Aging related symptoms, disease and cancer in digestive system: A reference for better performance to health evaluation and promotion

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A. Changes in digestive organs due to aging

1. Common symptoms in digestive organs among the elderly

The “Statistical Abstracts on Health and Welfare in Japan 2010” published every year by the Health and Welfare Statistics Association include data under the heading “ratio of subjective symptoms”. This indicates how many people per thousand of population have felt specific symptoms on a daily basis, divided into 10-year age groups. In terms of symptoms affecting the digestive organs, the statistics include “upset stomach or heartburn”, “diarrhea”, “constipation”, “loss of appetite”, “abdominal or stomach pain” and “pain or bleeding due to hemorrhoid”. Between 15-74 age group and 55-64 age group, the symptom that increased more than 20% or more are “upset stomach or heartburn”, “constipation” and “abdominal or stomach pain”. In the case of appetite loss, in particular, “upset stomach or heartburn”, “diarrhea”, “constipation”, “loss of appetite”, “abdominal or stomach pain” and “pain or bleeding due to hemorrhoid”. Between 15-74 age group and 55-64 age group, the symptom that increased by 20% or more are “upset stomach or heartburn”, “constipation” and “abdominal or stomach pain”. In the case of appetite loss, in particular, the ratio is relatively low at 9.3 persons per thousand in the 55-64 age group, but the figure almost doubles at 55-64 age and again almost doubles at 75-84 age to 26.7 per thousand (Fig. 1)[1].

2. Aging related gastrointestinal alterations and diseases

Aging is understood to entail both mental and physical changes due to a reduction in the somatic cell count followed by decrease of organ function with increasing age[2][3]. Aging phenomena in physiological functions of the digestive organs include those described below, in addition to constipation and chewing-swallowing dysfunction.

1) Esophagus

Compared to younger people, the elderly have a higher incidence of sliding type hiatal hernia. Since this hiatal hernia obstructs the reflux prevention mechanism in the lower esophageal sphincter (LES), gastro-esophageal reflux disease (GERD) is prone to occur, and this can cause heartburn, dysphagia, chest pains and others. Tonaga, et al. cite hiatal hernia and old age (65 years and over) as significant risk factors related to GERD showing abnormality in the mucosal surface, and report odds ratios of 2.3 and 2.5, respectively[4]. Although the reason for this increase among the elderly is unclear, it is thought to be because of the slack of valve function in the esphago-cardial junction and increased prevalence of sliding hernia by aging. The course of sliding hernia is thought to due to the slack of ligaments which support the digestive tract. Diagnosis is carried out using endoscopy, and severity is normally diagnosed in accordance with Los Angeles classification[5]. However, cases of “non-erosive reflux disease (NERD)”[6], in which reflux symptoms are recognized but changes in the mucosal surface are not observed, are thought to account for 30-40% of the whole.

2) Stomach

The gastric mucosa is known to show atrophy with increasing age[7]. Tarnawski, et al. have pointed out, from studies using elderly rats, that a decrease in gastric mucosal blood flow and an increase in low oxygen and apoptosis markers are involved as factors promoting the occurrence of gastric mucosa disorders among the elderly[8]. Gastric mucosal atrophy causes decrease of number in parietal cell, followed by the decrease of acid secretory capacity. It is thought to cause a fall in protein digestion capacity and is thought to cause seniors taste preference from heavy protein food such as beef steak to light protein food such as tofu and fish. Moreover, since the gastric mucosal blood flow is central to protection functions, a decline with age creates a risk of mucosal damage, which could give rise to atrophic gastritis.

On the other hand, Helicobacter pylori are the principal offender of the aggressive factor. In our study performed in 2008, the 30s-40s age group had an infection rate of 21-22%, but in the 50s-60s it was 32-34%, in the 70s it was 41%, and in the 80’s it was 56%, showing a clear increase of infection rates with age but total prevalence was decreased when com-

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pared to previous reports. The reported prevalence is different among the investigated area and year, however every report showed age related increase in H. pylori infection[9]. Many elderly people, moreover, suffer from more than one disease and simultaneously take different types of medication. This can cause acute or chronic gastritis, and particular care is needed when taking nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids or platelet aggregation inhibitors. Interestingly, Torisu et al. reported that H. pylori negative gastric atrophy was associated with body mass index (BMI) suggesting influence of the life style[9].

3) Small and Large Bowels

The mucosal wall of small intestine also tends to show atrophy with age, and the absorption efficiency of fats and proteins is thought to fall in conjunction with this. However, the speed of this change is slow and there is reserve capacity for absorption; as a result, this hardly ever causes a problem in daily life[11].

An age-related change in the colon is increase in colonic diverticula, whereby weak loci of the intestinal track wall protrude in sack-like formation into the abdominal cavity due to internal pressure. Most of these are false diverticula caused by a histological deficiency in the muscularis propria; when many of these exist they trigger diverticulosis. Of all patients with diverticula, 80% live out their lives without any symptoms. However, the remaining 20% are thought to suffer from complications, and the frequency of these increases with age. The main complications are diverticulitis and hemorrhage, and if these are aggravated they can develop into life-threatening conditions including peridiverticulitis, abscesses and perforative peritonitis, and hypovolemic shock. Another disease typically found among the elderly is ischemic colitis; this is particularly prevalent among patients of arteriosclerosis, hypertension diabetes, and is triggered by vasospasm or obstruction of the intestine[11]. In many cases it can be alleviated by conservative treatment, but can become serious with perforation or poor control of hemorrhaging, and can sometimes become life-threatening.

3. Aging and constipation

1) What is constipation?

There is no clear definition of constipation in Japan. Conceptually, it is understood to be “a condition characterized by reduced stool bulk and defecation frequency”, but it generally seems to refer to a state in which bowels have not been opened for four or more days. However, evacuation every four days is still regular, and as long as there are no accompanying symptoms such as abdominal pain or bloatedness, there is no pathological significance or need for treatment in the majority of cases. More than anything, the interval between evacuations varies greatly from person to person, and it is considered difficult to prescribe a set time. As a result, a good rule of thumb for identifying morbidity in cases of delayed evacuation or fecal impaction might be: “A state in which there is no bowel movement beyond the interval that is comfortable in view of the individual’s habits, giving rise to abdominal pain, a sensation of bloatedness, difficulty in evacuation and various other complaints”.

2) Prevalence of constipation

In Japan, 2.0% of males, 4.9% of females and 3.5% of the overall population have experienced constipation. The rate of those with subjective symptoms tends to increase with age; this corresponds to 2.5% of the overall population in the 45-55 age group, but 3.9% in ages 55-64, 6.7% in ages 65-74, 9.9% in ages 75-84 and 12.4% in ages 85 and over, showing a clearly rising trend[1].

3) Characteristics of the constipation in elderly person and managements

Susceptibility to constipation is determined by the presence or absence of causative factors, and these are tremendously varied. Atonic constipation caused by reduced tension in the smooth muscle and bowel peristalsis, a type most common amongst the Japanese especially women and the elderly. Constipation that occurs secondarily as a result of various illnesses is important for elderly. This defecation disorder is particularly common among patients of depression, hypothyroidism, amyloidosis, diabetes accompanied by nervous disorders, uremia, and other ailments.

On the other hand, incidence of the colon cancer is increasing in Japan in recent years especially in senior woman. When the passage of intestinal contents is physically obstructed is called organic constipation. This can be caused by not only colorectal cancer but also surgical scar stenosis, large colorectal polyps, intestinal tuberculosis, healing scars caused by ischemic colitis, wall thickening due to recurrent diverticulitis, intestinal edema following radiation treatment, extraintestinal pressure due to intra-abdominal tumor, and so on.

In case of elderly person, they are relatively easy to fall into the dehydration, and thus making them more prone to constipation. The colon is an organ that absorbs water, and when the body is dehydrated it tries to absorb as much moisture as it can. This reduces the moisture contained in the stool, the stool harden and become more difficult to pass. Drinking and taking of dietary fiber needs to be encouraged to elderly person. because lack of dietary fiber is also a risk for constipation. Dietary fiber, with its function of retaining moisture, not only softens stools but also increases stool bulk and promotes evacuation.

4. Aging and the liver

1) Changes in the shape and physiological functions of the liver

Organs tend to become atrophy due to the loss of cells with age, and the liver is no exception to this rule. In the results of a study of autopsy cases, Katayama, et al. reported that the average liver weight was 1300-150g at age 30, decreasing to 1,000-1,100g in the late 60s and 700-800g at age 80 or over. As a proportion of body weight, it was about 2.5% up to age 60 but 2.0% from age 90 and over[10]. In research by Wynne, et al. on the relationship between age, liver weight and liver blood
An important function of the liver is that of drug metabolism. Drugs metabolism is divided into those that depend on metabolic enzymes such as P450 or glucuronate conjugation, while another states that the reaction decreases in men but not in women. On the other hand, Zoli, et al., from their study on portal vein blood flow using the pulse doppler method, found that the portal vein blood flow was significantly lower at ages 71 and above compared to 40 and below; this is seen as a major contributor to the reduction of liver blood flow with age.

In any case, however, drug metabolism is thought to decrease with reduced liver weight and liver blood flow in the elderly. Care is therefore required when deciding dosages.

2) Changes in liver function tests

ALT(GOT) and AST(GPT) are both representative indicators of liver cell destruction. In histological terms, AST(GPT) reflects abnormalities in the portal vein region and ALT(GOT) in the terminal portal branch region. However they tend to reduce slightly with age. Here again, γ-GTP is thought to be high among men in their 30s-50s but to decrease in older age, though this is affected by fatty liver and drugs taken. ALP is thought to gradually rise in women after the menopause, but it is affected by fatty liver and drugs taken. ALP is thought to gradually rise in women after the menopause, but it needs to be ascertained whether such rises are due to hepatic or bony in nature. Cholinesterase, serum total protein (TP) and albumin are indicators of protein synthesis in the liver, but both tend to decrease in the elderly. ICG tolerance tests, indicators of liver blood flow and metabolism, reflect the decrease in blood flow as stated above; R15 rises slightly while K values decrease. Besides these, no time-related change is thought to occur in bilirubin, hyaluronic acid or prothrombin. However, these age-related changes are within the standard range; when this range is exceeded, more detailed testing is required.

Metabolic syndrome is well known as a factor that accelerates aging. In anatomical terms, visceral fat adheres to the omentum and mesentery. The liver is positioned downstream of these hemodynamically, and is responsible for metabolizing, storing and re-synthesizing of various nutrients for example as the primary target organ of insulin. From this, fatty liver is thought to be visceral fat itself, and the increase in fatty liver patients in recent years is seen as a major problem that could shorten the lives of the Japanese.

Although the liver is the largest organ in the human body, there is absolutely no problem in daily life as long as it is functioning at full capacity. This may be more easily understood if we consider that, in living liver transplants, only the left lobe of the donor’s liver is transplanted. There have even been cases in the United States of liver transplants from donors aged over 80. The liver could therefore be seen as an organ that is resistant to aging. Protecting this organ from fatty liver due to hyperalimentation, alcohol, drugs, viruses and others is seen as fundamental to achieving a healthy long life.

5. Aging and cancers in digestive system

1) Epidemiological trends in gastrointestinal cancers

Since 1981, cancer has continuously been the number one cause of death among the Japanese. In 2010 it accounted for 30.4% of all deaths, about twice the rate of the second biggest cause, heart disease. Moreover, while the latter has leveled off and cerebrovascular disease in third place is in a decreasing trend, cancer continues its gradual upward climb (Fig. 2). It is estimated that, if cancer could be controlled, men would live 4.02 more years and women 3.01 more years on average, making this a disease that has a most significant impact on Japan’s national demographics. Gastrointestinal cancers account for...
more than half of all cancers for both men and women (Fig. 3), and these cancers are increasing at a pace far outstripping the rate of increase in cancer deaths overall. For while the number of deaths from all cancers increased 1.58 times from 206,702 in 1975 to 325,941 in 2005, all gastrointestinal cancers except stomach cancer and esophageal cancer are increasing in excess of this rate, as shown in Figure 4[1]. Meanwhile, an increase in cancer incidences accompanying the increase in elderly persons is clearly shown while the general incidence rate increased 2.7 times from 206,702 in 1975 to 560,694 in 2001, the rate among the over 65’s increased 3.7 times from 98,570 to 363,388 in the same period, and the proportion of over 65’s within the whole increased markedly from 47.7% in 1975 to 64.8% in 2001.

Thus, when considering gastrointestinal cancers as a disease entity, there is an undeniable possibility that this field will impact the average life expectancy as well as population demographics and medical economy of Japan and the Japanese in future.

2) Characteristics and risk factors of gastrointestinal cancers

- **a) Esophageal cancer**
  It commonly occurs among elderly men. It is prevalent in the central thoracic region, in pathological terms it often consists of squamous cell carcinomas. As for risks, meanwhile, a group at the National Cancer Center Hospital has reported that excessive smoking and alcohol as well as flushing when consuming alcohol play a part in its occurrence[23]. In the west, adenocarcinomas have been increasing in recent years; Barrett's epithelium has been identified as the substrate, together with the involvement of obesity, hiatal hernia and gastro-esophageal reflux disease (GERD) as causative factors[24]. Recently, moreover, it has been demonstrated in large-scale tests that Helicobacter pylori infection poses a high risk[25].

- **b) Stomach cancer**
  Although stomach cancers are seen across all age groups, there have been several reports of a strong causative correlation from atrophic gastritis, Helicobacter pylori infection and others that increase with increasing age. Here again, then, there is a clear increase in occurrence among the elderly[26]. Besides these, smoking, and salted foods are known to be risk factors, while it has been suggested that consuming vegetables and fruits could reduce the risk of occurrence[27].

- **c) Colorectal cancer**
  Colorectal cancer also increases with age, the most commonest forms being rectal and sigmoidal cancers. Among the elderly, however, there is a higher frequency of cancers in the right colon, typically discovered in an advanced state including intestinal obstruction, peritonitis and bloody bowel discharge. In recent years, screening by the simple two-step fecal occult blood method has been widely used, but guidelines issued by the Ministry of Health, Labour and Welfare recommend that those testing positive should be given total colonoscopy[27]. This examination is much stressful and poses risk for elderly patients. Although enema tests exist as secondary tests, elderly persons find it difficult to make smooth body position changes, and the usefulness of virtual colonoscopy using CT has been pointed out in recent years[29]. The westernization of lifestyle habits has also been reported as a risk factor; obesity, overweightness, lack of exercise and excessive fat intake have been pointed out as risks, while exercise and an active intake of dietary fiber, calcium and vitamins have been suggested as ways of reducing risks[27].

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prospects of health check-up system focused on prevention for aging-related various abnormalities. HEP 38(2), 30-40, 2011


