Awareness of memory impairment does not predict progression to dementia in Mild Cognitive Impairment

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Objective: The level of awareness of memory deficit in Mild Cognitive Impairment (MCI) does vary in either clinical or research setting[1]. Only a prospective study is available[2] showing that low awareness predicts conversion to dementia, but the selected sample is insufficient to draw firm conclusions.
The aim of this study was to evaluate the predictive utility of self-reported memory deficits in patients with mild cognitive impairment (MCI) for the follow-up diagnosis of dementia.

Methods: Between January 2003 and May 2014, 349 amnestic MCI[3] (both single and multi-domain) were consecutive recruited in the Center for Research and Treatment on Cognitive Dysfunctions of the Luigi Sacco Hospital, included in the study and followed up annually.
To assess the awareness of memory complaints we employed a specific question included in the Geriatric Depression Scale (GDS): "Do you think you have more problems with memory than most people?".
The outcome of our study was the progression to dementia and AD. To verify if awareness of memory impairment was associated with the risk of progression of MCI to dementia and AD we used a Cox regression model. The covariates included in the model were: age, sex, education, subtypes of MCI (amnestic single or multi-domain), Minimental State Examination (MMSE), Cumulative Illness Rating Scale (CIRS) severity index, APOE genotype.

Results: During a follow up of 27.7 ± 20.8 months, 205 (63.3%) of 324 amnestic MCI subjects progressed to dementia, including 141 AD. GDS were available for 282 subjects (87%).
Univariate analysis showed that MCI subjects who developed dementia were older (75.9 ± 6.3 vs. 74,3 ± 7.5; p = 0.05), were more likely to be women (60% vs. 47.1%; p = 0.01), had a lower MMSE score (24.4 ± 2.8 vs. 25.8 ± 2.4; p <0.001) and fewer comorbidities (CIRS severity index 0.5 ± 0.3 vs. 0.6 ± 0.3; p<0.001). No statistically significant difference regarding the awareness of memory disorder was found. The multivariate Cox analysis, built to adjust for confounding covariates, showed no association between awareness of memory impairment and the risk of progression to dementia (HR 0.76, 95% CI 0.52-1.11, p = 0.16) and AD (HR 0.84, 95% CI 0.78-0.91, p =0,38).

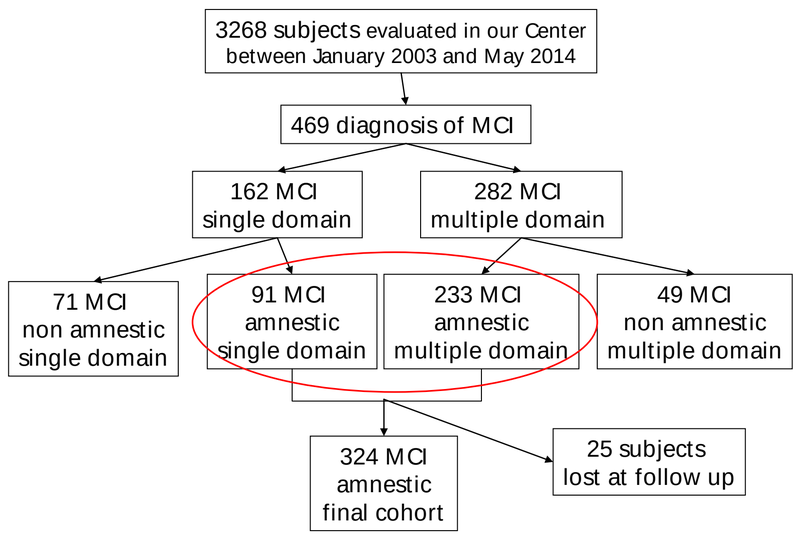

Table 1 Demographic and clinical characteristics at baseline of whole sample and by outcome at follow-up

	Study population N=324	No dementia at follow-up N=119	Dementia at follow-up N=205	p
Age	75,32 ± 6,81	74,35 ± 7,48	75,88 ± 6,34	0,05
Females, n (%)	179 (55,2)	56 (47,1)	123 (60)	0,01
Education	7,89 ± 4,07	7,85 ± 4,06	7,91 ± 4,09	ns
MMSE score	24,89 ± 2,77	25,76 ± 2,39	24,39 ± 2,85	<0,0001
MCI subtype **Amnestic single domain, n (%)** **Amnestic multiple domain, n (%)**	 91 (28,1) 233 (71,9)	 39 (32,8) 80 (67,2)	 52 (25,4) 153 (74,6)	ns
CIRS- Severity index	0,53± 0,27	0,60 ± 0,28	0,49 ± 0,26	<0,0001
Depression GDS* ≥ 11	0,49± 0,26	49 (45)	61 (35,3)	ns
Awareness of memory impairment (GDS* item14)	118 (41,8)	47 (39,5)	71 (34,6)	ns
ApoE4 genotype ** **ε 4 allele absent, n (%)** **ε 4 allele present, n (%)**	 149 (63,7) 85 (36,3)	 60 (72,3) 23 (27,7)	 89 (58,9) 62 (41,1)	0,02

MMSE = Mini Mental State Examination GDS= Geriatric Depression Scale
CIRS = Cumulative Illness Rating Scale
**** calculated on a subgroup of 282 MCI subjects***
***** calculated on a subgroup of 234 MCI subjects***

Table 2 Hazard ratios (HR) and 95% confidential interval (CI) of progression to dementia and AD in relation to baseline characteristics: Cox regression model adjusted for the potential confounding variables

	Dementia			AD		
	HR	**95%CI**	**p-value**	**HR**	**95%CI**	**p-value**
Age	1,06	1,09 - 1,03	<0,001	1,06	1,02 - 1,10	<0,001
Sex	1,06	0,75 - 1,11	0,15	0,66	0,40 – 1,07	0,09
Education	0,75	1,00-1,11	0,22	1,07	1,01-1,13	0,01
MMSE score	0,84	0,78 - 0,91	< 0,001	0,82	0,75-0,90	< 0,001
MCI subtype	1,08	0,68 - 1,74	0,72	1,07	0,61-1,86	0,80
CIRS- Severity index	0,45	0,20 – 1,00	0,51	0,27	0,09-0,77	0,01
Depression (GDS ≥ 11)	0,79	0,52 – 1,19	0,27	0,70	0,43-1,15	0,16
Awareness of memory impairment	0,76	0,52 – 1,11	0,16	1,22	0,77-1,93	0,38
ApoE4 genotype	0,83	0,57 – 1,22	0,35	0,72	0,47-1,12	0,15

Discussion: These findings indicate that in subjects with MCI, the patient's awareness or anosognosia of memory deficits identified by GDS is not useful to predict future progression to dementia.

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