DOI:10.4274/tnd.2022.48347
Turk J Neurol 2022;28:248-253

Original Article / Özgün Araştırma

Self-perspective Versus Caregiver-perspective on Cognitive Impairment at Different Stages of the Alzheimer's Continuum

Alzheimer Hastalığının Farklı Evrelerindeki Bilişsel Bozukluklarda Hasta ve Bakım Veren Perspektifinin İncelenmesi

Mustafa Seçkin[1], Gülcan Öztürk[2], Ecem Dilmaç[3], Hakan Gürvit[4]

[1]Acibadem Mehmet Ali Aydinlar University Faculty of Medicine, Department of Neurology, Istanbul, Turkey

[2]Istanbul University Aziz Sancar Experimental Medicine Research Institute, Department of Neuroscience, Istanbul, Turkey

[3]Lund University, Department of Psychology, Lund, Sweden

[4]Istanbul University Faculty of Medicine, Department of Neurology, Behavioral Neurology and Movement Disorders Unit, Istanbul, Turkey

Abstract

Objective: To understand how the patients' and their study partners'/caregivers' perspectives on cognitive decline change at the subjective cognitive decline (SCD), mild cognitive impairment (MCI), and probable Alzheimer's disease (PRAD) stages of the Alzheimer's disease (AD) continuum.

Materials and Methods: Twenty-three individuals with the diagnosis of SCD, 33 individuals with the diagnosis of MCI, and 17 individuals with the diagnosis of PRAD were included. A cognitive testing battery including the standardized mini-mental state examination (MMSE), digit span forward and backwards tests, and the semantic fluency test were administered to all patients. The cognitive function instrument (CFI) was used for the subjective assessment of cognitive decline. The same questions in the CFI were answered both by the patients (CFI-self report) and the study partners (CFI-partner report).

Results: In the SCD and the MCI groups, the CFI-self report scores were higher than the CFI-partner report scores, whereas an opposite pattern was found in the PRAD group with higher CFI-partner report scores and lower CFI-self report scores. The CFI self report scores positively correlated with the MMSE scores in the PRAD group showing higher ratings in cognitively less impaired individuals, and vice versa. The CFI partner-report scores did not show a significant correlation with the MMSE scores in any of the groups, however a trend for a negative correlation was observed in the MCI group. Finally, the CFI-self report and partner report scores significantly correlated only in the MCI group.

Conclusion: Report-based assessment of cognitive decline can be informative, particularly in the early stages of the AD continuum. However, the loss of insight in PRAD may mask the symptoms when the subjective cognitive assessment relies on the patients' perspective. The greatest concordance between the patients' and their partners' perspectives was evident in the MCI stage which represented a transitional period between SCD and PRAD.

Keywords: Cognitive function instrument, Turkish, subjective cognitive decline, mild cognitive impairment, Alzheimer's disease

Öz

Amaç: Alzheimer hastalığının (AH) subjektif bilişsel gerileme (SBG), hafif bilişsel bozukluk (HBB) ve olası Alzheimer hastalığı (OAH) demansı evrelerinde hastaların ve eşlerinin/bakım verenlerin bilişsel bozulma ile ilgili perspektiflerinin nasıl değiştiğinin incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Yirmi üç SBG, 33 HBB ve 17 OAH tanılı hasta çalışmaya dahil edildi. Katılımcılara standardize minimental test (SMMT), sayı menzili testi ve semantik akıcılık testleri uygulandı. Kognitif fonksiyon enstrümanı (KFE) bilişsel bozukluğun subjektif değerlendirmesi için kullanıldı. Aynı sorular hastalar tarafından katılımcı bildirimi (KFE-KB), çalışma partnerleri tarafından ise çalışma partneri bildirimi (KFE-ÇPB) kullanılarak yanıtlandı.

Bulgular: SBG ve HBB gruplarında KFE-KB skorlarının KFE-ÇPB skorlarına göre daha yüksek olduğu görüldü. OAH grubunda ise tam tersi bir durum gözlendi ve KFE-ÇPB skorlarının KFE-KB skorlarına göre daha yüksek olduğu görüldü. Ayrıca OAH grubunda SMMT skorları ile KFE-KB skorları arasında pozitif korelasyon saptandı ve bilişsel bozukluğu daha ağır olan hastaların KFE-KB skorlarının daha düşük olduğu, bilişsel bozukluğu daha hafif olan hastaların ise KFE-KB skorlarının daha yüksek olduğu görüldü. Grupların hiçbirinde KFE-ÇPB skorları ile SMMT skorları arasında anlamlı korelasyon saptanmadı ancak HBB grubunda negatif korelasyon eğilimi görüldü. KFE-KB ve KFE-ÇPB skorları arasında anlamlı korelasyon sadece HBB grubunda gözlendi.

Sonuç: Bilişsel bozuklukların subjektif değerlendirmesi özellikle AH'nin erken evrelerinde bilgilendirici olabilir. Ancak, OAH olgularında içgörü kaybı gelişmesi nedeniyle hastaların perspektifine dayanan subjektif bilişsel değerlendirme yanıltıcı olabilir. Hastaların ve eşlerinin perspektifleri arasında en yüksek uyumluluk SBG ve OAH arasında bir geçiş dönemini temsil eden HBB evresinde saptanmıştır.

Anahtar Kelimeler: Kognitif fonksiyon enstrümanı, Türkçe, subjektif bilişsel gerileme, hafif bilişsel bozukluk, Alzheimer hastalığı

Address for Correspondence/Yazışma Adresi: Lec. Mustafa Seçkin MD, Acibadem Mehmet Ali Aydinlar University Faculty of Medicine, Department of Neurology, Istanbul, Turkey
Phone: +90 535 863 36 73 E-mail: seckin.dr@gmail.com ORCID: orcid.org/0000-0003-1342-8084
Received/Geliş Tarihi: 11.05.2022 **Accepted/Kabul Tarihi:** 12.08.2022

Introduction

Cognitive impairment associated with Alzheimer's disease neuropathological change (ADNC) presents as a continuum (1) ranging from an asymptomatic preclinical stage (2,3) to a severe, disabling cognitive decline as in the case of probable Alzheimer's disease (PRAD) dementia (4). Although PRAD develops slowly and insidiously, some clinical phenotypes have been defined to characterize the evolution of symptomatology at different stages of the disease. It has been proposed that the first symptoms of Alzheimer's disease (AD) may not be visible to a casual observer, instead these symptoms can be reported based on the "subjective" experience of the patients and/or observation of close partners, family members, or friends. This stage is also known as subjective cognitive decline (SCD) (5). Moreover, such a subjective complaint may not be detected using traditional clinical assessment tools such as pencil and paper tests (6,7).

As the disease progresses, the cognitive decline becomes detectable through examination in individuals with ADNC even though the activities of daily living (ADLs) are relatively spared (8). This stage between the SCD and the PRAD is known as the mild cognitive impairment (MCI) stage (9). Epidemiological studies revealed that the prevalence of MCI ranged from 2.4% to 74.2% which tended to increase with age (10,11,12). On the other hand, annual conversion rates from MCI to PRAD dementia may range from 9.6% to 91.2% being lowest in the age groups of 65-70 years and ≥85 years (13). Since MCI may affect a large population, early diagnosis is vital for slowing down cognitive decline.

Finally, neurodegeneration progresses to a stage where the cognitive decline interferes with the ADLs including work, travel, shopping, household care and even personal care. At this stage, which is also known as PRAD dementia, patients may have a loss of insight while the caregivers experience significant distress associated with the impact of the disease (4,14,15).

Due to the subjectivity of the symptoms reported by the patients and their partners, particularly in the early stages of cognitive decline, cognitive function instrument (CFI) has been developed as a standardized measure to understand how patients define their symptoms and to characterize the magnitude of the cognitive decline based on their partners' observation. CFI provides a subjective description of the status of cognitive abilities including memory, orientation, language, calculation, and functioning in the ADLs such as household care, shopping, traveling, employment, and recreational activities (16). This instrument is particularly beneficial in patients in whom objective measures of cognitive decline are not evident in the cognitive exams. So-called "subjective" decline reported in those patients has a predictive value for the prognosis as SCD may be a precedent clinical phenotype of AD dementia (5). It has been shown that the CFI instrument is valid in predicting whether a group of older adults will develop cognitive decline or preserve a stable cognition over 4 years (16). Several studies have confirmed the validity, reliability, and robustness of the CFI when translated to other languages and populations, such as Italian and Norwegian, and have demonstrated the usefulness of the CFI to screen for the early subjective cognitive changes over time (17,18).

In this study, we aimed to understand how the patients' and their partners' perspectives on cognitive decline changed at the SCD, MCI, and PRAD stages of the AD continuum. We hypothesized that the CFI-self report would be more reliable in the early stages compared to the later stages of AD. We also wanted to reveal how CFI-self report interacted with the CFI-partner report to understand the relationship between the two perspectives in AD-associated cognitive decline; patients' perspective, and their partners' perspective, respectively.

Materials and Methods

Participants

Twenty-three individuals with the diagnosis of SCD, 33 individuals with the diagnosis of MCI, and 17 individuals with the diagnosis of PRAD were included. Diagnosis of SCD was made if "self-experienced persistent decline in cognitive capacity in comparison with a previously normal status was evident and standardized cognitive tests showed normal age-gender-education adjusted performance" (5). Diagnosis of MCI was made if "concern about a change in cognition, in comparison with the person's previous level, was obtained directly from the patient and/or from a relative or friend (i.e. spouse, children, etc), lower performance in one or more cognitive domains that was more than would be expected for the patient's age and educational background was evident, and functionality in ADLs was relatively preserved" (19). Diagnosis of PRAD was made if "the cognitive impairment involved a minimum of two domains (i.e. memory and attention), represented a decline from previous levels of functioning, and interfered with the ability to function at work or usual activities" (4).

All participants in the SCD and MCI groups and 5 out of 17 participants in the PRAD group were recruited prospectively. Additional 12 participants with the diagnosis of PRAD were included retrospectively from the patient database. The study was approved by the Istanbul University Ethics Committee and was performed according to the ethical guidelines of the Declaration of Helsinki and its later amendments (decision no: 18, date: 26.10.2018). All prospectively involved participants provided informed written consent before enrolling in the study. All groups were matched for age [$F(2.72)=1.76$, $p=0.18$]. However, groups differed from each other in years of education [$F(2.72)=4.54$, $p=0.014$]. Please see Table 1 for the details of the demographics.

Neurocognitive Assessment

All participants were administered the Turkish version of the standardized mini-mental state examination (MMSE) to test global cognition (20). Digit span forward and backwards tests were performed to test attention (21). Additionally, the semantic fluency test was performed in which participants were asked to name animals from memory as many as they could in 60 seconds (22). Please see Table 1 for the details of the cognitive tests.

Cognitive Function Instrument

The original version of the CFI introduced by Amariglio et al. (16), was translated to Turkish by an experienced behavioral neurologist for Turkish adaptation. The CFI included two versions. One version of the CFI was completed by the patients to obtain information for the patients' perspective (CFI-self report). The other version included the same questions and was completed by the partners of the patients to obtain information about the patients' cognitive decline from the partners'/caregivers' perspective (CFI-partner report). Participants and their partners

Table 1. Details of the demographics and the cognitive tests

	Diagnosis		
	SCD (n=23)	MCI (n=33)	PRAD (n=17)
Demographics			
Age	64±7.6	66.7±9.2	69.2±9.7
Education	13.3±5.2	9.4±4.7[a]	10.5±4.3
Male/female	9/14	10/23	4/13
Cognitive tests			
MMSE	28.6±1.5	27.3±2.6	20.5±4.9[a, b]
DS-forward	5.8±1.1	5.2±0.9	4.3±1.2[a, b]
DS-backwards	4.7±0.9	3.6±0.8[a]	2.9±1.1[a]
Verbal fluency	18.8±4.6	13.9±5.2[a]	13.2±6[a]

[a]: p<0.5 versus SCD, [b]: p<0.5 versus MCI. SCD: Subjective cognitive decline, MCI: Mild cognitive impairment, PRAD: Probable Alzheimer's disease, MMSE: Mini-mental state examination

completed the CFI independently. Each response was coded as "Yes", "No", or "Maybe", and the responses were scored as 1, 0, or 0.5, respectively. Afterwards, the scores were summed together to obtain a total score for CFI-self report and CFI-partner report, separately.

Statistical Analysis

The main effect for the group (SCD, MCI, and PRAD) and report type (CFI-self and CFI-partner) were calculated using a 3×2 repeated measures mixed-model ANOVA. Follow-up 2x2 ANOVAs were then conducted to determine which pairs of groups differed from each other (SCD/MCI, SCD/PRAD, and MCI/PRAD). Paired samples t-tests were performed to reveal within-group differences in the scores of the CFI-self report and CFI-partner report. Finally, CFI-self report and CFI-partner report were subjected to One-Way ANOVA which was followed up by post hoc group comparisons when significant. Age and years of education were added as covariates in all of the between-group analyses.

Results

A significant interaction was found between group and report type [$F_{(2.68)}$=26.5, p<0.001]. Follow-up 2x2 ANOVA showed that the magnitude of cognitive impairment reported by the patients (CFI-self report) and the study partners (CFI-partner report) did not differ between the SCD and the MCI groups [$F_{(1.52)}$=0.03, p=0.85]. On the other hand, the PRAD group significantly differed from both the SCD [$F_{(1.36)}$=31.13, p<0.001] and MCI groups [$F_{(1.46)}$=40.5, p<0.001].

Moreover, reversal of the perspectives on cognitive impairment was evident in paired sample t-test. While the magnitude of cognitive impairment reported by the patients via self-assessment (CFI-self report) was greater than the impairment reported by the study-partners (CFI-partner report) in the SCD [t(22)=2.43, p=0.024] and the MCI [t(32)=2.15, p=0.039] groups, the cognitive impairment reported by the study-partners (CFI-partner report) was greater than the impairment reported by the patients (CFI-self report) in the PRAD group [t(16)=-5.3, p<0.001].

Although the SCD group had the lowest scores and the MCI group had the highest scores on average in CFI-self report, the group differences did not reach significance [$F_{(2.68)}$=2.8, p=0.064]. A One-Way ANOVA revealed significant group differences in CFI-partner report [$F_{(2.68)}$=48.2, p<0.001]. Post-hoc comparisons showed that the magnitude of impairment reported by the study partners in the PRAD group was greater than the MCI (p<0.001) and the SCD groups (p<0.001). However, the reports of the study partners in the SCD and the MCI groups did not significantly differ from each other (p=0.06) despite the tendency for greater impairment reported in the MCI group (please see Figure 1).

A correlation analysis conducted between the scores of the CFI-self report and the MMSE scores was significant within the PRAD group (r=0.62, p=0.008) (Figure 2). On the other hand, CFI-self report showed no significant correlation with the MMSE scores in

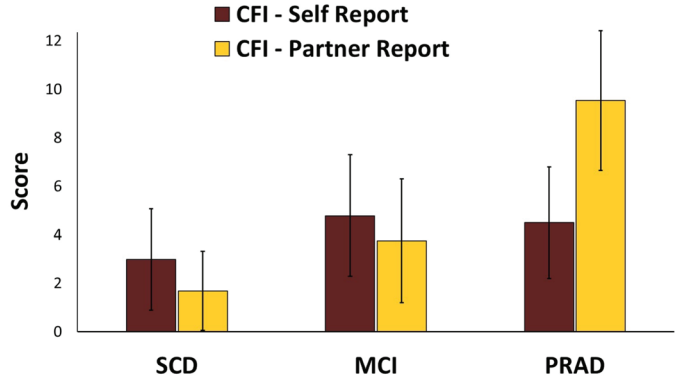

Figure 1. Self-perspective (self report) versus study partners' perspective (partner report) assessed by cognitive function instrument (CFI) in patients with subjective cognitive decline (SCD), mild cognitive impairment (MCI), and probable Alzheimer's disease (PRAD)

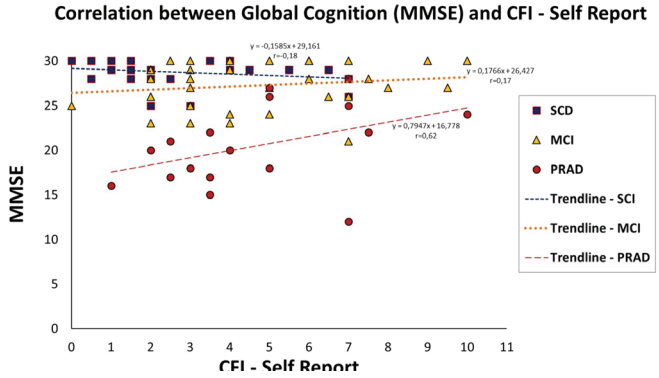

Figure 2. Correlation between global cognition (MMSE) and the CFI-self report in three patient groups

SCD: Subjective cognitive decline, MCI: Mild cognitive impairment, PRAD: Probable Alzheimer's disease, MMSE: Mini-mental state examination, CFI: Cognitive function instrument

the SCD (r=-0.18, p=0.4) and the MCI groups (r=0.17, p=0.34). Since the within-group variance of the MMSE scores was very low in the SCD and the MCI groups, a significant correlation might not appear despite the variance in the CFI – Self Report scores in the SCD and MCI groups (please see Figure 2).

The second correlation analysis was performed between the CFI-partner report and the MMSE scores and no significant correlation was found in any of the groups including the SCD (r=0.12, p=0.58), the MCI (r=-0.22, p=0.22), and the PRAD groups (r=-0.11, p=0.66). However, there was a tendency for a mild negative correlation in the MCI group (please see Figure 3).

The third correlation analysis was performed between the scores obtained from the self report and the partner report of the CFI to understand whether the patients' perspective correlated with the caregivers' perspective on the global cognitive decline at different stages of the AD continuum. No significant correlation between the patients' perspective and the caregivers' perspective was detected in the SCD (r=0.08, p=0.68) and the PRAD groups (r=-0.04, p=0.88) whereas, a significant correlation was found in the MCI group (r=0.41, p=0.019) (please see Figure 4).

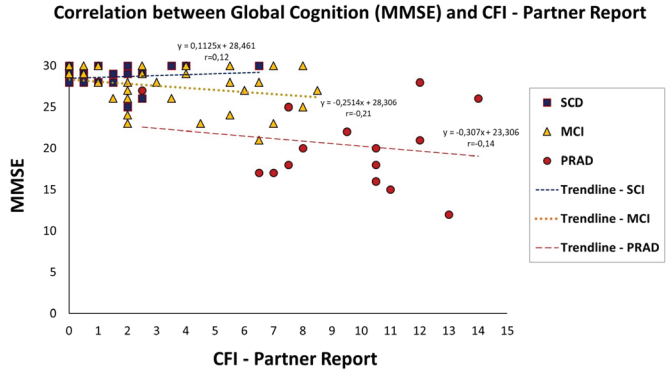

Figure 3. Correlation between global cognition (MMSE) and the CFI partner report in three patient groups

SCD: Subjective cognitive decline, MCI: Mild cognitive impairment, PRAD: Probable Alzheimer's disease, CFI: Cognitive function instrument, MMSE: Mini-mental state examination

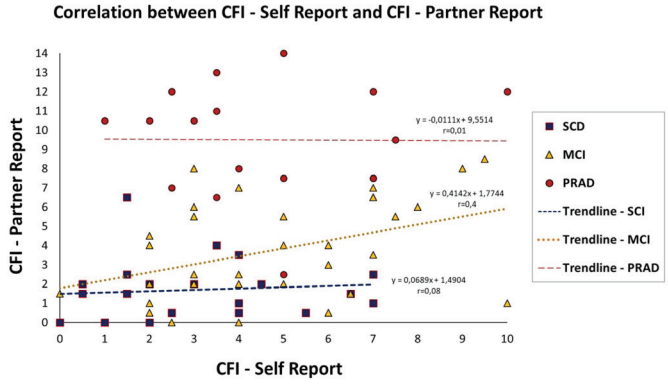

Figure 4. Correlation between the CFI-self report and CFI-partner report in three patient groups

SCD: Subjective cognitive decline, MCI: Mild cognitive impairment, PRAD: Probable Alzheimer's disease, CFI: Cognitive function instrument

Discussion

In this study, we investigated the similarities and the differences in the perspectives of the patients and their study partners on the cognitive decline associated with different stages of the AD continuum (SCD, MCI, and PRAD). We also wanted to understand how different perspectives correlated with global cognitive impairment (MMSE). The CFI was used as a measure for subjective assessment of cognitive decline. Our findings indicated that the patients in the SCD and the MCI groups reported a greater cognitive decline (CFI-self report) compared to the study partners' assessments (CFI-partner report). On the other hand, an opposite pattern was evident in the PRAD group with greater CFI-partner report scores compared to the CFI-self report scores.

It was striking that, although the MCI group had the highest scores on average, the CFI-self report scores did not significantly differ between groups. Moreover, CFI-partner report scores were significantly higher in the PRAD group compared to the SCD and the MCI groups. However, the comparison of the CFI-partner report scores in the SCD and the MCI groups did not reach statistical significance. The results of the correlation analysis revealed that patients in the PRAD group with higher MMSE scores tended to give higher ratings during self-assessment for their cognitive impairment and patients with lower MMSE scores tended to give lower ratings. This may be associated with the level of insight into the global cognitive decline in the PRAD group. CFI-partner report scores only showed a mild but not significant negative correlation with the MMSE scores in the MCI group. Finally, a significant correlation between the CFI-self report and the CFI-partner report scores was evident only in the MCI group.

Our results strongly suggest that the cognitive decline may not be clearly visible to an observer during the SCD stage of the AD continuum. On the other hand, the cognitive decline can be ignored and/or underestimated by the patients with PRAD although it is highly frustrating for their caregivers/partners. Therefore, a dissociation between the perspectives of the patients and their study partners on cognitive decline was observed in the PRAD group. Whereas, the perspective of the patients on the cognitive decline were concordant with the perspectives of their partners in the MCI stage.

As a novel and practical tool for the assessment of cognitive decline based on patient and partner interviews, the CFI has been fundamentally used in individuals with SCD (16,23). However, our findings indicate the usefulness of the CFI in MCI and PRAD, as well. It was striking that the CFI-self report scores were strong indicators of global cognitive decline in the MCI group. Although the group differences did not reach statistical significance, CFI-self report scores were the highest in the MCI group on average compared to the SCD and the PRAD groups. Within the AD continuum, the MCI stage represents a transitional state between the subtlety of early clinical symptoms at the SCD stage and the markedness of the advanced symptoms at the PRAD stage (9,19). Thus, understanding both patients' and their partners' perspectives may be extremely useful during the cognitive assessment, particularly in the MCI stage.

In a recent study, the CFI-self report was found to be more accurate in predicting future cognitive decline compared to the CFI-partner report in cognitively normal individuals, as well as in individuals with possible MCI (24). There is growing evidence

indicating the significance of patient-reported outcome measures for predicting the disease course in the AD continuum (25). Based on the most recent studies and our findings, we also recommend the use of assessment tools that include both patient and partner reports such as the CFI. Particularly in individuals with very subtle or no objective deficits of cognitive impairment, a subjective report may provide clues for transitional cognitive decline that can be defined as "decline in the previous level of cognitive function". Such a transitional decline may represent "a change from the individual baseline within the past 1-3 years" (1). Although the early studies used the term "impairment" for subjective cognitive complaints, the term "decline" was preferred by other researchers as it reflected the "temporal course of subjective cognitive change" that might be associated with the "progressive nature of cognitive deterioration" in AD (5).

A change from the individual baseline can be objectively documented in individuals that are enrolled in longitudinal studies. However, in the absence of objective clinical assessments on the individual baseline of a patient, self report may be informative, as well. In previous studies, partner reports were also found to be useful in reflecting the cognitive performance, particularly in patients with advanced symptoms of AD and accompanying anosognosia (16,24). During a 48-month follow-up of cognitively normal individuals, the self-report showed stronger correlations with the cognitive performance at the baseline and at 24 months, while the partner report showed stronger correlations at 36 and 48 months. Although the partner reports in our study did not show significant correlations with the cognitive performance, the MCI and the AD groups showed numerically greater correlations compared to the SCD group.

In summary, the findings of our study indicate the usefulness of the CFI in the assessment of individuals in the AD continuum. However, our study had a relatively small sample size, particularly in the PRAD group and the CFI questionnaire has relatively limited coverage for AD-associated symptomatology. Involvement of larger cognitive testing batteries in larger cohorts and improvement of the subjective cognitive assessment tools would help obtain more comprehensive information about the effectiveness of subjective reports on global as well as specific cognitive impairment including memory, attention, language, executive functions, visuospatial functions, and behavior.

Conclusion

The CFI is an effective tool for the subjective assessment of cognitive decline. At the early stages of the AD continuum (the SCD and the MCI stages), self report scores may overweigh the partner report scores as the symptoms can be subjective or very subtle to be noticed by an observer. On the other hand, there is a reversal of perspectives at the PRAD stage where the partners report a greater decline. The loss of insight may also be misleading while interpreting the CFI-self report at the PRAD stage. Finally, the CFI was more informative in the MCI group compared to the SCD and the PRAD groups.

Ethics

Ethics Committee Approval: The study was approved by the Istanbul University Ethics Committee and was performed according to the ethical guidelines of the Declaration of Helsinki and its later amendments (decision no: 18, date: 26.10.2018).

Informed Consent: All prospectively involved participants provided informed written consent before enrolling in the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.S., H.G., Concept: M.S., H.G., Design: M.S., H.G., Data Collection or Processing: M.S., G.Ö., E.D., Analysis or Interpretation: M.S., Literature Search: M.S., G.Ö., E.D., H.G., Writing: M.S., G.Ö., E.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Jack CR Jr, Bennett DA, Blennow K, et al. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. Alzheimers Dement 2018;14:535-562.
2. Jack CR Jr, Knopman DS, Jagust WJ, et al. Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. Lancet Neurol 2010;9:119-128.
3. Sperling RA, Aisen PS, Beckett LA, et al. Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011;7:280-292.
4. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011;7:263-269.
5. Jessen F, Amariglio RE, van Boxtel M, et al. A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. Alzheimers Dement 2014;10:844-852.
6. Slot RER, Verfaillie SCJ, Overbeek JM, et al. Subjective Cognitive Impairment CohorWt (SCIENCe): study design and first results. Alzheimers Res Ther 2018;10:76.
7. Weintraub S, Carrillo MC, Farias ST, et al. Measuring cognition and function in the preclinical stage of Alzheimer's disease. Alzheimers Dement (N Y) 2018;4:64-75.
8. Johnson N, Barion A, Rademaker A, Rehkemper G, Weintraub S. The Activities of Daily Living Questionnaire: a validation study in patients with dementia. Alzheimer Dis Assoc Disord 2004;18:223-230.
9. Petersen RC, Caracciolo B, Brayne C, et al. Mild cognitive impairment: a concept in evolution. J Intern Med 2014;275:214-228.
10. Lu Y, Liu C, Yu D, et al. Prevalence of mild cognitive impairment in community-dwelling Chinese populations aged over 55 years: a meta-analysis and systematic review. BMC Geriatr 2021;21:10.
11. Lara E, Koyanagi A, Olaya B, et al. Mild cognitive impairment in a Spanish representative sample: prevalence and associated factors. Int J Geriatr Psychiatry 2016;31:858-867.
12. Petersen RC, Lopez O, Armstrong MJ, et al. Practice guideline update summary: Mild cognitive impairment: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology 2018;90:126-135.
13. Zhang Y, Natale G, Clouston S. Incidence of Mild Cognitive Impairment, Conversion to Probable Dementia, and Mortality. Am J Alzheimers Dis Other Demen 2021;36:15333175211012235.
14. Kaufer DI, Cummings JL, Christine D, et al. Assessing the impact of neuropsychiatric symptoms in Alzheimer's disease: the Neuropsychiatric Inventory Caregiver Distress Scale. J Am Geriatr Soc 1998;46:210-215.
15. Rymer S, Salloway S, Norton L, et al. Impaired awareness, behavior disturbance, and caregiver burden in Alzheimer disease. Alzheimer Dis Assoc Disord 2002;16:248-253.
16. Amariglio RE, Donohue MC, Marshall GA, et al. Tracking early decline in cognitive function in older individuals at risk for Alzheimer disease dementia: the Alzheimer's Disease Cooperative Study Cognitive Function

Instrument. JAMA Neurol 2015;72:446-454. Erratum in: JAMA Neurol 2015;72:608.

17. Chipi E, Montanucci C, Eusebi P, et al. The Italian version of Cognitive Function Instrument (CFI) for tracking changes in healthy elderly: results at 1-year follow-up. Neurol Sci 2019;40:2147-2153.
18. Michelet M, Engedal K, Selbæk G, et al. The Validity of the Norwegian Version of the Cognitive Function Instrument. Dement Geriatr Cogn Disord 2018;46:217-228.
19. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011;7:270-279.
20. Güngen C, Ertan T, Eker E, Yaşar R, Engin F. Reliability and validity of the standardized Mini Mental State Examination in the diagnosis of mild dementia in Turkish population. Turk Psikiyatri Derg 2002;13:273-281.
21. Wecshler D. Wechsler Adult Intelligence Scale-Revised. San Antonio, TX: Psychological Corporation. 1987.
22. Aki ÖE, Alkan B, Demirsöz T, et al. Effects of age, gender and education on phonemic and semantic verbal fluency. Turk Psikiyatri Derg 2022;33:53-64.
23. Li C, Neugroschl J, Luo X, et al. The Utility of the Cognitive Function Instrument (CFI) to Detect Cognitive Decline in Non-Demented Older Adults. J Alzheimers Dis 2017;60:427-437.
24. Nuño MM, Gillen DL, Alzheimer's Disease Cooperative Study. Study partner types and prediction of cognitive performance: implications to preclinical Alzheimer's trials. Alzheimers Res Ther 2019;11:92.
25. Frank L, Lenderking WR, Howard K, Cantillon M. Patient self-report for evaluating mild cognitive impairment and prodromal Alzheimer's disease. Alzheimers Res Ther 2011;3:35.