




The instruments used by the Italian centres for cognitive disorders and dementia to diagnose mild cognitive impairment (MCI)

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Abstract

Aims The purpose of this study was to examine the tools used in Italy to diagnose mild cognitive impairment (MCI).

Methods In collaboration with the Luigi Amaducci Research Consortium, the Italian Network of Alzheimer Evaluation Units prepared a questionnaire to describe how MCI is diagnosed in the Italian Centres for cognitive disorders and dementia (CCDD).

Results Most of the ninety-two CCDDs participating in the survey were located in hospitals (54.7%); large percentages were coordinated by neurologists (50.8%) and geriatricians (44.6%). Almost all (98.5%) used the Mini Mental State Examination to diagnose MCI; the Clock Drawing Test was also frequently used (83.9%). Other neuropsychological, imaging and biomarker tests were utilized less frequently and a wide diversity in the instruments used was noted.

Conclusions According to the results, diagnoses of MCI are based on a multitude of instruments, with major differences in the clinical assessment of geriatricians and neurologists. Standardized testing protocols, validated instruments and cut-off points need to be identified and adopted by the CCDDs for assessing MCI.

Keywords Mild cognitive impairment · Diagnosis tools · Italian centres for cognitive disorders and dementia

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Introduction

Mild cognitive impairment (MCI) is an intermediate stage of cognitive impairment that often, but not always, represents a prodromal phase of dementia. In accordance with the international criteria based on the Key Symposium held in 2003, MCI is considered a clinical syndrome that has different aetiologies and clinical profiles including impairment not only in memory but also in other cognitive domains [1, 2]. New criteria for dementia recently published by the American Psychiatric Association in the fifth edition of the diagnostic and statistical manual for mental disorders (DSM-5) identified a pre-dementia stage of cognitive impairment defined as mild neurocognitive disorder (NCD). Sharing many features with MCI, the condition represents an initial phase of cognitive impairment that precedes the major neurocognitive disorder that corresponds to outright dementia [3].

Objective cognitive impairment, defined as poor performance on one or more neuropsychological tests or batteries, can refer to any cognitive domain such as executive functions, attention, language, memory and visuospatial skills. Depending on the type and number of cognitive domains

found to be impaired, MCI has been classified into four subtypes: amnesic MCI (isolated memory deficit); multi-domain amnesic MCI (difficulty of memory accompanied by a deficit in at least one other cognitive function, such as language, executive functions, visuo-spatial abilities); single domain non-amnesic MCI (cognitive decline involves a single domain not linked to memory, such as an isolated deficit in visuo-spatial functions); multidomain non-amnesic MCI (cognitive decline is linked to at least two cognitive functions, with the exclusion of memory) [1].

According to a recent review [4], MCI prevalence rates range between 16 and 20% in the general population. The incidence rate of dementia in patients with MCI is much higher than that observed in MCI-free individuals. The rate of progression to dementia in MCI patients varies from 20 to 40% [5]. However, individuals with MCI do not necessarily progress to dementia, and several studies have shown that they can remain cognitively stable or even recover normal cognitive status [6]. The high variability in prevalence rates and in the rate of conversion to dementia are undoubtedly linked to differences in the populations studied, in the duration of study's follow-up and, above all, in the diagnostic criteria utilized, as well as to the number and types of neuropsychological tests employed [7]. Currently, there is no consensus for agreed guidelines specifying the neuropsychological tests or batteries, the cut-off points and the number of tests or subtests that should be used to define impairment in a cognitive domain. Although many studies use the same or similar diagnostic criteria, the manner in which they are utilized is not necessarily the same [2, 8]. The most frequently proposed screening tests include the Montreal Cognitive Assessment (MoCA [9]), the Mini-Mental State Exam (MMSE [10]) and the Mini-cog test [11, 12]. The MoCA is a screening tool that was developed specifically to detect MCI. Thirty items assess multiple cognitive domains including short-term memory, visuospatial abilities, executive functioning, attention, concentration, and working memory, language and orientation in time and place. The MMSE is a brief screening tool that is useful in estimating the severity of cognitive impairment and in assessing cognitive changes over time. The MMSE provides a measure of individual's orientation in time and place, immediate recall, short-term verbal memory, calculation, language, and construct ability. With respect to the MMSE, some researchers consider the MoCA more sensitive in differentiating MCI from normal cognition and dementia; it has been validated in diversified setting [13]. The Mini-Cog test only takes 3 min, and is slightly influenced by education level. Mini-Cog is mainly used in screening patients with dementia and little research has been undertaken on whether it performs better than MMSE for screening MCI patients [14].

Cross-national comparative studies examining the prevalence and incidence rates of MCI and its progression to

dementia provide important data for public health decisions and interventions for clinical research, but the lack of standardized instruments for its assessment often do not allow such studies.

Although the CRONOS project first [15] and the "Italian Dementia National Plan" of the Ministry of Health [16] later, have highlighted the challenge in Italy of formulating appropriate health care policies and of creating an integrated and coordinated care network for dementia, there are no specific indications on how to diagnose and manage MCI.

The current study aimed to evaluate the tools used in Italy by the Centres for Cognitive Disorders and Dementia (CCDD), formerly called Alzheimer Evaluation Units (AEUs), to diagnose MCI.

Methods

In collaboration with the Luigi Amaducci Research Consortium, the Italian Network of Alzheimer Evaluation Units (UNIVA) formulated a questionnaire (available upon request) to evaluate the tools used by the CCDDs to diagnose MCI. All the CCDDs located in the various regions of Italy were sent an e-mail with a description of the project and an invitation to participate. When a CCDD accepted the invitation, the credentials (username, password) needed to access the web form questionnaire which was to be completed between November 2017 and February 2018, were provided.

The questionnaire included three sections: the first collected information on the CCDD's characteristics (geographic location, a list of the individuals coordinating and managing the team, the days of the week the centre is open, the services it provides, the research activities it participates in). The second section regarded the centres' activity during the preceding month's time. It was dedicated to questions about the number of patients that were evaluated, including information regarding their ages and sex. There were also specific items concerning the patients who had been evaluated for the first time during that period and the diagnoses that were formulated. The third section focused on the tools used to formulate the diagnosis of MCI.

Statistical analysis

After the data quality control, categorical variables were summarized using percentages and frequency distributions and the continuous ones using median and interquartile range. The CCDDs groups were defined depending upon the type of coordination (neurologists vs geriatricians vs psychiatrists). The differences between the groups with regard to the patients' ages, the tests prescribed and the instruments used to formulate a MCI diagnosis were evaluated using the χ^2 or Fisher's exact test for categorical variables and

the Wilcoxon rank-sum test for quantitative ones. All the analyses were performed using SAS 9.4 software.

Results

Ninety-two CCDDs had access to the web form questionnaire; 70 completed the questionnaire.

More than half of the participating CCDDs ($n = 35$; 54.7%) were set up in a hospital context, 12 (18.8%) in University Clinics, 14 (21%) in other types of health care services, and only 3 (4.7%) in residential facilities for the elderly. Most of the centres were coordinated by neurologists ($n = 33$; 50.8%) or by geriatricians ($n = 29$; 44.6%); less than 5% ($n = 3$) were coordinated by psychiatrists. The professional teams frequently included psychologists [present in 57 centers (87.7%)], neurologists [46 centers (70.8%)], nurses [41 centers (63.1%)] and geriatricians [39 centers (60.0%)]; psychiatrists, speech and rehabilitation therapists were present in less than 25% of the teams.

The total number of patients evaluated by the CCDDs participating in the survey during the preceding month was 7535; the median number of patients evaluated by each CCDD was 85 (Q1 = 48, Q3 = 120). There were 4300 females who represented 60.3% of the patients, 552 (8%) patients were younger than 65, 1578 (24.2%) fell into the 65–74 age groups, 3015 (43.7%) fell into the 75–84 age groups and 1750 (24%) were 85 or older. An analysis of study results showed that the CCDDs coordinated by geriatricians evaluated a lower percentage of individuals who were 65 or younger (4%) and a higher percentage of patients

who were 85 or older (30%), with respect to the CCDDs coordinated by neurologists (12% and 18.5%, respectively).

A total of 1916 individuals underwent a first evaluation over the previous month by the participating CCDDs; each CCDD evaluated a median of 21 persons (Q1 = 10, Q3 = 38) for a first evaluation. The characteristics of the individuals evaluated for the first time by the CCDDs are outlined in Figs. 1, 2 and 3. One-fifth of the patients ($n = 372$) had a score of 26 or higher on the MMSE; 1151 patients (61.9%) had a score that was lower than 24. A diagnosis of Alzheimer's disease was formulated for 509 patients (25.4%), of vascular dementia for 216 (11.6%) and of Alzheimer's plus vascular dementia for 380 patients (17.9%). Overall, 1210 patients (65%) were diagnosed with some type of dementia. Three hundred and twenty-two patients (17.5%) who were being evaluated for the first time were diagnosed with MCI. A diagnosis was not formulated for approximately 10% of the patients undergoing evaluation by a CCDD for the first time.

The tests and exams most frequently prescribed during the first appointment were neuropsychological tests (for $n = 1166$ patients; 82.4%), brain computed tomography (CT scan) or brain magnetic resonance imaging (MRI) (for 938 (52.5%) and 700 (44.9%), respectively) and cerebrospinal fluid analysis (CSF) (for 240 patients; 15.8%). Less than 10% of the individuals undergoing a first visit were prescribed genetic tests (apoE or others), amyloid positron emission tomography (PET) or single photon emission computed tomography (SPECT). CT scan was prescribed more often in the CCDDs coordinated by a geriatrician with respect to those coordinated by a neurologist (64.8% vs 40.8%, respectively; $p = 0.0175$). The CCDDs coordinated by neurologists

Fig. 1 The distribution of the Mini-Mental State Examination (MMSE) score among individuals evaluated by the CCDDs at the time of the first diagnosis

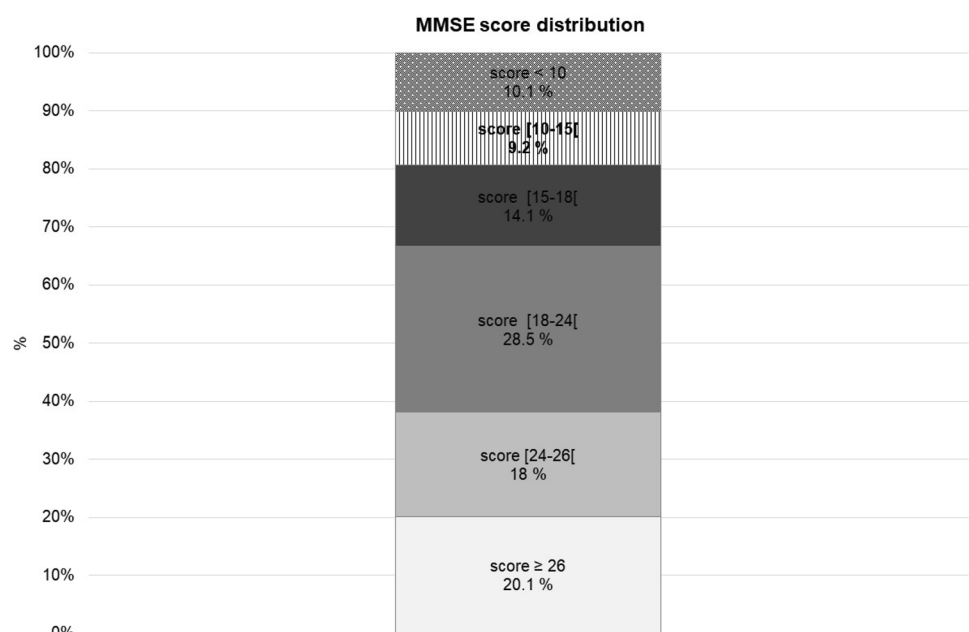


Fig. 2 Percentage of patients diagnosed with different disorders after the first visit to a CCDD

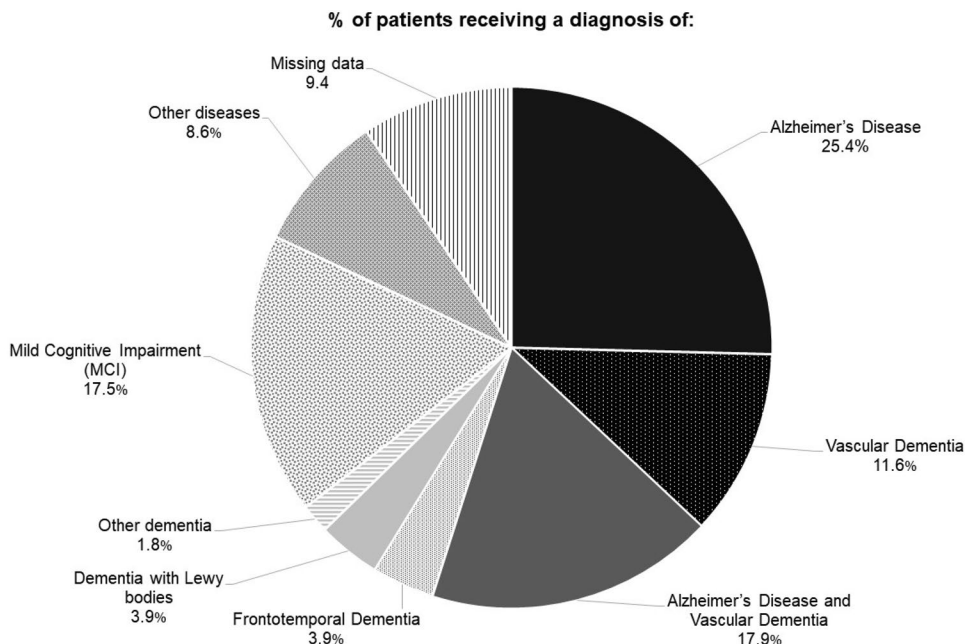
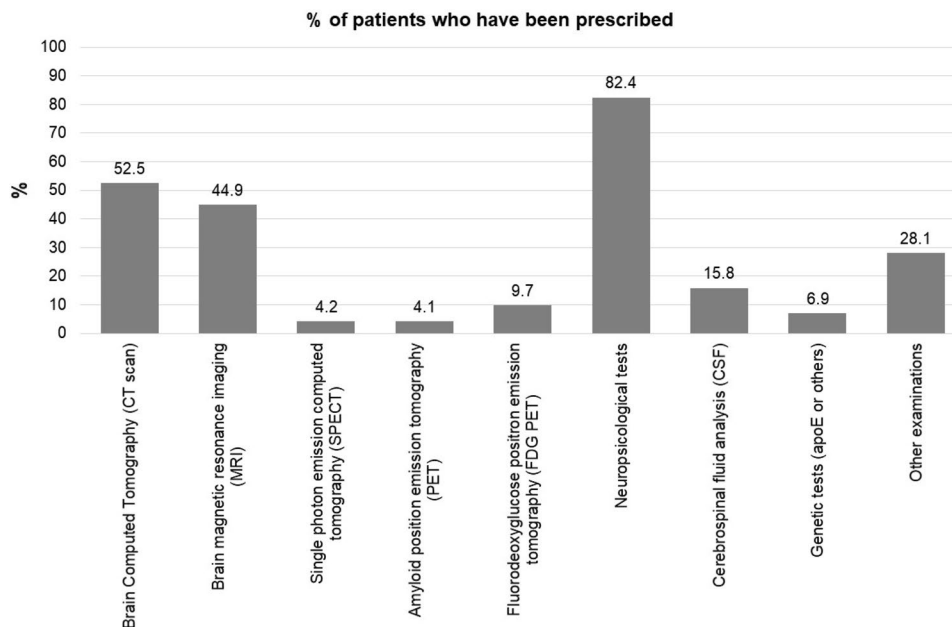


Fig. 3 Percentage of patients who were prescribed specific examinations (multiple answers allowed) after the first visit to a CCDD



more frequently prescribed genetic tests (11.4% vs 0.8%; $p=0.0206$) or CSF analysis (21.0% vs 11.0%; $p=0.0149$).

Table 1 concerns the third section of the questionnaire which focused on the instruments used to reach a diagnosis of MCI. Almost all the centres (64/65 responded to this question) used the MMSE. The Clock Drawing Test [17] was used by 52/62 centres (83.9%). Less than 10% of the CCDDs (6/63) reported using the Alzheimer's Disease Assessment Scale (ADAS-cog; [18]). Eighty-five percent of the participating CCDDs (51/60 responded to this question) also evaluated depression but without specifying the instruments

used; 80.7% (50/62) used the Neuropsychiatric Inventory (NPI; [19]). Sixty-nine percent of the CCDDs used other neuropsychological tests to formulate a diagnosis of MCI; the most frequently used were the MoCA (14/55 centres (25.5%)), the Rey Auditory Verbal Learning Test (15/55 centres (27.3%); [20]) and the Rey Complex Figure (15/55 centres (27.3%); [21]).

The CCDDs coordinated by geriatricians less frequently reported using the Rey Complex Figure test, with respect to the CCDDs coordinated by neurologists (12.5% and 41.4%, respectively; $p=0.0202$). No other significant differences

Table 1 A profile of the tools used to assess MCI at the first visit to a CCDD

	Number of centres that answered this item	Number of centres that acknowledge using this instrument	%
Mini-Mental State Examination (MMSE)	65	64	98.5
Alzheimer's Disease Assessment Scale (ADAS-cog)	63	6	9.5
Clock drawing test (CDT)	62	52	83.9
Activities of daily living (ADL)	58	62	93.6
Instrumental activities of daily living (IADL)	59	63	93.7
Cumulative Illness Rating Scale (CIRS)	58	26	44.8
Neuropsychiatric inventory (NPI)	62	50	80.7
Depression or depressive symptomatology scales	60	51	85.0
Scale caregiver stress assessment	59	36	61.0
Other tests:	55	38	69.2
Rey auditory verbal learning test	55	14	27.3
Rey complex figure	55	15	27.3
Montreal Cognitive Assessment (MoCA)	55	14	25.5
Semantic and phonemic verbal fluency	55	12	21.8
Trail making test	55	12	21.8
Digit span	55	10	18.2
Frontal assessment battery	55	9	16.4
Visual search test	55	7	12.7
Raven's progressive matrices	55	7	12.7
Story recall test	55	6	10.9
Token test	55	5	9.1
Free and cued selected reminding	55	5	9.1
Mental deterioration battery (MDB)	55	4	7.3
Milan Overall Dementia Assessment (MODA)	55	4	7.3
Stroop's test	55	4	7.3
Apraxia test	55	4	7.3
Corsi block-tapping task	55	3	5.5
Babcock Story Recall Test	55	3	5.5
Esame Neuropsicologico Breve	55	2	3.6
Boston Naming Test	55	2	3.6
Screening for Aphasia in Neurodegeneration	55	1	1.8
Cinq mots test	55	1	1.8
Three-objects-three-places test	55	1	1.8
Dual task	55	1	1.8
Tower of London test	55	1	1.8
Visual object and space perception battery	55	1	1.8

emerged regarding the instruments to formulate a diagnosis of MCI and the CCDD coordination.

Discussion

The survey described here uncovered that there was high variability in the diagnostic investigation process and the test batteries used to evaluate specific cognitive domains in the CCDDs surveyed in Italy. Conversely, there was a high homogeneity with regard to the instruments used to evaluate

the level of global cognitive function (99% of the practitioners declared that they used the MMSE), behavioural and psychological symptoms (81% used NPI) and depression (85% used specific instruments, although these were not specified).

According to the guidelines of the Italian Association of Psychogeriatrics (AIP) and the Dementia Study Group of the Italian Neurological Society (SINDEM), which are based on the diagnostic criteria proposed by the National Institute of Aging and the International Working Group, early detection of dementia can be achieved only if the cognitive tests

and the tools utilized are capable of assessing behavioural and psychological symptoms. Since not only memory but also other cognitive functions need to be evaluated when individuals are being assessed for MCI [22], both rapid and global assessment tools such as the MMSE and tests investigating specific cognitive domains must be utilized, as they were by most of the CCDDs surveyed here.

Our questionnaire showed that psychiatrists play only a marginal role in the clinical work-up of CCDD team, thus arguing for behavioural and psychological symptoms being not extensively assessed during MCI assessment.

Another finding that emerged from the survey was the high percentage of patients who were diagnosed with dementia already during the first appointment (65%). This would confirm the importance of setting up screening programs or protocols able to identify early stage cognitive decline and/or MCI-subtypes in the general population. Specific, targeted educational programs should train General Practitioners (GPs) and other health professionals to carry out cognitive screening in patients at early stages of the disease and to refer them to the nearest CCDDs that are located throughout the country. Until now the efficacy of cognitive impairment screening programs set up in primary care setting [23] has not been demonstrated, although screening tests performed by GPs seem to be useful if signs or symptoms of cognitive impairment are present [24]. It has been claimed that a therapeutic approach, based on pharmacological and non-pharmacological therapies (such as physical and cognitive stimulation) and monitoring cardiovascular risk factors, may be able to delay MCI progression and improve quality of life if it begun at an early stage of the disease [22, 25]. Timely MCI diagnoses could presumably lead to early interventions, as well as to integrated care pathways, better symptoms management, cost containment and delayed institutionalization [26].

The survey has some limitations, the major one being that not all the CCDDs responded to the questionnaire. Since questionnaires were anonymous, it was not possible to evaluate the difference between the centres that responded and those that did not. We can presume, however, that, on the basis of a self-selection principle, quality of the cognitive assessment was higher in the CCDDs participating in the survey, with respect to those that did not. The results cannot, therefore, be generalized to the overall Italian network. The fact that data collected did not allow us to evaluate if tests were used routinely or occasionally can be considered another limit.

In conclusion, the scientific community and the population at large are waiting the introduction of new pharmacological protocols that will be able to treat or slow down cognitive impairment progression. When this will become available, CCDDs will need to be better organized and to follow homogeneous diagnostic protocols and integrated care

pathways. It is important that the numerous CCDDs located throughout Italy adopt standardized testing protocols, validated instruments and cut-off points to diagnose MCI and its subtypes. This would allow to obtain standardized rates of MCI and dementia and to reduce variability in reported rates of conversion from MCI to dementia. Moreover, in international comparative studies in the epidemiology of MCI and dementia.

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Compliance with ethical standards

Conflict of interest The sponsor was in no way involved in selecting the participants, reviewing the literature, analysing the data collected, drafting or reviewing the paper, or in the decision to submit the manuscript for publication. All the views expressed here are exclusively

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