

Research Article

Association between the controlling nutritional status (CONUT) score and mortality in elderly individuals with dementia followed in a neurology outpatient clinic

Nöroloji polikliniğinde takip edilen demanslı yaşlı bireylerde nütrisyonel durum kontrolü (CONUT) skoru ile mortalite ilişkisi

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Abstract

Introduction: Dementia is a medical condition that has become more prevalent around the world due to rising life expectancy. It leads to dependency and eventual death. Individuals over the age of 65 with dementia are at an increased risk of malnutrition due to various problems with food intake. Adequate nutrition intake and nutritional status throughout the disease process is crucial. Loss of muscle mass with body weight loss and functional decline has been reported to be related to increased morbidity and mortality in patients with dementia. Guidelines emphasize that nutritional interventions should be a component of dementia care. However, the increased dependency in the later stages of dementia makes it difficult to measure weight and calculate weight changes. Although several indexes and scales have been developed to quantify nutritional status, no gold standard of reference exists. Controlling Nutritional Status (CONUT) scoring, based on serum albumin, total cholesterol, and total lymphocytes, has been reported to be useful for early diagnosis and monitoring of malnutrition in a variety of patient groups. Therefore, this study aims to evaluate the correlation between the CONUT score and the Mini Nutritional Assessment–Short Form (MNA-SF) in determining the malnutrition status of individuals with dementia aged 65 and over. It also aims to examine the relationship between the CONUT score and mortality among those who are followed in a neurology outpatient clinic.

Methods: In the neurology outpatient clinic of a municipal day hospital, 113 patients aged 65 and over were included in the study from among 187 patients with a dementia diagnosis of at least one year, whose retrospective data were accessible. Their weight, height measurements, MNA-SF scores, serum albumin, total lymphocyte, and total cholesterol values were recorded from the system. The CONUT score was calculated based on biochemical data, and their three-month mortality statuses were obtained from the e-Nabız system.

Results: The mean age of the patients were 80.9 (± 7.48) years, with 63.7% were female. Most of the patients had Alzheimer's type dementia (76.9%), and 53.9% had a body mass index (BMI) below $<23 \text{ kg/m}^2$. Based on the MNA-SF (≤ 7) and CONUT score (≥ 2), the malnutrition rates were 61.9% and 61%, respectively, and a negative correlation was found between them. Malnutrition, as identified by the CONUT score was positively correlated both the number of years with dementia, and weight loss of $>5\%$ in the last three months, while negatively correlated with BMI. Although no difference was observed in the number of hospital admissions, individuals with malnutrition had a significantly higher need for hospital admission ($p = 0.029$). Mortality status was statistically significantly associated with a CONUT score ≥ 2 , regardless of age and duration of dementia (AUC = 0.63, 95% CI: 0.57–0.73).

Conclusion: A negative correlation was demonstrated between the CONUT score (≥ 2 points), calculated using biochemical markers, and the MNA-SF, which is recommended for the assessment of malnutrition in the elderly. The CONUT score's association with BMI and involuntary weight loss highlights its importance as an objective calculation method, particularly for individuals with dementia whose weight cannot be measured or known. Furthermore, the CONUT score was found to be associated with mortality status, independently of age and duration of dementia.

Keywords: CONUT Score, Dementia, Elderly, Malnutrition, Nutrition Assessment

Öz


Giriş: Demans, dünya genelinde beklenen yaşam süresinin uzaması ile yaygın hale gelen, bağımlılığa ve sonunda ölüme yol açan bir sağlık sorunudur. 65 yaş üstü demanslı bireyler, besin alımındaki çeşitli problemler nedeniyle artan yetersiz beslenme riski altındadırlar. Hastalığın seyri sırasında yeterli besin alımının ve beslenme durumunun korunması önemlidir. Vücut ağırlığındaki kayıp ve fonksiyonel azalma ile zayıflığın eşlik ettiği kas kütlesi kaybının demanslı bireylerde artan morbidite ve mortalite riskiyle ilişkili olduğu belirtilmektedir. Rehberler beslenme müdahalelerinin demans tedavisinin mutlak bir parçası olması gerektiğine vurgu yapmaktadır. Ancak demansın ilerleyen dönemlerinde bağımlılık durumlarının artması ağırlık ölçümünü ve ağırlıktaki değişimin hesaplanmasını zorlaştırmaktadır. Beslenme durumunun değerlendirilmesi için farklı ölçekler ve indeksler kullanılabilmekle beraber, altın bir standart yoktur. Serum albümin, total kolesterol ve total lenfositin skorlanması ile oluşturulan, Nütrisyonel Durum Kontrolü (Controlling Nutritional Status-CONUT) skorlamasının farklı hasta gruplarında malnütrisyonun erken teşhisi ve takibinde kullanılabileceği gösterilmiştir. Bu nedenle bu çalışmada, nöroloji polikliniğinde takip edilen 65 yaş ve üstü demanslı bireylerin malnütrisyon durumlarının belirlenmesinde CONUT skoru ile Mini Nütrisyonel değerlendirme-Kısa Form (MNA-SF) korelasyonunun değerlendirilmesi ve mortalite ile ilişkisinin incelenmesi amaçlanmıştır.

Yöntem: Belediyeye bağlı bir gündüz hastanesinin nöroloji polikliniğinde, en az 1 yıldır demans tanısı bulunan 187 hastadan, geriye dönük verilerine ulaşılabilen 65 yaş üstü 113 hasta çalışmaya dahil edilmiş olup, ağırlık, boy ölçümleri ve MNA-SF puanları ile serum albümin, total lenfosit ve total kolesterol değerleri sistemden kaydedilmiştir. CONUT skoru biyokimyasal verilerinden hesaplanmış ve 3 aylık mortalite durumları e-nabız sisteminden kontrol edilmiştir.

Bulgular: Hastaların yaş ortalamaları 80,9 ($\pm 7,48$) yıl olup, %63,7 si kadındır. Bireylerin çoğunluğu Alzheimer tipi demansa (%76,9) sahiptir ve %53,9 unun beden kütle indeksi (BKİ) $<23 \text{ kg/m}^2$ dir. Beslenme durumları açısından MNA-SF (≤ 7) ve CONUT skoruna (≥ 2) göre malnütrisyon oranları sırasıyla %61,9, %61 dir ve aralarında negatif yönlü korelasyon bulunmuştur. CONUT ile belirlenen malnütrisyon ile demans yılı ve son 3 ayda $>5\%$ ağırlık kaybı arasında pozitif yönde, BKİ ile negatif yönde korelasyon bulunmuştur. Hastaneye en az bir kez başvuru ve başvuru sayısında fark olmamasına rağmen malnütrisyonu olanların daha fazla hastaneye yatış ihtiyacı olmuştur ($p=0,029$). Hastaların herhangi bir sebeple mortalite durumları açısından yaş ve demans yılından bağımsız olarak. CONUT skor ≥ 2 olması ile istatistiksel olarak (AUC = 0.63, 95% CI: 0.57–0.73) anlamlıdır.

Sonuç: Malnütrisyonun belirlenmesinde biyokimyasal belirteçler ile hesaplanan CONUT skor (≥ 2 puan) ile yaşlılarda sıklıkla kullanılması önerilen MNA-SF arasında negatif yönlü korelasyon gösterilmiştir. CONUT skorunun, BKİ ve istemsiz ağırlık azalması ile ilişkili olması özellikle ağırlığı ölçülemeyen ve/veya bilinemeyen demanslı hastalarda objektif bir hesaplama olarak kullanılabilir bir yöntem olması açısından önemlidir. CONUT skor ile herhangi bir sebeple yaş ve demans yılından bağımsız olarak mortalite durumunun ilişkili olduğu gösterilmiştir.

Anahtar kelimeler: Demans, Yaşlılık, Malnütrisyon, CONUT skor, Beslenme Değerlendirmesi

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Key Points

1. The prevalence of malnutrition is high among elderly individuals with dementia.
2. The CONUT score is appropriate for assessing malnutrition in individuals with dementia and shows a correlation with the MNA-SF.
3. Malnutrition, as determined by the CONUT score, is associated with mortality.

Introduction

Dementia is a chronic progressive neurodegenerative process of late age and one of the leading causes of death. It leads to activities of daily living disabilities due to a loss of intellectual capacity and affecting at least two cognitive functions such as memory, speech, perception, calculation, judgment, abstract thinking, and problem-solving. This syndrome is not a normal part of the aging process, and the ultimate result is dependence and death. Dementia is becoming more prevalent not only in Europe and North America but also worldwide due to the rise in life expectancy. In 2010, the World Health Organization reported that 35.6 million people worldwide had dementia, and 7.7 million new cases were identified each year. The most clinically significant diseases that result in dementia are vascular dementia and Alzheimer's dementia [1, 2]. According to Turkish Statistical Institute (TÜİK) data, Alzheimer's disease as the underlying cause of death increased from 3.4% in 2012 to 4.3% in 2019 [3].

Epidemiological studies in our country reveal that most patients with Alzheimer's dementia are females, the majority of whom are in the age range of 79-84 years and in the advanced stages of the illness. Among the many issues suffered by this category of patients, nutritional disorders are reported as the most common, seen in approximately 82% of the cases [4, 5]. In the elderly aged 65 and above with dementia, the risk of malnutrition is increased by multiple impairments in food consumption. Optimal intake of nutrients and nutrition status are crucial during the disease course. Weight loss, functional decline, and loss of muscle mass, which is often followed by frailty, have been found to be strongly associated with increased risk of morbidity and mortality in this population [6]. In the early stages of dementia, alterations in dietary intake are not perceived by carers or individuals because they do not yet lead to weight loss. In late stages, individuals with dementia may lose the ability to respond to hunger and thirst stimuli and are unable to feed themselves due to visuospatial defects or apraxia. Additional factors to inadequate oral intake include loss of interest in food, food refusal, inability to identify familiar objects, cognitive confusion, mistrust of care givers due to psychotic symptoms, and dysphagia, which significantly hampers the swallowing process in the later stages of the disease [7, 8]. Guidelines emphasize that nutritional interventions be included in dementia care. Nutritional status is generally evaluated using screening tools that quantify malnutrition in terms of body mass index (BMI), weight loss, decreased appetite or dietary intake, and disease-related stress. None of these, however, have specifically been designed for individuals with dementia, and there is no gold standard in this area. In general, the Mini Nutritional Assessment (MNA) and MNA short form (MNA-SF) are increasingly being used in both dementia and non-dementia groups, particularly in the elderly [1, 2, 9].

Malnutrition can be assessed using various indices and biochemical markers, particularly when the weight cannot be measured directly (e.g., bedridden patients) and/or when anthropometric measurements cannot be obtained reliably. Albumin is a widely utilized clinical biomarker, and its serum concentration reflects hepatic synthetic function. Total lymphocyte count is a simple, rapid, and useful indicator of nutritional status in all ages with a progressive fall with worsening malnutrition. In elderly individuals, serum cholesterol level is recognized as a biochemical indicator of malnutrition [10]. The Controlling Nutritional Status (CONUT) score, developed by combining serum albumin, total cholesterol, and total lymphocyte count and validated in 2005, has been shown to be useful for the early detection and long-term monitoring of malnutrition [11, 12].

This study aims to evaluate the correlation between the CONUT score and the MNA-SF in determining the malnutrition status of individuals with dementia aged 65 and over. It also aims to examine the relationship between the CONUT score and mortality among those who are followed in a neurology outpatient clinic.

Methods

This cross-sectional, descriptive study retrospectively analyzed the medical records of individuals aged 65 and older with a confirmed diagnosis of dementia who were under the care of a specialist neurologist at a municipality-affiliated day hospital between January 2023 and January 2024. Mortality data were retrieved from the e-Nabız system. Ethical approval and institutional authorization were obtained. The study population comprised 187 patients aged 65 and older who had been diagnosed with dementia for at least one year and had consulted a specialist neurologist within the past year, either through the home care unit or direct outpatient visits. The retrospective file review included patient data with recorded weight and height measurements, nutritional screening completed using the MNA-SF ($n=128$), and serum albumin, total lymphocyte count, and total cholesterol levels available at evaluation ($n=113$). During follow-up, information that was collected routinely and recorded in the system by the specialist neurologist during regular follow-ups was recorded in the patient information form. These included demographic characteristics, diagnosis and duration of dementia, weight (kg), height (cm), body mass index (BMI, kg/m^2), weight loss over the previous three months, calculated MNA-SF scores, and biochemical parameters. In addition, the number of hospital visits over a six-month period and hospitalization, if any, during the visits were extracted from the system and recorded. The Controlling Nutritional Status (CONUT) score was calculated based on available biochemical parameters.

CONUT score; developed by Ulibarri, is calculated using serum albumin, total lymphocyte, and total cholesterol values obtained from the system [11]. This index, ranging from 0 to 12 points, classifies nutritional status as follows: 0–1 indicates normal nutrition, 2–4 mild malnutrition, 5–8 moderate malnutrition, and 9–12 severe malnutrition. The CONUT score of ≥ 2 is indicative of malnutrition. The calculation is performed as follows:

CONUT score = Serum albumin score + total cholesterol score + total lymphocyte score

Serum albumin score: 0, ≥ 3.5 g/dL; 2, 3.0–3.49 g/dL; 4, 2.50–2.99 g/dL; 6, <2.50 g/dL

Total cholesterol score: 0, ≥ 180 mg/dL; 1, 140–179 mg/dL; 2, 100–139 mg/dL; 3, <100 mg/dL

Total lymphocyte score: 0, ≥ 1600 mL; 1, 1200–1599 mL; 2, 800–1199 mL; 3, <800 mL

MNA-SF; For the assessment of malnutrition in older adults, a scale validated for Turkish reliability by Sarikaya et al. is applied. Six questions measuring modifications of appetite, weight loss over the past three months, status of mobility, recent psychological distress or recent illness, presence of neuropsychological complications, and BMI are included in this scale. Based on total score, individuals are classified as well-nourished (11–14 points), risk of malnutrition (8–11 points), or malnourished (≤ 7 points) [13]. In correlational analysis for the detection of malnutrition, CONUT ≥ 2 and MNA-SF ≤ 7 were taken as indicators of malnutrition..

Ethical approval, informed consent and permissions

Ethical approval was obtained from the İzmir Tınaztepe University Non-Interventional Clinical Research Ethics Committee on May 17, 2024 (Decision No: 2024/23). Institutional permission was granted by the chief physician before accessing the study data from the system. Additionally, verbal notification was provided to the patients and/or their relatives, and their informed consent was obtained.

Statistical analysis

Normality of continuous variables gathered in the study was verified using Shapiro-Wilk W and Kolmogorov-Smirnov tests. Frequency (n) and percentage (%) were employed to represent categorical data, while normally distributed quantitative variables were summarized as mean (\bar{X}) and standard deviation (SD). Spearman's correlation analysis was applied to estimate the correlation among the MNA-SF, CONUT score, and other variables. The chi-square test was applied for non-categorical variables and the t-test was applied for non-categorical variables. ROC analysis was conducted to explore the relationship between malnutrition status and all-cause mortality and CONUT and MNA-SF scores. Statistical significance was established at $p < 0.05$ level of a 95% confidence interval. Statistical analysis was done using SPSS Statistics 25.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

Results

A total of 113 individuals with dementia were included in the study. Of the participants, 63.7% were female, with a mean age of 80.9 (± 7.48) years, and 77% had a diagnosis of Alzheimer's disease. Nutritional status assessment revealed that 61.9% of patients were classified as malnourished based on the MNA-SF, while 61% were identified as malnourished using the CONUT score. The distribution of patients' nutritional status according to MNA-SF and CONUT scores is presented in Table 1.

Table 1. Nutritional status of patients based on MNA-SF and CONUT scores

CONUT Score	n	%	MNA-SF Score	n	%
0–1: Normal nutrition	44	38.9	12–14: Normal nutrition	11	9.7
2–4: Light malnutrition	47	41.6	8–11: Risk of malnutrition	32	28.3
5–8: Moderate malnutrition	21	18.6	≤ 7 : Malnutrition	70	61.9
9–12: Severe malnutrition	1	0.9			

CONUT; Nutritional Status Check-MNA-SF: Mini Nutritional Assessment Short Form

The evaluation of patients with and without malnutrition, based on the CONUT score and their respective characteristics, is presented in Table 2. Specifically, there were no significant differences in mean age ($p=0.458$); however, statistically significant differences were observed in the year of dementia diagnosis ($p=0.013$), BMI ($p=0.001$), and weight loss over the past three months ($p=0.031$). Although no significant difference was found in the number of hospital readmissions between the groups, individuals with malnutrition were significantly more likely to be hospitalized compared to those without malnutrition ($p=0.029$).

Table 2. Comparison of general characteristics of individuals with and without malnutrition according to CONUT score

	NORMAL (CONUT<2) n=44	MALNUTRITION (CONUT ≥ 2) n=69	Total n=113	p
Mean Age (year)	79.9 \pm 6.21	81.5 \pm 8.16	80.9 \pm 7.48	**p=0.458
Serum Albumin (g/dL)				
≥ 3.5	44	27	71	*p=0.001
3.0–3.49	-	22	22	
2.50–2.99	-	17	17	
<2.50	-	3	3	
Total Lymphocyte (mL)				
≥ 1600	34	36	70	*p=0.021
1200–1599	10	22	32	
800–1199	-	8	8	
<800	-	3	3	
Total Cholestrol (mg/dL)				
≥ 180	30	9	39	*p=0.012

	140–179	14	28	42	
	100–139	-	32	32	
	<100	-	-	-	
Sex					
	Female	30	42	72	*p=0.548
	Male	14	27	41	
Diagnosis					
	Alzheimer	31	51	87	*p=0.875
	Vascular Dementia	5	12	17	
	Parkinson	2	4	6	
	NPH	1	2	3	
Year of Dementia					
	1-5	39	45	84	*p=0.013
	6-10	4	23	27	
	>10	1	1	2	
Presence of comorbidities					
	Yes	40	55	95	*p=0.091
	No	4	14	18	
At least 1 hospital admission in the last 6 months		44	69	113	*p=0.431
Number of hospital admissions in the last 6 months		3.77 ± 1.95	3.83 ± 1.50	3.81 ± 1.68	**p=0.561
Need for hospitalisation in the last 6 months		1	10	11	*p=0.029
BMI					
	<19	2	9	11	*p=0.001
	19-23	14	36	50	
	23-27	17	20	37	
	>27	11	4	15	
Weight loss in the last 3 months(%)					
	0-5	25	20	45	*p=0.031
	>5	5	6	11	
	>10	14	43	57	
MNA-SF					
	No Malnutrition	9	2	11	*p=0.001
	Risk of Malnutrition	17	15	32	
	Malnutrition	18	52	70	

CONUT; Nutritional Status Check-BMI: Body Mass Index-MNA-SF: Mini Nutritional Assessment Short Form*Pearson χ^2 **Independent t test

A statistically significant negative correlation was observed between the MNA-SF and the CONUT score in relation to malnutrition ($r = -0.44$, $p = 0.001$). Additionally, a positive correlation was identified between malnutrition, as measured by the CONUT score, and the year of dementia diagnosis ($r = 0.28$, $p = 0.007$), while a negative correlation was found with BMI ($r = -0.32$, $p = 0.023$). Furthermore, a weak positive correlation was observed with weight loss greater than 5% over the past three months ($r = 0.30$, $p = 0.001$) (Table 3).

Table 3. Correlation between CONUT score and factors related to dementia patients with malnutrition

	r*	p
MNA-SF	-0.44	p=0.001
Year of Dementia Diagnosis	0.28	p=0.007
BMI	-0.32	p=0.023
Weight loss >5% in the last 3 months	0.30	p=0.001

BMI: Body Mass Index-MNA-SF: Mini Nutritional Assessment Short Form- Spearman correlation (r)

Both the MNA-SF and the CONUT score were found to be statistically significant in relation to patient mortality from any cause, independent of age and year of dementia diagnosis. Receiver operating characteristic (ROC) analysis was conducted, and the area under the curve (AUC) was calculated, revealing a value of 0.63 (95% CI: 0.57–0.73) for CONUT score ≥ 2 and 0.64 (95% CI: 0.53–0.74) for MNA-SF ≤ 7 , both of which were statistically significant ($p = 0.027$, $p = 0.014$). No significant difference was observed between the two assessments (CONUT score and MNA-SF) ($p = 0.745$).

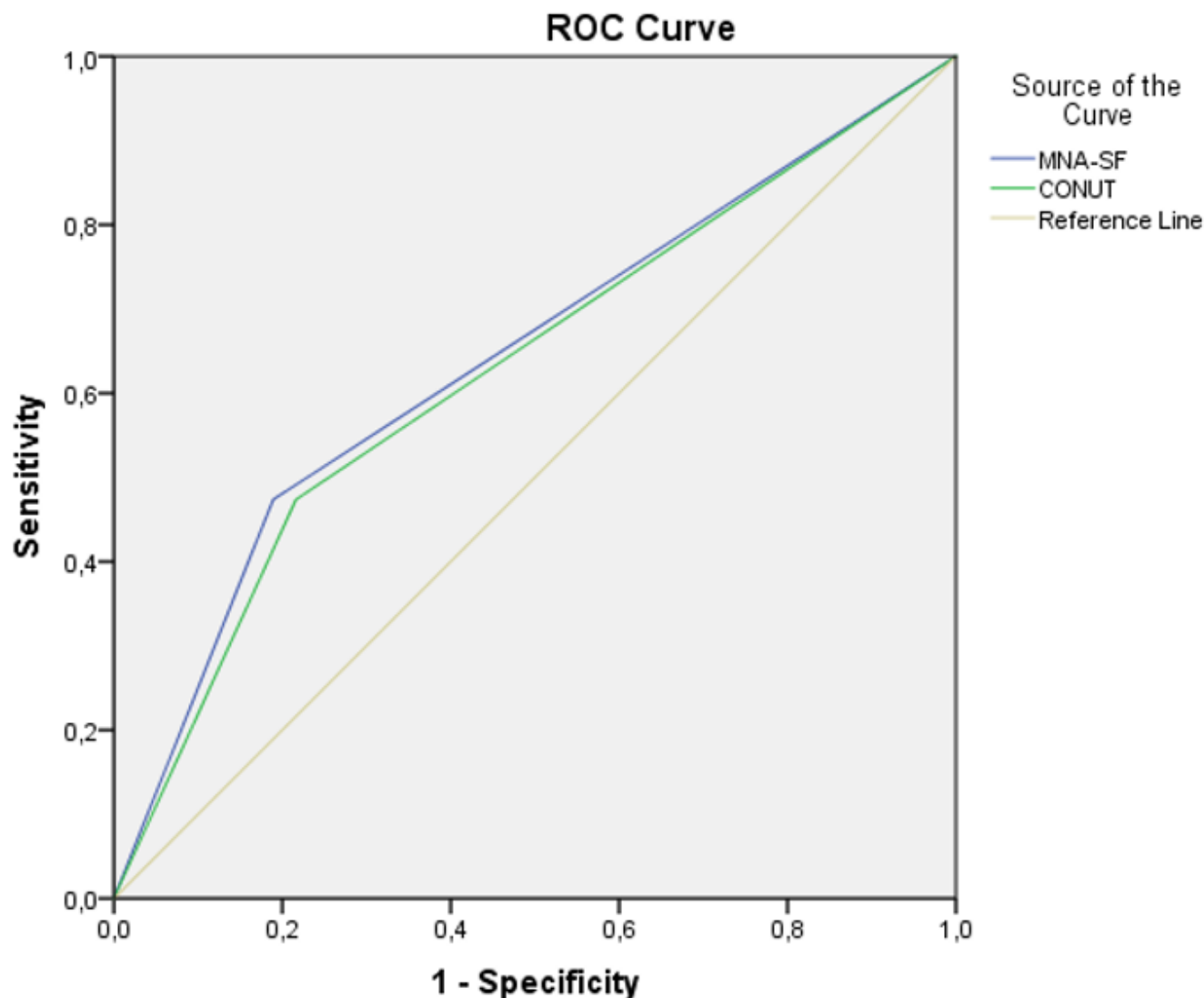


Figure 1. ROC analysis graph for mortality with CONUT score and MNA-SF in the diagnosis of malnutrition in patients with dementia.

Discussion

CONUT score is a quantitative index that is used in the assessment of malnutrition using serum albumin, total cholesterol, and the total lymphocytes. In this research, 61% of the patients were found to be malnourished according to the CONUT score. The prevalence of malnutrition according to MNA-SF was 61.9%, and malnutrition risk was 28.3%. Guidelines note that weight loss in individuals with dementia is more severe than in those without dementia, and the magnitude of weight loss may increase with increasing dementia severity. Thus, it is recommended to track weight measurements and changes in weight on each evaluation. While numerous screening and assessment tools are utilized to identify malnutrition, no gold standard for malnutrition in patients with dementia exists. It was interesting to find that the use of MNA and MNA-SF, including weight items and weight changes, is acceptable both for the community of the elderly and in demented patients. However, increasing dependency during the course of the disease towards its advanced stages renders measurement of weight and computation of weight change challenging [1, 2, 9, 14].

A systematic meta-analysis asserted that the prevalence of malnutrition among individuals suffering from dementia ranged from 6.8% to 75.6%, while the risk for malnutrition was between 36.5% and 90.4%. The prevalence of malnutrition in individuals with dementia in long-term care facilities was seen as a mean 26.9% (95% CI: 22.0–32.26, $p < 0.0001$, $I^2 = 94.12\%$) [15]. Another study using the Global Leadership Initiative on Malnutrition (GLIM) criteria found the prevalence of malnutrition to be 28.7% in individuals with dementia [16]. In the present study, there was a statistically significant negative correlation found between the MNA-SF and the CONUT score in predicting malnutrition. Since weight and/or weight change in the past three months were not measurable or queryable at the onset of our study, 59 patients were excluded from evaluation. For conditionally dependent diseases such as dementia, by applying another tool, e.g., the objective CONUT score regardless of the measurement of weight, an accessible approach to the detection of malnutrition may be available.

A meta-analysis of 111 studies comprising 52,911 subjects was conducted by Zhang et al. and revealed that malnutrition, as measured by the MNA, was associated with low albumin, total cholesterol, and BMI levels in elderly individuals [17]. Malnutrition, as measured by the CONUT score, in the present study was inversely associated with BMI and positively associated with weight loss over the previous three months. Several studies have also pointed out that the progression of dementia, the longer course, and the advancing stages of dementia are associated with malnutrition. It has been suggested that the nutritional status in dementia patients should be evaluated at an early stage and interventions should be implemented for treating malnutrition [1, 8, 18]. Likewise, our research found a positive correlation between malnutrition, as quantified by the CONUT score, and the duration of dementia.

Malnutrition is a very common geriatric syndrome in the elderly. Malnutrition has been demonstrated to be associated with an increased rate of hospital readmission and length of stay, with powerful associations with mortality [18, 19]. Malnutrition in patients with dementia has also been found to be associated with greater risk of morbidity and mortality compared to non-demented patients [1, 16, 18, 20, 21]. In the present study, no difference was found in the number of hospitalizations between malnourished and non-malnourished patients as indicated by the CONUT score, but the requirement for hospitalization was more in the case of malnourished patients.

While the relationship between malnutrition, as measured by the MNA, and mortality among dementia patients has been examined, there is a lack of studies regarding the application of CONUT score in such patients. However, prior research has established that low levels of albumin, total cholesterol, and total lymphocyte counts are associated with increased mortality in the elderly [21, 22, 23]. Correlation between mortality and CONUT score has been evaluated in various patient populations and has been established as a prognostic factor [24, 25, 26]. In the present study, malnutrition, classified by the MNA-SF (≤ 7) and CONUT score (≥ 2), was independently associated with mortality, regardless of age or year of dementia diagnosis. The presence of malnutrition has been shown to be linked to more advanced dementia and increased risk of morbidity and mortality. Thus, assessment of nutritional status, one of the preventable risk factors in patients with dementia, and detection of malnutrition are mandatory [16, 21, 27].

Limitations

Limitations of the study include that this was a single-centre study, it was conducted from retrospective records, and the other pathologies present before death were not known. Prospective multicentre studies with larger sample sizes are needed.

Conclusion

In conclusion, malnutrition is prevalent in elderly patients with dementia. Although the CONUT score does not have a weight-based parameter in its definition of malnutrition, its correlation with BMI, three-month weight loss, and its association with mortality have been determined. The CONUT score therefore provides a viable and objective method of nutritional status evaluation, particularly in dementia where weight cannot be measured or is unavailable. Further prospective studies on larger patient populations are required to validate the use of the CONUT score in this patient population.

Conflict of interest: The authors declare no conflict of interest related to this article.

Author Contributions		Author Initials
SCD	Study Conception and Design	MY, HK
AD	Acquisition of Data	HK
AID	Analysis and Interpretation of Data	MY
DM	Drafting of Manuscript	MY
CR	Critical Revision	MY, HK

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