and **B** (× 20). **C** Reconstructed schema of the rupture point. Arrows show the rupture point. This is located in the longitudinal vein connecting to the submucosal vein

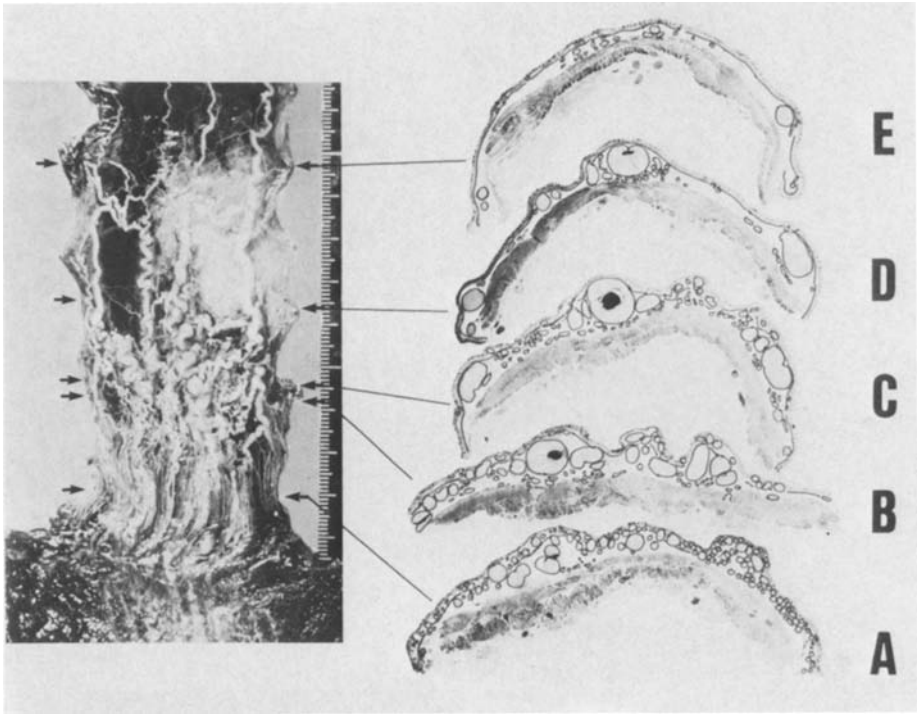

Fig. 6. Distribution of dilated veins at each level of typical esophageal varices. The line just below the squamous epithelium represents the muscularis mucosae

Discussion

The CIBA collection of medical illustrations describes esophageal varices as "spheres", but such dilatation was not demonstrated in this study. Nodules or a "string of pearls" (Demling 1982), which is clinically recognized on endoscopic and/or radiographic examinations, are mainly caused by the meandering of dilated submucosal veins. In the area of sudare-like veins in particular many longitudinal veins overlay the tortuous submucosal varices, and sometimes "varices on varices" were seen.

Although Kegaries (1934), Butler (1951), and others stated that there were no cross anastomoses among the fine longitudinal veins (sudare-like veins in this study) this observations by microscopic stereoscope disclosed branchings and anastomoses of these veins (Fig. 9). From the angioarchitectural investigation a typical model of venous structure of esophageal varices was as represented in Fig. 10.

The mechanism of rupture of esophageal varices has not yet been clarified (Chiles et al. 1953; Wagenknecht et al. 1953; Tisdale et al. 1959; Liebowitz 1961; Orloff 1963; Dagradi et al. 1966; Lebrec et al. 1980). There

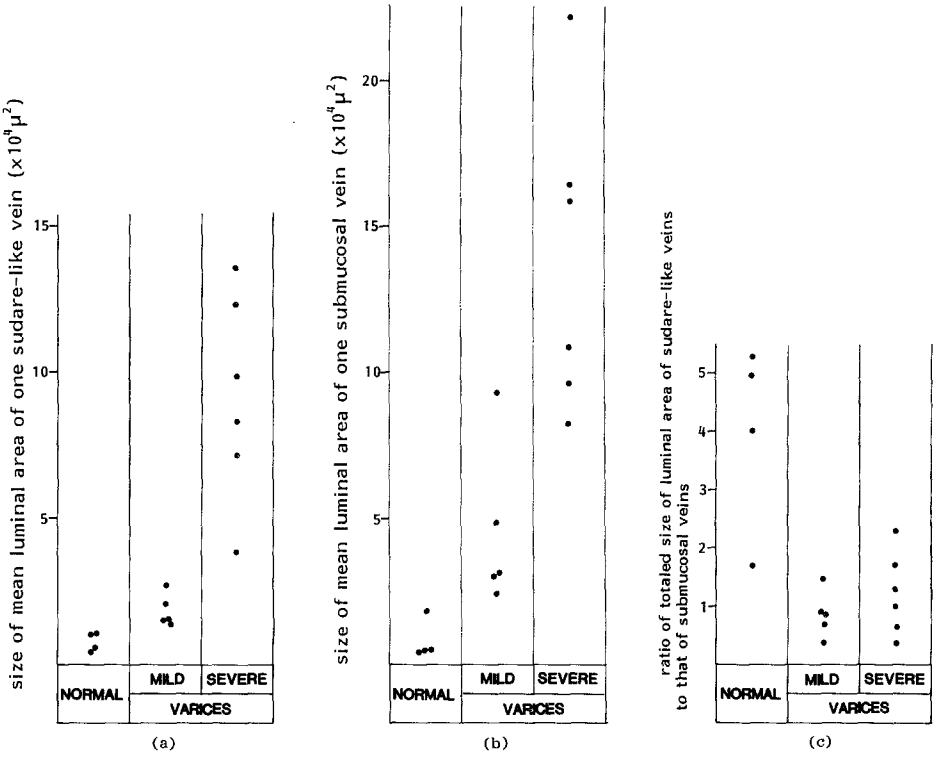

Fig. 7. Morphometric data for the veins at the lower end of the esophagus. The veins both above and below the muscularis mucosa are obviously dilated in severe varices

are three different points of view (1) bursting of varices due to increased hydrostatic pressure in the portal venous system; (2) erosion of variceal wall due to reflux acid-peptic esophagitis; (3) a combination of both. In general it is rather difficult to confirm the rupture point at autopsy. Among the 75 cases with esophageal varices, the rupture point could be confirmed in 8 cases by careful injection and observation. Histologically, the evidence of fibrinous thrombus covering broken venous walls might be the indication of the actual rupture point. Although mucosal clefts or fissures on the middle part of the esophagus and/or ulcerations on the esophagogastric junction were seen in some cases, these findings were interpreted as mechanical damages in using the Sengstaken-Blackmore tube, and these cases were excluded from rupture cases. In concern to the erosion hypothesis, marked infiltration of neutrophils in the squamous epithelium was found in only 1 case out of the 8 cases. Although the possibility that mucosal erosion might play some role in variceal rupture cannot be ignored, it might be minimal.

From the interesting finding that rupture points were located in the

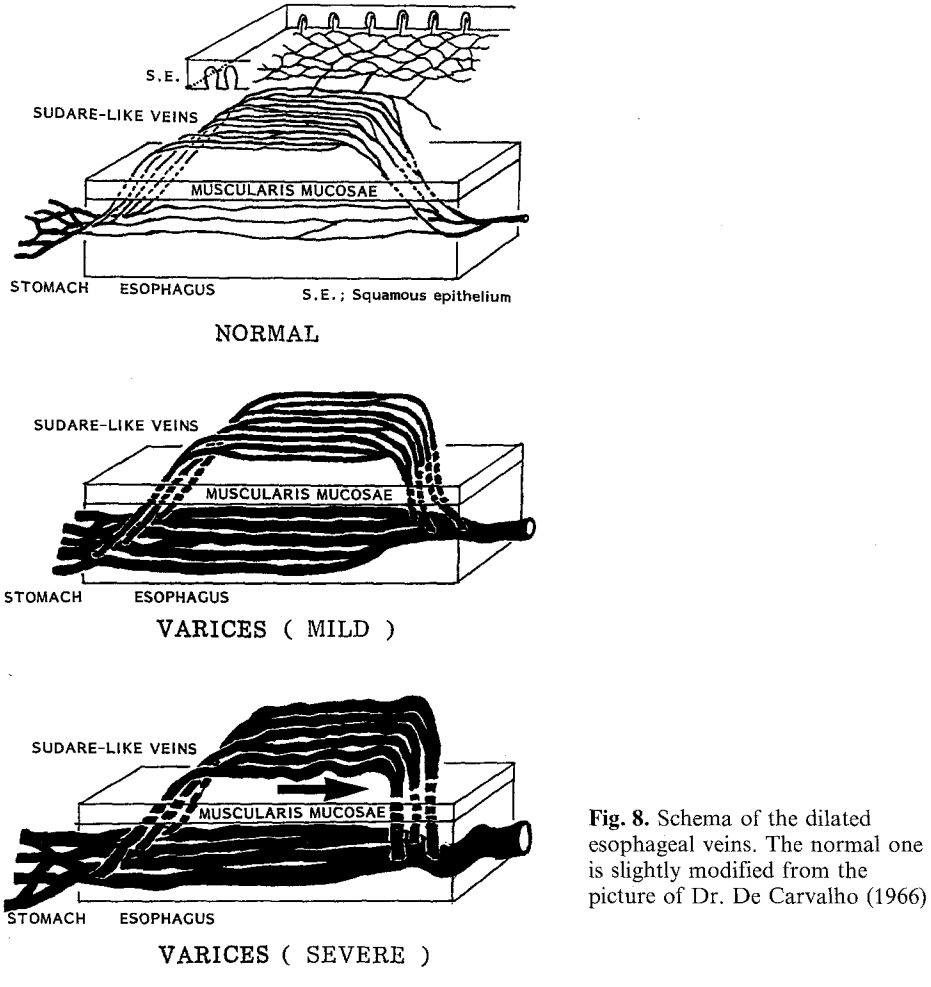

Fig. 8. Schema of the dilated esophageal veins. The normal one is slightly modified from the picture of Dr. De Carvalho (1966)

critical area, it was presumed that the sudare-like veins might have an important role in rupture of varices. As to cause of rupture of these veins at the critical area, it could be explained by the following three factors; (1) In portal hypertension, because of the characteristic venous structure of this region, the fluid stream resistance at the critical area may increase; (2) when highly congested sudare-like veins make sharp penetration at the critical area, the venous wall may become fragile due to the effects of changes in fluid dynamics; (3) since the submucosal veins dilate the most, the sudare-like veins shift to be superficial the most at the critical area. Consequently, the thinning of the squamous epithelium is frequently observed at this area. When sudden elevation of pressure in the portal system occurs by physical exertion, belching, vomiting, coughing, these three factors may be implicated and spontaneous rupture may occur at this area. Although McCormack et al. (1983) described that the direction of local blood flow in the lower

Fig. 9. Branchings and anastmoses of the fine longitudinal veins in normal esophagus. (transparent preparation)

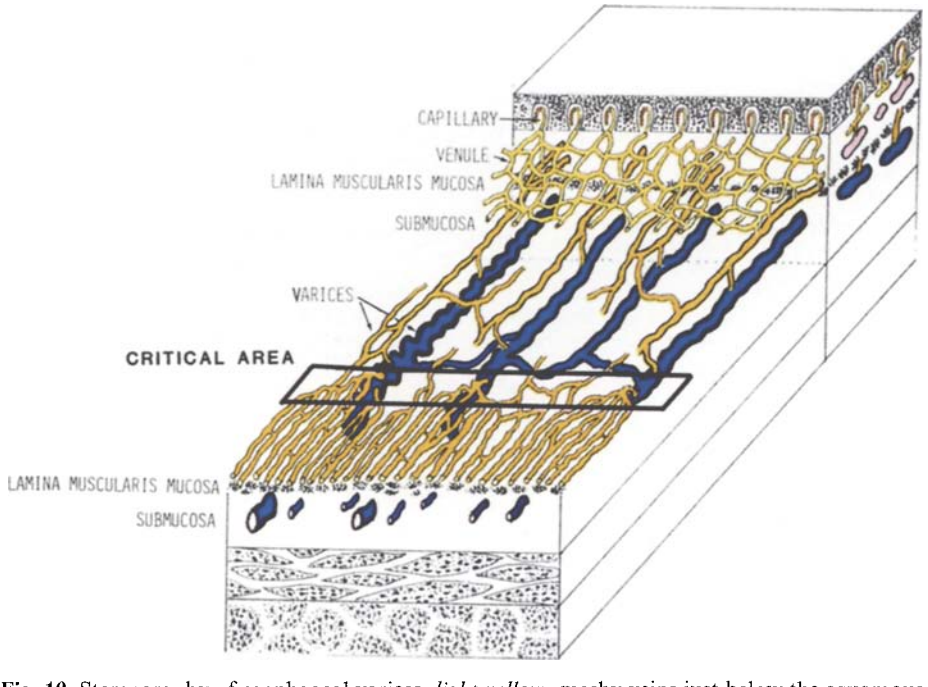

Fig. 10. Stereography of esophageal varices. *light yellow;* meshy veins just below the squamous epithelium. *dark yellow;* veins in the lamina propria. *blue;* submucosal veins

part of the esophagus might vary during the respiratory cycle, from the fact that the most remarkable angioarchitectural changes were not seen at the esophagogastric junction but at the critical area, it is most likely that the basic blood flow in the cases with severe varices may be presumed to cephalad. Thus, the critical area appeared to be of the greatest significance in the pathogenesis of spontaneous variceal rupture. Sometimes rupture of capillaries and hemorrhage into the papillae are seen histologically in the epithelium. However, these findings should not be misinterpreted as the rupture of the sudare-like veins in the lamina propria.

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