

Chapter 1

Overview of Dementia: Epidemiology, Definitions, Terms

What are the diagnostic criteria for dementia?

Answer

Representative diagnostic criteria for dementia include the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) published by the World Health Organization, the diagnostic criteria proposed by the National Institute on Aging–Alzheimer’s Association Workgroup (NIA-AA), and Diagnosis and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) published by the American Psychiatric Association.

Comments and evidence

In ICD-10 (1993), dementia is described as “a syndrome due to disease of the brain, usually of a chronic or progressive nature, in which there is disturbance of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgement”. Detailed diagnostic criteria are provided in ICD-10¹⁾.

In the diagnostic criteria of dementia proposed by the NIA-AA (2011), impaired ability to acquire or remember new information, impaired executive function, impaired visuospatial abilities, and impaired language functions are treated equally, and the diagnostic criteria include behavioral impairment and subtypes of dementia other than Alzheimer’s disease dementia²⁾.

DSM-5 (2013) introduced a new term, “neurocognitive disorders”, and replaces the term “dementia” with “major neurocognitive disorder”. DSM-5 details six cognitive domains that may be affected in neurocognitive disorders. A diagnosis of major neurocognitive disorder (dementia) requires evidence of significant decline in one or more of the following cognitive domains: complex attention, executive function, learning and memory, language, perceptual-motor function, and social cognition, and that the cognitive deficits interfere with independence in activities of daily living³⁾. DSM-5 provides new information sources for these criteria.

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- 1) World Health Organization. International Statistical Classification of Diseases and Related Health Problems. 10th Revision. Geneva: World Health Organization; 1993.
- 2) McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer’s disease: recommendations from the National Institute on Aging–Alzheimer’s Association workgroups on diagnostic guidelines for Alzheimer’s disease. *Alzheimers Dement*. 2011; 7(3): 263-269.
- 3) American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition: DSM-5. Arlington, VA: American Psychiatric Association; 2013.

■ Search formula

PubMed search: July 3, 2015 (Friday), August 8, 2015 (Friday)

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What other terms are related to dementia?

Answer

The DSM-5 introduces the new terms of major neurocognitive disorder (replacing dementia) and mild neurocognitive disorder (replacing mild cognitive impairment or MCI). Other terms include subjective cognitive impairment (SCI) and subjective cognitive decline (SCD).

Comments and evidence

The National Institute on Aging–Alzheimer’s Association (NIA-AA) workgroup classifies Alzheimer’s disease into three disease stages based on the pathophysiological process of Alzheimer’s disease: preclinical Alzheimer’s disease¹⁾, mild cognitive impairment (MCI) due to Alzheimer’s disease²⁾, and dementia due to Alzheimer’s disease (Alzheimer’s disease dementia)³⁾. In addition, the preclinical stage is divided into stage 1 (asymptomatic amyloidosis), stage 2 (amyloidosis + neurodegeneration), and stage 3 (amyloidosis + neurodegeneration + subtle cognitive decline).

In DSM-5 (2013), the new term “neurocognitive disorders” was introduced. Neurocognitive disorders are classified into delirium, major neurocognitive disorder, and mild neurocognitive disorder. DSM-5 details the diagnostic criteria for these three types⁴⁾.

Vascular cognitive impairment (VCI) is a concept that comprehensively encompasses a range of cognitive deficits from mild cognitive impairment caused by cerebrovascular disorder to vascular dementia (VaD)⁵⁾. Vascular cognitive disorder (VCD) has been proposed as a diagnostic category that includes VCI, post-stroke dementia, genetic VaD [cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy (CARASIL), Binswanger disease, and Alzheimer’s disease with VaD⁶⁾. (See CQ14-1).

Multiple definitions have been proposed for mild cognitive impairment, and the concept has undergone changes. Apart from the diagnostic criteria proposed by Peterson et al.⁷⁾ in 2004, diagnostic criteria have been provided in DSM-5, NIA-AA and ICD-10⁸⁾, all of which differ to some extent (see CQ4B-5). In addition to mild cognitive impairment, other conditions such as age-associated memory impairment (AAMI), aging-associated cognitive decline (AACD), mild cognitive disorder (MCD), mild neurocognitive decline (MNCD), and cognitive impairment no dementia (CIND) have been included in the concept of prodromal stage of dementia⁹⁾.

■ References

- 1) Sperling RA, Aisen PS, Beckett LA, et al. Toward defining the preclinical stages of Alzheimer’s disease: recommendations from the National Institute on Aging–Alzheimer’s Association workgroups on diagnostic guidelines for Alzheimer’s disease. *Alzheimers Dement*. 2011; 7(3): 280-292.
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- 4) American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition: DSM-5*. Arlington, VA: American Psychiatric Association; 2013.
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- 9) “Treatment Guideline for Dementia” Preparation Joint Committee (Ed.) Japanese Society of Neurology (Supervision). *Treatment Guideline for Dementia 2010*. Tokyo: Igaku Shoin; 2010. (In Japanese)

■ Search formula

PubMed search: July 3, 2015 (Friday), August 8, 2015 (Friday)

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What are the causes of dementia and how are they classified?

Answer

Dementia is caused by a variety of diseases and conditions. In DSM-5, the etiological subtypes of major neurocognitive disorder (dementia) comprise Alzheimer's disease, frontotemporal lobar degeneration, Lewy body disease, vascular disease, traumatic brain injury, substance/drug use, HIV infection, prion disease, Parkinson's disease, Huntington's disease, other medical conditions, multiple etiologies, and unspecified.

Comments and evidence

Many diseases and conditions may cause dementia or dementia-like symptoms¹⁾.

ICD-10 classifies dementia into Alzheimer's disease dementia, vascular dementia, dementia in other diseases classified elsewhere, and unspecified dementia²⁾.

In the neurocognitive disorder category of DSM-5, the etiological subtypes of major neurocognitive disorder (dementia) and minor neurocognitive disorder (mild cognitive impairment) are listed as follows: Alzheimer's disease, frontotemporal lobar degeneration, Lewy body disease, vascular disease, traumatic brain injury, substance/drug use, HIV infection, prion disease, Parkinson's disease, Huntington's disease, other medical conditions, multiple etiologies, and unspecified³⁾.

Among these causative diseases and conditions, some neurosurgical diseases such as normal pressure hydrocephalus and chronic subdural hematoma, as well as some medical diseases such as hypothyroidism and vitamin B₁₂ deficiency are being treated under the concept of treatable dementia, and early diagnosis and appropriate treatments and interventions are desirable.

■ References

- 1) "Treatment Guideline for Dementia" Preparation Joint Committee (Ed.) Japanese Society of Neurology (Supervision). Treatment Guideline for Dementia 2010. Tokyo: Igaku Shoin; 2010: 4-7. (In Japanese)
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What pathological conditions should be differentiated from dementia?

Answer

Pathological conditions that should be differentiated from dementia, especially Alzheimer's disease dementia, include normal cognitive decline accompanying aging (physiological amnesia), delirium, depression, other learning disabilities, and mental retardation.

Comments and evidence

DSM-5 lists pathological conditions that should be differentiated from dementia as follows: normal cognitive decline accompanying aging, delirium, depression, other learning disabilities, and mental retardation¹⁾. Important points for differentiation of Alzheimer's disease dementia from the above disorders are summarized below.

1. Physiological amnesia accompanying aging

In general, physiological amnesia is differentiated from dementia by partial forgetfulness of past experience, with no or slow progression, preserved self-recognition of the disability, preserved orientation to time, and little disturbance in activities of daily living.

2. Delirium

Delirium is an acute psychiatric symptom accompanied by impaired consciousness, causing difficulties to focus and maintain attention. Common triggering factors include physical illnesses, environmental changes, and effects of drug. The symptoms fluctuate, which differ from symptom persistence in dementia, but delirium and dementia are often found concomitantly.

3. Depression

Pseudodementia due to depression or a depressive state may cause psychomotor retardation and difficulties in concentration, as well as memory decline and impaired judgement. Patients complain of reduced memorizing ability, which may be mistaken as dementia. Unlike Alzheimer's disease dementia, memory and executive dysfunctions usually do not persist in pseudodementia, and patients often over-estimate their functional impairment (while dementia patients underestimate their functional impairment, reflecting decreased awareness of disease). Response to antidepressants is another point of differentiation.

■ Reference

- 1) American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition: DSM-5. Arlington, VA: American Psychiatric Association; 2013.

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PubMed search: July 3, 2015 (Friday)

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What is the prevalence of dementia in Japan?

Answer

In the first half of the 2010s, the prevalence of dementia in older people aged 65 years and above in Japan was estimated to be approximately 15%. A

Comments and evidence

During the period from the 1980s to the 2000s, the prevalence of dementia in older people aged 65 years and above in Japan was reported to be 3.8-11%, and the prevalence of dementia has shown a tendency of increase¹⁾. A survey on the prevalence of dementia in 8 municipalities nationwide estimated that there were 4.26 million older people with dementia in 2012, and the prevalence was reported to be about 15%^{2, 3)}. Based on a longitudinal survey conducted in Hisayama Town, Fukuoka Prefecture, the future prevalence of dementia was estimated and reported. Assuming that the prevalence of dementia in each age group remains constant after 2012, the number of people with dementia in 2025 is estimated to be 6.75 million [95% confidence interval (CI); 5.41 million to 8.44 million]. When assuming that the frequency of diabetes increases by 20% in the future, the number of people with dementia in 2025 is estimated to be 7.3 million (95% CI: 5.7 million to 9.36 million)⁴⁾.

The number of people with dementia in the world is estimated to be 46.8 million in 2015, and predicted to increase at a pace of doubling every 20 years, reaching 74.7 million in 2030 and 131.5 million in 2050. Furthermore, the increase in low- to middle-income countries is predicted to be markedly higher compared to high-income countries⁵⁾. On the other hand, a study in the UK has reported decrease in prevalence of dementia⁶⁾, while studies in the Netherlands, Germany, Sweden and US have reported decreases in incidence of dementia⁷⁻¹⁰⁾.

References

- 1) Dodge HH, Buracchio TJ, Fisher GG, et al. Trends in the prevalence of dementia in Japan. *Int J Alzheimers Dis.* 2012; 2012: 956354.
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- 5) Alzheimer's Disease International. World Alzheimer Report 2015: The Global Impact of Dementia: an analysis of prevalence, incidence, cost and trends. London: Alzheimer's Disease International; 2015.
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Search formula

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PubMed search: May 28, 2015 (Thursday), October 19, 2015 (Thursday)

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Ichushi search: May 28, 2015 (Thursday)

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Are there changes in prevalence depending on subtype of dementia?

Answer

Dementia shows a tendency of increase in Japan, and Alzheimer's disease dementia is increasing compared to vascular dementia. B

Comments and evidence

According to a nationwide survey conducted in the first half of the 2010s, the frequency of Alzheimer's disease dementia was the highest at 67.6%, followed by vascular dementia at 19.5%, and dementia with Lewy bodies /dementia with Parkinson's disease at 4.3% ¹⁾. In the 1980s, vascular dementia was more prevalent than Alzheimer's disease dementia in Japan, but Alzheimer's disease dementia has shown a trend of increase since the latter half of the 1990s, especially in older people aged 80 years and above ²⁻⁵⁾

■ References

- 1) Ministry of Health, Welfare and Labour Grant-in-aid for Dementia Control Integrated Research Project. Prevalence of dementia in urban areas and measures for impaired daily living functions in dementia. General Study Report for 2011-2012; 2013. (In Japanese)
- 2) Dodge HH, Buracchio TJ, Fisher GG, et al. Trends in the prevalence of dementia in Japan. *Int J Alzheimers Dis.* 2012; 2012: 956354.
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■ Search formula

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Ichushi search: May 28, 2015 (Thursday)

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Is the disease duration of dementia getting longer?

Answer

Studies have reported a possibility that the survival period of people with dementia may be prolonged. However, there is no report showing that the death rate of people with dementia is clearly lower compared to the general population.



Comments and evidence

In the United States, the hazard ratio (HR) for death in people with dementia aged 70 years and above compared to those without dementia was 2.53 in 1993 and 3.11 in 2002, with no significant change during the 9-year period ($p = 0.09$)¹. In a study conducted in Stockholm, Sweden, the mortality rate of people with dementia decreased by 29% over the 14-year period from 1988 to 2002, but the HR compared to non-dementia subjects was 2.42 in 1988 and 2.47 in 2002, with no significant change during the 14 years². In these reports, while the incidence of dementia has declined, prevalence has not changed, suggesting that the duration of dementia may be prolonged^{1, 2}. In a study using medical insurance claim data in Germany, the death rate of people with dementia increased by 1% in men ($p = 0.75$) and 11% in women ($P < 0.001$) over a 3-year period from 2004 to 2007³.

When the mean loss of life expectancy (%) (survival period from dementia onset to the mean age of death divided by the mean life expectancy of the general population at the age of dementia onset) was analyzed by period, many reports show that loss of life expectancy in people with dementia decreases after mid-1990s when compared to that from the 1980s to early 1990s⁴.

■ References

- 1) Langa KM, Larson EB, Karlawish JH, et al. Trends in the prevalence and mortality of cognitive impairment in the United States: is there evidence of a compression of cognitive morbidity? *Alzheimers Dement*. 2008; 4(2): 134-144.
- 2) Qiu C, von Strauss E, Backman L, et al. Twenty-year changes in dementia occurrence suggest decreasing incidence in central Stockholm, Sweden. *Neurology*. 2013; 80(20): 1888-1894.
- 3) Doblhammer G, Fink A, Fritze T. Short-term trends in dementia prevalence in Germany between the years 2007 and 2009. *Alzheimers Dement*. 2015; 11(3): 291-299.
- 4) Brodaty H, Seeher K, Gibson L. Dementia time to death: a systematic literature review on survival time and years of life lost in people with dementia. *Int Psychogeriatr*. 2012; 24(7): 1034-1045.

■ Search formula

PubMed search: October 19, 2015 (Thursday)

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What is the pathological background of dementia?

Answer

Various underlying pathologies are associated with dementia, such as degenerative disease, cerebrovascular disorder, infection, inflammation, and tumor, and the clinical picture is strongly influenced by the lesion distribution. The frequency of degenerative diseases is high, and in the majority of these cases, abnormal protein accumulation is the core feature of the pathology.

Comments and evidence

Alzheimer's disease is characterized by the formation of large numbers of senile plaques [amyloid β ($A\beta$) plaque formation] and neurofibrillary tangles (fibrous aggregates of tau protein). Both senile plaques and neurofibrillary tangles also appear in older people without dementia, but they are particularly abundant in Alzheimer's disease. It remains unclear how the formation of senile plaques and neurofibrillary tangles leads to neuronal degeneration and loss. The main lesion of dementia with Lewy bodies is abnormal accumulation of α -synuclein in neurons. In Parkinson's disease, Lewy lesions are confined to the brain stem, whereas in dementia with Lewy bodies, Lewy lesions spread to the cerebrum. Alzheimer's lesions are observed in many patients with dementia with Lewy bodies ¹⁾.

Fronto-temporal lobar degeneration (FTLD) is broadly divided into a disease group showing tau accumulation and a group showing TDP-43 accumulation, while there are rare cases of fused in sarcoma (FUS) protein accumulation ²⁾. Although there is not always a good correlation between clinical features and pathological diagnosis, many cases of semantic dementia and cases with coexisting motor neuron disease are associated with TDP-43 accumulation. In Japan, familial FTLD is often caused by tau gene mutations.

Argyrophilic grain dementia showing granular accumulation of tau inside neurites, and primary age-related tauopathy (PART) showing abundant neurofibrillary tangles (similar to Alzheimer's disease) localized to the hippocampal limbic system but no significant $A\beta$ accumulation are increasingly common in older people aged 80-90 years and above ³⁾. Hippocampal sclerosis is a general term for disease conditions showing severe neuronal loss and gliosis in hippocampal CA1 and subiculum, with diverse underlying diseases.

Vascular dementia is frequently caused by ischemic brain lesions, and the culprit vascular lesions are broadly classified into those caused by macrovascular atherosclerosis and those caused by microvascular lesions. Microvascular lesions cause multiple lacunar infarcts and white matter lesions, and are strongly associated with dementia ⁴⁾. Amyloid angiopathy also causes dementia, and in this case is often accompanied by Alzheimer's lesions. The coexistence of Alzheimer's lesion and vascular lesion is not simply comorbidity, but is thought to influence each other in pathological mechanisms (see CQ14-4).

References

- 1) McKeith IG, Dickson DW, Lowe J, et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. *Neurology*. 2005; 65(12): 1863-1872.
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PubMed search: July 24, 2015 (Friday)

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