



Factors associated with increased Alzheimer's disease severity at presentation:

data from the ICTUS study

A longitudinal observational study of 1380 AD patients in Europe

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BACKGROUND

- Reasonable to assume that dementia should be diagnosed as early as possible.

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BACKGROUND

- Why?
 - Treatment exists (AChE I) that slows cognitive decline and delays nursing home placement for up to 6 months.
 - **But** other evidence showing the benefit of early diagnosis is difficult to find.

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BACKGROUND

- Early diagnosis currently incorporated in UK health strategy
 - Scottish Government HEAT (*Health Efficiency Access and Treatment*) target.

“Target 4: Each NHS Board will achieve agreed improvements in the early diagnosis and management of patients with a dementia (March 2011)”

- National Dementia strategy (England and Wales)

The Dementia Strategy sets out 17 recommendations that the government wants the NHS, local authorities and others to take to improve dementia care services. The recommendations are focused on three key themes of:

- *Raising awareness and understanding*
- *Early diagnosis and support*
- *Living well with dementia*

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BACKGROUND

- Postulate
 - Provide education and training to patients and their families.
 - Improve QOL of patients and their careers.
 - Improve advance care planning for end of life.
 - The advent of disease modifying treatment will necessitate early diagnosis

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BACKGROUND

- Therefore
 - an understanding of the presenting characteristics of the Alzheimer's disease population is important in order to increase the capture of those individuals at risk of late presentation

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Methods ICTUS Study

- DESIGN:
 - Cross-sectional with longitudinal prospective follow-up 6 monthly for 3 yrs
- SETTING:
 - 29 EADC centres
- PATIENTS:
 - Mild to moderate Alzheimers Disease living at home. (MMSE 10-26)



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Patient Assessment

Alzheimer Disease Assessment Scale-Cognitive Section (ADAS-Cog)

- measures cognition.
- Consists of 11 subtests covering domains:
 - memory,
 - orientation,
 - attention,
 - language,
 - reasoning,
 - praxis
- Range of total score is 0 to 70.
- The higher the score the larger the deficit.

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Patient Assessment

Basic ADL



- 6 item scale assessing
 - bathing,
 - dressing,
 - toileting,
 - continence,
 - transferring
 - feeding
- These activities rated by the carer;
 - 0 (total dependence),
 - 0.5 (partial assistance)
 - 1 (autonomous).
- Total score 0 (fully dependant) – 6 (independent)

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Patient Assessment

Instrumental ADL



- Eight item scale assessing functional ability to
 - use the telephone,
 - cook,
 - shop,
 - Drive/ use public transport,
 - wash their clothes,
 - do the housework,
 - look after their finances
 - administer their medication.
- Completed by the caregiver.
- Gender-dependant items of cooking, housework and clothes washing excluded due to missing data

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Patient Assessment: Neuro-psychiatric inventory **NPI**

- 12 item scale assessing behavioral and psychiatric symptoms.
- The carer rates presence of
 - delusions,
 - hallucinations,
 - dysphoria,
 - anxiety,
 - agitation/aggression,
 - euphoria,
 - disinhibition,
 - irritability
 - apathy,
 - aberrant motor behavior,
 - sleep disturbance
 - appetite and eating disturbance
- **Severity** (range from 1 to 4) and **frequency** (range from 1 to 3) are independently assessed
- Total score ranges from 1 to 144 (with no symptoms present scoring 0).

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Methods

- New patients defined as those with date of diagnosis = date of baseline visit (- 0-3 months) (n=473) selected from the ICTUS cohort
- Divided into two groups depending on disease severity at diagnosis

More severe : MMSE 10-20

Less severe: MMSE 21-26

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Methods: Analysis

- Bivariate analysis
 - » Continuous variables - student t-test
 - » Categorical variables – Odds ratio and 95% CI (X_2 for significance testing)
- Multivariate analysis- Logistic regression analysis. Model created adding variables with $P < 0.25$ in stepwise fashion



Results

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Demographics

Characteristic	Total ICTUS cohort	<u>New Patients (n=473)</u>		P
		<u>MILD</u> MMSE 21-26	<u>MODERATE</u> MMSE 10-20	
Number	1377	253	220	
Age, years (mean ± SD)	76.3 ± 7.7	75.81 ± 8.09	77.31 ± 7.53	0.0384
Female (%)	891 (64.71)	149 (47%)	167 (52.8%)	
Education years (mean ± SD)	8 ± 4.6	8.25 ± 4.48	7.13 ± 4.39	0.0021
ADAS-Cog	21 ± 9.6	16.38 ± 6.87	25.69 ± 9.95	<0.0001
ADL Total Score	5.4 ± 0.9	5.67 ± 0.61	5.25 ± 1.05	<0.0001
IADL (/5) Tot Score		3.45 ± 1.28	2.40 ± 1.44	<0.0001
NPI Total score	13.0 ± 13.7	12.8 ± 14.10	12.59 ± 13.65	0.8618
Burden Interview	21.1 ± 14.65	17.9 ± 14.61	21.77 ± 15.27	0.0068

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Predictors of later presentation

Multivariate analysis

Covariates in initial model

- Age, gender, level of education
- Comorbidity hypercholesterolaemia/ IHD
- BMI
- ADL, iADL
- NPI agitation/ appetite and eating disorders
- Income
- Living arrangements/ Caregiver burden -Zarit
- Country

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Predictors of late presentation

Multivariate analysis



Variable in final model	Odds Ratio	95% CI	p (χ^2)
Male	0.48	0.29-0.80	0.0044
Treatment with psychotropic medication	0.60	0.37-0.98	0.0404
NPI Agitation score ≥ 4	0.42	0.20-0.86	0.0173
IADL ≥ 2 incapacities	3.89	2.40-6.32	<0.0001

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Discussion

- Female sex or two or more IADL incapacities are associated with an increase risk of presentation of AD at a more severe stage (MMSE 10-20)
- The prescription of psychotropic medication or the presence of agitation appear to be associated with earlier disease presentation

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What does this mean?

- Patients present to medical practitioners due to the neuropsychiatric symptoms of AD rather than their functional or cognitive decline
- Good home coping environment delays the “social crisis” and therefore disease presentation
- “Social admission”, “acopia” = cognitive / functional decline of dementia until proved otherwise.

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Discussion

- Urgent need for further research to assess whether early diagnosis does improve outcomes (patient / health / social).
- If there is a benefit to early diagnosis, patients with cognitive decline should be encouraged to present for assessment
- Medical practitioners will need to be familiar with methods of cognitive and functional assessment and should understand the mechanisms by which patients are referred onto the appropriate diagnostic pathway

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ICTUS STUDY Group

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