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Clinical Dementia Rating Scale (CDR) and dementia risk in the Mild Cognitive Impairment patients**

Skala Klinicznej Oceny Stopnia Otępienia (CDR) a ryzyko otępienia u osób z łagodnymi zaburzeniami poznawczymi

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S u m m a r y

Introduction. Mild Cognitive Impairment (MCI) is a syndrome defined as cognitive decline greater than expected for an individual's age and education level but that does not interfere notably with activities of daily life. The main criterion of MCI is memory impairment, and the most common method of diagnosis is Clinical Dementia Rating (CDR), scored in MCI as 0.5.

Aim. We tried to estimate the utility of particular CDR's boxes scores in dementia risk estimation.

Material and methods. Boxes of CDR (Memory, Orientation, Judgment & Problem Solving, Community Affairs, Home & Hobbies, Personal Care) baseline scores of 103 MCI persons (mean age 69.32; 80 females and 23 males) were analyzed in 2 groups: non demented – ND (n = 80; mean age 68.71; 56 females and 24 males), and demented – D (n = 23; mean age 71.82; 14 females and 9 males) after 3-year follow up.

Results. Any significant difference weren't observed in Memory, Orientation and Judgment. The most differentiating were Community Affairs and Home & Hobbies, which were on favor in the non-demented group (p = 0.05).

Conclusions. MCI subjects who later develop dementia differ from stable ones in functional domains of CDR at baseline evaluation. Analysis of particular CDR's boxes scores might be helpful in further patients' management.

Key words: Mild Cognitive Impairment, Clinical Dementia Rating, Alzheimer's disease, dementia risk

S t r e s z c z e n i e

Wstęp. Łagodne zaburzenia poznawcze (ŁZP) to zespół objawów definiowany jako pogorszenie funkcjonowania poznawczego w stopniu większym niż przewidywany dla wieku i poziomu wykształcenia, ale niezakłócający w sposób znaczący aktywności dnia codziennego. Głównymi kryteriami rozpoznawania ŁZP są deficyty pamięci. Jedną z metod ich diagnozy jest Kliniczna Ocena Stopnia Otępienia (ang. *Clinical Dementia Rating* – CDR), której wynik dla ŁZP wynosi 0,5.

Cel pracy. Celem pracy była ocena przydatności wyników poszczególnych podskali CDR w ocenie ryzyka wystąpienia otępienia u osób z ŁZP.

Materiał i metody. W badaniu wstępnym uzyskano wyniki poszczególnych podskali CDR (Pamięć, Orientacja, Osądzanie i rozwiązywanie problemów, Czynności związane z życiem w społeczności, Dom i hobby oraz Czynności osobiste) od 103 osób z ŁZP (śr. wieku 69,32; 80 kobiet, 23 mężczyzn). Po trzyletnim okresie obserwacji osoby zostały podzielone na dwie osobne grupy: bez otępienia – ND (n = 80; śr. wieku 68,71; 56 kobiet i 24 mężczyzn) i z otępieniem – D (n = 23; śr. wieku 71,82; 14 kobiet i 9 mężczyzn), a ich wyniki poddano odrębnej analizie.

Wyniki. Różnice pomiędzy wynikami podskali Pamięci, Orientacji oraz Osądzania i rozwiązywania problemów nie osiągnęły istotności statystycznej. Najbardziej różnicujące okazały się wyniki podskali: Czynności związane z życiem w społeczności oraz Dom i hobby, na korzyść osób bez otępienia (p = 0,05).

Wnioski. Pacjenci z ŁZP, u których w przyszłości wystąpi otępienie, uzyskują odmienne wyniki podskal pozapoznawczych CDR niż osoby bez otępienia. Analiza poszczególnych podskal CDR może być przydatna dla późniejszej opieki nad pacjentami.

Słowa kluczowe: łagodne zaburzenia poznawcze, Kliniczna Ocena Stopnia Otępienia, choroba Alzheimera, ryzyko otępienia

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INTRODUCTION

Mild Cognitive Impairment (MCI), is often a prodromal state of Alzheimer's disease (AD), however it seems to be a heterogeneous group with a variety of clinical outcomes. Most subjects will convert to dementia, but some MCIs may never progress to any significant extent or may even improve. The MCI prevalence varies from 15 to 30% of the population aged 60 and over according to different studies. Individuals with MCI are at an increased risk of developing dementia ranging from 1 to 25% per year. There is considerable heterogeneity in the rates of conversion in these studies, with annual conversion rates ranging from 2 to 31%. The overall 10.24% conversion rate is five-fold higher than the expected incidence of dementia in people at this age (1).

One of the popular instruments in the field of ageing research is the Clinical Dementia Rating (CDR) (2). CDR seems to be the major tool in establishing the diagnosis of MCI in Europe, where almost half of the memory clinics use CDR to assess patients with cognitive decline (3). For the most part, MCI subjects will be classified as CDR 0.5. However, the CDR is a severity rating and not a diagnostic classification. Therefore, subjects with a CDR of 0.5 may have the clinical diagnosis of MCI or AD (1).

AIM

The aim of this study was to point out the utility of CDR's boxes scores in predicting dementia risk in the MCI group. There are few papers analyzing particular boxes scores, most research focus on dementia staging provided by CDR overall score (3).

MATERIAL AND METHODS

The Clinical Dementia Rating was developed at Washington University School of Medicine, first published in 1982 and revised in 1993 (4). The CDR is a clinical staging instrument for dementia. It characterizes six domains of cognitive and functional performance: Memory, Orientation, Judgment & Problem Solving, Community Affairs, Home & Hobbies, and Personal Care. The necessary information to make each rating is obtained through a semi-structured interview of the patient and a reliable informant or collateral source (e.g., a family member). The CDR Table provides descriptive anchors that guide the clinician in making appropriate ratings based on interview data and clinical judgment. In addition to ratings on a 5-point scale for each domain (except Personal Care, which is rated on a 4-point scale) an overall CDR score is derived by standard algorithm. This score is useful for globally staging the level of impairment: 0 – No impairment, 0.5, 1, 2, and 3 indicate Very Mild, Mild, Moderate and Severe Dementia, respectively (2).

The CDR is used in both research and clinical settings to characterize the level of cognitive and functional performance in patients at risk for or suspected of being demented. Common applications include patient evaluation in memory assessment clinics, research studies of normal elderly and those with dementia, and clinical trials of therapeutic agents that might influence dementia progression (4).

The usefulness of the CDR may result from several factors: (1) it is clinically based (i.e., independent of psychometric test scores); (2) the six categories used for rating dementia severity are directly linked to validated clinical diagnostic criteria for AD; (3) it has high inter-rater reliability for physicians and nonphysicians; and (4) an expanded and more quantitative version of the scale can be achieved by summing the ratings in each of the six categories to provide the Sum of Boxes.

The CDR has been standardized for multicenter use. Criterion validity for both the global CDR and scores on individual domains has been demonstrated, and the CDR also has been validated neuropathologically, particularly for the presence or absence of dementia. Standardized training protocols are available. Although not well suited as a brief screening tool for population surveys of dementia because the protocol depends on sufficient time to conduct interviews, the CDR has become widely accepted in the clinical setting as a reliable and valid global assessment measure for dementia (4).

Our sample included 103 MCI individuals participating in a longitudinal study at the Department of Neurodegenerative Disorders of the Polish Academy of Sciences (DND/PAS) in Warsaw. The subjects were selected consecutively from attenders who had come to the DND/PAS for an evaluation of cognitive difficulties. All subjects lived independently in the community at the time of their baseline evaluation. Informed consent was obtained from each participant or their relatives. The local Ethics Committee for Medical Research approved the study (5).

The diagnosis of MCI was made if the subject met the following criteria: the presence of memory complaints, normal activities of daily living, objective memory impairment or an impairment in another area of cognitive function, normal global cognitive function, overall CDR score of 0.5, and not demented (1). Stages of the severity of cognitive disturbances were determined by the CDR conducted according to the published rules (2). The MCI participants were rated at entry as CDR 0.5 (6).

The outcome for each patient at 3 years was determined according to rules mentioned above, as well as observations and interviews with subject and subject's caregiver. Only particular CDR's boxes scores are analyzed.

All participants went neuropsychological evaluation, however all results except Mini Mental State Examination (MMSE) (7) scores were purposely disregarded in this paper, as well as demographic factors as educational level and occupation.

RESULTS

After three years of follow-up, 80 subjects remained non-demented and 23 converted to dementia. Nineteen of those converted patients had possible Alzheimer's Disease (5 with an Amnestic-MCI [A-MCI],

14 with Multi Domain-MCI [MD-MCI], 2 with MD-MCI were classified as Vascular Dementia, one MD-MCI as mixed dementia and one MD-MCI as Frontotemporal dementia). The overall rate of conversion to dementia was 21.9% at three years (an annual rate of 7.3%, calculated by dividing the observed conversion rate by the follow-up time). The mean time of follow-up was 3.05 years (SD: 0.675, median: 3.2 years). Those findings were published in the earlier report of observed group (6).

MCI patients were divided in 2 groups. Non demented (ND) group consisted with 80 persons, and demented group (D) consisted with 23 patients. Differences between groups were measured using the Mann-Whitney U-test. The threshold value of statistical significance was $p < 0.05$. The statistical analysis was carried out using the Analytical Software SPSS for Windows.

Following CDR's boxes scores were analyzed Memory (M), Orientation (O), Judgment & Problem Solving (J), Community Affairs (C), Home & Hobbies (H).

Overall CDR score and Personal Care box weren't taking into consideration, because all patients scored the same, Total CDR scored 0.5, and Personal Care box scored 0 (10).

Analysis revealed that at baseline both groups showed no differences in cognitive domains: Memory (M), Orientation (O), Judgment & Problem Solving (J). However there was a significant difference in functional, non-cognitive categories: Community Affairs (C) ($p = 0.042$) and Home & Hobbies (H) ($p = 0.036$) (tab. 1).

Demented group scored higher in Community Affairs and Home & Hobbies Boxes than non demented one. Their level of cognitive abilities was similar, not differentiating in terms of remembering, being oriented or able to abstractive thinking. However, the ability to conduct everyday activities in this group was decreased.

MMSE baseline scores were also calculated, and Demented group's mean result was 26.65 (SD: 2.08) compared to the mean score of stable group, which was equal to 27.35 (SD: 1.67). Both groups were similar in terms of baseline MMSE evaluation ($p = 0.262$).

Additionally, correlation between MMSE baseline scores and CDR's boxes scores was performed with r-Pearson statistics. However, obtained results weren't statistically significant. Results are presented in table 2.

DISCUSSION

The Washington University Clinical Dementia Rating (CDR) is a global scale developed to clinically denote the presence of Alzheimer's Disease (AD) and stage its severity. As it was proved, in some cases, MCI can be considered as preclinical stage of AD. Therefore CDR might be useful as dementia predictor in patients with MCI.

Data from longitudinal investigations conducted all over the world revealed that CDR is valuable tool in predicting the occurrence of dementia. In one of the studies stable and progressive MCI subjects differed only by CDR's boxes scores and delayed verbal recall, which were significant predictors of conversion to dementia (8).

Memory Box is primary category and the remaining ones are secondary. Patients with higher scores only in memory and orientation are on different level of functioning than patients with score 0.5 in all five boxes (except Personal Care box). The first one can be considered as amnestic MCI, the other one as generalized, global or multi-domain MCI. Data suggest that two types of MCI present the higher risk of developing dementia (9). Our results seem to point the dominance of general deficits profile as being a risk of dementia.

Table 1. CDR's boxes scores – comparison – between the groups.

CDR's domains	Demented (D) n = 23 mean (SD)	Non-demented (ND) n = 80 mean (SD)	U	p-value
Overall CDR	0.5 (0.00)	0.5 (0.00)	0.00	1.00
Memory	0.48 (0.10)	0.46 (0.15)	-0.455	0.649
Orientation	0.11 (0.21)	0.11 (0.56)	-1.302	0.193
Judgement & Problem Solving	0.46 (0.21)	0.39 (0.27)	-1.164	0.244
Community Affairs	0.35 (0.23)	0.18 (0.24)	-2.100	0.036*
Home & Hobbies	0.26 (0.25)	0.15 (0.23)	-2.035	0.042*
Personal Care	0 (0.00)	0 (0.00)	0.00	1.00

*$p < 0.05$

Table 2. Correlation between MMSE and CDR baseline scores.

MMSE	CDR – Overall score	CDR – Memory	CDR – Orientation	CDR – Judgment and Problem Solving	CDR – Home and Hobby	CDR – Community Affairs	CDR – Personal Care
Pearson Correlation	.(a)	.140	-.109	-.106	-.044	.003	.(a)
Sig. (2-tailed)	.	.160	.273	.288	.661	.977	.

The CDR shows progression of changes in patients functioning as well as its profile. It enables to indicate the typical features in case of mild dementia of the Alzheimer type, in which most scores in the different domains would hover around 0.5 or 1. However, in non-typical cases of AD or other neurodegenerative disorders reporting only overall CDR score is not sufficient. The analysis of individual domain of CDR allows to stress the predominating change, which present valuable assistance in diagnosis. The presence of widely divergent scores (such as a mixture of 0 s, 2 s and 3 s) would alert the clinician to the possibility of a non-Alzheimer cause of dementia (2). Establishing level of functioning as questionable dementia: CDR = 0.5 is useful in MCI diagnosis, but insufficient in predicting dementia, which was also found in our study.

The other research confirmed that presence of both higher CDR and lower verbal memory and executive function at baseline predicted greater likelihood of probable AD and decline (10).

Another study reported that in subjects with Mild Cognitive Impairment, the CDR score (especially when combined with word list recall) is a good predictor of progression to Alzheimer's disease, which corroborated the utility of CDR staging in describing predictive features of progression, and its major strength in discriminating ability even in the very mild or incipient stages of dementia. This could be attributable to the CDR's emphasis on cognitive and functional decline relative to one's past performance, as opposed to an absolute definition of clear-cut cognitive impairment with loss of functional independence (11).

Other findings claim that CDR score was significantly associated with a higher probability of being demented ($p < 0.001$). The sum of scores in boxes provides additional information to the CDR overall score in mild cases. It needs to be stressed that CDR score is a helpful indicator in making/excluding a diagnosis of dementia in people with mild cognitive deficits (12).

The CDR's boxes scores might be useful in future longitudinal analyses as either an indicator of global status or broken down into functional and cognitive subsets, or both (13).

There are studies, in which predictable validity of some CDR's boxes were analyzed. However, only those domains, which scores proved to be statistically insignificant in our study, were taken into consideration (Memory and Orientation boxes). Cross-sectionally the Orientation box score correlated substantially with an independent neuropsychological measure of orientation, but the Memory box score correlated more poorly with an independent measure of memory than with any other neuropsychological measure. The relationship of the overall CDR score and particular boxes' score to the results on neuropsychological measures was comparable to that of the Orientation and Memory boxes' scores. Longitudinally, Memory box's score a year later was predicted equally well by the other boxes' scores (Personal Care excepted) (3).

Data from our research revealed the opposite results, in which Memory and Orientation scores measured at baseline evaluation of MCI patients had no predictive value.

It may explain why Memory as a primary category has no predictable value in MCI patients, although delayed memory and learning impairments can surely predict the risk of developing dementia. Most of those patients are well oriented, show no judgments problems, are able to take care of themselves and other people, but present memory decline (14). The current findings suggest that individuals with MCI demonstrate deficits in a wide range of everyday functions but that the magnitude of these changes is greater for those functional abilities that rely heavily on memory (15). Neuropsychological assessment of memory is probably more exact than one used in CDR's questionnaire, but appearance of amnestic disturbances is not enough to predict development of dementia.

The lack of significant correlates between CDR's and MMSE's scores also indicates that simple cognitive screening and using methods focused only on memory dysfunctions are not sufficient in dementia prediction. As it was mentioned above, MMSE scores were similar in both presented groups.

It implies the necessity of more than memory assessment of all MCI patients. Our results suggest that patients with generalized impairment, not only in cognitive domain, but mostly in functional ones are more predisposed to be demented. Recent papers also confirms that the subjects with global impairment had greater decline in the planning and organizing process than in the initiation process and effectiveness in the performance of more complex everyday activities. They may be able to assume relatively independent functioning, but they may require some assistance and supervision (16). A greater executive dysfunction at initial assessment is associated with more rapid decline in everyday functioning. Perhaps executive function is particularly important with respect to maintaining everyday functioning. Alternatively, executive dysfunction may be a sentinel event indicating widespread cortical involvement. Changes in everyday life activities can result from motivational or cognitive deficits (17). In previous reports on this group, it was proved that lower mood in MCI patients, is conversion to dementia risk factor (5). The presence of depression may manifest in worse dealing with activity and lack of interests. It is worth mentioning that none of MCI patients were severely depressed, however further analysis is essential, but exceeds the frames of this paper, as well as additional description of combined results of neuropsychological examination scores and education level. Therefore, they were purposely disregarded.

CONCLUSIONS

MCI is a heterogeneous, dynamic group of disturbances, with different course. Moment of establishing the diagnosis of MCI can occur on the very beginning,

middle or final phase of that stage. Reporting only overall CDR score is not enough to evaluate that moment, or to predict duration or risk of conversion. However, since intentionally all components measure aspects of cognitive functioning, they are closely related. Focusing only on memory disturbances in MCI patients, especially not confirmed in objective testing might lead to misdiagnosis, if status of MCI is considered as predementia stage. Data from meta-analysis study (18), which also included our trial, suggest that most MCI patients will not progress to dementia, even after 10 years of follow up. Therefore, reports on cognitive and functional status of MCI patients are essential, and analysis of CDR's particular boxes seems to be an attractive and useful tool, both in establishing as well as in possible deterioration predicting in MCI patients, which could lead to dementia. MCI subjects with higher boxes' scores are at greater risk of conversion. Global or multi-domain MCI patients are more predisposed to develop dementia. The occurrence of functional disabilities together with impaired cognition can be a warning signal of the early phase of dementia. Physician's awareness of patient's functional disturbances might be helpful in disease management.

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