CHAPTER 48

Aspiration pneumonia

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Aspiration pneumonia and aspiration pneumonitis

Pneumonia is a common cause of death among older people despite the availability of potent novel antimicrobials. Whereas the death rate of juvenile pneumonia has decreased nearly to zero, that of old people has remained unchanged over the past 100 years. In other words, the traditional approach has proven a limited success: as Osler put it over 100 years ago, 'pneumonia is actually a friend to the old'.[1] Both the increased incidence of pneumonia and high mortality among older people are a consequence of a number of age-related factors including coexisting illnesses, therapeutic interventions and decreased host defence mechanisms. In these, aspiration is possibly the most important risk factor for pneumonia in the elderly.[2] Aspiration is defined as the inhalation of oropharyngeal or gastric contents into the larynx and the lower respiratory tract. Several pulmonary syndromes may occur after aspiration, depending on the amount and the nature of the aspirated material, frequency of aspiration and the host's response to the aspirated material.[3] Aspiration pneumonia is an infectious process caused by an inhalation of the oropharyngeal secretions that are colonized by pathogenic bacteria, whereas aspiration pneumonitis including Mendelson syndrome is a chemical injury caused by an inhalation of sterile gastric contents.[3] Although there is some overlap between these syndromes, they are distinct clinical entities. This chapter focuses on the pathophysiology and the management of aspiration pneumonia and aspiration pneumonitis.

Mechanisms for development of aspiration pneumonia or aspiration pneumonitis

Aspiration pneumonia

Pneumonia in the elderly is often caused by a non-apparent swallowing disorder.[2] Such 'silent aspiration' frequently occurs and is a more important cause of pneumonia than acute aspiration of gastric content in older people.[4] Silent aspiration of oropharyngeal bacterial pathogens to the lower respiratory tract is an important risk factor for community-acquired pneumonia[5] and also nosocomial pneumonia in the elderly.[6] Normal hosts are less likely to develop pneumonia because they aspirate smaller volumes or are able to clear bacteria rapidly.[7] However, an extremely small volume (0.01 ml) of saliva contains pathogenic numbers of bacteria.[7] Elderly patients with a predisposition to aspiration frequently aspirate oropharyngeal secretions and the development of pneumonia occurs when normal pulmonary defence mechanisms are overwhelmed.[8] Adequate protective reflexes in the airway are important and suppression or absence of these reflexes has led to pneumonia.[8] For example, Nakajoh *et al.* reported that the incidence of pneumonia was higher in patients having both a latency of swallowing response longer than 5 s following stimulation with 1 ml of distilled water and a cough threshold for inhalation of citric acid aerosol higher than a concentration of 1.35 (log mg ml^{-1}).[9] Thus, the progressive loss of protective reflexes (i.e. swallowing and cough reflexes) with age is thought to be one of the mechanisms for aspiration pneumonia, which is often seen in older people.[10] In fact, impaired swallowing and cough reflexes have been shown in patients suffering from aspiration pneumonia.[11] However, re-evaluation of age-related changes in protective reflexes in individuals who lead active daily lives has shown that both reflexes do not decrease with the advance of age,[12,13] indicating that involutional and degenerative changes associated with ageing often result in marginally compensated protective reflexes.[14] Disorders of the central nervous system are more likely to develop in the elderly and pneumonia has been estimated to occur in about one-third of patients with stroke.[15] The most important factor contributing to the development of pneumonia in patients with stroke is suggested to be dysphagia with aspiration.[16] Nakagawa *et al.* have shown that the risk of

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pneumonia was significantly higher in patients with basal ganglia infarcts than in patients with or without cerebral hemispheric strokes in other locations.[8] They found that multiple episodes of pneumonia occurred only in patients with bilateral basal ganglia infarcts and that there was a higher mortality rate associated with pneumonia in these patients.[8] Delayed triggering of the swallowing reflex occurs in patients with infarcts in the basal ganglia.[14] These results strongly suggest that disruption of basal ganglia functions is critically important in the development of aspiration pneumonia. The pharyngeal, laryngeal and tracheal epithelia, the most important sites for the initiation of swallowing and cough reflexes, have an extensive plexus of nerves that contains substance P.[17,18] Capsaicin desensitization, which diminishes substance P from the airway and upper digestive tract, or an administration of neurokinin (NK)-1 receptor antagonist remarkably attenuated the cough response to tussive stimuli[19,20] and distilled water-induced swallowing reflex in guinea pigs,[21] suggesting an important role of substance P-containing nerves in the initiation of these protective reflexes. Thus, irritation of laryngeal and pharyngeal mucosa by stimuli may activate capsaicin-sensitive sensory nerves, releasing substance P, with the result that protective reflexes are initiated by stimulation of the glossopharyngeal and vagal sensory nerves.[19] Treatment with a dopamine agonist in the rat brings about a heightened striosomal expression of substance P and both dopamine D1 and D2 antagonists decrease substance P.[22] Mice lacking the dopamine D1 receptor[23] and those treated with dopamine D1 receptor antagonist[24] showed abnormal motor activities and feeding and swallowing problems. An impairment of dopamine metabolism in the basal ganglia is observed in patients with infarcts in the basal ganglia.[25] Taking these facts together, the mechanisms of silent aspiration may be speculated as shown in Figure 48.1. Patients with basal ganglia infarcts may suffer from reduced dopamine metabolism, which decreases substance P in the glossopharyngeal and vagal sensory nerves. Reduction in substance P concentration in these nerves impairs both swallowing and cough reflexes, which increases the frequency of silent aspiration. Because the action of swallowing and coughing is a fundamental defence mechanism against aspiration of oropharyngeal contents into the respiratory tract, impairment of both reflexes is one of the major reasons for the development of aspiration pneumonia (see Figure 48.1). In patients with aspiration pneumonia, unlike those with aspiration pneumonitis, the episode of aspiration is generally not witnessed. The diagnosis is therefore inferred when a patient at risk for aspiration has radiographic evidence of an infiltrate in a characteristic bronchopulmonary segment. Elderly

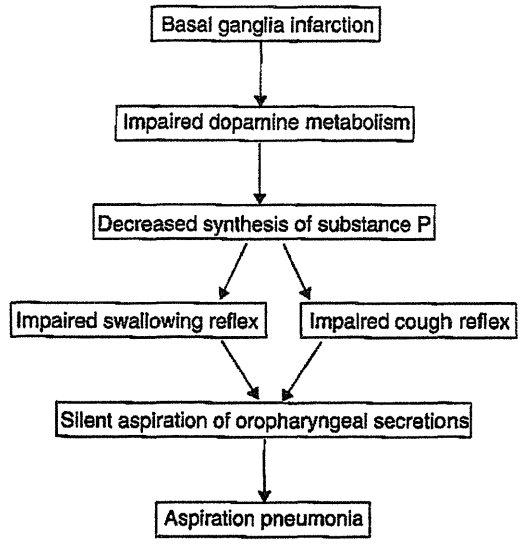

Figure 48.1 Possible mechanisms for development of aspiration pneumonia in patients with basal ganglia infarction.

persons frequently receive poor oral care, resulting in oropharyngeal colonization by potential respiratory tract pathogens, including Enterobacteriaceae, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. These pathogens are aspirated and may cause pneumonia.[3]

Aspiration pneumonitis

Aspiration pneumonitis is defined as acute lung injury after the inhalation of regurgitated sterile gastric contents. This syndrome occurs in patients who have a marked disturbance of consciousness such as that resulting from a drug overdose, seizures, a massive cerebrovascular accident or the use of anaesthesia.[3] The syndrome most commonly described as aspiration pneumonitis is Mendelson syndrome.[26] Reflux of gastric fluids into the airway can damage the respiratory tract.[27] Marked damage to the tracheal mucosa can occur even when the volume of aspirated gastric fluid is too small to cause clinically significant aspiration pneumonitis and repeated long periods of aspiration of gastric fluid may even cause interstitial pulmonary fibrosis. Damage is always more severe when the pH of the gastric contents is low, but gastric fluid also contains substances other than acid which cause airway damage and delay healing of the airway epithelial damage.[3,27] Since airway epithelial damage by gastric content probably arises from the additive effects of acidity,[27] treatment of gastroesophageal reflux using antiacids such as histamine-H2 receptor antagonists alone may not improve symptoms caused by aspiration of gastric fluids.[3]

Treatments for aspiration pneumonia and aspiration pneumonitis

Aspiration pneumonia

Antibiotic therapy is unequivocally indicated in patients with aspiration pneumonia. The choice of antibiotics should depend on the setting in which the aspiration occurs and also the patient's general health. However, antibiotic agents with activity against Gram-negative organisms, such as third-generation cephalosporins, fluoroquinolones and piperacillin, are usually required.[3] Kanda *et al.* evaluated an additive effect of angiotensin-converting enzyme (ACE) inhibitor and amantadine to the conventional antibiotic therapy for pneumonia and found that the combined administration of these drugs can shorten the duration of hospitalization and antibiotic use, inhibit methicillin-resistant *Staphylococcus aureus* (MRSA) infection and lower the medical cost for treatment of pneumonia.[28]

Aspiration pneumonitis

Although it is common practice, the prophylactic use of antibiotics in patients in whom aspiration is suspected or witnessed is not recommended.[3] However, empirical antibiotic therapy is appropriate for patients who aspirate gastric contents and who have small-bowel obstruction or other conditions associated with colonization of the gastric contents.[3] Antibiotic therapy should be considered for patients with aspiration pneumonitis that fails to resolve within 48 h after aspiration. Empirical therapy with broad-spectrum agents such as fluoroquinolone or piperacillin is recommended. Corticosteroids have been used for decades in the management of aspiration pneumonitis. However, there are limited data on the role of these agents.[29]

Strategies for the prevention of aspiration pneumonia (Figure 48.2)

Pharmacological therapy

Capsaicin

Because substance P is a neurotransmitter of the swallowing reflex and is depleted in patients with aspiration pneumonia,[30] capsaicin, a pungent substance in red peppers that stimulates sensory nerves, may improve the swallowing reflex in these patients.[2] Ebihara *et al.* measured the swallowing reflex with a bolus injection of 1 ml of distilled water into the pharynx through a nasal catheter and suggested that the addition of a low dose of capsaicin to liquid or food may stimulate the swallowing reflex and help to prevent aspiration pneumonia in the elderly.[31]

1. Pharmacological therapy
   a. Capsaicin
   b. Angiotensin-converting enzyme inhibitors
   c. Dopamine and amantadine
   d. Cilostazol
   e. Folic acid
   f. Menthol
   g. Banxia houpu tang
   h. Black pepper oil
   i. Mosapride
2. Oral hygiene
3. Sitting position
4. Avoid neuroleptics
5. Handwashing

Figure 48.2 Preventive strategies for aspiration pneumonia.

Angiotensin-converting enzyme (ACE) inhibitors

A well-known adverse effect of ACE inhibitors is a dry cough.[32] Since substance P is degraded by ACE,[33] its action is potentiated by ACE inhibitors.[34] Using ACE inhibitors, substance P might accumulate in the upper respiratory tract because of inhibited ACE activity and cause an increase in the sensitivity of the cough reflex.[2,20] In a similar way to the cough reflex, ACE inhibitors improve the swallowing reflex in older patients with aspiration pneumonia.[2] Sekizawa *et al.* compared the rate of pneumonia in stroke patients with hypertension treated by ACE inhibitors with that in stroke patients treated by other antihypertensive drugs and found that the risk of pneumonia is reduced by about one-third if ACE inhibitors are used for hypertension compared with the use of other antihypertensive drugs.[35] ACE inhibitors, therefore, may have beneficial effects on the prevention of pneumonia in these patients. Arai *et al.* reported that the rate of pneumonia was significantly lower in elderly hypertensive patients given ACE inhibitors than that in those treated with calcium channel blockers.[36] However, Teramoto and Ouchi refuted the advantage of ACE inhibitors over calcium channel blockers in preventing pneumonia in adult and elderly subjects with hypertension.[37] In elderly individuals, the severity of the underlying cerebrovascular disease greatly affects susceptibility to pneumonia. ACE inhibitors could be useful in the prevention of aspiration pneumonia in elderly patients with stroke but not in those without stroke.

Dopamine and amantadine

Delayed triggering of the swallowing reflex occurs in patients with basal ganglia infarctions[2] and an impairment

of dopamine metabolism in the basal ganglia is observed in these patients.[25] Kobayashi *et al.* investigated whether levodopa improves the swallowing reflex in patients with basal ganglia infarctions who had a history of aspiration pneumonia.[38] The subjects were given an intravenous drip infusion of levodopa (50 mg in 20 ml of saline) for 30 min. They found that the administration of levodopa improved the impaired swallowing reflex in these patients. Since dopamine supplementation improves the swallowing reflex in patients with cerebral infarctions, Nakagawa *et al.* investigated whether amantadine, a drug that acts as a dopamine releaser from dopaminergic nerve terminals, lowers the incidence of pneumonia in patients with cerebral infarctions.[39] Patients were randomly assigned amantadine 100 mg per day or no active treatment and were investigated for 3 years. During follow-up, the relative risk of developing pneumonia in patients on no active treatment compared with that in those on amantadine was 5.92. These findings suggest that the risk of pneumonia is lowered by about 20% if amantadine is used in patients with previous stroke. Amantadine may, therefore, have beneficial effects on the prevention of pneumonia in these patients. Of course, other recognized effects of amantadine might also have impacted the incidence of pneumonia in these studies. For example, amantadine improves the conscious state in patients with brain injury[40] and more active stroke patients may be less likely to aspirate. In addition, dopaminergic receptors have been identified in the lower oesophageal sphincter and amantadine might reduce gastroesophageal reflux[41] and thereby lower the risk of aspiration pneumonia. Finally, antiviral effects and prevention of influenza infection might also lower the incidence of pneumonia over a 3 year period. Hence the mechanism by which amantadine might positively affect the incidence of pneumonia remains to be proven.[42]

Cilostazol

Disorders of the central nervous system including dementia and atherosclerotic cerebrovascular disease are more often associated with aspiration than other specific neuromuscular disorders.[2] The mechanisms by which brain injury affects the risk of aspiration are beginning to be delineated. For example, in healthy people, the frequency of swallowing during sleep is slightly less than that when awake,[43] but severe delay of the swallowing reflex during nighttime compared with that during daytime was observed in patients with multiple lacunar infarctions.[44] Cough reflex and spontaneous cough are also suppressed during sleep in patients with evidence of cerebrovascular damage.[2] Hence patients with cerebrovascular disease are particularly susceptible to the development of aspiration pneumonia during sleep. Other evidence exhibiting the importance of cerebrovascular disease comes from studies of patients with silent cerebral infarction, that is, patients with radiographic evidence of infarction without frank signs of neurological impairment. Silent cerebral infarction is fairly common among the elderly. Silent cerebral infarction was observed in 23% of elderly people in the USA, in 42% of older adults in one Japanese study and in 51% in another Japanese study.[2] Not only is silent stroke a risk factor for clinical stroke that obviously increases the risk of aspiration pneumonia, but Nakagawa *et al.* reported that patients with silent cerebral infarction were more likely to develop pneumonia (20%) than were controls (5%) without silent cerebral infarction over a 2 year period.[45] In this study, deep silent infarcts were more closely associated with the incidence of pneumonia (29%) than that in superficial infarcts (7%).[45] Hence silent cerebral infarction should be considered as a potential risk for the development of aspiration pneumonia. Taken together, it is reasonable to propose that treatment aimed at reducing the incidence and severity of cerebrovascular diseases, for example, antihypertensive therapy or anticoagulation and anti-platelet therapy in selected populations, may not only prevent future stroke but also reduce the incidence of aspiration pneumonia. In a comparison between a group receiving cilostazol, an anti-platelet agent, for 3 years and a cilostazol non-receiving group, the incidence of cerebral infarction decreased to 50% in the cilostazol group.[2] Furthermore, the incidence rate of pneumonia also decreased by approximately half.

Folic acid

Folate plays a pivotal role in the synthesis of dopamine and its deficiency is common in older people, especially in institutionalized subjects. Folate deficiency may be an independent marker for increased risk of aspiration pneumonia in older people.[46] Folic acid supplementation may prevent the incidence of pneumonia by improving the swallowing function in these susceptible subjects.[46] Therefore, for older people, in order to prevent pneumonia, nutrition also has to be taken into consideration.

Menthol

Ebihara *et al.* found that menthol stimulation and also cold stimulation restore impaired swallowing reflex in patients with dysphagia through the activation of transient receptor potential (TRP) M8.[47] Thus, an addition of menthol to liquids or food may improve swallowing reflex and help to prevent aspiration pneumonia in the elderly with dysphagia.

Banxia houpu tang

Iwasaki and co-workers reported that a traditional Chinese herbal medicine, banxia houpu tang (BHT), improves both swallowing and cough reflexes in patients with stroke.[48,49] Furthermore, they reported that treatment with BHT reduces the risk of pneumonia and pneumonia-related

mortality in elderly patients with neurodegenerative disorders.[50]

Black pepper oil

Ebihara *et al.* reported that olfactory stimulation by nasal inhalation of volatile black pepper oil (BPO) increases the cerebral blood flow of the right orbito-frontal and left insular cortexes, increases serum levels of substance P and improves swallowing function.[51] Inhalation of BPO might improve swallowing movement and might have benefits in older post-stroke patients with dysphagia, regardless of their consciousness level or physical and mental status.

Mosapride

Percutaneous endoscopic gastrostomy (PEG) is widely used for gastrointestinal tract access to provide artificial feeding in patients with neurological dysphagia. PEG tube placement is frequently requested to address problems of dysphagia with aspiration pneumonia. However, pneumonia is the most common cause of death and might explain the lack of survival benefit in patients fed using a PEG tube. A quantitative scintigraphic study with Tc-99m-labelled enteral infusion demonstrated frequent episodes of gastroesophageal reflux (GER) and subsequent aspiration of gastric contents into the airway in patients with gastrostomy.[52] Mosapride citrate is a gastroprokinetic agent that enhances upper gastrointestinal motility and is known to prevent GER in patients with GER disease. He *et al.* found that mosapride citrate lowers the rate of developing pneumonia after PEG and improves the survival rate in patients with PEG.[53]

Oral hygiene

The microbiological aetiology of aspiration pneumonia is usually traced to organisms that inhabit the oropharynx and aspiration of pharyngeal contents has been suggested as the mechanism by which these bacteria reach the lower respiratory tract.[2] Johanson and Harris speculated that the pulmonary infections caused by bacteria following the introduction of pathogenic organisms by aspiration of oropharyngeal contents is one of the major reasons for pneumonia in the elderly.[54] Since aspiration of bacteria in the oropharyngeal secretions is an important risk factor for nosocomial pneumonia in the elderly, poor oral health may also contribute to the development of pneumonia. Yoneyama *et al.* assessed the rate of pneumonia in elderly people receiving oral care and in those who were not.[55] During 2 years of follow-up, pneumonia was diagnosed in 19% of the participants who did not receive oral care and in 11% of those who received it. The relative risk of developing pneumonia in no active oral care compared with that in oral care was 1.67 (95% CI, 1.01–2.75; $p < 0.05$). Thus, monitoring the attention given to the oral hygiene of dependent patients can probably lower the incidence of aspiration pneumonia. Furthermore, Yoshino *et al.* stimulated the gum-ridge with a brush without toothpaste immediately after a meal.[56] No matter where in their mouth they stimulated, the swallowing reflex improved after the stimulation on the gum-ridge. This result indicates that stimulation in the mouth is transmitted to the brain and certainly improves the swallowing reflex, which is one of the most important defensive reflexes against microorganisms with which the human body is equipped. Brushing in the mouth is not only good for the prevention of dental caries and gumboils but also very good for improving the reflexes. Stimulation of the mouth requires less time and effort than stimulation of the arms and legs. All we need is a small amount of stimulus to care for older people.

Sitting position

GER is very common in general and more common in elderly subjects. It has been estimated that more than one-third of older people have intermittent symptoms of GER. In addition, the supine position, possibly by increasing the likelihood of aspiration of gastric contents into the lung, may lead to pneumonia in patients on mechanical ventilators.[2] Finally, nasogastric tubes promote aspiration of gastric contents by impairing swallowing function, causing stagnation of oropharyngeal secretions and reducing the tone of the lower oesophageal sphincter.[2] The simple approach to all of these problems may involve elevating the position of the bed. Meguro *et al.* showed that elevating the bed after each meal for 2 h may lower the febrile days presumptively caused by aspiration of gastric contents.[57] Matsui *et al.* also emphasized the importance of a patient's sitting position for the prevention of respiratory tract infections.[58]

Avoid neuroleptics

The cough reflex can, of course, be suppressed by sedative drugs. Irwin *et al.* reported a consensus panel report of the American College of Chest Physicians, 'Managing Cough as a Defense Mechanism and as a Symptom,' and did not identify any age-related changes in cough reflex.[59] However, depression of cough reflex by anaesthesia, sedative hypnotics or analgesic narcotics should be considered to be a major risk for aspiration pneumonia in older patients, especially during sleep. Attention to minimizing the use of agents that suppress the cough reflex is crucial in caring for elderly patients. When older people take benzodiazepines, their swallowing reflex will not decrease significantly. However, when they take neuroleptics, which mostly act as a dopamine receptor antagonist, their swallowing reflex clearly does decrease, which makes things even more troublesome and leads to pneumonia.[60]

Handwashing

Gram-negative bacilli and *Staphylococcus aureus* commonly colonize the hands of healthcare providers. Although usually transient, hand colonization may persist, particularly in workers with dermatitis. Handwashing before and after contact with patients is an effective method for removing transient bacteria,[2] but this is often a neglected behaviour by medical personnel. The use of gloves and gowns can significantly reduce nosocomial infection and pneumonia. Hospitals with effective surveillance and infection control programmes have rates of pneumonia 20% lower than hospitals without such programmes. Adherence to infection control practices such as handwashing is fundamental for the prevention of nosocomial pneumonia. Unfortunately, such barrier methods will not be effective in preventing infection with organisms that are part of the critically ill patient's endogenous flora; hence most Gram-negative pneumonias cannot be avoided by isolation methods.[61] Improved handwashing practices and appropriate handling of mechanical feeding, suction and respiratory devices should reduce the spread of infectious agents in institutional settings.

Prevention of pneumonia among the elderly by vaccines

Influenza vaccines

Influenza vaccination is effective in older adults in preventing not only primary influenza pneumonia but also secondary bacterial pneumonia. Although an increased risk of pneumonia mortality is found in patients with limitations in activities of daily living, even bedridden elderly patients can be effectively immunized against influenza and the duration of febrile days and all respiratory conditions associated with influenza can be reduced.[62]

23-Valent pneumococcal vaccines

The efficacy of pneumococcal vaccine among high-risk patients has been the subject of some controversy. Some investigators estimate an ~60–95% prevention rate of pneumonia by 23-valent pneumococcal vaccine in immunocompetent elderly and in other high-risk patients.[63] It is currently recommended in the USA that all adults aged 65 years or older and those at risk because of underlying illnesses receive both of these vaccines. Chiba *et al.* demonstrated that pneumococcal vaccination significantly shortened the overall febrile days and significantly reduced the rate of hospitalization for pneumonia even in bedridden patients.[64] Pneumococcal vaccination is of benefit and recommended for elderly disabled patients at high risk for pneumonia.

Bacillus Calmette–Guérin (BCG) vaccines

The tuberculin skin test is an easy way to check the cell-mediated immunity in elderly people.[65] Almost all Japanese people over 65 years old may have a positive tuberculin skin test. If a person shows negative, it means that his or her cell-mediated immunity is depressed. We undertook a trial to vaccinate bedridden elderly people with BCG vaccine. During follow-up, new pneumonia was diagnosed in 42% of the elderly disabled patients with negative tuberculin responses, in 15% of the tuberculin converted patients by BCG and in 13% of the patients with positive tuberculin responses. BCG inoculation might reactivate the depressed T helper-1 mediated cellular immunity and prevent pneumonia in immobile elderly patients.[66]

Conclusion

Silent aspiration, which is frequently observed in patients with basal ganglia infarctions, might be an important risk factor for pneumonia in elderly patients. Measurement of a swallowing latency is useful for identifying a subject susceptible to pneumonia. The swallowing function might be partly regulated by dopaminergic neurons and substance P-containing sensory nerves. Disruption of the basal ganglia leads to an impairment of the swallowing function and may predispose stroke patients to pneumonia. ACE inhibitors and amantadine may have beneficial effects for the prevention of pneumonia. Similarly, oral care improves swallowing reflexes and lowers the risk of pneumonia. Vaccines are also effective even in disabled elderly patients in a bedridden condition. Since pneumonia in elderly patients frequently recurs and is often lethal, it is important to identify and protect high-risk patients from pneumonia.

Key points

- The main theme is to discuss how aspiration pneumonia develops in older people and to suggest preventive strategies that may reduce the incidence of pneumonia among older adults.
- Silent aspiration of oropharyngeal bacterial pathogens to the lower respiratory tract is one of the most important risk factors for elderly pneumonia. Impairments in swallowing and cough reflexes among older adults, for example, related to cerebral basal ganglia infarctions, increase the risk of pneumonia.
- Since both swallowing and cough reflexes are mediated by endogenous substance P contained in the vagal and glossopharyngeal nerves, pharmacological therapy using ACE inhibitors,

which decrease substance P catabolism, can improve both reflexes and result in the lowering of the risk for pneumonia.

- Since the production of substance P is regulated by dopaminergic neurons in the cerebral basal ganglia, treatment with dopamine analogues or potentiating drugs such as amantadine can reduce the incidence of pneumonia.

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発表研究論文 14

老年内科入院患者における MNA-SFによる栄養評価と摂食嚥下状態ならびに各種身体計測との関連の検討

田中　文彦[1)]　　葛谷　雅文[2)]

1. 緒　言

高齢入院患者の約40%では蛋白質の欠乏とエネルギーの欠乏が複合しておこるProtein-Energy Malnutrition (PEM) を呈すると報告されており[1)]，栄養不良のリスク要因である摂食嚥下機能低下や痩せの評価及び対策は重要である．今回我々は大学病院老年内科入院患者に対して簡易栄養評価ツールであるMini Nutritional Assessment Short Form (以下，MNA-SFと略)[2)]を実施し，対象者の栄養評価と摂食嚥下状態ならびに各種身体計測との関係を検討した．

2. 方　法

2010年5月18日から2011年8月10日の期間に調査可能であった名古屋大学医学部附属病院老年内科入院患者100名 (65歳以上，男性：49名，女性：51名，平均年齢± SD：81.4 ± 6.6歳) を対象とした．

本研究で使用した検討項目は入院1週間以内に看護師より行われた入院時摂食嚥下評価，同じく入院1週間以内に管理栄養士より行われたMNA-SF及び各種身体計測である．入院時摂食嚥下評価は当院独自のもので，(1) 飲み込みにくさ，(2) 口腔内食物残留，(3) 痰がらみ，(4) 咽頭食物残留，(5) むせ込みの5項目の問診を，それぞれ「よくある」，「ときどきある」，「ない」に分類するものである．今回の検討では (1) ～ (5) のすべての問診で「ない」に分類されている場合を摂食嚥下状態「問題なし」，(1) ～ (5) のすべての問診に「よくある」もしくは「ときどきある」が一つでもある場合を摂食嚥下評価「障害あり」，評価を行える状態ではなかった場合を摂食嚥下評価「評価不可能」とした．また，各種身体計測は，インサーテープ®，簡易キャリパー®(いずれもアボットジャパン株式会社) を用いて上腕周囲長 (arm circumference：AC)，上腕三頭筋皮下脂肪厚 (triceps skinfold thickness:TSF)，下腿周囲長 (calf circumference：CC) を計測し，AC及びTSFから上腕筋囲 (arm muscle circumference：AMC) と上腕筋面積 (arm muscle area:：AMA) を算出した．これら各種計測結果と「日本人の新身体計測基準値 (Japanese anthropometric reference date 2001：JARD2001)」[3)]に記された年齢・性別ごとの中央値から% TSF・% AC・% CC・% AMC・% AMAを算出した．MNA-SF評価群と摂食嚥下評価の結果ならびに各種身体計測(%)との関係について検討を行った．

3群間の比較にはカイ2乗検定，もしくは一元配置分散分析を用いた．解析にはSPSS18.0を用い，$p<0.05$を統計的有意とした．

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表1 対象者の特性

	MNA-SF			p
	良好群 (n=24)	risk群 (n=46)	低栄養群 (n=30)	
男 / 女(n)	8 / 16	25 / 21	16 / 14	ns
年齢(歳)*	79.2±7.1	80.7±6.0	81.4±6.1	p=0.011
MNA-SF(range:0-14)*	13.0±0.9	9.7±1.1	4.7±1.8	p<0.001
摂食嚥下評価(n)				
問題なし	24	38	11	
障害あり	0	5	10	p<0.001
評価不可能	0	3	9	
身体計測*				
TSF(cm)	1.4±0.6	0.9±0.4	0.7±0.4	p<0.001
%TSF(%)	116.6±47.7	80.5±37.7	70.3±32.7	p<0.001
AC(cm)	26.8±3.2	24.0±3.2	22.5±2.9	p<0.001
%AC(%)	109.2±14.4	96.9±14.0	92.8±13.0	p<0.001
CC(cm)	33.2±3.8	30.4±3.5	27.5±2.6	p<0.001
%CC(%)	107.9±10.8	98.1±11.3	90.6±8.8	p<0.001
AMC(cm)	22.5±2.6	21.2±2.6	20.2±2.4	p=0.006
%AMC(%)	108.8±12.7	100.5±13.9	97.2±12.5	p=0.007
AMA(cm)	40.9±9.7	36.3±8.9	33.1±8.1	p=0.007
%AMA(%)	120.4±30.8	103.1±29.9	96.4±27.1	p=0.012

* Mean ±SD

ns : not significant

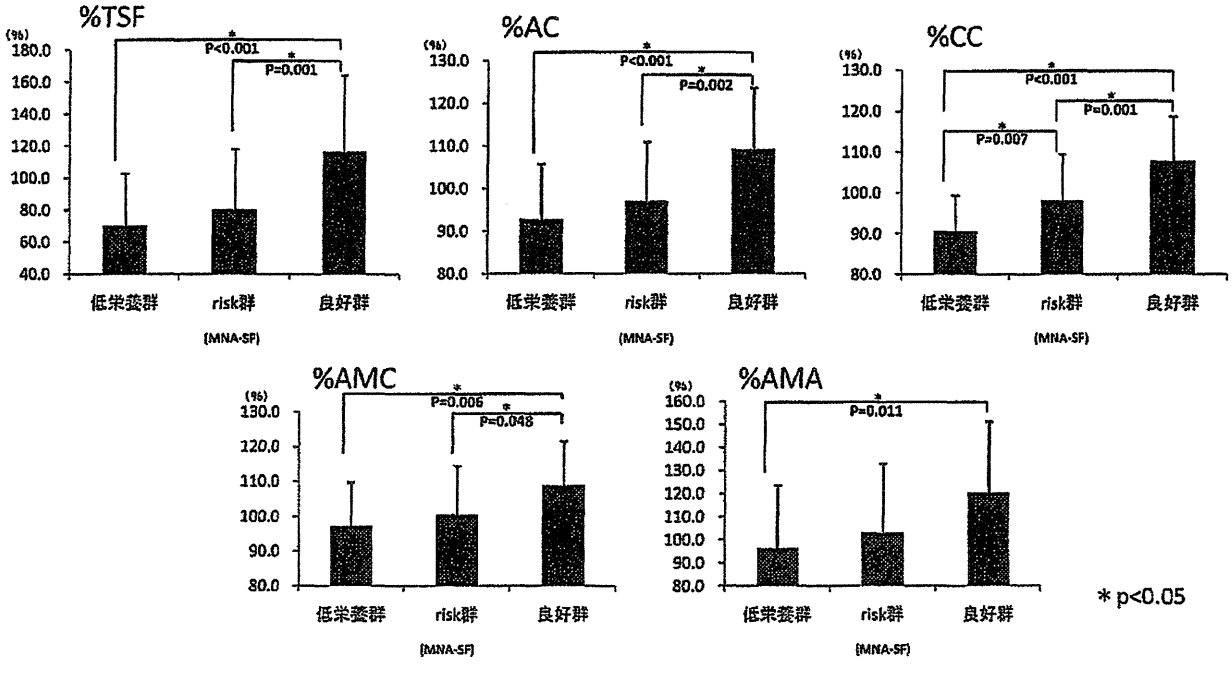

図1 NMA-SF と各種身体計測（%）

3. 結 果

対象者の特性を表1に示した.

MNA-SF の結果は「栄養状態良好」が24名（以下, 良好群),「At risk」が46名（以下, risk 群),「低栄養」が30名（以下, 低栄養群）で, 良好群は全体の24%に留まった. 摂食嚥下評価の結果,「問題なし」が73名,「障害あり」が15名,「評価不可能」が13名であった.

MNA-SF 評価群と摂食嚥下評価の結果を比較検討すると，MNA-SF 良好群では摂食嚥下評価結果「問題なし」が 24 名（100%），「問題あり」及び「評価不可能」はともに 0 名であった．また，MNA-SF risk 群では摂食嚥下評価「障害有り」が 5 名（11%），「評価不可能」が 3 名（7%），MNA-SF 低栄養群では摂食嚥下評価結果「障害有り」が 10 名（33%），「評価不可能」が 9 名（30%）となった．

MNA-SF 評価群と JARD2001 より算出した各種身体計測（%）との検討では，MNA-SF 良好群でのすべての各種身体計測（%）の平均は 100% を超えていた．また，MNA-SF 良好群，risk 群，低栄養群での各種身体計測（%）の平均は，すべてで良好群＞risk 群＞低栄養群との結果となり，図 1 より良好群と低栄養群にはすべてで有意な群間差（$p<0.05$）を認めた．

4. 考　察

本研究では，大学病院急性期病棟での高齢入院患者に対して入院時栄養評価，摂食嚥下評価，各種身体計測について調査を行った．

今回の検討では，MNA-SF 評価で「低栄養」と評価された割合は 30%，「At risk」と評価された割合は 46% と高率に栄養の問題がある患者が存在していた．MNA-SF の平均値が低値で栄養不良と判定されると，摂食嚥下障害がある群が高率となり，また，% TSF，% AC，% CC，% AMC，% AMA のすべての各種身体計測（%）の平均値が低値となる傾向が認められた．これらのことより，高齢患者に対して入院時に MNA-SF を実施することで，摂食嚥下機能ならびに身体状態のリスクを予想し，早期に管理栄養士，言語聴覚士，摂食・嚥下障害看護認定看護師などが介入することによって，食事形態の調整や投与栄養量の検討などが可能になると思われる．したがって，MNA-SF による高齢入院患者の栄養評価は極めて重要であり，今後も継続した使用が望まれる．

最後に，本研究では入院時摂食嚥下評価を病棟看護師が行っており，客観的かつ定量的な嚥下機能を基盤とした評価ではないため，嚥下障害の判断が適切でない可能性があることは本研究の限界である．

5. 結　語

今回の検討により，MNA-SF と摂食嚥下状態ならびに身体計測との間には，密接な関係があることが示唆された．今後は入院時だけではなく，在院中や退院時の栄養・摂食嚥下評価，各種身体計測を実施して，経時的な検討を行っていきたい．

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REVIEW ARTICLE

Cognitive dysfunction: An emerging concept of a new diabetic complication in the elderly

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The incidence of type 2 diabetes mellitus (T2DM) has risen, and this trend is likely to continue. Recent advances suggest that T2DM is a risk factor for cognitive decline. We are now encountering novel complications of T2DM, namely cognitive dysfunction and dementia. Although the treatment strategy for diabetic patients with neurocognitive dysfunction has received a great deal of attention, the appropriate level of glycemic control for the prevention of the development and/or progression of cognitive decline in elderly diabetic patients remains to be elucidated. Another issue in diabetic treatment in patients with cognitive dysfunction is the selection of medicines. The best choice and combination of antidiabetic medications for the preservation of cognition should also be studied. Ample studies suggest that exercise helps to preserve cognitive function, although existing evidence does not necessarily indicate its effectiveness exclusively in diabetic patients. Exercise is a helpful non-pharmacological therapy. Considering the progressive aging of the worldwide population, more research to investigate the best way to manage this population is important. **Geriatr Gerontol Int 2013; 13: 28–34.**

Keywords: Alzheimer's disease type dementia, hypoglycemia, insulin resistance, neurocognitive assessment, vascular dementia.

Introduction

The incidence of type 2 diabetes mellitus(T2DM) has risen, and this trend is expected to continue.[1] Recent remarkable advances in pharmacological therapy in T2DM have resulted in a wide variety of treatments. Many large clinical trials have been carried out, and a variety of interventions are now available to prevent and treat the classic microvascular and macrovascular complications that occur with DM, so that people are living longer with the condition.[2] Recent studies suggested that T2DM is a risk factor for cognitive dysfunction and dementia in the elderly. With the increase in the number of elderly individuals with DM, the number of diabetic patients with cognitive dysfunction has been increasing. We are now encountering novel complications of T2DM that are not targeted by the current management strategies. As one of these new targets, cognitive impairment and dementia in patients with T2DM has generated a great deal of interest, and diabetic treatment in this population that takes brain protection into consideration should be provided.

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Cognitive impact of T2DM

Large epidemiological studies have shown the cognitive impacts of T2DM. In the Rotterdam Study,[3] T2DM patients showed an increased risk of developing dementia. The study also showed that patients treated with insulin were at a 4.3-fold higher relative risk for dementia. The Hisayama Study showed that the incidence of all-cause dementia, Alzheimer's disease (AD) and vascular dementia were significantly higher in patients with diabetes than in those with normal glucose tolerance[4] The same study showed that systemic insulin resistance was associated with the pathogenic process of AD, neuritic plaques formation.[5] The Religious Orders Study, which observed some 800 nuns and priests longitudinally for 9 years, showed that diabetic people had a 65% increased risk of developing AD.[6] The Honolulu Asia Aging Study, a cohort of Japanese Americans in Hawaii, showed that the diabetic population had a 1.8-fold higher risk of developing AD and a 2.3-fold risk of vascular dementia.[7,8]

Prospective trials also suggested that T2DM caused cognitive function to deteriorate in the elderly.

A diagnosis of diabetes increased the odds of cognitive decline 1.2-fold to 1.7-fold (95% CI 1.3–2.3) in several neurocognitive assessments.[9] A recent systematic review of large prospective trials reported that T2DM increased the risk of AD by a factor of 1.59 (range 1.15–2.7).[10] Another systematic review reported that T2DM has a risk of vascular dementia of 2.0–4.2.[9,11]

The advances in the research in this field strongly suggest that T2DM is a risk factor for cognitive dysfunction or dementia.[12,13]

Assessment of diabetes-associated cognitive dysfunction

To screen patients with cognitive impairment, several neuropsychological assessment tools might be applied. The Mini-Mental State Examination (MMSE) is an assessment scale for global cognition including orientation, memory, calculation, verbal ability and constructional disability.[14] A full score is 30, and a cut-off point of 23 out of 24 is usually used for the screening of dementia. The MMSE subset analysis identified impaired attention and calculation as specific characteristics of DM patients,[15] whereas patients with AD had lower scores in temporal orientation and recall.[16]

As a part of a large cohort study of older DM patients (Japanese Research of Cholesterol and Diabetes Mellitus, UMIN000000516 Japan CDM), we carried out MMSE on diabetic patients aged older than 65 years in a diabetic outpatient clinic (52 males, 61 females; mean age 74.7 ± 4.6 years). Of these patients, 75 were aged less than 75 years (younger-old mean age 69.9 ± 4.7 years) and 38 patients were aged older than 75 years (older-old mean age 80.7 ± 4.4). In the younger-old group, 76.0% of patients (57/75) had a MMSE score of more than 24 (mean score 25.3 ± 4.7), and in the older-old group, 52.6% (20/38) had a MMSE score of more than 24 (mean score 24.2 ± 4.6). This small assessment showed that many diabetic patients had lower cognitive scores indicative of dementia, especially in the older-old.

Diabetes affects a wide range of cognitive domains.[17] Among the domains affected by T2DM, cognitive speed might provide early detection of diabetes-related cognitive decline[18,19] The digit symbol substitution test (DSST) is a test of cognitive speed that can be carried out relatively easily. It consists of a number (e.g. nine) of digit-symbol pairs (followed by a list of digits). Under each digit, the patient is asked to write down the corresponding symbol as quickly as possible. The number of correct symbols written within the allowed time (e.g. 90 or 120 s) is measured.

In clinical settings, the diagnosis of dementia is generally made based on the Diagnostic and Statistical Manual of Mental Disorders III revised criteria in patients with or without DM.[20] The disturbance in memory impairment with at least one of the following is required for the diagnosis of dementia: abstract thinking, judgement, higher cortical function and personality changes interferes with work or social activities. The leading cause of dementia in diabetic patients is AD, as is those without DM. DM patients often have cerebrovascular disease, and clinical-pathological studies support the notion that vascular lesions aggravate the deleterious effects of AD pathology by reducing the threshold for cognitive impairment.[21]

Pathogenesis of diabetes-associated cognitive dysfunction

The precise mechanisms underlying T2DM-related cognitive dysfunction or the development of dementia, especially AD-type dementia, remain to be elucidated; however, several hypothetical mechanisms have been proposed (Fig. 1). To develop pharmacological and non-pharmacological strategies for treating the diabetic elderly with cognitive impairment, elucidating the pathogenesis of this complication might be essential.

High glucose concentration, a major pathological characteristic of diabetes, might have toxic effects on neurons in the brain through osmotic insults and oxidative stress, and the maintenance of chronic high glucose also leads to the enhanced formation of advanced glycation end-products (AGE).[22] AGE couple with free radicals and create oxidative damage, which in turn leads to neuronal injury,[23] and they also reactivate microglia, the resident innate immune cells in the brain. A wealth of evidence shows that activated microglia can become deleterious and damage neurons.[24]

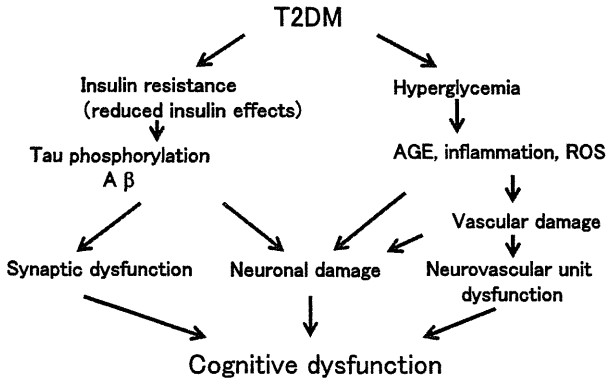

Figure 1 Pathogenesis of type 2 diabetes mellitus (T2DM)-associated cognitive dysfunction. Cognitive dysfunction in T2DM is induced by multiple pathways. Insulin resistance might be associated with Alzheimer's disease pathology, and hyperglycemia induces advanced glycation end-products (AGE) formation, inflammation and reactive oxygen species (ROS) production, which might lead to neuronal damage and neurovascular dysfunction.

T2DM, especially in conjunction with obesity, is characterized by insulin resistance and/or hyperinsulinemia. Insulin degrading enzyme (IDE) catabolizes insulin in the liver, kidneys and muscles.[25,26]

It is generally agreed that insulin located within the brain is mostly of pancreatic origin, having passed through the blood–brain barrier, although there is debate about the amount of insulin that is produced de novo within the central nervous system.[27] Major known actions of insulin in the brain include control of food intake (through insulin receptors located in the olfactory bulb and thalamus) and effects on cognitive functions, including memory.[28,29] Insulin also regulates acetylcholine transferase expression, which is an enzyme responsible for acetylcholine (ACh) synthesis. ACh is a critical neurotransmitter in cognitive function, and it might be relevant to neurocognitive disorders in diabetics.[30] Recent basic research showed that insulin signaling in the central nervous system prevents the pathological binding of amyloid beta (Aβ) oligomers.[31] Aβ oligomers are soluble molecules that attach with specificity to particular synapses, acting as pathogenic ligands.[32]

Insulin has multiple important functions in the brain, as aforementioned. These functions are disrupted in insulin-resistant states. The transport of insulin into the brain across the blood–brain barrier is reduced in insulin-resistance-associated hyperinsulinemia, and insulin levels in the brain are subsequently lowered.[33,34] Intranasal insulin showed some benefits in early AD patients.[35] With intranasal administration, insulin bypasses the periphery and the blood–brain barrier, reaching the brain and cerebrospinal fluid within minutes through extracellular bulk flow transport along olfactory and trigeminal perivascular channels, as well as through more traditional axonal transport pathways.[36,37]

Some basic research suggests that insulin signaling is involved in AD-related pathology through its effects on the Aβ metabolism and tau phosphorylation.[38] Insulin signaling activates PI3K/Akt pathway, which leads to inactivation of glycogen synthase kinase-3β (GSK-3β). GSK-3β regulates tau phosphorylation, one of the main pathological components in AD. Less insulin signaling might also induce increased activity of GSK-3β, which leads to the enhanced phosphorylation of tau protein and the formation of neurofibrillary tangles.[39] Decreased insulin signaling reduces the synthesis of several proteins, including IDE. IDE degrades Aβ as well as insulin, and reduced amounts of IDE might result in greater amyloid deposition. The results of pathological assessments in AD with or without DM, however, are highly controversial.[40,41] More research would be warranted to elucidate the relevance of insulin and insulin resistance in the underlying mechanism of T2DM-associaiated cognitive dysfunction.

Diabetic patients often have ischemic brain lesions.[42] Even asymptomatic cerebral infarctions have affects on the cognition in elderly diabetic patients.[18,43] On cerebral magnetic resonance imaging, white matter hyperintensities and lacunae, both of which are frequently observed in the elderly, are generally viewed as evidence of small vessel disease in the brain (white matter lesions and lacunae). Small vessel diseases affect cognitive function in older diabetics.[18,44] DM also affects the function of microvascular endothelial cells. The deterioration of the endothelial cell function leads to the disruption of blood–brain barrier function, which might induce neuroinflammatory reactions and neurodegeneration.[45] The endothelial cells play a critical role in the control of hemodynamic coupling among neuronal, glial and vascular components; that is, "neurovascular units". Dysfunction of "neurovascular units" might have some impact on cognition in diabetic patients.[46]

Treatment of vascular risk factors including T2DM was reportedly associated with a lower conversion rate from mild cognitive impairment to AD[47] or slower cognitive decline in AD patients.[48] Comprehensive management in DM patients should be warranted.

Treatment and management of diabetic patients with cognitive impairment

T2DM is associated with cognitive dysfunction; however, it has not yet been made clear whether glycemic control leads to the preservation or improvement of cognitive function. Several prospective studies[19,49,50] have shown that higher glycated hemoglobin (HbA1c) levels at baseline are associated with cognitive decline. A recent prospective study by Christman *et al.*, however, showed that HbA1c levels at baseline had no effects on cognitive function.[51] A large cohort study, the Action to Control Cardiovascular Risk in Diabetes–Memory in Diabetes (ACCORD-MIND) trial, has found that HbA1c levels were cross-sectionally associated with worse performance on several cognitive functional tests.[52] However, the results of the interventional study were rather disappointing.[53] Although total brain volume in the intensive glycemic control group was significantly greater than in the standard treatment group after 40 months, there was no significant difference in cognitive assessment. The results of the study, however, should be interpreted cautiously because of the early drop-outs in the intervention group.

In the ACCORD-MIND study, the intensive control group achieved a HbA1c level of 6.6% compared with 7.5% in the standard treatment group. Several smaller studies involving less intensive glycemic treatment, however, indicated that modest cognitive decrements in patients with T2DM are partially reversible with the improvement of glycemic control,[54–59] although not invariably.[60] Postprandial hyperglycemia is associated

with atherosclerosis and diabetic complications,[61] and a control of postprandial hyperglycemia might prevent cognitive decline in older diabetic individuals.[59] These studies suggested that metabolic control might have beneficial effects in terms of cognitive function; however, the appropriate levels of blood glucose control remain unclear. In contrast, a recent report has suggested that a history of severe hypoglycemic episodes is associated with a greater risk of dementia.[62] The diabetic control in this population should be balanced between the merits of treatment and the risk of hypoglycemia.

Another issue related to the treatment that pertains to cognitive dysfunction is the selection and combination of antidiabetic medicines. The Rotterdam Study reported that insulin use increased the incidence of dementia.[3] However, many confounding factors must be considered when interpreting the results of that study. The patients who used insulin might have had worse diabetic control, a longer history and more complications, and these factors might have some impact on the incidence of dementia. Greater insulin resistance means that a greater amount of insulin is required to control the blood glucose level. The association of the use of an excessive amount of insulin with insulin resistance status might be undesirable, the appropriate prescription of insulin for maintaining a desirable blood glucose level has not yet been determined for individuals with insulin resistance. A small study reported that pioglitazone, an insulin sensitizer, has some beneficial effects on cognition in AD.[63] Comprehensive management in combination with insulin use would be necessary to achieve appropriate glycemic control, and efforts to reduce insulin resistance would be warranted.

Recently, a new class of diabetic pharmacological treatments known as incretin-related medicines has emerged. Glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP), whose activity is reduced in insulin resistance, have been implicated in central nervous system function, including cognition, synaptic plasticity and neurogenesis.[64] An animal study showed that GLP-1 prevented the neurodegenerative developments in AD model mice.[65] Further clinical investigation from the perspective of brain protection is warranted.

Many studies suggested that exercise has the potential to protect brain function. A systematic review of the Cochran database by Angevaren *et al.* reported the effects in elderly individuals without known cognitive impairment, and another systematic review of a prospective cohort study by Hamer *et al.* reported that exercise reduces the risk of incidence of dementia by 28% and of AD by 45%.[66,67]

Exercise also has effects on patients with mild cognitive impairment and dementia.[68] Although existing evidence does not indicate the effects of exercise on the protection of brain function exclusively in the diabetic population, exercise has multiple established effects on diabetic patients, including the improvement of insulin resistance. Studies to investigate the effects of exercise on diabetic cognitive dysfunction are warranted.

Cognitive dysfunction is associated with poor ability of self-care in elderly diabetics, and the use of both health and social services.[69] In addition, physical function is often more compromised in those with cognitive impairment. Individuals with DM with cognitive impairment might have difficulty carrying out the daily tasks of DM self-care effectively,[70] which might result in worse glycemic control than in individuals without cognitive impairment. A study reported that cognitively impaired DM patients were at increased risk of mortality and functional disability.[71] The relationship between cognition and self-management ability might be bidirectional. While it could be that poor self-management practices lead to poorer metabolic control and therefore brain dysfunction, cognitive deterioration would lead to changes in self-management ability.

A depressive mood is often comorbid with dementia,[72] especially in diabetics.[73] Depressed mood might also be associated with cognitive impairment and might interfere with effective self-management.[74–77]

People with dementia often experience behavioral and psychological symptoms of dementia (BPSD) during the course of their illness. The management of dementia is complicated by BPSD, such as psychosis, depression, agitation, aggression and disinhibition. BPSD also disrupts the daily diabetes care routine, with "denial" of having diabetes or memory loss (anosognosia) being the most disruptive.[78] Caregivers often report that caring for both diabetes and dementia is highly burdensome, that they feel overwhelmed by BPSD, and that they want more support from family and from the patients' healthcare providers.

To control BPSD, antipsychotic medication is sometimes prescribed. Antipsychotic drugs, especially second-generation drugs including olanzapine and quetiapine, have the potential to induce weight gain and elevate plasma glucose levels.[79] The use of these drugs in demented diabetic patients should be avoided.

Conclusion

Cognitive dysfunction might be a novel class of diabetic complication in the elderly. The management of diabetic patients with this complication is challenging and presents many unresolved problems. Considering the progressive aging of the worldwide population, it will be important to carry out investigations to improve our understanding of the association between T2DM and cognitive dysfunction, and to determine the best way to manage these populations.

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Disclosure statement

Nothing to declare.

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ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Cognitive impairments and functional declines in older adults at high risk for care needs

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Aim: Functional status of those who have very mild cognitive impairment have not been sufficiently investigated. In the current study, we analyzed the characteristics of functional awareness in older adults who had cognitive impairment and were at high risk of requiring support/care (termed as specified elderly at high risk for care needs in the long-term care insurance scheme).

Methods: The answers of a health check, which is provided by the local municipal government for those aged 75 years or older who have not been certified as eligible for care services, were analyzed. The differences of the variables between the two groups regarding yes/no answers to each of three cognition-related questions were analyzed. Then, a multiple logistic analysis was carried out to investigate the association of yes/no answers of the three cognition-related questions and the awareness of functional decline.

Results: The participants who had cognitive impairment had greater awareness of functional declines. Multiple logistic regression analysis showed that subjective memory impairment and disorientation were significantly associated with a wider range of awareness of functional decline.

Conclusions: Subjective cognitive impairment was associated with a wide range of awareness of functional decline in older adults at high risk for care need. **Geriatr Gerontol Int 2013; 13: 77–82.**

Keywords: depressive mood, dysphagia, instrumental activities of daily life, memory impairment, physical activity, vitality.

Introduction

Screening for cognitive impairment is essential for better health outcomes. Early identification and intervention holds the promise of improving overall care for affected persons through the use of chronic disease management strategies. In general, the existing literature does not support screening of unselected older adults for cognitive impairment;[1] however, screening in a high-risk population might be valid.

Several factors are closely associated with mild cognitive impairment (MCI) and very early dementia. Depressive mood might be a risk factor or an early manifestation of dementia.[2–4] Subtle impairments of instrumental activities of daily living (IADL) might also be very early manifestations.[5,6]

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In Japan, the public long-term care insurance system provides services to older adults who have been certified as requiring support (level 1 and 2) or care (levels ranging from 1 to 5 depending on their care needs). Uncertified, but not quite healthy, older adults who are considered at high risk of requiring support/care are categorized as specified elderly at high risk of care needs (specified elderly are provided with preventive care services by the municipalities in which they reside). The specified elderly are community-dwelling and have neither basic activities of daily living (B-ADL) impairments nor dementia. The specified elderly, however, is supposed to be the transitional stage to requiring care. Elucidating the characteristics of this group and developing some adequate intervention on this population to prevent the transition to requiring care are warranted. The local governments provide a health check of the uncertified elderly annually, in which all examined subjects complete a basic yes/no questionnaire that consists of simple assessments of their instrumental activities of daily living (7 items), memory problems (3 items), walking status (5 items), dysphagia (3 items), nutritional

status (2 items) and depressive mood (5 items).[7] Subjective memory complaint might be an easy method to screen cognitive impairment, and a report showed that subjective memory complaint was associated with depressive mood and difficulties of activities of daily living (ADL).[8] In this assessment, subjective cognitive dysfunction was evaluated by three questions, and in the same assessment awareness of functional declines were also evaluated.

However, the functional characteristics of those who have subjective cognitive impairment by this assessment in the specified elderly at high need for requiring care have been unclear. Elucidating the characteristics of this population might lead to the development of intervention for the prevention of the transition to dementia and/or the status of requiring care.

In order to portray the characteristics of awareness of functional decline in those who are considered to have subjective cognitive impairment by this assessment, we examined the associations between non-cognitive items and cognitive items of the questionnaire in older adults at high risk of requiring support/care.

Methods

Measurements

To screen the elderly at high risk for care, a health check is provided by the local municipal government for those elderly aged 75 years or older who have not been certified as eligible for care services.

The health check includes a yes/no questionnaire that consists of simple assessments of their IADL (7 items), subjective cognitive problems (3 items), walking status (5 items), dysphagia (3 items), nutritional status (2 items) and depressive mood (5 items). In the current study, we calculated the scores for each of these six domains, with higher scores indicating worse functioning. The data for 1163 men and 2651 women who were determined to be specified elderly were obtained from annual health checks implemented in one of the urban municipalities in central Japan during October and November in 2009.

Continuous variables (age, blood pressure, hemoglobin, serum albumin and body mass index) were compared by Student's *t*-test, and others were compared by χ^2 analysis.

The questionnaire was as follows;

1) IADL

1. Do you go out alone using transportation? 2. Do you shop for daily necessaries by yourself? 3. Do you manage your bank account on your own? 4. Do you visit your friends alone? 5. Are you consulted by your family or friends?

2) Waking status

6. Do you climb up the stairs without holding onto handrails or walls? 7. Do you stand up without assistance? 8. Can you walk for more than 15 min without rest? 9. Have you fallen within a year? 10. Are you anxious about falls?

3) Nutrition

11. Have you lost more than 2–3 kg in weight in the recent 6 months? 12. BMI < 18.5 kg/m^2

4) Dysphagia

13. Do you have difficulty in eating hard food? 14. Do you choke with liquid? 15. Do you care about dry mouth?

5) Vitality

16. Do you go out more than once a week? 17. Do you go out less frequently than last year?

6) Cognition

18. Are you told that you repeatedly ask the same things? 19. Do you look up the numbers, dial and make phone calls without help? 20. Do you sometimes forget the date?

7) Depressive mood

21. Do you feel unfulfilled with daily life? 22. I do not enjoy my life as I used to (recent 2 weeks). 23. I feel more bothered to do everyday things than before (recent 2 weeks). 24. I do not feel that I am useful (recent 2 weeks). 25. I feel tired for no reason (recent 2 weeks).

The differences of the variables between the two groups regarding yes/no answers to each of the three cognition-related questions (Are you told that you always ask the same things? [memory]; Do you look up numbers, dial and make calls without help? [telephone]; Do you sometime forget what day it is? [orientation]) were analyzed. In the analysis, answers for related questions were scored as follows: IADL, 0–5; walking status, 0–5; depressive mood, 0–5; dysphagia, 0–3; vitality, 0–2; and nutritional status, 0–2. The difference of the distribution was analyzed by Student's *t*-test, Mann–Whitney *U*-test, or χ^2 analysis. Then, a multiple logistic analysis was carried out to investigate the association of yes/no answers of these three cognition-related questions and the awareness of functional decline.

Results

The characteristics of the participants are shown in Table 1.

IADL, walking status, depressive mood, vitality, and nutrition were all associated with subjective memory impairment and disorientation in univariate analysis (Tables 2 and 4). IADL, walking status, depressive mood and vitality were associated with an inability to call by themselves, but dysphagia and nutritional status were not significantly associated (Table 3).

Multiple logistic regression analysis showed that vitality was not associated with each of the three