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Clinical commentary

Natural course and predictors of severe disability and death in Thai patients with dementia

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ABSTRACT

More than half of patients with dementia lived in countries with low and middle incomes. However, there have been few studies on the natural course of disease in these countries. The purpose of this study was to study the natural course and the predictive factors of advanced stage and death in Thai patients with dementia. Patients with dementia who were treated in neurologic and psychiatric clinic from September 2004 to February 2016, were included. Data about natural course of diseases, behavioral and psychological symptoms in dementia (BPSD) and complications were studied. 207 patients were included. Mean age was 77 years old. Mean Thai Mental State Examination (TMSE) was 17.5. Alzheimer's disease was the most common cause of dementia (55%). With the mean follow-up of 39 months (range from 2 to 126 months), 64% of the patients had BPSD. Sixty-two patients (30%) had complications required admission. Seven patients died. Fifty-four patients (29%) ended in the advanced stage of dementia. Mean duration from diagnosis to the advanced stage was 49 months. Complications that required admission usually occurred in moderate to severe dementia and were strongly associated with the advanced stage or death (OR 6.1, 95%CI 2.57–14.49, p -value < 0.0001). Alzheimer's disease was the most common cause of dementia in the study. Most demented patients presented in moderate severity of dementia. Mean duration from diagnosis to the advanced stage of dementia was approximate 4–5 years. Complications required admissions related to the progression to advanced stage or death.

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Dementia affects 5–7% of the population over 60 years old and its prevalence further increases with age [1,2]. It was estimated that 35.6 million people lived with dementia worldwide in 2010, with numbers expected to almost double every 20 years, to approximately 115.4 million in 2050. Prevalence of dementia is expanding rapidly, particularly in countries with low and middle incomes [2]. In 2010, 58% of all people with dementia lived in countries with low and middle incomes, with this proportion anticipated to rise to 71% in 2050. Thailand has become an ageing society since 2002 as the proportion of elderly constituting more than 10 percent of population [3]. In the community-based studies, surveyed in 2004–2006, prevalence of dementia in Thai adults was 2.35–3.1% [3,4].

Dementia causes a significant financial burden to society. One-hundred and forty-one billion Euros per year was an estimated cost

for the whole of Europe [5]. Life expectancy of elderly people with dementia is shorter than those without dementia. Reports on survival after a diagnosis of dementia vary from 3 to 12 years [6]. However, less data on survival came from Asian countries. The purpose of this study was to study the natural course and the predictive factors of advanced stage and death in Thai patients with dementia.

1. Methods

The study population was patients who were diagnosed with dementia and treated in the neurologic and psychiatric clinic, Thammasat University Hospital, from September 2004 to February 2016. The International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) with the search term of 'dementia' was used to identify the patients. All demented patients who were (1) diagnosed and followed up by neurologists, psychiatrists (dementia experts), (2) investigated per Thai clinical practice guidelines for dementia to excluded medical- and

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surgical-treated conditions mimicking dementia, and (3) had available medical records to retrieve necessary data since the diagnostic date, were included. The Thai Mental State Examination (TMSE) was used to evaluate cognitive function with the cutoff point of ≤ 23 to define cognitive impairment [7]. The diagnosis of dementia was based on a decline in cognitive function that affect the subject's activities of daily living. Neuroimaging, such as computed tomography (CT), magnetic resonance imaging (MRI), or MRI with dementia protocol, was recommended mainly to exclude surgical-treatable causes of dementia. All neuroimaging films were reviewed by a neuroradiologist. Fazekas scale and medial temporal lobe atrophy visual rating scale (MTA scale) were used to evaluate white matter lesions and severity of medial temporal lobe atrophy, respectively. Combining clinical data and neuroimaging data was used to accurately diagnose the cause of dementia in each patient.

TMSE scores were used to classify severity of dementia; 21–23, 11–20 and 0–10 for mild, moderate and severe dementia. Global Deterioration Scale (GDS) was used to describe the clinical progression of dementia [8]. The scale ranges from stages 1 to 7, with higher scores indicating more severe dementia; GDS 4 – clear-cut memory deficits, poor knowledge of current events, inability to handle finances or travel to new places, GDS 5 – no longer function without some assistance, unable to recall major aspects of current life, may need assistance dressing, but still independent in eating and toileting, GDS 6 – occasionally forgets name of primary care giver, largely unaware of recent personal events, substantial assistance required with activities of daily living, can still recall his or her own name and distinguish a familiar face. Stage 7 of GDS, which was unable to recognize familiar faces, verbal abilities limited to <5 words, incontinent of urine and stool, total functional dependence and unable to walk, provided clinical features of advanced dementia [9].

Information about chief complaint, who brought the patients to see the doctors, baseline characteristics of the patients and duration of symptoms were reviewed. About dementia, types and stages of dementia, behavioral and psychological symptoms in dementia (BPSD), complications that required admission, time from diagnosis to stage of advanced dementia (GDS of 7), medication (anticholinesterase inhibitor), mortality and cause of death were studied. Data was retrospectively collected. However, most of the final status of the patients was prospectively evaluated for GDS. If the patients could not go to the clinic, a well-trained research assistant would call to evaluate the GDS. Univariate analysis was used to find the factors that related to advanced stage or death. Differences between groups were assessed by the Chi-square test for categorical variables and the nonpaired *t*-test for normally distributed continuous variables. Multivariate logistic analysis was performed to test for confounding factors in the association to advanced stage or death. A $p < 0.05$ was considered significant. The study was approved by the institute ethical review committee.

2. Results

There were 277 patients identified by ICD10 in the study. Seventy patients were excluded due to wrong diagnosis (29 patients), lack of important information such as no TMSE data (20 patients), no follow-up or diagnosis by dementia experts (10 patients) and mild cognitive impairment (11 patients). Two-hundred and seven patients were included. Mean age of the patients was 77 years old. Alzheimer's disease (AD) was the most common cause of dementia in our study (114 patients, 55%). Other types of dementia were vascular dementia (42 patients, 20%), mixed dementia (AD with cerebrovascular disease, 29 patients, 14%), Parkinson's disease dementia (PDD, 20 patients, 10%) and

fronto-temporal dementia (2 patients, 1%). Baseline characteristics of the patients were presented in Table 1. Mean TMSE at the presentation was 17.5 (range from 1 to 23). Fifty-seven percent of the patients presented with moderate dementia, one-third with mild dementia and 10% with severe dementia. Most patients (205 patients) was brought to the clinic by their closed relatives. One-hundred and fifty-nine patients had at least one neuroimaging study, for which the findings supported the diagnosis. Most patients (191 patients, 92%) received acetylcholinesterase inhibitor.

2.1. Behavioral and psychological symptoms in dementia (BPSD)

With a mean follow-up duration of 39 months (range from 2 to 126 months), BPSD occurred in 133 patients (64%); which were agitation (31%), apathy (25%), hallucination (24%), aggression (14%), delusion (13%), depression (10%), wandering (8%) and obsessive behavior (8%).

2.2. Medical and surgical complications

Complications requiring admission were found in 62 patients (62/207 patients, 30%) during follow-up; medical complications in 47 patients, surgical complications in 13 patients, both medical and surgical complications in 2 patients. Most complications occurred in moderate to severe stage of dementia (TMSE < 20) (54/62 patients, 87%). Medical complications were infection (15 patients), coronary artery disease (6 patients), arrhythmia (5 patients), acute ischemic stroke (5 patients), intracerebral hemorrhage (2 patients) and other medical complications 16 patients. Surgical complications were fall and fractures (8 patients), bed sore (2 patients), others in 5 patients. After complications, almost half of the patients (28/62 patients, 45%) deteriorated and had severe disability (GDS 7).

2.3. Disability

At the final follow-up, (54/186) 29% of the patients were in stage of advanced dementia (GDS7), 30% in GDS 6, 20% in GDS5 and 19% in GDS 4. In the subgroup of AD (114 patients); there were 27 patients with GDS 7. Mean duration from diagnosis to stage of advanced disease was 57 months (range from 4 to 105 months). In subgroup of vascular dementia (42 patients), 15 patients were in stage of advanced dementia, with mean duration from diagnosis to GDS7 of 42 months (range from 12 to 98 months). In subgroup of Parkinson's disease dementia (20 patients), 8 patients were in stage of advanced dementia, with mean duration from diagnosis of 48 months (range from 23 to 81 months). If patients were classified by disease severity at the diagnosis, 64 patients had mild dementia, 120 patients moderate dementia and 23 severe dementia. With a mean follow-up of 39 months, there were 20%, 24% and 53% in the subgroups of mild, moderate and severe dementia at the diagnosis, ended up with the advanced stage of dementia (GDS7). Univariate analysis showed that advanced dementia or death were related to older patients, more severe dementia, hypertension, some types of dementia (vascular dementia, Parkinson's disease dementia), having BPSD and complications that required admission (Table 2). However, multivariate analysis reviewed that only the presence of any complications that required admission was associated with having advanced dementia or death (OR 6.1, 95% CI 2.57–14.49, p -value < 0.0001).

2.4. Death

Twenty-one patients were lost to follow-up and unable to be contacted in anyway. Seven patients (4%) died. Causes of death

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