Recommendations for the Diagnosis and Treatment of Dementia 2012

Based on the Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (4th CCCDTD) 2012

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Potential Conflicts of Interest

- 4th CCCDTD participant
- No other conflicts to declare

Objectives

- Review the updated recommendations made at the 4th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia
  - New diagnostic criteria
  - Neuroimaging
  - Update on symptomatic therapies
- Address a number of specific issues
  - Why "bother" diagnosing dementia
  - Why monitor patients with MCI or dementia for change over time
  - When and how to say "no" for requested investigations or therapy
  - Communication strategies for those with dementia and their families

CCCDTD4 Participants (Alphabetically)

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Overview

- Did not review all the areas previously covered
- Topics:
  - **Definitions and diagnostic criteria**
    - **Criteria for MCI and dementias**
    - **Biomarkers and amyloid imaging**
  - Early onset dementia (should refer)
  - Rapidly progressive dementia (should refer)
  - **Neuroimaging**
  - **Update on symptomatic treatments**
- Will note if the information presented here is part of previous recommendations or represent newer (2012) recommendations

Overview – Bottom Line

- Little day-to-day change in practice for most treating physicians in Canada
- Do not endorse using biomarkers such as imaging studies (e.g., Positron Emission Tomography or PET) to detect pre-symptomatic disease
- Consider treatment trials in most patients with Alzheimer's Disease (AD) or Parkinson's Disease Dementia (PDD), including those with concomitant vascular cognitive impairment, but not pure vascular dementia

Why Diagnose?

- Reasons from the perspective of the practitioner -
  - Treatment (e.g., prescribe drugs, withdrawing drugs that may harm like anticholinergics & consider drugs that are unproven [i.e., research studies])
  - Prognostication (e.g., higher risk of delirium when hospitalized, future need for various forms of care including residential)
  - Planning & Care (e.g., allow patients to be involved in decisions around enduring power of attorney or other substitute decision-making, management of co-morbidities, identify potential safety issues down the road like driving cessation & medication management)

Why Diagnose?

- From the perspective of the person with the condition
  - Growing evidence that many people with dementia want to know their diagnosis and experience less anxiety after being told
  - Without this, they are denied access to support, information and potential treatments that could help them to live well with their condition

Background

- Three earlier Canadian Consensus Conferences on the Diagnosis and Treatment of Dementia (CCCDTD)
- Evidence-based recommendations on the diagnosis and treatment of AD and related dementias
- Dissemination targeted to those who treat people with dementia, both primary care practitioners & specialist physicians (geriatricians, neurologists, psychiatrists, etc…)

Background

- 4th CCCDTD convened in May 2012 in Montreal

- **Primary aim**: to update the diagnostic approach to AD in light of revised diagnostic criteria proposed by the International Working Group (IWG) and the recommendations made by the National Institute on Aging/ Alzheimer Association workgroups (NIA/AA)

Methods

- Guided by the AGREE (Appraisal of Guidelines for Research and Evaluation) instrument (20/23 criteria met)
- Prior CCCDTDs graded evidence with the Canadian Task Force on Preventive Health Care system
- CCCDTD4 followed the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) system where possible to be in keeping with current recommendations for the conduct of consensus conferences

Pre-conference

- Background articles (written by work groups) were posted to a password protected website that was accessible to conference participants
- Recommendations, modified where appropriate as a result of feedback, were posted for on-line voting
  - Closed May 03, 2012 (one day in advance of the conference assembly)
- Organizations relevant to the care of people with dementia appointed delegates
  - Delegates had access to the background articles and could vote on recommendations

Conference

- Each topic briefly reviewed before voting on each recommendation
- All participants (except for the 2 industry observers) were permitted to vote
- In the event of failed consensus, on-line votes of conference participants not in attendance were taken into account

Consensus

- Consensus defined as 80% or more of conference participants voting for the recommendation
  - Partial consensus defined as 60-79% of votes
- Recommendations presented here reached consensus
  - See full article for discussion of items that failed to reach consensus available

Changes in How AD Viewed

- AD pathological changes and cognitive deficits develop over many years
  - Dementia is the end stage (i.e., dementia and AD decoupled) – but need to recall some people with AD pathology don't have cognitive deficits/ dementia
- Initial event felt to be disordered beta amyloid metabolism (but still hypothesis)

Biomarkers

- Biomarkers – three major
  - Beta amyloid pathology
    - Amyloid PET imaging and low levels of beta amyloid $_{1\text{-}42}$ in CSF
  - Neuronal injury
    - High levels of tau and phospho-tau in CSF
  - Neuronal dysfunction
    - Decreased metabolism in parietal-temporal lobes on FDG PET
  - Neurodegeneration
    - Temporal, parietal, and/or hippocampal atrophy on MRI

Precipitant to Re-evaluate Diagnostic Criteria

- New criteria developed by the National Institute on Aging (NIA) and the Alzheimer Association (AA) in the US and the International Working Group (IWG) would have an impact on Canadian practice
- The American Heart Association/American Academy of Neurology issued a statement about vascular contributions to cognitive impairment (VCI) and dementia

New Definitions/Diagnostic Criteria: NIA/AA and the IWG

- In 2011 three work groups of the National Institute of Aging (NIA) and the Alzheimer Association (AA) recommended criteria for the diagnosis of
  - Dementia due to AD
  - MCI due to AD (IWG: called prodromal/ predementia)
  - Preclinical AD (note: like the proposed IWG preclinical states, utilize biomarkers)

Preclinical Stage (Asymptomatic AD)

- Solely intended for research purposes and “do not have any clinical implications at this time”
- Three stages
  - Asymptomatic cerebral amyloidosis (beta amyloid in CSF, PET amyloid imaging)
  - Amyloid positivity + evidence of neuronal injury (tau, FDG-PET, MRI)
  - Amyloid + neuronal injury + subtle cognitive changes

Note: International Working Group suggested the term *Pre-symptomatic AD* for those carrying causative mutation - Lancet Neurology 2010, 9:1118-27

MCI due to AD – Establish Clinical and Cognitive Criteria

- **Cognitive Concern**
  - Change in cognition from previous level reported by patient, informant, or clinician (i.e., historical or observed evidence of decline over time)
  - Objective evidence of impairment in 1+ cognitive domains (e.g., memory, executive function, attention, language, visuospatial skills) greater than expected for age & educational background (episodic memory most common in those who progress to AD dementia)
- **Preservation of independence in functional abilities**
- **Not demented**

MCI due to AD – Look to See it Etiology Consistent with AD

- Rule out other systemic or brain diseases that could account for the decline in cognition (e.g., vascular, traumatic, medical)
- Genetics
  - Autosomal genetic mutations for AD
  - Genetic factors that increase risk for AD (APOE ε4)
- Research criteria using biomarkers
  - Not for clinical use

New Criteria - Dementia Due to AD

- Probable AD dementia
  - Dementia + insidious onset, clear history of worsening, amnestic (most common) or nonamnestic (language, visuospatial, executive) presentation
  - No cerebrovascular disease, dementia with Lewy body, frontotemporal degeneration, or other neurological or non-neurological condition (co-morbidity or medication) that could have substantial effects on cognition
  - More certain if documented decline or carry causative gene (carriage of E4 not sufficiently specific)

Dementia Due to AD

- Possible AD dementia
  - Either atypical course (e.g., abrupt onset or insufficient data on decline) or have mixed causation

- Probable or Possible AD dementia with evidence of the AD pathophysiological process
  - Biomarkers of amyloid deposition or downstream neuronal degeneration … but not recommended for routine use

4th CCCDTD Recommendations: Definitions/ Diagnostic Criteria

- Recommended 2011 NIA/AA criteria for dementia & probable and possible AD dementia
- Recommended use of 2011 NIA/AA criteria for MCI due to AD ("… *but to be used cautiously and only in specialized clinical practice*")
- Recommended using ASA/ AHA criteria for VCI

Preclinical/ Prodromal AD

- Reassess utility of the concept of prodromal AD in the future when biomarkers are available, validated, and ready for use in Canada
- IWG asymptomatic at-risk for AD only for research
- As the presence of brain amyloid in normal people is of uncertain significance, discouraged amyloid imaging in individuals without memory loss, outside of a research setting
- The medical community should be clear in discussions with patients, media and the general population that the presence of brain amyloid in normal people is of unclear significance

AHA/ ASA Criteria for VCI

- VCI – all forms of cognitive deficits from vascular dementia (VaD) to MCI of vascular origin
- Dementia – decline in cognitive function and deficits in 2+ cognitive domains (assess at least 4 - executive/ attention, memory, language, visuospatial) of sufficient severity to affect the person's ADL deficits (and not due to motor/ sensory sequelae of vascular event)

AHA/ ASA Criteria for VCI

- Probable VaD: cognitive impairment and imaging evidence of CV disease plus
  - Clear temporal relationship between vascular event & onset of cognitive deficits, or
  - Clear relationship in severity/ pattern of cognitive deficits and presence of diffuse, subcortical CV disease (note: executive dysfunction common but not specific/ memory deficits suggest AD; WMLs of less diagnostic utility in older patients)
  - No history of gradually progressive decline before or after a stroke

AHA/ ASA Criteria for VCI

- Possible VaD – cognitive impairment + evidence of CV disease but no clear relationship, insufficient information, aphasia interferes with assessment, and/or other condition
- VaMCI – IADL normal or mildly impaired
  - Probable VaMCI (no history of gradual decline before or after stroke)
  - Possible VaMCI
  - Unstable VaMCI (symptoms revert to normal)

Stroke 2011, 42:2672-2713

A Note on the Importance of Communication

NY Times Headline, August 10, 2010

In Spinal-Fluid Test, an Early Warning on Alzheimer's

By Gina Kolata

- *"… Researchers are finding simple and accurate ways to detect Alzheimer's long before there are definite symptoms … "*

NY Times Correction, Sept 16, 2010

- "… incorrect impression that the test can predict future disease with 100 percent accuracy in all patients … [up to] 100 percent accurate in identifying a signature level of abnormal proteins in patients with memory loss who went on to develop Alzheimer's — not in identifying [asymptomatic] patients who 'are on their way' … patients who had memory loss and developed Alzheimer's within five years, every one had protein levels associated with the disease five years before; it was not the case that 'every one of those patients with the proteins developed Alzheimer's within five years.'"

Neuroimaging

- Structural neuroimaging "… not required in all (although will be indicated in most) …"
  - "Although more costly and less available, MRI is preferable to CT" (for use by specialists when patterns of atrophy and other features may provide additional diagnostic/ predictive information)
- "Where available, PET-^{18}FDG and/or PET amyloid imaging can be used for clinical purpose [sic] in patients with atypical dementias" (not routine/ by dementia specialists only; PET amyloid imaging not currently approved in Canada; SPECT if PET unavailable)
- Against use of other neuroimaging modalities (e.g., functional MRI and MR spectroscopy)

Recommended Criteria for Neuroimaging

- Age < 60
- Rapid, unexplained decline in cognition or function
- “Short” duration (< 2 yrs)
- Recent/ significant head trauma
- Unexplained neurological symptoms (e.g., new onset severe headache, seizures)
- History of cancer (sites/ types that metastasize)
- Use of anticoagulants or bleeding disorder
- Early history of gait disorder & urinary incontinence (i.e., Normal Pressure Hydrocephalus)
- New localizing neurological sign (e.g., hemiparesis, Babinski)
- Unusual or atypical cognitive symptoms or presentation (e.g., speech)
- Gait disturbance

“Liquid” Biomarkers

- Plasma Aβ1-42 not recommended for clinical practice
- CSF Aβ1-42 and tau did not reach consensus (64%) – “The practical message is that, for now, measurement of CSF Aβ1-42 and tau have no clinical utility in Canada, although they are part of research protocols in observational and therapeutic studies”

Monitoring Over Time

- MCI
  - Progression - increased risk of developing dementia
- Dementia
  - Response to therapy (stabilization, improvement, deterioration)
  - Identify emerging issues (e.g., caregiver stress, safety concerns, functional problems, behavioural challenges, need to mobilize community-based resources)
  - Care is a complex and evolving task (Hogan DB et al. CMAJ 2008;179:787-793)

Symptomatic Treatments

- Recognizes that many cases have more than one contributing cause (management based on dealing with predominant contributing causes)
- Trial of a cholinesterase inhibitor for most patients with AD
  - Cholinesterase inhibitors an option for AD with cerebrovascular disease
    - No recommendation for or against their use in the treatment of vascular dementia
  - Cholinesterase inhibitors an option for Parkinson's disease dementia
- No recommendation for or against combination therapy (cholinesterase inhibitor and memantine)

Discontinuation of Cholinesterase Inhibitors

- Discontinuing may lead to a worsening but this must be balanced with the risk of side effects and costs of therapy
  - Criteria for stopping
    - Decision of patient &/or proxy decision-maker
    - Non-adherence that can't be corrected
    - Decline greater than before treatment started
    - Intolerable side effects
    - Co-morbidities (risky or futile)
    - At a stage where there is no clinically meaningful benefit
  - If done for lack of effectiveness, suggested that you taper and monitor for evidence of deterioration (with consideration of restarting if occurs)

Choosing Wisely

- Campaign to have patients & care provides think and talk about medical tests and procedures that may be unnecessary and in some instances harmful (http://www.choosingwisely.org/)
- National organizations representing medical specialists asked to "choose wisely" by identifying 5 tests or procedures commonly used in their field whose necessity should be questioned and discussed
  - When you need a brain scan and when you don't - amyloid PET scanning (http://consumerhealthchoices.org/wp-content/uploads/2013/02/ChoosingWiselyAlzheimersSNMMI-ER.pdf)
  - Don't use antipsychotics as first choice to treat behavioral and psychological symptoms of dementia
  - Don't recommend percutaneous feeding tubes in patients with advanced dementia; instead offer oral assisted feeding (http://www.choosingwisely.org/wp-content/uploads/2013/02/AGS-5things-List_Web.pdf)

Dealing with Requests for Tests, Procedures, and Treatments

- Try to understand why the request is being made
  - Clear up misperceptions
- Give it serious consideration
  - Base decision on evidence, how the results would modify care, feasibility and whether it is good use of resources
- Communicate your recommendation (with justification) and discuss it with your patient and/or family

Communicating with Dementia Patients

- Encourage communication – may need to be pro-active
- Identify and involve family members where possible and appropriate
- Explore the patient's perspective/ understanding
- Respond to their reaction – elicit and address questions & concerns
- Effective communication techniques – develop rapport, use appropriate verbal/ non-verbal communication (write things down), active listening, involve the patient, and structure the session (agenda, summarizing, signposting); specific needs may arise as dementia progresses

Thank You for Your Attention – Any Questions?

References

- First
  - CMAJ 1991, 144:851-53
- Second
  - CMAJ 1999, 160 (12 suppl):S1-20
- Third
  - CMAJ 2008 - http://www.cmaj.ca/cgi/collection/diagnosis_and_treatment_of_dementia_series
- Fourth
  - Can J Neurological Sci 2012, 39 (Suppl 5):S1-8
  - Can Geriatr J 2012, 15(4):120-26 - http://www.cgjonline.ca/index.php/cgj/article/view/49/88

For More Information

An online CME for physicians will be available in early 2013.

Check www.lifeandminds.ca for updates and a link to this.

Webinars aimed at the inter-professional health teams will be available in 2013 via the CDKTN.

Check www.lifeandminds.ca for updates and links to these.

Publications:

The main paper is available in the Canadian Journal of Neurological Sciences, Volume 39 Number 6 (Supplement 5) November 2012: *4th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia*

Background articles are in press at Alzheimer Research and Therapy.

Check www.lifeandminds.ca for updates and links to these.

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