

# **1 Introduction**

## **1.1 Dementia**

### **1.1.1 The definition of dementia**

Dementia is an acquired, generalized, and usually progressive impairment of cognitive function that affects the contents, not the level of consciousness. A typically early sign is the impairment of recent memory; with the progression of memory disorder other aspects of cognitive deficits such as disorientation, anomia, aphasia and acalculia may develop. As the disease progresses, physical functions relentlessly are impaired, psychiatric symptoms may appear and previous social graces are lost. In the later stage, most patients lose the ability to perform activities of daily living independently and fall into dependency in daily living. Dementia is characterized by progressive cognitive decline and relentless debilitation. At this stage of development of medical science, the course of dementia cannot be reversed. On average, cognitive function declines at a rate of approximately three or four points per year in patients with Alzheimer's disease (AD) based on the commonly used cognitive screening instrument of Mini Mental Examination Score (MMSE) [1, 80], and the rates of functional decline in mild to moderate AD would be expected to decline approximately 11-13 points on the Disability Assessment for Dementia (DAD) scale [2]. Three-year and five-year mortality risk of patients with dementia living in the community reached 45% to 48% and 70% respectively. Median length of life from diagnosis was reported to be 5.3 to 5.4 years [3]. The natural course of dementia is around 5 to 10 years and average survival is 8-10 years [4-7].

#### **1.1.2 The incidence of dementia increases dramatically with age**

Due to the higher life-expectancy, the population of developed countries is characterized by a rising proportion of old and very old people [8]. According to projections made by the United States Census Bureau, by the year 2050, up to 20% of the total United States population will be aged 65 and older [9-10]. Dementia is an age-related disease and the incidence of dementia increases dramatically with age [11-13]. Annual incidence rates of dementia were 2.3% for persons aged 75 to 79 years, 4.6% for those aged 80 to 84 years, and 8.5% for those aged 85 to 89 years in United Kingdom [13], and 1.3% for

persons aged 75 to 79, 3.5% for those aged 80 to 84, 6.0% for those aged 85 and older in America [12], and 0.24% for those aged 65 to 69 years, 0.55% for those aged 70 to 74 years, 1.6% for those aged 75 to 79 years, 3.1% for those aged 80 to 84 years, 4.9% for those aged 85 to 89 years, 7.0% for those aged 90 to 94 years in Germany [149]. The majority results of epidemiological studies generally showed a prevalence of dementia of 5% to 20% in persons aged 65 years and older [4], the prevalence of dementia being 8.3% in USA [14], 5.9% to 9.4% in Europe [15], 8.0% in Canada [16], 4.5% for men, 7.3% for women in Germany [148]. One remarkably uniform finding in studies all over the world is the association between dementia and age. The prevalence rates of dementia and AD double approximately every 5 years: from 2% to 3% in the 65 to 74 age group to over, 30% in persons aged 85 years and over for dementia, and 1%-2% in the 65 to 74 age group to 25% and over in those aged 85 years and older for AD [11]. Up to 2000, the number of persons with dementia was estimated at about 25 million persons worldwide (about 0.5% of the whole worldwide population), of which 59% were female. 46% live in Asia, 30% in Europe and 12% in North America. 52% live in less developed country. The number of new cases of dementia in 2000 was estimated to be 4.6 million. And it is forecast that by 2030, 63 million people will have dementia, and by 2050, 114 million people will suffer from dementia. 71% of dementia people will live in developing countries [17-18]. Dementia becomes a public health issue facing the whole world in the next decades.

### 1.1.3 The etiology of Alzheimer's disease and related dementia remains unclear; consequently few treatment options are available

Dementia is a clinical syndrome. There is a wide variety of diseases that are associated with dementia [4]. It is estimated that it can be caused by more than 55 different diseases [7]. It is generally agreed that Alzheimer's disease is the main cause of dementia. It could account for about two-third of patients with dementia. Another major cause is ischemic and brain hemorrhage lesion, i.e., vascular dementia accounting for approximately 10%-15% of all cases, followed by dementia with Lewy bodies, Parkinson's disease and other type of dementia [4, 7, 11]. The causes of dementia can be classified into two major categories. The first category includes Alzheimer's disease and other degenerative diseases of the central nervous system. So far it remains incurable. The second category is curable causes including normal pressure

hydrocephalus, intracranial mass lesions, vitamin B12 deficiency, hypothyroidism etc. Alzheimer's disease is a neurodegenerative disease. It mainly appears in elderly people. With increasing age the incidence of Alzheimer's disease (AD) increases dramatically [4, 11]. The etiology of Alzheimer's disease is unclear, i.e., about 5% of the cases with genetic factors such as Trisomy 21, Presenilin 1 and 2, Apo E4, BACE, Neprilysin and so on. The genetic factors may only modify susceptibility to Alzheimer's disease without being directly causal. The pathogenesis leading to AD is also unclear. The major pathological change of AD is cerebral degeneration with selective neuronal cell death associated to two characteristic pathological lesions: intracellular neurofibrillary tangles and extracellular amyloid deposits in the form of senile plaques. Cholinergic neurons are lost and the acetylcholine-synthesizing enzyme choline acetyltransferase is markedly depleted in cerebral cortex and hippocampus of patients with Alzheimer's disease [4, 19]. In the last three decades there has been much research into the risk factors of AD and related dementia. It is generally believed that the main risks of AD are: age, family history, gender, education, life style, head injury, vascular risk factors, chemical exposure, inflammatory stress, depression, hypothyroidism, diabetes, environmental exposure, aluminum, zinc, smoking, estrogen-replacement therapy, non-steroidal anti-inflammatory drugs, antioxidants [11, 20-21]. Dementia remains an incurable condition of major significance to the world's ageing population [22]. So far there is no cure for AD and the treatment options are scarce. Choline acetyltransferase inhibitors can relieve some symptoms but they do not stop the progress of the disease and have no effect on the prognosis. Some neuron protective agents are still undergoing clinical trials [2, 11]. Some non-pharmacology therapy programs try to preserve the remaining functions and improving the quality of life [23-25].

#### 1.1.4 Dementia is one of the main causes of disability in the later stage of life

Dementia is characterized by irreversible progressive cognitive decline. With the decline of cognition, physical functions are relentlessly impaired and subsequently non-cognitive behavioral psychiatric symptoms could appear, which together lead to the loss of ability to perform activities of daily living and become ADL disability. According to ICD-10 [147] and DSM-IV [99], the diagnostic criteria for dementia, progressive decline in physical functions is an important hallmark of dementia. As the disablement process model applied to dementia described by Barberger-Gateau et al. in 2002 the physical functional

limitations involved in patients with dementia are limitations in generic cognitive tasks such as remembering a list of words or orientating oneself in time and space, they are responsible for the disability in performing activities of daily living including basic ADL and more complex IADL. And some complex functional impairment could appear even at the preclinical stage [26]. Research has demonstrated that executive control functions are strongly associated with the functional status of patients with dementia, which could be impaired in the preclinical phase of dementia. Executive abilities include planning, active problem solving, anticipation of an intended action, initiation of activity, inhibition of inappropriate behavior and the capacity to monitor the effectiveness of one's behavior which closely correlates with instrumental activities of daily living (IADL) disability in the early stage of patients with dementia even before the diagnosis of dementia [27-29].

With the progress of cognitive impairment, physical functions are impaired; subsequently the basic ADL such as bathing, grooming, toilet use, feeding, transfer, mobility, and bladder and bowels control could be affected. The impairment of basic ADL makes the patients with dementia functionally disabled and ADL dependent, as a result of which they need help and support in daily activities. This imposes a burden on the family and society. Recently, large numbers of population-based studies have demonstrated that cognitive function was closely associated with the functional status of patients with dementia, and dementia is one of the major pathologies leading to impairments, functional limitations and disability in the elderly [30-47, 58-69]. Sauvaget et al. demonstrated that dementia is an important determinant of functional status of elderly people [32]. Barberger-Gateau et al. showed that dementia has a strong significant effect on progression to IADL and then ADL disability [30]. Blaum et al. found that low cognitive performance, regardless of its relationship to clinical dementia, coexists with multiple chronic diseases and conditions. It is independently associated with a broad array of functioning difficulties, even after adjusting for demographic characteristics, educational attainment, and chronic conditions [42].

#### 1.1.5 Dementia burdens the family and society

Dementia is one of the major causes of ADL disability in elderly people, and the process of disability progresses as the dementia process worsens [30]. They are emerging as major threats to the health and well-being of the elderly [2]. Dementia burdens the family and society by imposing demands on the medical services, home help in the daily living

and institutionalization. Many studies have shown that dementia not only debilitates the patients with dementia but also burdens the caregiver and society. Dementia affects caregivers in several ways, i.e. by psychological effects: more than half of primary caregivers are thought to be at risk of clinical depression, by social effects: caregivers' leisure and other social activities are severely disrupted, by physical effects: caregivers are at increased risk of hospitalization, and use about 70% more prescribed drugs than control individuals, and by financial effects: caregivers incur indirect costs [46-50]. There is strong consensus that caring for an elderly individual with dementia is burdensome and stressful to many family members and contributes to their own psychiatric morbidity [2].

Costs of dementia patient care vary greatly but a general trend for the costs is to escalate on a yearly basis throughout the world. It has been estimated that the national annual costs of caring for patients with dementia in the USA range from 60 to 120 billion US dollars [2, 11, 50]. In the UK costs range from £ 5,360 to 5,837 million [2], in Sweden annually range from SEK16 to 40 billion [48], in Canada Can \$ 3.9 billion [51], in Germany 43.767 € per dementia person per year [150]. It is estimated that the costs of care of dementia patients and their impact on the society will continue to rise [46-52]. It is feared that they will reach epidemic proportions worldwide by the year 2020 [2].

## 1.2 The functional status of patients with dementia

### 1.2.1 The ability to perform activities of daily living (ADL)

The functional status of patients with dementia refers to the functional outcome of dementia, which is represented by the ability to perform activities of daily living (ADL). It is supposed to be affected by many factors such as cognitive function, motor function, age, comorbidity, socio-demographic factors etc [53-55]. The ability to perform activities of daily living is measured in terms of mobility, instrumental activities of daily living (IADL) and basic activities of daily living (ADL). The theoretical framework for classifying ADL into mobility, instrumental ADL and basic ADL was proposed by Katz [56]. The present concept of ADL is commonly categorized as either instrumental ADL or basic ADL: Instrumental ADL comprises the more complex activities required for independent living such as meal preparation, shopping, telephone use, handling correspondence, personal finances, traveling alone by car or public transportation, and participating in leisure activities and hobbies, whereas basic ADL encompasses personal care activities such as

dressing, grooming, bathing, toileting, eating and ambulation [24]. The basic activities of daily living (basic ADL) are understood as physical abilities (self-care) and instrumental activities of daily living (IADL) include physical and cognitive elements (self-management) [57]. Studies have shown that IADL as self-management depend more on cognitive functions and that they decline earlier and faster than basic ADL [26, 30, 37, 41], and basic ADL as a basic ability to perform the activities of daily living is more significant to maintain independency in daily living than IADL [32].

According to literatures, it is generally agreed that the prevalence of functional disability in patients with dementia is higher than in cognitively normal elderly and the cognitive function is the dominant factor of the functional status of patients with dementia, although many factors are involved as well [30-32, 37-38, 42-43, 62-63]. However, the results derived from different studies were incomparable due to different scales and different methodologies were used to measure the functional disability.

Stuck et al. reviewed the predictors of functional decline in aging people living in the community: chronological age, cognitive impairment, comorbidity, depression, low frequency of social contact, low level physical activity, low physical performance, poor self-perceived health and vision impairment were reported to have strong associations with functional status [54-55]. And the disablement process model applied to dementia described: dementia is one of the main pathways leading from pathology to impairments, functional limitations and disability. Functional limitations are limitations in generic cognitive tasks which are responsible for disability in activities of daily living; meanwhile the process of progressing disability could be modulated by some predisposing risk factors as well as intra-individual and extra-individual factors [26]. And Greiner et al. pointed out that there are three possible scenarios for the role that cognitive functions may play in the disablement process leading to loss of ADL independency. The first was a cognitive decline that preceded ADL dependency. The second was a concomitant cognitive and functional decline following an acute condition. And the third was a cognitive decline due to normal aging [43].

#### Commonly used measurements of ADL

1. Barthel Index is a basic ADL scale to measure the basic activities competence of daily living in ten areas: eating, dressing, grooming, bathing, transfer, stairs, mobility, toilet use, bladder, and bowel [70].

2. The eight items of the Lawton IADL Scale assess housekeeping, shopping, traveling to places out of walking distance, doing the laundry, handling finances, taking medications, using the telephone, and meal preparation [71].

3. The Pfeffer Functional Assessment Questionnaire (FAQ) comprises 10 items that assess a variety of IADL and complex cognitive/social functions. They include writing checks, paying bills, and keeping financial records; assembling tax or business records; shopping alone; playing games of skill; making coffee or tea; preparing a balanced meal; keeping track of current events; paying attention and understanding while reading or watching a TV show; remembering appointments, family occasions, and to take medications; and traveling out of the neighborhood [72].

4. The Direct Assessment of Functional Status (DAFS) Scale is a behavior-based measurement of abilities of daily living skills in persons with Alzheimer's disease and related disorders. It includes: 1) dialing a phone number; 2) selecting shopping items with a written list; 3) reading a clock; 4) preparing a letter for mailing; 5) counting money; 6) writing a check; and 7) balancing a checkbook [73].

5. The Disability Assessment for Dementia (DAD) was designed to assess functional disability in people with dementia [88].

6. The Echelle Comportment Adaptation Scale (ECA) is used to measure the ability of daily living which covers dressing, putting on and taking off shoes, putting oneself in bed, bathing and washing, dental hygiene, self-feeding and ability to manipulate cutlery, use the telephone, ability to use toilet and mobility (ability to go up and down stairs and move about the house) [36].

7. The Functional Independent Measure (FIM) is used to identify cognitive impairment, assess depression, and to describe the level of functional dependence. It has an 18-item, 7-level ordinal scale designed to measure ADL [75].

8. Social Adaptive Functioning Evaluation (SAFE) is a 17 items social-interpersonal, basic, and instrumental daily life skills on a 0-4 scale. Items include bathing, dressing,

feeding, neatness, mobility, communication, conversational skills, instrumental social skills, social appropriateness, friendships, recreation, and participation in activities [76].

9. The Alzheimer's Disease Co-operative Study-Activities of Daily Living Inventory (ADCS-ADL) is a 23-item scale used to determine levels of functional ability, with higher scores indicating better functioning [77].

10. The Medical Outcome Study Short Form-36 (SF-36) comprises eight domains to judge three scales to be particularly likely to be impaired in severe dementia: mental health (calmness, sadness, happiness owing to emotional health problems), physical health (owing to physical health problems) [78].

11. Physical Performance Test (PPT) is a performance-based measurement of physical performance in daily activities consisting of the following seven tasks: writing a sentence simulated eating, lifting a book to a shelf above shoulder level, putting on a jacket, picking up a penny from the floor, turning by 360 degrees, and walking 15.2 m (50 ft)[79].

### 1.2.2 Cognitive function

Cognitive function is a higher mental function including memory, orientation, language, attention, concentration, judgment, abstraction, reasoning, calculation, perception, visual spatial, executive, function etc. It is a mental process resulting in understanding (perception), which is based on an intact nervous system, physical health, and healthy mental condition [4]. The cognitive function is regarded as the core component of dementia which is characterized by progressive and irreversible decline of cognitive function. Studies have shown that the cognitive function is the dominant factor of functional status in patients with dementia [26-30]. The methods used in research to measure cognitive functions vary depending on the research aim and design. In general, cognitive measurements can be classified into global cognitive tests and specific cognitive function domain tests. The measurements commonly used are: Mini Mental Status Examination (MMSE) [80], Clock Completion Test (CCT) [81], Clinical Dementia Rating (CDR) [82], The Mattis Dementia Rating Scale (MDRS) [83], Boston Naming Test [84], The Cambridge Examination for Mental Disorder of the Elderly Cognitive Subsection (CAMCOG) [85], Alzheimer's Disease Assessment Scale (ADAS-cog) [86], Modified Mini



Mental Status examination (3MS) [87]. Generally, the global cognitive function could be classified into five grades of non-cognitive impairment, very mild, mild, moderate, severe cognitive impairment according to CDR overall score of 0, 0.5, 1, 2, 3, [82], and it could also be graded into very mild, mild, moderate, and severe cognitive impairment in terms of MMSE scores of more than 24, 18-24, 11-17, and less than 11 [33, 59, 80].

### 1.2.3 Mobility

In general, mobility is defined as a person's ability to move around in the living surrounding without assistance [88]. Mobility has not been adequately defined in most studies. A wide range of proxies for mobility such as ADL, walking, falls, motor system disease, balance, and gait etc., have been used. All these elements formed an operational definition of mobility [89]. Mobility as functional outcome depends largely on physical functions and sufficient cognition [90-93]. Research has demonstrated that mobility is critical for elderly people to maintain independent living and a high quality of life [88]. According to the theoretical framework of ADL proposed by Katz, mobility itself is a part of ADL [56]. In most studies mobility is measured by walking ability and speed, maximal step length, step height, rapid step test, tandem walk, gait, balance etc. Commonly used measurements are: Timed "up and go" , Tinetti-Gait, Tinetti-Balance [94], Bergs Balance Scale (BBS) [95], Walking in Figure of Eight [96], Talking while walking, and the Performance Oriented Mobility Assessment (POMA) [97] etc.

## 1.3 The relationship between physical functions and ADL

### 1.3.1 The relationship between cognitive function and ADL

Population-based studies have demonstrated that dementia is a major disabling disease in elderly people [32], and that cognitive function is a dominant factor of functional status of patients with dementia [26, 30]. According to ICD-10 and DSM-IV diagnostic criteria for dementia, progressive decline of physical functions is an important characteristic of dementia [99, 147]. Functional decline is a part of the symptoms of dementia [98-99]. Cognitive and functional decline appear to influence the development of one another [44]. Recently, cognitive function has been regarded as the most important determinant of functional status of patients with dementia [30-45, 62-63]. There is evidence that executive function significantly predicts IADL functioning, even in normal ageing; IADL

deficit could present in preclinical stage of dementia, and difficulties in the performance of everyday activities were observed in people with mild cognitive impairment (MCI) [27-29,45,100]. Agüero-Torres et al. reported that the prevalence of functional dependence is significantly higher among demented subjects than among those cognitively impaired non-dementia subjects and than cognitively normal elderly in turn; the decreasing of MMSE was strongly associated with the probability of IADL and ADL disability [37]. Caro et al. reported that the odds ratio of dependence was significantly higher among the patients with worse cognitive impairment, adjusting for age, gender and antipsychotic medication use, and even relatively small degrees of cognitive functional impairment increased the risk of losing the ability of ADL [60]. An American national panel survey (n=6600) carried out in 2002 reported that low cognitive performance, regardless of its relationship to clinical dementia, coexists with multiple chronic diseases and conditions, and that it is independently associated with a broad array of functional difficulties, even when adjusted for demographic characteristics, educational attainment, and chronic conditions [42]. Suh et al. and Holtzer et al. found that the rate of cognitive decline is related to functional outcome in Alzheimer's patients and the annual average rate of decline in the MMSE, neither gender, duration of formal education, nor duration of AD since onset was a significant predictor of cognitive and functional decline [33, 61]. Leckey et al. and Mok et al. demonstrated that the MMSE is the best predictor of functional status in patients with dementia [62-63]. Furthermore some researchers found that some special cognitive function domains were more closely related to some ADL tasks [45, 65].

### 1.3.2 The relationship between mobility and ADL

Diminished mobility often accompanies dementia and has a great impact on independence and the quality of life in patients with dementia [101]. Researchers have demonstrated that mobility is critical for elderly people to maintain independent living and high quality of life [88,102-103]. It is hypothesized that motor dysfunction in demented patients is a potent mediator of disability [104]. Both basic ADL and IADL depend largely on mobility. Some basic ADL tasks overlap with mobility such as transfer, climbing stairs and mobility tasks. Mobility as a functional outcome comprises a core component of ADL [56]. Sonn et al. demonstrated that walking speed impairment had the greatest influence on dependence in ADL [105]. Guralnik et al. found that gait speed alone is nearly as good

a predictor of disability outcome as the full performance battery [106]. Brach et al. found that walking speed, risk of falling, and muscle force contributed independently to the characterization of the activities of daily living of old man living in community [107]. Park et al. demonstrated that the activities of daily living of elderly people could be related mainly with motor function of the limbs and severity of dementia [53]. Konno et al. showed that advanced age, difficulty in walking and poor interest are significant predictors of loss of independence in ADL [55]. Among several factors which were considered to define the functional status in the patients with dementia such as increasing age, progressive cognitive impairment, gender risk, education level, only mobility is modifiable and mobility is regarded as a vital prognostic factor. [89-90,104]. Furthermore, poor mobility is postulated to affect survival both by increasing the risk of falls and through secondary disease related immobility [89]. In summary, mobility is closely associated with ADL and mobility itself is a part of ADL.

### 1.3.3 The relationship between cognitive function and mobility

Motor dysfunction and diminished mobility are very common in patients with dementia [53, 97,101,104]. Mobility as a part of ADL is associated with cognitive function too. Van Schoor reported that immediate memory impairment is most closely related to falls [89-93]. It is a widely held view that motor disability is a late stage symptom of AD. Recent researches showed that motor dysfunction could appear in the early stage of dementia and in the elderly with mild cognitive impairment [91-93, 96-97]. Over the years, eventually most people with dementia will develop mobility problems, and dependency in the activities of daily living [91, 93,108]. Motor deficit increases with the severity of dementia in a stage-related manner [92,101]. Gait and balance disorder, walking slower, shortening of step length are common motor dysfunctions in patients with dementia. Gait and balance disorder result in a high risk of falls in patients with dementia and gait disorder could present in any type of dementia independent of etiology [12, 92, 104, 108-111]. It is well known that dementia is linked to falls and fractures [110-112]. Kluffer et al. pointed out that motor impairment is an important aspect of cognitive decline in older persons; complex and fine motor control deficits precede gross motor performance [89, 93]. Sala et al. demonstrated that walking disorder in patients with Alzheimer's disease may result from gait apraxia and focal neurological damage [113]. Moreover, Abbott et al.

found that walking is associated with a reduced risk of dementia, and active lifestyle in physically fit men could promote cognitive function in late-life [113-115].

#### 1.3.4 The relationship between age and functional status

Population-based studies have demonstrated that age is significantly associated with all patterns of decline including cognition, motor function and ADL [5, 109]. It has been confirmed that dementia is an age-related disease [12, 18, 20] and the incidence of dementia increases dramatically with age [12-13, 22]. Howieson et al. documented that the elderly are at high risk of developing cognitive decline and many will not progress to dementia in next 2 to 3 years [5]. Larrabee et al. found that the content of memory is preserved with aging but the speed of recall and flexibility of thought are reduced. More than half of the elderly population will demonstrate some measurable loss of memory function of this type but the rate of conversion to dementia is not beyond that expected for age [117-118]. The majority of studies consistently agree that age is closely related to cognitive decline [5, 22].

Rapp et al. found that both cognitive and functional status were negatively associated with age, functional disability ( $r=-0.108$ ;  $P=0.038$ ) and overall cognition as measured by the MMSE ( $r=-0.154$ ;  $P=0.010$ ) in community-dwelling and nursing home residents [35]. Functional dependency is prevalent in old people, in those aged 65 and older it range from 5% to 35%, in contrast to 4.2% in those aged 55 to 65, the prevalence of functional dependence increases drastically to 20% to 40%, in selected population of those aged 75 and older [119]. Spector et al. reported that the proportion of people receiving help of ADL or IADL was about 1% for persons aged 18-29, 10% for persons aged 70-74%, and 80% for those aged 95 and over, and people aged 80 and older had more severe disability than those who were younger [120-121]. Japanese researchers documented that disability in ADL increases with advanced age in non-dementia older adults [55, 105,122]. Sato et al. point out both ADL ability and life satisfaction of independent elderly tend to decline with age, decrease in the group of octogenarians was extreme [103].

In addition, some researchers have indicated that walking speed decline progresses with age and there was a clear age-related deterioration in gait and balance in most of normal old subjects [55,109,123-124]. Rantanen et al. demonstrated that with increasing age, the muscle strength may eventually decline to a level where weakness starts to restrict the ability to carry out everyday tasks. It is confirmed by many studies that muscle weakness

is a powerful risk factor for functional limitations, disability and mortality in old age [125-126]. It was shown that mobility is a particularly important functional ability that can be impaired with age and age was negatively associated with all patterns of motor functions [88,102,109,135]. Lauretani et al. reported that walking speed declines progressively with age and in both men and women, the magnitude of decline per year increased with age [124]. Waite et al. reported that age was significantly associated with gait abnormalities and disability. It is hypothesized that age may be acting as a proxy for the potentially preclinical dementia and other age related systemic diseases, such as arthritis and visual impairment [104].

The majority of population-based studies reviewed have demonstrated that the functional status of elderly people including cognitive function, mobility, and ADL are attributed to age. However, the impact of increasing age on the functional status of hospitalized patients with dementia is supposed to be not the same as in population-based studies due to the fact that the majority of hospitalized patients with dementia suffered from multiple acute medical conditions as well as advanced cognitive impairment. Mok et al. reported that in hospitalized patients with dementia, age was not a significant factor ( $p=0.89$ ) contributing to the decline in functional abilities when compared with the stage of dementia (mean age  $80.18 \pm 8.15$ , mean MMSE  $11.51 \pm 6.75$ ) [66]. Farias et al. reported that among patients in the memory disorder clinic, age was not significantly associated with performance on any of functional domains (mean age  $71.67 \pm 8.52$ , mean MMSE  $22.02 \pm 5.1$ ) [65].

### 1.3.5 The relationship between comorbidity and functional status

Comorbidity is very common in the elderly, especially in the cognitively impaired old population. Frequently impaired physical performance caused by comorbidity may confound the clinical assessment of dementia patients [127-131]. It is generally believed that comorbidity increases sharply with age [104, 131]. Clinical and research findings have demonstrated that a variety of diseases affecting cognitions are associated with deteriorating physical functions [129-130]. Comorbidity as an organic impairment could result in multiple functional limitations and disability [26, 42-43]. Recently, some research-based informations about comorbidity in people with dementia has become available but the true prevalence of comorbidity in patients with dementia is still unknown due to the fact that accurate information about comorbidity in elderly people is difficult to

obtain, especially for patients with dementia. Cognitive impairment may potentially lead to inaccurate symptom reporting, noncompliance, and delayed or inadequate treatment. It is still a challenge to formalize the identification and measurement of comorbidity for research purpose and so far no standard approach to assess comorbidity existed [127,130]. A variety of assessment techniques have been used for measurement of comorbidity. The most basic measurement of comorbidity is a sum of the number of coexisting medical conditions [129]. Although the arithmetical sum of coexisting medical conditions cannot predict how comorbidity will affect functional status [129]. The prevalence of comorbidity very much depends upon how many medical conditions are being considered [54,129]. It is still a useful approach and it is quite straightforward and easy to understand [129]. The methods commonly used to measure comorbidity by other authors are as follows: 1) A summed total number of coexisting medical conditions; 2) Assignment of severity scores to all relevant medical conditions with summation of these scores; 3) Assignment of comorbidity severity based on the most severe comorbid disease present [129]. Each of these approaches has strengths and limitations. A variety of research results of the relationship between comorbidity and age, cognitive and functional status were observed due to different research design and measurements used.

#### 1.4 Summary of the relationship between cognitive and functional status

Cognitive decline is a core component of dementia. Dementia is one of the major pathways leading pathologies to impairments, functional limitations and disability. And functional limitations are limitations in generic cognitive tasks, which are responsible for ADL disability. Although the process of disability could be affected by many intra-individual and extra-individual factors, cognitive function is the dominant factor of functional status of patients with dementia. Age and comorbidity as intra-individual factors could speed up the disability process. Additionally, age expedites cognitive decline and with ageing comorbidity increases. Mobility as a functional outcome is a basis of ADL; meanwhile it could be affected by cognitive function, comorbidity and age. However, the relationship between cognitive function and comorbidity remains unclear.

## 1.5 The significance of present study

With the population ageing, the incidence of dementia increases dramatically. Dementia is characterized by relentless debility, thus dementia is regarded as one of the major causes of ADL disability in the later stage of life [30, 32]. Moreover, as the dementia process worsens the process of debilitation is progressive and irreversible. Subsequently, functional disability directly affects well-being and the quality of life of patients with dementia. So far dementia remains incurable and few treatment options are available. According to reviewed literatures, the majority of studies on dementia were based on population-based samples. Few studies focus on hospitalized patients with dementia, especially on those in geriatric hospitals. Patients with dementia were admitted to the geriatric hospital due to a variety of acute medical conditions. This group of patients not only suffered from acute medical conditions but also showed advanced cognitive impairments as well as marked multiple functional deficits. These patients represented the frailest part of the ageing population. The functional status of this group of patients is largely impacted by cognitive impairment, coexisting medical conditions and very old age. It is assumed that the economic and social burdens of this group of patients are very high as comparing with the healthy elderly and the majority of social and economic burdens of dementia could be attributed to functional disability. Dealing with this special group of patients, it is very important to better understand the functional status and the relationship between cognitive function and functional status. It will be helpful to improve the stratagem of intervention in these patients and to preserve the remaining functions of these patients and to improve their quality of life. Although the functional status of patients with dementia has been extensively investigated in population-based studies, it is assumed that the knowledge of population-based studies cannot be generalized for hospitalized patients with dementia due to the fact that the functional status of these selected patients is severely impacted by advanced cognitive impairment, acute medical conditions and very old age. The present study focuses on this special group of very old patients with dementia to investigate the physical functional status and the relationship between cognitive function and functional status. The findings from the present study will help to fully understand the disablement process in these patients such that more specifically suited stratagem of interventions can be developed to fit their complex needs.