IS AMYLOID IMAGING REALLY HELPFUL IN DIAGNOSING AD? NO

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Recently two relevant decisions for our debate were published by US agencies. The United States Preventive Services Task Force (USPSTF) decreed that routine screening of all older individuals for cognitive impairment is not supported by the available evidence. After reviewing 55 studies examining the accuracy of screening instruments, and more than 130 studies of interventions aimed at slowing or stopping cognitive decline in patients who tested positive for cognitive impairment or relieving caregiver burdens, the USPSTF resolved that a clear benefit for screening has not been recognized, relative to the potential for harm. Thus, notwithstanding many new studies of cognitive screening and interventions since 2003, when the USPSTF last examined the issue, the overall conclusion remained the same. The task force emphasized that the review covered only routine, universal screening for older patients without clear signs or symptoms of cognitive impairment. Nearly at the same time the US Food and Drug Administration (FDA) has approved a third agent for imaging β-amyloid, florbetaben F18 injection (*Neuraceq*, Piramal Imaging). Florbetaben is indicated for positron emission tomography (PET) of the brain to estimate β-amyloid neuritic plaque density in adults with cognitive impairment who are being evaluated for Alzheimer's disease (AD) and other causes of cognitive decline. It was lately also approved in Europe. As with other imaging agents, a positive florbetaben scan does not establish a diagnosis of AD or any other cognitive disorder, but a negative scan indicating sparse to no amyloid plaques "is inconsistent with a neuropathological diagnosis of AD at the time of image acquisition; a negative scan result reduces the likelihood that a patient's cognitive impairment is due to AD," the company notes.

In the last year the impact of measuring fibrillar amyloid-beta load and glucose metabolism on the diagnostic process in a memory clinic population was assessed. One hundred fifty-four patients underwent paired dynamic and static scans soon after the administration of a standard dementia screening. Two-year clinical follow-up data were available for 39 patients. Clinical diagnosis and confidence in said diagnosis before and after disclosing imaging results were defined as the outcome measures. PIB scans were positive in 40 of 66 (61%) patients with a clinical diagnosis of AD and in 3 of 10 (30%) patients with other dementias. FDG uptake patterns matched the clinical diagnosis in 38 of 66 (58%) of AD patients. PET results led to a change in diagnosis in 35 (23%) patients. Diagnostic confidence increased from 71% before to 87% after PET ($p<0.001$). The authors concluded that in the setting of a memory clinic combining PIB and FDG PET are of additional value on top of the standard diagnostic work-up, especially when prior diagnostic confidence is low (Ossenkoppele et al, 2013). I would suggest that this may be an optimistic reading of the results. While diagnostic certainty increased by employing imaging studies this can more easily and with better clinical outcome can be achieved by practice and education of personnel.

Nearly at the same time an investigation of AD and other dementia diagnoses in three national registers in Finland was undertaken. The Hospital Discharge Register (HDR), the Drug Reimbursement Register, and the Causes of Death Register (CDR) were examined. The researchers had the benefit of basing their baseline "gold" standard on the Cardiovascular Risk Factors, Aging and Dementia (CAIDE) study wherein participants were first evaluated in 1972 to 1987, and were reexamined in 1998 and in 2005 to 2008. Sensitivity of the HDR was for AD diagnosis was55.6%.

The positive predictive value was 100% for AD. Sensitivity and PPV of the HDR were greater after 1998. For AD in the Drug Reimbursement Register alone, sensitivity was 63.5% and PPV was 97.1%. The authors conclude that diagnoses in registers have very good accuracy (Solomon et al, 2013).

The accuracy of clinical diagnoses in registers is notoriously low. The fact that this is not upheld in the diagnosis of AD emphasizes the fact that practice, clinical acumen and dedication are the infrastructure of AD diagnosis.