ORIGINAL

Evaluation of stress reactions during upper gastrointestinal endoscopy in elderly patients : assessment of mental stress using chromogranin A

Sayuri Fujimoto, Masahiro Nomura*, Miyako Niki**, Hideki Motoba*, Kiyoshi Ieishi, Toshifumi Mori, Hiroyuki Ikefuji, and Susumu Ito

*Department of Digestive and Cardiovascular Medicine, Institute of Health Biosciences, The University of Tokushima Graduate School, *Faculty of Integrated Art and Sciences, Department of Human and Social Sciences, The University of Tokushima ; and **Division of Internal Medicine, Okinosu Hospital, Tokushima, Japan*

Abstract :
Objective : **Salivary chromogranin A (CgA) was recently reported to be a useful marker of mental stress. In this study, mental stress during upper gastrointestinal endoscopy was evaluated by measuring salivary CgA levels in young and elderly subjects.** ***Methods :*** **The subjects were 9 healthy subjects aged less than 50 years (young group) and 15 subjects aged 70 years or older (elderly group). The heart rate, blood pressure, blood oxygen saturation level, and salivary CgA concentration were measured before and after upper gastrointestinal endoscopy and compared.** ***Results :*** **In the young group, the CgA level decreased significantly ($p<0.05$) during endoscopy compared with the level during rest before endoscopy. In the elderly group, it also decreased significantly ($p<0.05$) during endoscopy compared with the level during rest before endoscopy. However, CgA levels were significantly higher ($p<0.05$) in the elderly group than in the young group both before and during endoscopy. The decrease in CgA levels was significantly greater ($p<0.05$) in the young group than in the elderly group.** ***Conclusions :*** **In this study, mental stress associated with endoscopy appears to be higher in elderly subjects than in younger subjects. Attention to complications due to increased stress is considered to be necessary in elderly patients during endoscopy.**
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Keywords **:** *chromogranin A, mental stress, gastrointestinal endoscopy, stress, elderly patient*

INTRODUCTION

With the arrival of an aging society, the percentage of elderly patients who are undergoing upper gastrointestinal endoscopy is increasing annually. Particularly, in elderly people, more attention to accidents as well as to the degree of distress is necessary than in younger patients, even under the same endoscopic conditions (1, 2). Vomiting reflex during insertion of the fiberscope and its operation in the upper gastrointestinal tract, in particular, may affect the blood pressure, heart rate, oxygen saturation, and autonomic nervous activities, cause changes in hemodynamics, and even induce lethal arrhythmia or sudden death (3-6). While there have been reports of respiratory and hemodynamic responses

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Address correspondence and reprint requests to Sayuri Fujimoto M.D., Department of Digestive and Cardiovascular Medicine, Institute of Health Biosciences, The University of Tokushima Graduate School, Kuramoto-cho, Tokushima 770-8503, Japan and Fax : +81-88-633-9235

to endoscopy, studies that related to the effects of mental stress during endoscopy are unknown.

Stress has been evaluated by measuring cortisol or a catecholamine as a marker. However, these hormones do not reflect genuine mental stress, because they respond to, not only mental, but physical stress as well. Salivary chromogranin A (CgA) levels, which respond specifically to mental stress, have recently become measurable (7). In the present study, mental stress during upper gastrointestinal endoscopy in elderly subjects using CgA as a marker was evaluated.

METHODS

1) Subjects.

Upper gastrointestinal endoscopy was performed in 9 healthy subjects aged less than 50 years (young group : 5 men and 4 women, aged 41.2 ± 6.9 years) and 15 subjects aged 70 years or older (elderly group : 6 men and 9 women, aged 77.3±5.5 years).

None of the subjects had a history of cardiovascular disease and all were found to be normal on physical examination, standard 12-lead ECG, and a chest X-ray examination. Individuals with hypertension or diabetes mellitus and those who had used autonomic drugs such as anticholinergic and β-blocking agents within the past month were excluded. The subjects were prohibited from eating or drinking after 21 : 00 on the day before upper gastrointestinal endoscopy, which was performed between 9 : 00 and 12 : 00 the next morning. All subjects were considered to require upper gastrointestinal endoscopy by a gastroenterologist. The present study was approved by the ethics committee of Hospital, and informed consent was given to the patients or their family after full explanation of the purpose of this study.

All subjects were premedicated by an intramuscular injection of diazepam (10 mg) and butyl scopolamine bromide (20 mg). Upper gastrointestinal endoscopy was performed by physicians with at least 6 years of prior experience and who were accredited by the Japanese Society of Digestive Endoscopy.

2) Measurement of percutaneous oxygen saturation, blood pressure, and heart rate during upper gastrointestinal endoscopy.

In the young and elderly groups, the percutaneous oxygen saturation, blood pressure, and heart rate were monitored using an automatic sphygmomanometer (MUE-200, Olympus, Tokyo, Japan), and the maximum percent changes between before the examination and during endoscopic procedure were compared. The heart rate was continuously monitored by attaching an ambulant ECG monitoring system. Blood pressure (MUE-200, Olympus, Tokyo, Japan) was measured every minute by the oscillometric method by applying a cuff to the right brachium. Percutaneous oxygen saturation (MUE-200, Olympus, Tokyo, Japan) was monitored by applying an arterial blood oxygen saturation sensor to the right second finger.

3) Measurement of the salivary CgA concentration.

Salivary CgA concentrations were determined at two points during rest before upper gastrointestinal endoscopy and during duodenal endoscopy. About 1 ml of saliva was collected, immediately cooled in ice, centrifuged after the end of endoscopy, and stored at -20℃ until used in the assay.

CgA was determined by an enzyme immunoassay using a Human Chromogranin A EIA kit (YK070, Yanaihara Institute, Tokyo, Japan). The observed CgA concentrations were corrected for the total protein concentration and expressed as pg/mg protein.

4) Statistical analysis.

The data are presented as the mean ± standard deviation (SD). Comparisons between the two groups were performed by the Student's unpaired t-test, and a comparison between the same groups (before endoscopy vs, during endoscopy) was performed using the paired t-test. $P<0.05$ was considered to be significant.

RESULTS

1) Changes in the respiratory and hemodynamic parameters during upper gastrointestinal endoscopy in young and elderly patients.

Figure 1a-c shows changes in respiratory and hemodynamic parameters during upper gastrointestinal endoscopy in the young and elderly subjects. The systolic and diastolic blood pressure (panel a) before endoscopy was 112.0 ± 15.1 mmHg and 70.3 ± 9.2 mmHg, respectively, in the young group and 133.7 ± 17.5 mmHg and 78.6 ± 8.4 mmHg, respectively, in the elderly group. Both systolic and diastolic pressures were significantly higher in the elderly group before the endoscopic procedure. During endoscopy, the systolic and diastolic blood pres-

sure was 108.4±15.0 mmHg and 70.9±11.5 mmHg, respectively, in the young group and 134.6±23.7 mmHg and 78.6±11.9 mmHg, respectively in the elderly group. The systolic pressure was significantly higher in the elderly group during the endoscopic procedure.

Heart rate (panel b) before endoscopy was 77.8 ± 12.5/min in the young group and 69.2 ± 8.1/min in the elderly group, with marginally significant difference (p=0.053). Moreover, the heart rate was 76.2 ± 12.8/min and 75.9 ± 17.6/min, respectively, with no significant difference during endoscopy.

The percutaneous oxygen saturation (panel c) before endoscopy was 98.0 ± 0.87% in the young group and 96.4 ± 0.74% in the elderly group, being significantly lower in the elderly group. The values during endoscopy were 97.1 ± 1.97% and 96.2 ± 1.32%, respectively, with no significant difference.

2) Comparison of changes in percutaneous oxygen saturation, blood pressure, and heart rate during upper gastrointestinal endoscopy between the young and elderly groups.

Figure 2 shows a comparison of changes in blood pressure, heart rate, and percutaneous oxygen saturation associated with the endoscopic procedure. The maximum changes in systolic and diastolic pressures associated with upper gastrointestinal endoscopy were -3.56 ± 13.8 mmHg and +0.56 ± 6.8 mmHg, respectively, in the young group and +0.87 ± 22.8 mmHg and +0.55 ± 14.0 mmHg, respectively, in the elderly group. Changes in the blood pressure associated with upper gastrointestinal endoscopy between the young and elderly groups were not significant.

The maximum change in heart rate associated with endoscopy was -1.56 ± 3.2 bpm in the young group and +6.67 ± 15.6 mmHg in the elderly group, with no significant difference between the two groups. The maximum change in percutaneous oxygen saturation due to upper gastrointestinal endoscopy was -0.89 ± 2.03% in the young group and -0.2 ± 1.08% in the elderly group, with no significant difference between the two groups.

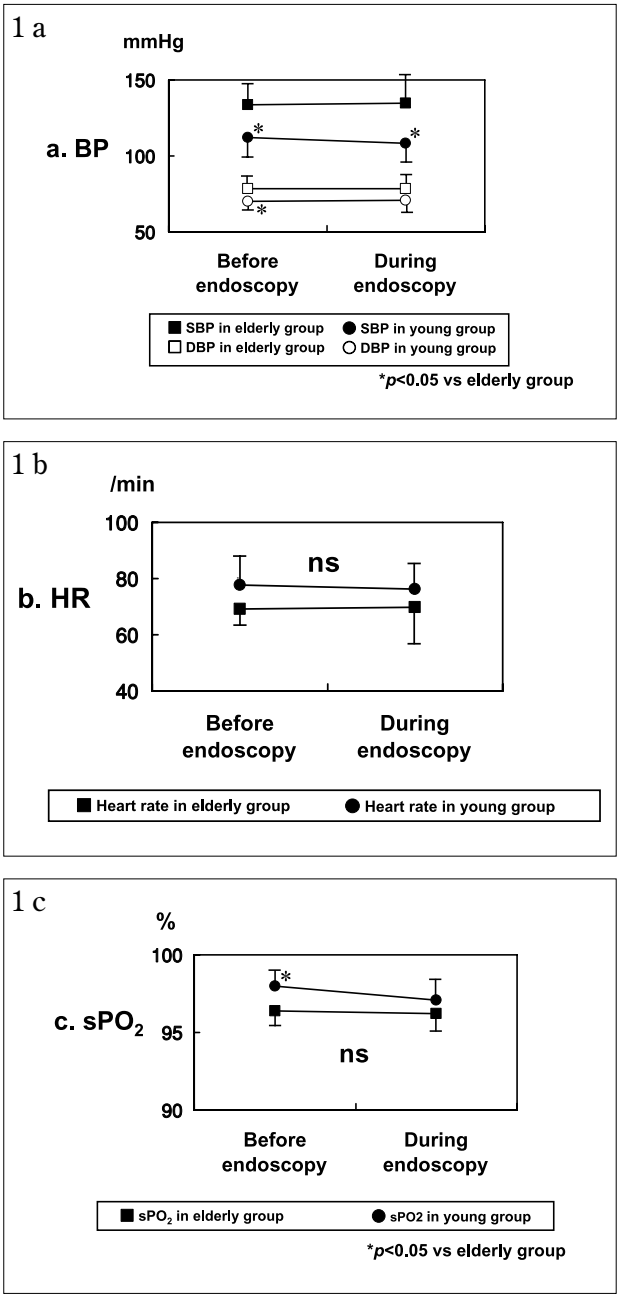

Figure 1 Changes in respiratory and hemodynamic parameters during upper gastrointestinal endoscopy in the young and elderly groups.
Panel a : systolic and diastolic blood pressure, Panel b : heart rate, Panel c : percutaneous oxygen saturation.
BP, blood pressure ; SBP, systolic blood pressure ; DBP, diastolic blood pressure ; HR, heart rate ; sPO_2, percutaneous oxygen saturation ; ns, not significant.

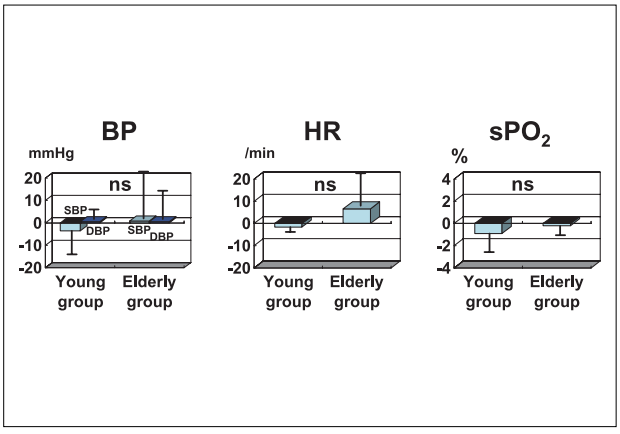

Figure 2 Changes in blood pressure, heart rate, and percutaneous oxygen saturation associated with an endoscopic procedure.
BP, blood pressure ; SBP, systolic blood pressure ; DBP, diastolic blood pressure ; HR, heart rate ; sPO_2, percutaneous oxygen saturation ; ns, not significant.

3) Comparison of the salivary CgA level between the young and elderly groups.

Figure 3 shows changes in CgA levels in the young and elderly groups. In the young group, the salivary CgA level was 52.1 ± 42.9 pg/mg protein during rest before endoscopy but 13.6 ± 13.5 pg/mg protein during endoscopy, showing a significant decrease during the examination ($p<0.05$). In the elderly group, the values were 103.1 ± 26.3 pg/mg protein and 77.5 ± 31.9 pg/mg protein, respectively, showing a significant decrease during the examination ($p<0.05$).

Moreover, salivary CgA levels were significantly higher in the elderly group than in the young group both during rest before endoscopy and during endoscopy ($p<0.05$).

4) Comparison of changes in the salivary CgA level between the young and elderly groups.

Figure 4 compares changes in salivary CgA levels between the young and elderly groups. The CgA level decreased by 36.6 ± 20.1 pg/mg protein in the young group but by 25.6 ± 22.9 pg/mg protein in the elderly group ; the decrease was significantly larger in the young group ($p<0.05$)

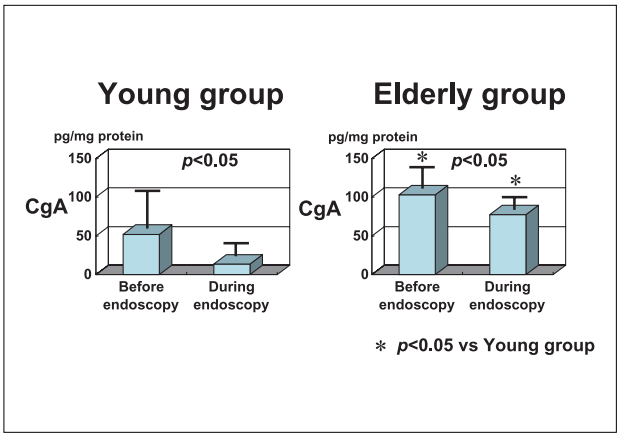

Figure 3 Changes in CgA levels in young and elderly groups.
CgA, salivary chromogranin A.

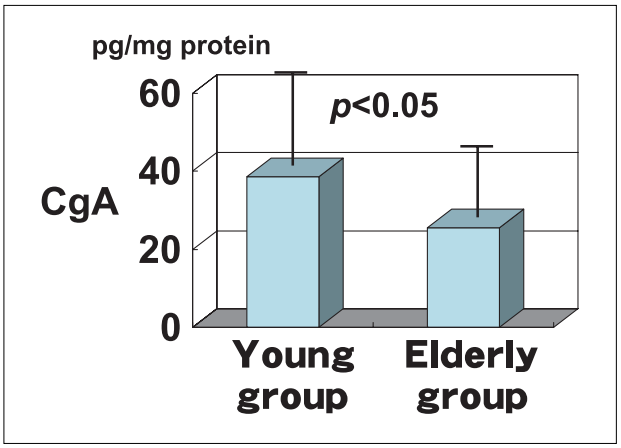

Figure 4 Comparison of changes in salivary CgA levels between the young and elderly groups.
CgA, salivary chromogranin A.

DISCUSSION

In the present study, no significant difference was observed in percutaneous oxygen saturation, or heart rate during an upper gastrointestinal endoscopic procedure between the young and elderly groups, but CgA levels, which are considered to be an index of mental stress, suggest that mental stress caused by the examination was greater in the elderly group. Caution concerning complications of upper gastrointestinal endoscopy due to increased mental stress is considered to be necessary in elderly patients.

CgA is widely distributed in the endocrine and nervous systems and can be detected at high levels particularly in the adrenal medulla and hypophysis. Since the CgA coexists with catecholamines, and is released with them, reflecting catecholamine secretion into the blood, it serves as an index of sympathetic-pituitary activities (8-13). O'Coner and Bernstein (7) first established a radioimmunoassay of human blood CgA using naturally occurring CgA as the antigen and reported that serum CgA levels were markedly higher in patients with neural or endocrine tumors, particularly those with melanocytoma and pituitary tumor, than in healthy individuals, leading to the use of blood CgA as a tumor marker.

The salivary CgA is also present in the ductal parts of the submandibular glands and is released into the saliva on stimulation of the autonomic nervous system, so that it has begun to attract attention as a new index of autonomic nervous activities, particularly mental stress (8-14). Since the salivary CgA concentration increases even under conditions of mild stress, it allows the sensitive evaluation of mental stress reactions. Unlike blood, saliva can be collected without stress, making a non-invasive evaluation possible. In addition, salivary CgA levels rapidly decrease with the disappearance of stress and respond specifically to mental but not physical stress.

Nakane, *et al.* (15) suggested the usefulness of salivary CgA levels as a highly sensitive index of mental stress since it increased more rapidly than salivary cortisol levels during an oral presentation in front of an audience or driving a car but showed no marked

change under exercise loading, which instantly increased blood catecholamine levels. Nakayama, *et al.* (16) also evaluated fatigue in long-distance truck drivers based on salivary CgA levels and reported that continuous driving for 6 hours or longer should be avoided and mental stress is milder when driving on a highway than on ordinary roads.

Concerning stress reactions during karaoke, an examination of the salivary CgA levels indicated a decrease in anxiety and mitigation of stress during singing despite an increase in heart rate (17). Coffee has also been reported to have a refreshing effect, based on changes in the salivary CgA levels (18).

Hayashi, *et al.* (6) and Saijo, *et al.* (19) reported that sympathetic nervous activities were significantly enhanced during compared with before upper gastrointestinal endoscopy, but mental stress was significantly reduced during endoscopy according to salivary CgA levels in the present study. In upper gastrointestinal endoscopy, mental stress is considered to be greater during insertion of the endoscope than during the actual endoscopy. After insertion of the endoscope, salivary CgA levels decreased in both the young and elderly groups, but the decrease was smaller in the elderly group, suggesting that mental stress during endoscopy remained high in the elderly patients. Therefore, attention to complications due to increased stress is considered to be necessary in upper gastrointestinal endoscopy for elderly patients.

STUDY LIMITATION

Because CgA level of elderly group before endoscopic procedure is higher than young group, it is not concluded that endoscopic stress is strong in elderly group. It is possible that baseline of CgA levels of elderly group is higher than young group. In this study, however, decreased ratio of salivary CgA levels was significantly smaller in the elderly group than young group after insertion of the endoscope, and this result suggests that the mental stress remains stronger in the elderly group than young group. On the other hand, it is suggested that premedication of diazepam influences mental stress in the present results. In future study, the mental stress without premedication of anti-anxiety agent should be examined during endoscopic procedure.

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