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Effect of Aging on the Esophageal Motor Functions

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Abstract

To clarify the changes of esophageal motility along with age, we performed esophageal manometry on 47 healthy volunteers, and compared the values of four groups under 49 years old (n=11), 50 to 59 (n=15), 60 to 69 (n=11), and over 70 years old (n=10). Resting lower esophageal sphincter (LES) pressure in the group over 70 years old showed the tendency of decrease, but not statistically significant. Nadir LES pressure on swallow-induced relaxation was not statistically different among 4 groups. On esophageal body testing, percentage of non-conduction sequence in the group 60 to 69 and over 70 years old was statistically higher compared with that of the group under 49 years old ($p<0.05$) but spared in some elderly subjects. Percentage of simultaneous contractions was not statistically different among 4 groups. Peristaltic contraction amplitude in the group over 70 years old was significantly lower than that of the group under 49 years old both at the level of 5 cm above ($p<0.01$) and 10 cm above LES ($p<0.05$). We speculate that the influence of aging on esophageal motility is the reduced transmission sequence of peristalsis and contractility of esophageal body. This alteration along with age may differ from the pathological condition of scleroderma or diffuse esophageal spasm.

Key words: esophageal motility, aging, presbyesophagus, esophagus

Introduction

Physical conditions alter according to age in human subject (Carid, 1987). Motor functions of human gasstrointestinal tract may also alter along with age. In the elderly human subjects, delayed gastric emptying (Moore *et al.*, 1983) and reduced postprandial contractility in small intestine (Anuras *et al.*, 1984) were reported.

Aging effect on human esophageal motility had been analyzed by means of cineradiological studies (Zboralske *et al.*, 1964 : Mandelstam *et al.*, 1970). Zboralske *et al.* showed that reduced peristaltic sequence, delayed barium emptying from the esophagus, and increased spontaneous

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contraction as characteristic changes in the elderly human esophagus, and they coined this condition as "presbyesophagus" (Zboralske *et al.*, 1964). The other cineradiological study by Mandelstam *et al.* (1970) showed that the reduced peristaltic sequence and the delayed barium emptying in the elderly subjects. However, radiological study is not suitable for the quantitative analysis of the esophageal motor events, as there could be considerable interobserver difference on analysis (Mandelstam *et al.*, 1970).

Esophageal manometry is the most objective and quantitative method to assess the esophageal motility. Only several studies, which studied manometric findings in the elder subjects, have been reported by 1994 (Hollis *et al.*, 1974 ; Kahn *et al.*, 1977 ; Csendes *et al.*, 1978 ; Richter *et al.*, 1987, Micklefield *et al.*, 1993 ; Adamek *et al.*, 1994) as far as we know. Studies reported by Hollis *et al.* (1974) and Khan *et al.* (1977) mainly compared the esophageal motor function between the two groups of young and elder. If the aging has influence on esophageal motility, changes in motility may occur gradually along with age. Richter *et al.* (1987) studied esophageal motility in 95 healthy volunteers. As the aim of their study was to establish normal value, they gave less attention to the elderly human subject and the eldest age of the volunteers was 74 years old (Richter *et al.*, 1987). Csendes *et al.* (1978) performed esophageal manometry in the subjects ranging from infants to the elderly. In their report, they did not describe the method to induce esophageal peristaltic activities whether wet or dry swallows.

Our aim of the study is to clarify the changes in the characteristics of the esophageal motility along with aging in the human subjects.

Method

Subjects

Forty-seven volunteers participated in this study. They were 26 males and 21 females. Their age ranged from 23 to 89 years old (yo), and both of the mean and the median were 57 yo. They had no upper gastrointestinal symptoms. The person who had diseases known to have influence on gastrointestinal motility such as diabetes mellitus, collagen diseases, or peptic ulcer was excluded. The person who was taking any drugs known to affect gastrointestinal motility was also excluded. To assess the effect of aging, the subjects were divided into 4 groups by age ; group under 49 yo (<49 yo. 11 subjects, 7 of whom were male), group between 50 and 59 yo (50's. 15 subjects, 7 males), group between 60 and 69 yo (60's. 11 subjects, 5 males) and group over 70 yo (>70. 10 subgects, 5 males). Proportion of male and female in the four groups were not statistically different ($\chi^2=1.185$, $p=0.76$). Study was performed according to the Declaration of Helsinki. Before participation, informed consents were obtained from all subjects.

Manometry

Esophageal manometric study was performed using 5 lumen polyvinyl catheter (outer diameter 4.5 mm). Three side holes located at 5 cm proximal from the distal end of catheter and radially oriented with difference of 120 degree each other. These three side holes were served for the monitoring of the lower esophageal sphincter (LES) pressure. The other 2 side holes were located 5 and 10 cm proximal to the three side holes, respectively. These two holes were used for recording contractions of esophageal body. Each lumen were connected to external pressure transducer (Statham P23ID, Gould, Oxnard, California, USA) and perfused with distilled water at a flow rate of 0.5 ml/minute by pneumohydraulic infusion pump (Arndorfer Medical Specialties Inc. Wisconsin, USA). Electrical signals from the transducers were amplified through bioelectric amplifier (Polygraph 360, NEC San-Ei, Japan) and recorded by pen-chart recorder (Recti-Horitz-8K, NEC San-Ei, Japan). This recording system has a pressure rise rate more than 300 mmHg/sec (Ujiie *et al*., 1987).

Esophageal manometry was performed at least after 8 hours fast. Each subject was in supine position during manometry. After pharyngeal local anesthesia, manometric catheter was introduced from nostril or oral cavity until three distal side holes reached into the stomach. Recording started after several minutes of adaptation. LES pressure was recorded with three distal side holes by 1 cm of step-wise station pull-through technic. After this procedure, three distal holes were placed at LES so that at least one pressure pattern suggested at respiratory inversion point, and 10 succesive swallow of 3-5 ml of tap water were given, with intervals of more than 30 seconds, to record esophageal body contractions and LES relaxation. The paper speed of chart recorder was 1 mm/sec at station-pull through and 2 mm/sec at wet swallows.

Data analysis

All the charts were reviewed and calculated without knowledge of the age of the subjects. For LES pressure measurement, and-expiratory intragastric pressure was used as baseline. Mean end-expriratory pressure of 3 distal channels in each point of station pull-through were calculated and the maximum of the mean value was defined as resting LES pressure. Minimum LES pressure at relaxation induced by wet swallow was measured on each 3 distal channels. On each wet swallow, LES pressures at relaxation were monitored with 3 radial side holes, and the mean of three values was calculated. The grand mean of LES pressure at relaxation in 10 wet swallows was calculated, and defined as nadir LES pressure at relaxation.

On measurement of esophageal body contraction, end-expiratory intraesophageal resting pressure was served as baseline. The onset and offset of each contraction waves were defined as the time of crossing points of baseline and main upward slope of contraction wave, and main downward slope, respectively (Dalton *et al*., 1987). Duration of contraction was defined as the time difference between the onset and offset of each contraction wave. Conduction velocity was defined from the time difference of onset of contraction between at 10 cm and 5 cm above LES. Contraction in manometry was defined as the $\geq$10 mmHg pressure increase. When the sequence of contractions at 2 different sites in the esophageal body, 5 cm and 10 cm proximal to LES, is separated by $\geq$0.5 seconds at the onset, this sequence was defined as peristaltic contraction. When the intervals of the onset of contraction sequence at 2 sites was $<$0.5 seconds, which means conduction velocity is $>$10 cm/sec, this sequence was defined as simultaneous contraction. When one of the recording sites failed to record contractions ($<$10 mmHg in amplitude), this sequence was defined as non-conducted sequence. Appearance of each sequence following 10 wet swallows was expressed in %. On peristaltic sequences, mean peristaltic contraction amplitude and duration were served for statistical analysis.

Contraction wave with 2 peaks or more, those were separated by ≥one second in time by their peaks and >10 mmHg in pressure difference between the peak and the bottom was defined as bi-peak or multi-peak wave (Clouse *et al.* 1983a). Repetitive contraction was defined as >2 contractions within 10 seconds, following a wet swallow, separated by ≥one second in time between the offset and the onset of the following wave (Clouse *et al.*, 1983b).

Statistical analysis

Kruskal-Wallis test was performed on each manometric parameter of four groups. If the result was statistically significant, values in the group <49 yo and in the other three groups were compared by Mann-Whitney test with correction by Dunnett's method. A p value less than 0.05 was accepted as significant. The data were expressed as median: [range].

Results

The values of manometric parameters in 4 groups by age are summarized in Table.

LES function

Resting LES pressure in the group <49 yo was 15: [8, 27] mmHg, while that of the >70 yo was 10.5: 4, 16] mmHg. Though the tendencyof decrease in resting LES pressure in the group>70 yo was noted, statistical significance was not observed among 4 groups. Nadir LES pressure on relaxation in the group of >70 yo was 2.7: [0.3, 8.2] mmHg, showing slightly

Table. Esophageal motor functions in groups by age.

	groups			
	≤49 yo (n=11)	50's (n=15)	60's (n=11)	70 yo≤ (n=10)
[**LES function**]				
resting pressure (mmHg)	15: [8, 27]	15: [7, 28]	17: [7, 22]	10.5: [4, 16]
nadir pressure on relaxation (mmHg)	1.7: [0, 6.8]	0.7: [0, 5.8]	0.6: [0, 7.1]	2.7: [0.3, 8.2]
[**body function**]				
sequence				
peristaltic sequence (%)	100: [90, 100]	90: [80, 100]	87: [10, 100]*	80: [60, 100]*
non-conducted sequence (%)	0: [0, 10]	10: [0, 10]	10: [0, 90]*	10: [0, 40]*
simultaneous contraction (%)	0: [0, 0]	0: [0, 10]	0: [0, 20]	0: [0, 20]*
amplitude of peristaltic contraction				
5 cm above LES	114: [58, 142]	78: [27, 149]	70: [18, 135]	37: [20, 54]*
10 cm above LES	72: [31, 137]	61: [21, 152]	51: [14, 101]	35: [14, 58]*
duration of peristaltic contraction				
5 cm above LES	3.4: [2.5, 5.9]	3.2: [2.5, 5.1]	3.3: [2.3, 6.1]	3.2: [2.5, 3.9]
10 cm above LES	3.4: [2.4, 5.3]	3.1: [2.5, 4.2]	3.1: [2.1, 7.6]	2.9: [2.1, 3.9]
conduction velocity of peristalsis (cm/sec)	4.7: [2.4, 6.5]	4.0: [2.1, 6.7]	3.2: [2.3, 6.1]	4.4: [2.5, 5.9]
% of bi-peak contraction (%)	0: [0, 10]	0: [0, 20]	0: [0, 20]	0: [0, 0]

Data are expressed as median: [range]. *; $p<0.05$, **; $p<0.01$ vs ≤49 yo.

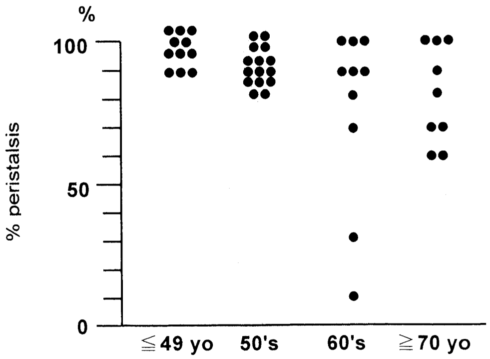

Fig. 1. The percentage of peristaltic sequence in the subjects. Compared with the group under 49 yo (≤49 yo), group between 60 and 69 yo (60's) and over 70 yo (≥70 yo) showed statistically significant decrease ($p<0.05$). However, some subjects in 60's and ≥70 yo seem to maintain the percentage in 90 to 100%.

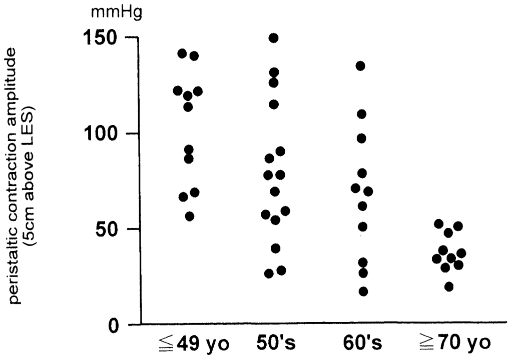

Fig. 2. The amplitude of peristaltic contraction at 5 cm above the LES. In 50's and 60's, several subjects showed weak peristaltic contraction amplitude, but there were considerable overlaps between the value of the group ≤49 yo. All subjects in the group≥ 70 yo showed weaker peristaltic contraction amplitude than the subjects <49 yo, and the difference were statistically significant ($p<0.01$).

higher walue than the other 3 groups, but not statistically significant.

Esophageal body function

Percentage of peristaltic contractions in the group<49 yo was 100 : [90, 100], while the % of peristaltic contractions in 60'9 and >70 yo were significantly lower compared with the group<49 yo ($p<0.05$. Fig. 1). The % of non-conducted sequence in the group <49 yo was 0 : [0, 10], while in 60's and in >70 yo were 10 : [0, 90] and 10 : [0, 40], respectively, and were significantly higher compared with the group <49 yo ($p<0.05$). Simultaneous contractions were observed in 7 subjects ; 2 subjects in 50's (15%), 2 in 60's (18%), and 3 in >70 yo (30%). The highest % of simultaneous contraction was 20% in two subjects ; one in 60's and another in >70 yo. Median value of % simultaneous contraction was 0% in all groups, and there was no statistical significance. Conduction velocity of peristaltic contraction did not significantly differ among 4 groups.

There was a tendency of a decrease in the peristaltic contraction amplitude at 5 cm proximal to LES with the increase of age. In 50's and 60's, several subjects showed weak perstaltic contraction amplitude, but there were considerable overlaps between the value of the group <49% (Fig. 2). All subjects in the group >70 yo showed weaker perstaltic contraction amplitude than the subjects <49 yo, and the difference was statistically significant ($p<0.01$). At 10 cm proximal to LES, the perstaltic contraction amplitude in group >70 yo was also significantly lower than that in the group <49 yo ($p<0.05$).

Duration of perstaltic contraction at both 5 cm and 10 cm proximal to LES was not significantly different among 4 groups by age.

The appearance rate of bi-peak waves was not significantly different among 4 groups.

The appearance rates of bi-peak waves in each subjects were below 20%. The contraction with three or more peaks was not observed in this study. Repetitive contraction was not observed during the entire period of this study.

Discussion

Our data showed that esophageal peristaltic sequence and peristaltic contraction amplitude reduce along with age in human subjects.

Decrese in the appearance rates of peristaltic contraction in 60's and in the group ≥70 yo was mainly due to increased occurrence of non-conducted sequence, but not due to the increase in simultaneous contractions. Influences of the aging on the appearance rates of peristaltic contraction in the previous reports are conflicting. One study showed no difference in the appearance rate of the peristaltic contractions between the young and the elderly as reported earlier (Hollis *et al.*, 1974), while some studies reported that the reduction of peristaltic contractions in the elderly along with an increase of the failed contractions and the simultaneous contraction (Kahn *et al.* 1977 ; Adamek *et al.*, 1994). In our data, simultaneous contractions were recorded in several subjects from the elder 3 groups, while not in the group ≤49 yo. However, the appearance rates were below 20% in each subject and did not show significant difference among all groups. Conduction velocity of peristaltic contraction did not change by age, in our data. Kahn *et al.* (1977) reported that in the upper third portion of the esophagus, that is, striated muscle portion of the esophagus in human, conduction velocity of peristalsis increased significantly in the elderly subjects. However, difference in the mean value between in the young and in the elderly was only 0.7 cm/sec in their study. Furthermore, there was no significant difference in the conduction velocity in the lower two-third of the esophagus, namely, in the smooth muscle portion, where we did not find significant changes with age.

Decrease of the peristaltic contraction amplitude of the esophageal body in the elderly had been previously reported (Hollis *et al.*, 1974 ; Kahn *et al.* 1977), while some studies reported such changes are not statistically significant (Micklefield *et al.*, 1993 ; Adamek *et al.*, 1994). Our data clearly shows the increase in the incidence of reduced peristaltic contraction amplitude along with age. Compared with the group ≤49 yo, % of peristaltic contraction was statistically lower in the group ≥70 yo, but 4 subjjcts showed peristaltic contractions in 90% or more. On the other hand, all subjects in the group ≥70 yo showed decreased peristaltic contraction amplitude, which was below the lower range in the group ≤49 yo, at 5 cm above LES. From these data we speculate that two kinds of alterations of the motility in the esophageal body motility along with age, decrease in the % of peristaltic sequence and decrease of peristaltic contraction amplitude, may progress in an independent way. Vagal nerves and myenteric plexus of the esophagus play an important role on regulation of esophageal peristaltic sequence (Kravitz *et al.*, 1978 Dodds *et al*, 1979 ; Gidda *et al.*, 1981 : Humphries *et al.*, 1981). Reduction of parasympathetic function with aging is shown through findings of heart rate variation tests (Oikawa *et al.*, 1984). Histologically, ganglion cells in esophageal myenteric plexus in the elderly subjects decreased in number (Eckhardt *et al.*, 1978). These functional and histological alterations in vagal and myenteric nerves may have relationship with the decreased appearance rate of peristaltic sequence in the elderly subjects. Alterations of nervous system, especially postsynaptic cholinergic nerves, may have influence on esophageal contractile force because stimulation of muscarinic receptors augments contractile force of the esophageal body (Humphries *et al.*, 1981). Another explanation of decreased contractile force in esophageal body is reduced contractility of the esophageal smooth muscle coat. Because the thickness of the smooth muscle layer of the human esophagus does not reduce with age (Eckhardt *et al.*, 1978), decrease in contractility in the elderly subjects might be due to the altered function of the smooth muscle fiber rather than the loss of the smooth muscle cells.

In the present study, resting LES pressure was lower in the group >70 yo, but was not significant, similar to the other data (Kahn *et al.* 1977 ; Csendes *et al.*, 1978). LES relaxation following wet swallows in the elderly subjects is controversial. Kahn *et al.* (1977) reported the relaxation response of LES in the elderly was impaired, while Hollis *et al.* (1974) reported that intact. Their observations on LES relaxation were performed by means of one pressure channel. Our measurement on LES relaxation was performed by three channels which may give more reliable information. As nadir LES pressure on relaxation was not significantly different among 4 groups, we speculate that aging has fewer effects on LES relaxation.

Some investigators reported that functional alteration of esophageal motility in the elderly mimics diffuse esophageal spasm (Zboralske *et al.*, 1964 ; Kahn *et al.* 1977). Our results were obtained from the subjects without esophageal symptom and any diseases known to have influence on esophageal motility. Some subjects over 50 yo showed simultaneous contractions but no significant difference in appearance rate among 4 groups. Furtermore, bi-peak contraction, which is ferquently observed in diabetic patients with autonomic neuropathy (Loo *et al.*, 1985), did not increase with age in our study. Therefore, neurogenic or myogenic alterations of motility in esophageal body with age may be different from pathological condition such as diffuse esophageal spasm or hypomotility in patients with scleroderma (Vantrappen *et al.*, 1979 ; Satake *et al.*, 1990).

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