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CACHEXIA AND COGNITIVE FUNCTION IN THE COMMUNITY-DWELLING OLDER ADULTS: MEDIATION EFFECTS OF ORAL HEALTH

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Abstract: *Background:* Cognitive impairment and poor oral health are common problems in older adults and are associated with malnutrition. However, it is unclear how they are related to cachexia in community-dwelling older adults. The aim of this study was to examine the relationships among cachexia, cognitive function, and oral health in community-dwelling older adults. *Methods:* This study is a secondary analysis of a data-set. Data were collected in the community setting on older adults who applied for government-funded long-term care services in Hong Kong in 2017. Subjects were community-dwelling and aged ≥60 years. The outcome variable was cachexia. The predictors were cognitive function and oral health. The covariates included demographics and comorbidities associated with cachexia or malnutrition. Path analysis was employed to examine the associations among cachexia, cognitive function, and oral health using the software SAS/STAT and Mplus. *Results:* This analysis included 12,940 subjects. The prevalence of cachexia was 1.3%. Cognitive function was also found to have a direct effect on the oral health indicators of chewing problems (OR=1.073, p<0.001), brushing teeth problems (OR=1.349, p<0.001), and swallowing problems (coeff.=0.177, p<0.001). Oral health indicators with a direct effect on cachexia included dry mouth (OR=1.250, p<0.001), brushing teeth problems (OR = 1.185, p<0.01), and swallowing problems (OR=1.231, p<0.001). Cognitive function had no significant direct effect, but had a significant indirect effect on cachexia (OR=1.100, p<0.001) which is mediated by brushing teeth problems (OR=1.052, p<0.001) and swallowing problems (OR=1.038, p<0.001). *Conclusion:* Cognitive impairment causes cachexia indirectly through poor oral health. This study recommends adding cognitive function when screening community-dwelling older adults for cachexia. Health policymakers should stress regular oral health screening and interventions, and encourage increased utilization of oral health services by community-dwelling older adults with cognitive problems.

Key words: Cachexia, cognitive function, oral health, older adults.

Introduction

Cachexia is a complex metabolic syndrome associated with underlying illnesses, characterized by muscle loss, and manifested by weight loss (1). The common underlying illnesses associated with cachexia in older adults include chronic heart failure, chronic renal failure, chronic obstructive pulmonary disease (COPD), cancer, and arthritis (2). Its prevalence ranges from 5-15% in end-stage chronic heart failure to 50-80% in advanced cancers (3). The prevalence in the general population is approximately 2% (4). In the process of ageing, decreased food intake related to declining smell and taste and the interplay between sarcopenia and inactivity make older adults particularly vulnerable to cachexia (4). Cachexia is also associated with an increased risk of function loss, care burden, and death (5), and is therefore an important clinical condition to prevent and treat in older adults.

Cognitive impairment, particularly when severe, is associated with cachexia. Studies have shown that adults with advanced dementia have a greatly increased risk of developing cachexia (6). This is because adults with advanced dementia have lost the cognitive ability to eat and interest in eating; thus, anorexia induces the cachexia. Cachexia is also a common natural cause of death in adults at the final stage of dementia (7). In older adults with less severe forms of cognitive impairment (e.g., cognitive decline, mild cognitive impairment, mild dementia dementia), cognitive impairment is also associated with the risk of undernutrition only (e.g., low BMI and low mid-arm circumference) (8, 9). Little is known about the relationship between cognitive function and cachexia.

Oral health is significantly affected by ageing. Older adults have poor oral health for many physiological reasons related to ageing, such as changes in teeth and oral mucosa, edentulism, dental caries, periodontal disease, and xerostomia (i.e., dry mouth) (10). In community-dwelling older adults, xerostomia (prevalence=34.8%) (11), swallowing problems (prevalence=11.4%) (12), and chewing problems (prevalence=10.1%) (13) are commonly observed. Cognitive function has also been observed to be associated with oral health. Poor oral health is conventionally perceived to be caused by cognitive impairment and its effect to be mediated by poor oral hygiene (14). Recent studies have proposed new physiological and mechanistic explanations of how oral health possibly causes cognitive impairment by speeding up the progression of Alzheimer's disease through prolonged exposure to bacterial infection (e.g., porphyromonas gingivalis) and an increase in a systemic pro-inflammatory state secondary to chronic periodontitis (15, 16). However, a recent systematic

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review showed that there is still insufficient evidence to clearly show how or whether oral health and cognitive status are related (17).

Oral health is a broad concept involving many clinical indicators. Oral health is conventionally perceived to be associated with nutritional status. However, in older adults, different oral health indicators show associations of different strengths with nutritional status. Denture problems, chewing problems, xerostomia, and swallowing problems were significantly associated with malnutrition in older adults, while dental caries, periodontal status, number of teeth, and number of occluding tooth pairs were not (18-20). From the perspective of nutritional status, some oral health markers (i.e., denture problems, chewing problems, and xerostomia) are more indicative than others. Tooth brushing is the world's most popular oral hygiene practice and is effective for maintaining oral health and preventing caries and periodontal diseases (21). Yet older adults do not brush as regularly as younger people (22). However, little is known about the association between oral health indicators and tooth brushing practices.

Studies have indicated that cognitive impairment, oral health, and cachexia are potentially inter-related, but their relationships are unclear. Apart from underlying diseases, the current evidence seems to support the hypothesis that cognitive impairment can independently cause cachexia. The effect may possibly be mediated by oral health. However, this hypothetical model is untested. Interventions that mitigate cognitive decline and promote oral health are available. Understanding these relationships can inform the development of interventions and health policies to reduce the risk of cachexia in community-dwelling older adults. Therefore, the aim of this study was to examine the associations among cognitive function, oral health, and cachexia. Specifically, the following four hypotheses were tested:

1. Cognitive function has a direct effect on cachexia,
2. Cognitive function has a direct effect on oral health,
3. Oral health has a direct effect on cachexia, and
4. The effect of cognitive function on cachexia is mediated by oral health

Methods

Study design

A cross-sectional design was employed in this study. This is a secondary analysis of a database of the "Well-being and Associated Factors of Vulnerable Population in Long-term Care in Hong Kong", which routinely collected health data from a large cohort of community-dwelling Chinese older adults who applied for government-funded long-term care services. This study is reported in accordance with The Reporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement (23).

Setting

This observational study was conducted on community-dwelling older adults in Hong Kong. The data collection period was January to December 2015.

Participants

In Hong Kong, eligibility for government funded long-term care services is based on an applicant's care needs. Older adults who want to apply for government funded long-term care services can submit an application to the Standardised Care Need Assessment Management Offices-Elderly Services (SCNAMO-ES) under the Hong Kong Social Welfare Department. Accredited personnel assessed applicant's care needs by using the Hong Kong version of the Minimum Data Set-Home Care (MDS-HC) instrument 24. In this study, all applicants who fulfilled the following eligibility criteria were selected for analysis:

Inclusion criteria

1. Completed the MDS-HC in the SCNAMO-ES assessment,
2. Community-dwelling (i.e., non-institutionalized in the last 12 months), and
3. Age ≥60 years

Exclusion criteria

1. Dependent on tube feeding or extensive feeding assistance measured by MDS-HC 24. This is because their nutritional status would not be affected by their oral health.

Variables

The outcome was cachexia. The predictors were cognitive function and oral health. The potential confounders included basic demographics, lifestyle, and comorbidities known to be associated with cachexia or malnutrition (e.g., age, gender, living alone, educational level, marital status, cancer, chronic obstructive pulmonary disease (COPD), a psychiatric diagnosis, Alzheimer's disease, arthritis, chronic heart failure, chronic renal failure, and depression) (2, 25, 26).

Data sources

MDS-HC is a government-mandated assessment tool used to determine the care needs of older adults and match them with appropriate government funded long-term care services. It is a comprehensive tool with 21 sections (e.g., personal items, cognitive patterns, nutrition/hydration status, oral health, and disease diagnoses). The assessment drew on multiple sources and included direct questioning of care recipients and primary family caregivers, observation of care recipients in their home environment, and a review of secondary documents such as medical records, if available. This study extracted data from the relevant sections of the MDS-HC to answer the research questions.

Outcome variable

Cachexia was a binary variable, diagnosed by registered medical practitioners according to the following criteria 1:

1) Weight loss of at least 5% in 12 months or less (or BMI<20 kg/m^2), and
2) Three of the following symptoms
   a. decreased muscle strength,
   b. fatigue,
   c. anorexia,
   d. low fat-free mass index,
   e. abnormal biochemistry (e.g., anaemia, low serum albumin)

Predictors

Cognitive function was measured using the five-item Cognitive Performance Scale (CPS) (27), a hierarchical scale assessing short-term memory, cognitive skills for daily decision-making, the ability to make oneself understood, comatose status, and dependence in eating. Scores ranged from 0 (cognitively intact) to 6 (very severe impairment).

Oral health was measured using four variables. The first variable was 'chewing problems', which is dichotomous. It refers to an inability to chew food easily and without pain or difficulty, regardless of the cause (e.g., ill-fitting dentures, a neurologically impaired chewing mechanism, temporomandibular joint pain, or a painful tooth). The second variable was 'dry mouth', which is dichotomous. It was determined by clients reporting that they had a dry mouth. Dry mouth was also determined through an inspection when the client had difficulty speaking (e.g., tongue sticking to the roof of the mouth) or when the client had difficulty in moving food bolus in the mouth. The third variable was 'problems brushing teeth and dentures', which is dichotomous. It means difficulty in cleaning one's teeth and/or dentures due to endurance, motivation, or fine motor skill problems. The fourth variable was 'swallowing problems', which is a five-item ordinal variable. It was determined by the presence of special dietary prescriptions for swallowing difficulties. It was coded as follows: 0 indicating normal, 1 requiring dietary modifications to swallow solid foods (a mechanical diet or an ability to ingest specific foods only), 2 requiring modifications to swallow solid foods and liquids (purees, thickened liquids), 3 combining oral and tube feeding, and 4 indicating no oral intake. A higher score indicates a higher level of difficulty with swallowing.

Covariates

Data on age, gender, living arrangement, marital status, and educational level were collected from interviews. Data on chronic diseases were obtained from the participants' medical records.

Depression was measured by the number of negative mood symptoms experienced by the participants. It was based on the occurrence of the following nine items, each dichotomous (experienced or did not experience that negative symptom): (1) feelings of sadness or depression; (2) persistent anger with oneself or others; (3) expressions of what appear to be unrealistic fears; (4) repetitive health complaints; (5) repetitive anxious complaints and concerns; (6) sad, pained, worried facial expressions; (7) recurrent crying and tearfulness; (8) withdrawal from activities of interest; and (9) reduced social interactions. Scores ranged from 0 to 9, with a higher score representing a higher level of depression.

Bias

There may have been a sampling bias because only older adults who applied for government funded long-term care services were included in the current study.

Study size

All older adults who applied for government funded long-term care services were included in the sample. Based on the current sample size, the error in estimating the proportion of those with cachexia was ±0.20% at a 95% confidence level.

Statistical methods

The outcome variable (i.e., severe malnutrition), predictors (i.e., cognitive function and oral health), and covariates were summarized in terms of mean, standard deviation, frequency, and percentages where appropriate. A chi-square test and two-sample t-test were used to compare the predictor and the covariate variables of the cachexia and non-cachexia groups. Path analysis was employed to test the four hypotheses of this study using the software SAS/STAT 14.1 and Mplus version 7.11 (28, 29). The strength of any associations was reported using odds ratios and path coefficients. The level of significance was 0.05.

Data access and cleaning methods

All subjects in the dataset who fulfilled the eligibility criteria were included in the analysis. Subjects with missing data in any of the variables in this study were excluded.

Results

Participants

Included in this study were 13,180 older adults aged 60 or above who lived in the community and had completed the assessment. When subjects who depended totally on tube feeding or needed extensive assistance in eating were excluded, 12,945 subjects remained. Five subjects with missing values in any of the variables of concern were excluded, resulting in a final sample of 12,940 older adults.

Descriptive data

As shown in Table 1, 12,940 subjects were selected for the data analysis. Their mean age was 81.88±7.83 years. The majority were female (60.0%), lived with family (78.0%), had received no formal education (70.0%), were not currently

Table 1
Participants' profile (n = 12,940)

	n (%) / mean ± SD		
	Total	**Cachexia**	**Non-cachexia**
Demographics			
Age (years) *	81.88 ± 7.83	80.60 ± 8.40	81.89 ± 7.82
Female	7767 (60.02)	93 (54.07)	7674 (60.10)
Living status			
Lives alone	2845 (21.99)	39 (22.67)	2806 (21.98)
Lives with spouse only	2072 (16.01)	23 (13.37)	2049 (16.05)
Lives with spouse and other(s)	2849 (22.02)	33 (19.19)	2816 (22.06)
Lives with child (not spouse)	3841 (29.68)	59 (34.30)	3782 (29.62)
Lives with other(s)	1333 (10.30)	18 (10.47)	1315 (10.30)
Level of education			
Primary school or above	3901 (30.15)	61 (35.47)	3840 (30.08)
Below primary school	9039 (69.85)	111 (64.53)	8928 (69.92)
Marital status			
Married	5532 (42.75)	65 (37.79)	5467 (42.82)
Not married	7408 (57.25)	107 (62.21)	7301 (57.18)
Alcoholism	116 (0.90)	3 (1.74)	113 (0.89)
Comorbidities			
Cancer	984 (7.60)	20 (11.63)	964 (7.55)
COPD	1172 (9.06)	21 (12.21)	1151 (9.01)
Psychiatric diagnosis *	1508 (11.65)	31 (18.02)	1477 (11.57)
Alzheimer's disease *	1573 (12.16)	10 (5.81)	1563 (12.24)
Arthritis *	2844 (21.98)	25 (14.53)	2819 (22.08)
Congestive heart failure	866 (6.69)	8 (4.65)	858 (6.72)
Renal failure	546 (4.22)	9 (5.23)	537 (4.21)
Chronic diseases	7155 (55.29)	91 (52.91)	7064 (55.33)
Depression ***	0.83 ± 1.57	1.61 ± 2.55	0.82 ± 1.55
Outcome and predictors			
Cachexia	172 (1.33)		
Cognitive function (CPS) *	1.46 ± 0.80	3252 (25.13)	1.58 ± 0.78
Oral health			
Chewing problems	50 (29.07)	1.45 ± 0.80	3202 (25.08)
Dry mouth ***	879 (6.79)	35 (20.35)	844 (6.61)
Brushing teeth problems ***	524 (4.05)	18 (10.47)	506 (3.96)
Swallowing problems ***			
Normal	6401 (49.47)	64 (37.21)	6337 (49.63)
Modification to solid food	5874 (45.39)	86 (50.00)	5788 (45.33)
Modification to solid food and liquids	626 (4.84)	19 (11.05)	607 (4.75)
Combined oral and tube feeding	39 (0.30)	3 (1.74)	36 (0.28)
No oral intake	0 (0)	0 (0)	0 (0)

COPD: chronic obstructive pulmonary diseases, CPS: clinical performance scale; * p-value < 0.05, *** p-value < 0.001

married (57.3%), and were non-alcoholics (99.1%). Subjects with known underlying diseases related to cachexia were not in the majority: cancer (7.6%), COPD (9.1%), psychiatric illnesses (11.7%), Alzheimer's disease (12.2%), arthritis (22.0%), chronic heart failure (6.7%), and renal failure (4.2%). More than half (55.3%) of them had at least one of the above chronic diseases. The mean score for negative mood was 0.83±1.6.

Data on outcome and predictors

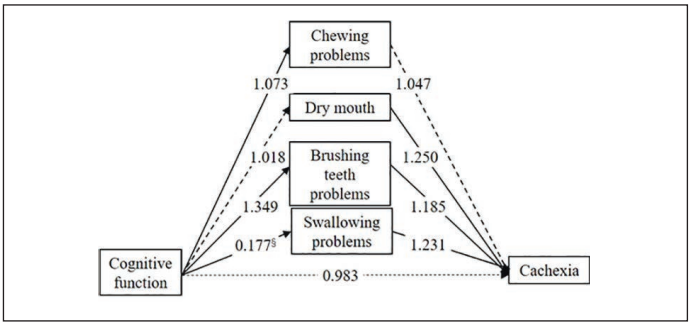
A total of 172 subjects (1.3%) were diagnosed with cachexia. The mean CPS score was 1.46±0.80. The majority did not have oral health problems: chewing problems (25.1%), dry mouth (6.8%), and brushing teeth problems (4.1%). Slightly less than half had various types of swallowing problems needing modifications to their ingestion of solid food (45.4%), modifications to solid food and liquids (4.8%), and combined oral and tube feeding (0.3%).

Main results

As shown in Table 1, cognitive function ($p<0.05$) and three oral health indicators including dry mouth ($p<0.001$), brushing teeth problems ($p<0.001$), and swallowing problems ($p<0.001$) had a significant association with cachexia. Older adults with cachexia had more severe cognitive impairment (mean=1.58 vs 1.45) than those without cachexia, and were more likely to have a dry mouth (20.4% vs 6.6%), brushing teeth problems (10.5% vs 4.0%), and swallowing problems (62.8% vs 50.4%).

Figure 1

Path analysis: A schematic illustration of the paths



As shown in Table 2 and Figure 1, the path analysis showed that cognitive function had no direct effect on cachexia. Cognitive function was also found to have a direct effect on oral health indicators, including chewing problems (OR=1.073, $p<0.001$), brushing teeth problems (OR=1.349, $p<0.001$), and swallowing problems (coeff.=0.177, $p<0.001$), but not dry mouth. All oral health indicators had a direct effect on cachexia including dry mouth (OR=1.250, $p<0.001$), brushing teeth problems (OR=1.185, $p<0.01$), and swallowing problems (OR=1.231, $p<0.001$), but not chewing problems.

Table 2

Path analysis: Odds ratio and coefficients of the paths

	Effects of oral health problems on cachexia	Effects of cognitive function on oral health problems
Chewing problems	1.047	1.073***
Dry mouth	1.250***	1.018
Brushing teeth problems	1.185**	1.349***
Swallowing problems	1.231***	0.177***§
Cognitive function	0.983	-

*p<0.05, **p<0.01, ***p<0.001; §coefficient

As shown in Table 3, cognitive function had a marginally non-significant total effect on cachexia (OR=1.081, $p=0.058$). Cognitive function had no significant direct effect on cachexia. Its apparent positive effect is better explained by a significant indirect effect (OR=1.100, $p<0.001$), than a direct effect. The effect of cognitive function on cachexia was significantly mediated by brushing teeth problems (OR=1.052, $p<0.001$) and swallowing problems (OR=1.038, $p<0.001$).

Table 3

Total, direct, and indirect effects of cognitive function on cachexia

	Odds ratio
Total	1.081
Direct	0.983
Indirect	1.100***
Chewing problems	1.003
Dry mouth	1.004
Brushing teeth problems	1.052***
Swallowing problems	1.038***

*p<0.05, **p<0.01, ***p<0.001

Discussion

This study analysed data from a large number of community-dwelling older adults to provide quality evidence on a few key points. First, the prevalence of cachexia in older adults in Chinese community settings is 1.33%. Second, cognitive function has a significant indirect effect on cachexia. The indirect effect is mediated by two important oral health factors, namely, brushing teeth problems and swallowing problems.

This is the first study to report on the prevalence of cachexia in the general population (i.e., not those with a specific disease) of Chinese older adults living in the community. The prevalence of cachexia in this population is similar to the figure reported for the general population (i.e., non-disease-specific cachexia) in the United States, Germany, and United Kingdom (i.e., approximately 1-2%) (4, 5, 30). This implies that

genetic, geographical, and environmental factors do not play important roles in the development of cachexia in older adults in community settings.

Cachexia is known to be associated with many underlying diseases (e.g., cancer, chronic heart failure, chronic renal failure) (2). These diseases can also cause cognitive impairment (31-33). Whether cognitive impairment and cachexia are only the result of these underlying diseases has been unclear. This study provided clear evidence that cognitive function is associated with cachexia and that this association is independent of the underlying diseases. Older adults with more cognitive deficits are at an even higher risk of developing cachexia.

A systematic review showed that existing instruments used to screen for the risk of cachexia mainly focus on the domains of weight loss, nutritional intake, disease states, and biochemical metabolic derangement (34). Rarely do they consider cognitive function a risk factor in identifying cachexia. This study therefore recommends that cognitive function should also be considered as an independent risk factor when identifying cachexia, particularly in the general population without specifically known underlying illnesses.

In the literature, the evidence only supported the argument that people with advanced dementia who have lost the capacity to feed themselves and require extensive feeding to survive, have a much higher risk of becoming malnourished. Cachexia only occurs in people with very severe cognitive impairment who are unable to feed themselves, and it signifies the end-stage of dementia (6). People requiring extensive feeding were excluded from this study. Adjustments were made for commonly known underlying diseases causing cachexia. The result still supports the argument that cognitive function is indirectly associated with cachexia. This finding extends our understanding that cachexia may not necessarily occur only in people with severe dementia, but also in people with cognitive impairment who have not yet lost their ability to feed themselves.

On why people with cognitive impairment who have not lost their ability to feed can develop cachexia, the mediation analysis yielded an important result to explain this phenomenon. In this study, people with poor cognitive function have significantly poorer oral health, particularly with regard to teeth brushing and swallowing. These two factors significantly mediated the effect of cognitive function on cachexia. Older adults with poor oral health (e.g., swallowing, dental caries) are more susceptible to malnutrition (20, 35). It has been well documented that swallowing abnormalities can be caused by different dementia pathologies (e.g., Alzheimer's disease, Lewy-body dementia, vascular dementia) and that the swallowing abnormalities may not necessarily become obvious when the dementia has progressed to the advanced stage (36-38). Cognitive impairment is also associated with poor oral self-care function and severe dental caries; thus, oral self-care plays a significant mediating role between cognitive impairment and dental caries (39). Therefore, this study enriched our understanding of these relationships, indicating that people with progressive cognitive decline may have been exposed to a prolonged period of swallowing problems caused by various dementia pathologies, and that the development of dental caries follows from the progressive loss of oral self-care function (e.g., tooth brushing). Cachexia can occur in people with progressive cognitive impairment because of prolonged malnutrition. Cachexia can be independent of other commonly known underlying diseases. Further studies should employ a more robust design to test these relationships.

This study therefore recommends that health policymakers emphasize regular oral health screenings, particularly of teeth brushing and swallowing, for people with different levels of cognitive impairment. Such screenings are also recommended because dysphagia (prevalence=27.2%) is prevalent in older adults who live independently 40, and also because infrequent tooth cleaning (OR=4.7) and ineffective tooth cleaning (OR=1.6) are the most common reasons why older adults develop dental caries 41. Effective interventions to promote oral health (e.g., dental hygiene education for denture hygiene, teeth cleansing) (42, 43) and enhance the function of swallowing (e.g., dietary modifications, postural modifications, medications) (44) are recommended to reduce the risk of cachexia in people with different levels of cognitive decline. Many oral health programmes for older adults target the more functionally dependent population (e.g., nursing home residents) (42). Even in developed countries, the utilization of oral health services by older adults remains low (22). To prevent cachexia, this study also recommends that health policies be developed to increase the utilization of oral health services by community-dwelling older adults, particularly those with cognitive impairment who are still functionally independent.

There are several limitations to this study. First, a cross-sectional approach was adopted, so the direction of the effects among the variables may not be certain. Second, the prevalence of cachexia was low, although very similar to the figures reported in other countries. Third, this was a secondary analysis in that the co-morbidities (e.g., cancer, COPD) were obtained only from interviews and the subjects' medical records; therefore, some disease conditions may have been overlooked because of under-diagnosis.

Conclusion

Cognitive impairment can cause cachexia indirectly, through poor oral health, particularly from swallowing and teeth brushing problems. This study recommends adding cognitive function to the procedures for screening for cachexia in community-dwelling older adults. Health policymakers should advocate regular oral health screening and interventions, and increased utilization of oral health services by community-dwelling older adults with cognitive problems.

Conflict of interest: None of the authors has any conflict of interest to declare.

Ethical standards: The study was approved by Human Research Ethics Committee of The University of Hong Kong (Ref no.: EA1904045).

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