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Distribution of the Bronchial Gland at Plastic Surgery for Tracheobronchial Plasty

Ryuichiro Yoshida

The First Department of Surgery, Nagasaki University School of Medicine

The purpose of the present study was to evaluate the change in the sizes of the gland following tracheoplasty and bronchoplasty, as well as to investigate the effect of steroid therapy on changes in the size of the bronchial gland following bronchoplasty.

The total number of the glands, the mean bronchial gland area (MGA), and the ratio of the total gland area to the bronchial wall area (G/W) were measured in 70 dogs after tracheoplasty and left upper sleeve lobectomy of the lung. Nine dogs were used as a control.

The results are as follows:

1) The mean gland area (MGA) and the G/W increased in both tracheoplasty and bronchoplasty groups, however the number of the bronchial gland has not increased. As a significant change in the bronchial gland following the plastic operations, hypertrophy of the bronchial gland develops.

2) In the tracheoplasty group, the MGA and the G/W much more increased at a resection of 14 tracheal cartilaginous rings than at that of 3 and 8.

3) In bronchoplasty group, the MGA and the G/W increased on day 7 than on day 21 and in the steroid-untreated group than steroid-treated group.

It is concluded that tracheobronchial plastic operation enables the size of the bronchial glands to enlarge, and the enlarged bronchial glands grately responded to corticosteroid.

Introduction

Recently, a successful tracheoplasty and bronchoplasty for patients with malignant tumors, traumatic injuries and the stenosis due to scar formation have been reported. However, anastomotic complications are still serious and ominous. Tracheal and bronchial anastomotic complications include air leakage, hemorrhage and stenosis, ensuing pulmonary infection and atelectasis. Especially, surgeons are aware of postoperative atelectasis and pneumonia due to increased secretion and retention in the airway for elder patients with a habit of heavy smoking and with a history of chronic bronchitis.

Materials and Methods

Seventy-nine mongrel dogs weighing 7 to 15kg were anesthetized with 25mg/kg of sodium pentobarbital, intubated with a cuffed endotracheal tube and ventilated with room air using a volume respirator (HARVARD).

Animals were divided into the following groups. In nine animals, their tracheobronchial trees were resected as a control.

In tracheoplasty group containing 25 dogs, the cervical trachea was exposed through mid-cervical skin incision in the supine position. The trachea was circumferentially removed by a resection of 3, 8 and 14 tracheal cartilaginous rings. Thereafter, the trachea was anastomosed end-to-end using continuous sutures of 4-0 nylon. Dogs were killed at the 7th and the 21st day postoperatively.

In bronchoplasty group containing 45 dogs, left upper sleeve lobectomy was performed and bronchial continuity was reestablished with a running stitch of 4-0 nylon. The dogs were divided into three groups as follows:

(A group) Steroid-untreated groups (15 dogs): Only upper sleeve lobectomy was performed. The animals were sacrificed at the 7th, the 14th, and the 28th day postoperatively.

(B group) Steroid-treated group (16 dogs): Prednisolone (2mg/kg body weight) was given intramuscularly from the first day of the operation for 7 days. The animals were sacrificed at the 7th, the 14th, the 28th day postoperatively.

(C group) Stenotic group (14 dogs): When sutured end-to-end a 50% stenosis was constructed by leaving an excess margin to sew up. Dogs were killed at the 28th day postoperatively. These dogs underwent the operation and cepharosporin was given at a dosis of 50mg/kg on day 0 and 1.

The lungs were inflated with intratracheal liquid formalin. After inflation the trachea was ligated and the lungs were fixed for 5 days. Sections were taken for the histological examination from the trachea and bilateral main and lobar bronchi. For the trachea and the main bronchi, the longitudinal sections were required because bronchial glands were normally situated between the rings of the caltilages (Fig. 1). In the lobar bronchi, the glands were

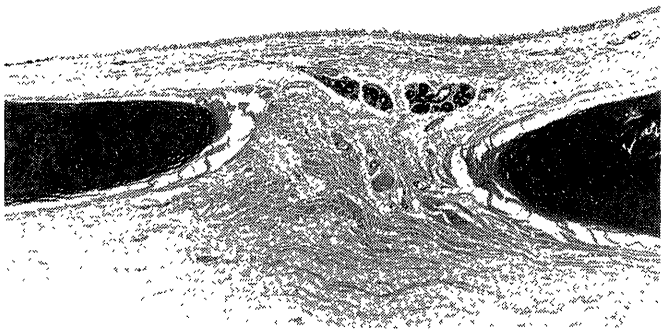

Fig. 1.

randomly distributed, so the sections were taken and cut transversely (Fig. 2). The paraffin sections were stained with haematoxylin and eosin, with a combined Alcian Blue and periodic acid-Schiff stain for glycoproteins.

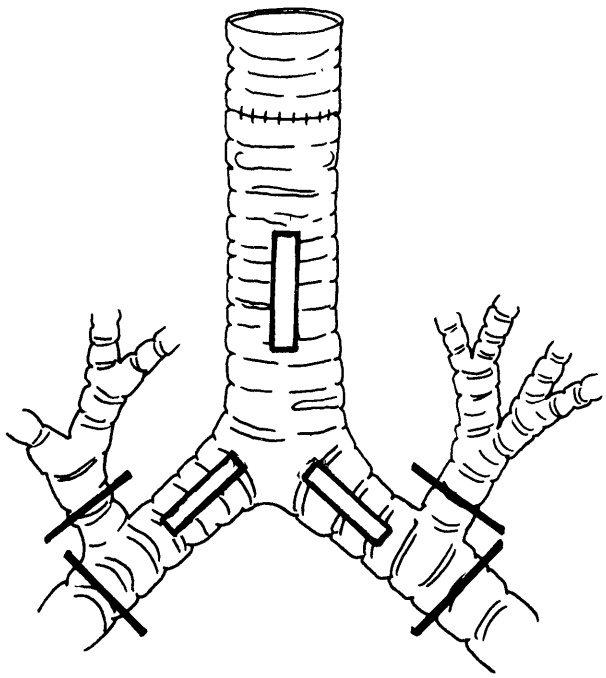

Fig. 2.

The area occupying the bronchial glands in each sections was photographed with a scale. Using the semi-autodigitizer (LEITZ-ASM), the area and the number of each individual gland were measured and areas were summed. Next, the area of the bronchial wall was measured from a drawing of the projected image of the sections. The mean gland area (MGA) was calculated. The G/W was determined as the ratio of the total gland area to the bronchial wall area, the calculation being performed by a microcomputer. Anastomotic site was not suitable for measurement because of the formation of inflammatory granulation and the infiltration of neutrocytes in submucosal layer.

Result

No death was encountered in the tracheoplasty group. However, there were 4 deaths in A group, 2 in B and 5 in C bronchoplasty groups. The causes were pneumonia and athelectasis.

1) Histologic findings of the normal dog's trachea

As shown in Fig. 1, the majority of the submucosal glands lay between the mucosa and the cartilage, but a few are found external to the cartilage ring. The submucosal glands consist mainly of mucous gland cells, serous gland cells and collecting ducts (Fig. 3).

2) tracheoplasty group

As shown in Fig. 4, MGA ranged from about one and a half to threefold at the 7th day as compared with the control group. MGA in 14 tracheal cartilaginous rings resected group was much greater than in 3 or 8 tracheal cartilaginous rings resected group. At the 21st day, it increased about 1.5 to 2 times rather than the control group (Fig. 5). In contrast, it did not show an increase as compared with that on day 7.

In the trachea and the main bronchi, the G/W increased at both the 7th and the 21st day, but did not increased in the lobar bronchi (Fig. 6, 7).

As shown in Fig. 8, 9, the number of the glands did not increase. The postoperative changes in tracheoplasty are due mainly to hypertrophy of the bronchial gland.

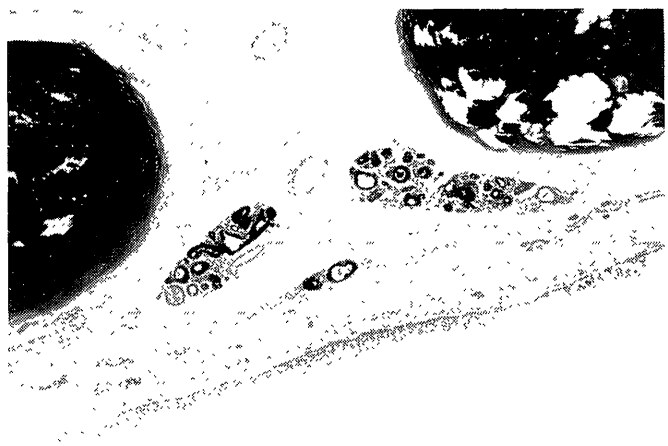

Fig. 3.

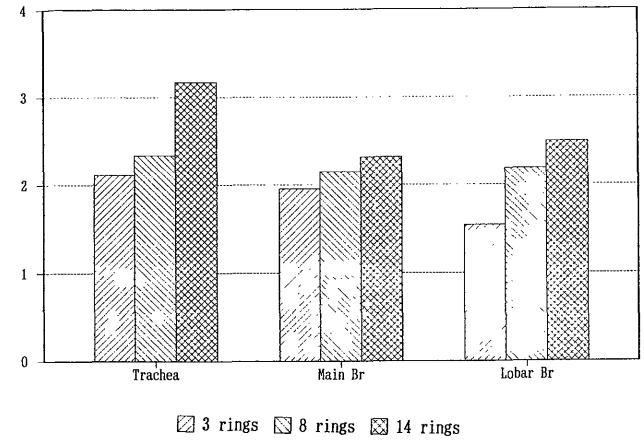

Fig. 4. Mean Gland area in Tracheoplasty group at 7th day (Control = 1)

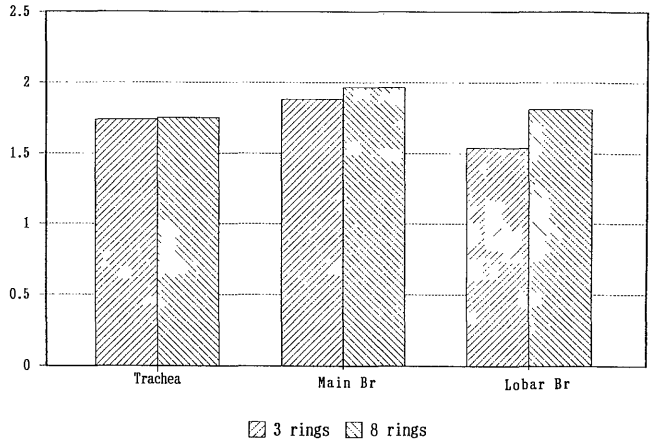

Fig. 5. Mean Gland area in Tracheoplasty group at 21st day (Control = 1)

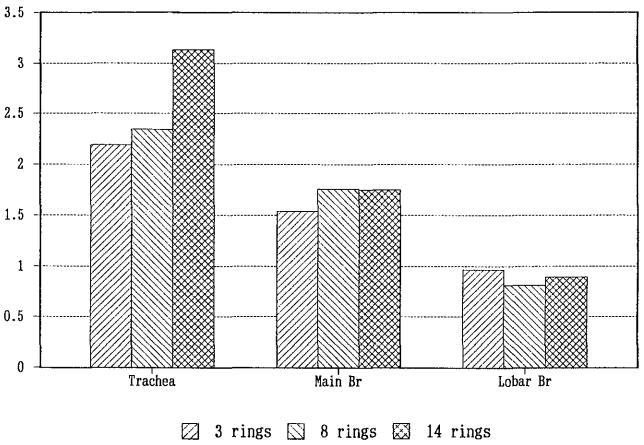

Fig. 6. G/W in Tracheoplasty group at 7th day (Control = 1)

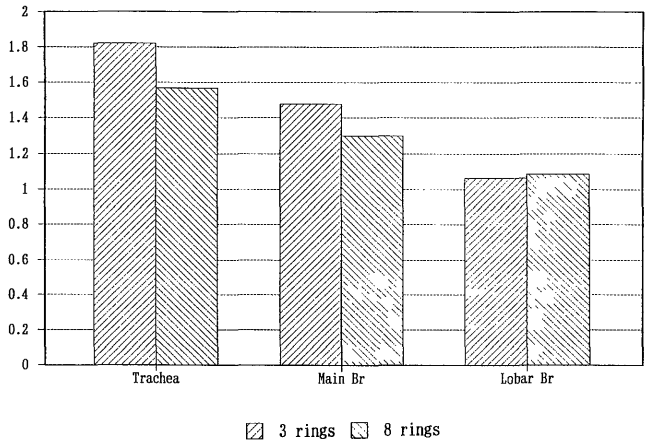

Fig. 7. G/W in Tracheoplasty group at 21st day (Control = 1)

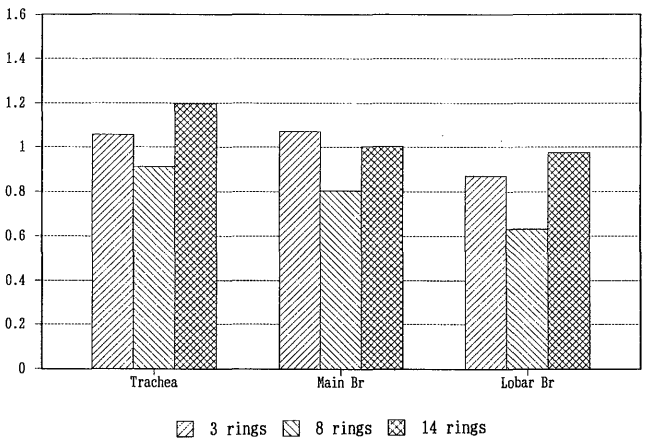

Fig. 8. Number of the gland in tracheoplasty group at 7th day (Control = 1)

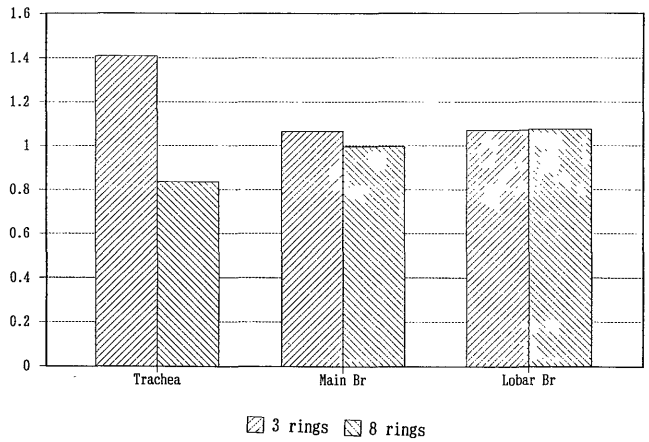

Fig. 9. Number of the gland in Tracheoplasty group at 21st day (Control = 1)

3) bronchoplasty

The MGA increased at the 7th day than the 14th and the 28th day, and in steroid-untreated group than steroid-treated group (Fig. 10, 11, 12). As shown in Fig. 13, the mean G/W in the four sites (trachea, the right main bronchus, the right upper and lower bronchi) was the same as the above. The MGA and the G/W in group C (stenotic-

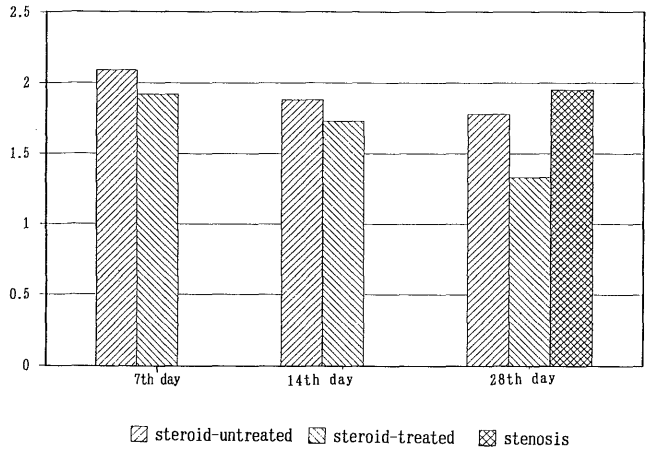

Fig. 10. MGA in bronchoplasty group at trachea (Control = 1)

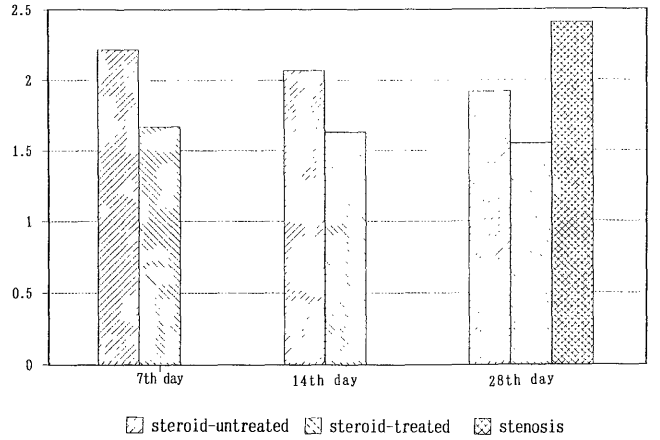

Fig. 11. MGA in bronchoplasty group at main bronchus (Control = 1)

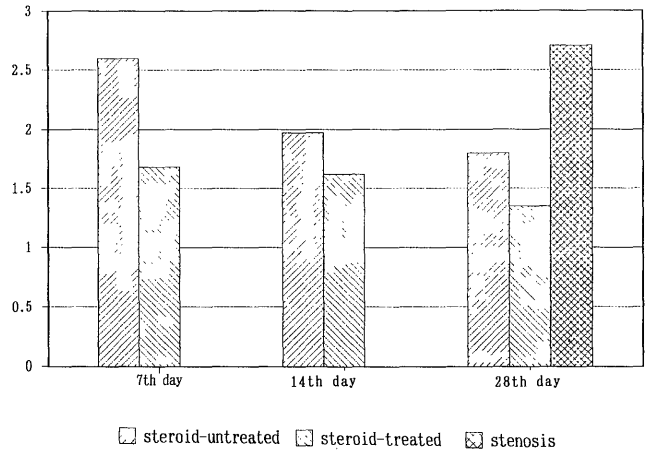

Fig. 12. MGA in bronchoplasty group at lobar bronchi (Control = 1)

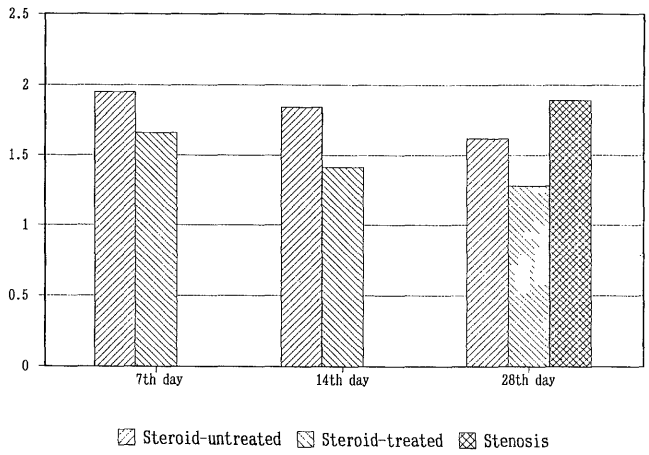

Fig. 13. G/W in Bronchoplasty group the mean of four sites (Control = 1)

group) were greater than those in steroid-treated and steroid-untreated groups.

In this study, all of the dogs which belonged to the stenotic group were sacrificed on day 28. An increase in the MGA was significantly indicated in the main and the lobar bronchi rather than that in the trachea.

Discussion

The important morphologic alteration in chronic bronchitis is enlargement of tracheobronchial glands. In 1960, Reid[1] described the measurement of the gland-to-wall ratio, generally referred to as the Reid index. She used the ratio of the thickness of mucous glands to the thickness of bronchial wall from the cartilage to the basement membrane to identify a trait of chronic bronchitis. She reported hypertrophy and hyperplasia of the bronchial mucous glands, and demonstrated that gland hypertrophy was in association with production of sputum and also that the degree of hypertrophy varied directly with the amount of sputum produced.

The major advantage of the Reid Index is that the measurement is easy and can be done quickly. However, Jamal[5] could not define a significant correlation between Reid Index and the amount of sputum produced.

Prior to the Reid's report, in 1959, Fukuda[6] evaluated the enlargement of the submucosal gland by the card-weighing method. He took photographs of the bronchial image projected on the wall with a scale. A paper that was cut off the glands and bronchial lumen were weighed on a delicate balancer. He reported that the increase in a bronchial gland/lumen ratio distribution (a coefficient of the mucus gland) correlated well with the occurence of postoperative bronchial fistula. In 1963, Restrepo and Heard[7] also evaluated the degree of enlarged mucous glands in chronic bronchitis by the card-weighing method.

In 1962 Dunnill[8] and in 1968 Hale[9] described their experience with a point-counting method that assesses all structures in the bronchial wall.

Bedrossian and associates[10] reported that the use of the Reid index, bronchial glandular acinar counts, and determination of percentage mucous acini was of no great benefit in assessment of the degree of hypertrophied bronchial mucous gland with any degree of precision as compared with planimetry. Furthermore, they showed the advantages of the accuracy and the convenience of the point count method and the card-weighing method. In 1971 Takizawa[11] also reported that the size of the mucous gland size increased in asthma in the case of assessment by the Dunnil point count, but not by the Reid index.

A computer-assisted digitizer (LEITZ-ASM) was used in this study. It slightly consumes time, but the data obtained was precise. Estimations were made of the total number of gland cells, the mean gland area (MGA) and the ratio of the total gland area to the bronchial wall area (G/W).

Concerning morphologic alteration of the bronchial gland in various diseases, Okada[12] clarified that the mucous glands were significantly proliferated rather than the serous gland in chronic bronchitis.

The acinus of the mucous gland used to display less than 50% in healthy state although it increased up to 60% or more in chronic bronchitis. Tomita[13] and associates reported that a distribution coefficient of the bronchial gland increased when occurring inflammation which was estimated round cell infiltration in the submucosal layer. They contemplated secretion of the bronchial gland was necessary for air-way cleaning at the time of infection. And also Tomita emphasized that hypertrophy of the bronchial gland was in association with postoperative polmonary complication and its degree correlated well with the disease time duration of inflammation of the bronchial wall.

Yamanaka[14] reported that histochemical differentiation of the bronchial gland which elapsed 6 months after gland regeneration in dogs whose trachea on the anterior wall was partially resected with the window type of 3 cartilaginous rings and replaced the inside out in which the bronchial glands began regrowth 3 months later.

Nagasawa[15] noticed that regeneration of the bronchial gland and wrapping of the regenerative epithelium was recognized on day 21 in the experiment in which retransplantation of the resected tracheal wall of dogs was performed after the thoracic trachea was removed with 5 cartilagenous rings.

Kawahara[16] reported that ischemic changes at bronchial anastomosis is most manifest on day 7 to 12 after anastomosis, and normal gross and histologic appearance was seen 19 days later.

Hasegawa[17] also reported in dogs that neovasucularity around the anastomosis was evident on day 7 after tracheal anastomosis by microangiography, and newly growing vessels were no longer observed on day 21.

In 1980 Douglas[18] estimated the enlargement of the bronchial gland by the gland index which is proportional to the mucous gland area existing in non-cartilaginous part of the bronchial wall from 30 lower lobe bronchi, which were taken from coal miners. He demonstrated that the enlarged bronchial mucous gland was primarily based on a hyperplastic change. It might be true that smoking and exposure to dust had serious consequence in the case of coal miners.

Generally, it is considered that glucocorticoids can inhibit the inflammatory process[19] and wound healing.[20] Lima[21] demonstrated that low-dose methylprednisolone (2mg/kg) and azathioprine (1.5mg/kg) significantly decrease the tensile strength of both bronchial anastomoses and healed skin incisions following canine lung autotransplantation. Namely, they reported that at 23 days, the breaking strength of the bronchial anastomosis in control animals was nearly twice as potent as that in immunosuppressed, and the breaking strength of healed skin wound was four times as great as that in immunosuppressed. It is probably due to not the effect of methylprednisolone but azathioprine.

In fact, Pinsker, Veith, and their associates[22] showed that prednisone (2mg/kg) does not only interfere with healing for up to 21 days, but also reduces inflammation at the bronchial anastomotic site. The dose of prednisone they used is equivalent to 120 to 140mg per day for a human lung transplant recipient. Hsiesh[23] also demonstrated that a short-term administration of corticosteroid (Prednisolone 2mg/kg) decreased inflammation and prevented excessive granulation at anastomotic site and only has a little inhibition on the early phase of bronchial healing.

The MGA and the G/W values in steroid non-treated group were 2 to 1.5 times as great as those in the control group and also those in the steroid treated group were much more lower than those in the steroid non-treated group. The data obtained in this study are in agreement with their experience.

Ohmagari[24] cited that a 75% stenosis of the bronchial lumen in 98 dogs had led to 14 deaths due to pneumonia. Thus it was clarified that the lung had become emphysematous on chest roentgenogram with elapse of one month after making a 75% stenosis, and 3 months later, the club-like shadow change was seen. This meant the irreversible changes in the lung even though bronchial reconstruction had been performed. Therefore, he emphasize that the indication of bronchial reconstruction for bronchial stenosis is within 3 months from the onset of bronchial stenosis. In this series, dogs with atelectasis expired within 7 days. It is needless to say that it is based on bronchial stenosis, however, partly due to an increase in bronchial secretion on the basis of the increase in the MGA and the G/W.

Prevention from occurring atelectasis and pneumonia is needed for an increase in bronchial secretion. The maximum of the MGA and the G/W on day 7 was seen in the following order, the trachea, the main bronchus and the lobar bronchus. On day 21, the increase in the MGA and the G/W was lessened because of elimination of inflammatory response. The number of cartilaginous ring was

almost similar with the fact that the more the resected cartilaginous ring increased, the more the tensile strength had become vigorous. It is concluded that early change of the bronchial gland is not hyperplastic but hypertrophic. The results showed that the change following the performance of plastic operations was attributable to hypertrophy of the bronchial gland without any increase of the number of bronchial gland.

Acknowledgement

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