Analysis of the relationship between cognitive decline and physical function in older adults who participated in health measurement events using classification and regression tree (CART)

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博　士　論　文

Analysis of the relationship between cognitive decline and physical function in older adults who participated in health measurement events using classification and regression tree (CART)

（健康測定会に参加した高齢者の認知機能低下と身体機能に関する決定木分析）

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神戸大学大学院保健学研究科保健学専攻

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Abstract

Objective: Investigate various factors related to cognitive decline and analyze combination of factors and priority.

Methods and Results: We measured the demographic data, physical, cognitive and executive functions of 219 older adults who were divided into 2 groups (a no cognitive decline group and a cognitive decline group). We performed Classification and Regression Tree (CART) analysis using the cognitive decline as dependent variables.

Conclusions: By CART, it was revealed that the combination of walking speed ≥ 1.01 m/s and TMT-A ≥ 107.47 seconds is a combination of strongest factors for cognitive decline. The classification accuracy was 92.2% by CART.

Keywords

older adults, factor of cognitive decline, physical measurement, classification and regression tree

INTRODUCTION

With an increasing aging population in Japan, the prevalence of cognitive decline is also increasing every year. Cognitive decline affects not only older people themselves but also the lives of families and caregivers (physical, mental, economic, etc.)[1]. Therefore, preventing the decline of cognitive function is an important issue, and it is also important to identify people who are likely to experience a decline in cognitive function, in a stage prior to the onset of the decline.

Many studies have reported various factors related to cognitive decline such as age, educational history, drinking history, past medical history, diabetes, hypertension, executive function, and physical function[2-7]. Previous studies to ascertain the level of physical function have measured various items such as state of gait[8,9], walking speed[10-12], grip strength[5,12], standing balance[5,12], chair stands[5,12], and skeletal muscle mass index (SMI)[13,14]. However, these studies have reported only the independent relationship between each measurement item and cognitive decline by using a traditional linear regression analysis method such as the logistic regression model, and the quantification of the importance and priority of each related factor remains unknown. Furthermore, since many older adults in clinical settings and communities have both negative and positive cognitive decline factors, it's difficult to use the cut-off point of previous studies properly due to the interrelationship between factors[15]. Hence, it is necessary to perform analysis by integrating multiple factors of an individual.

Recently, several reports have used decision tree analysis as an analysis method to show the importance and priority of various factors[16,17]. Decision tree analysis has the advantage of being able to read the results in a flowchart, and to interpret them visually. In addition, this analysis can be used for determination of cut-points[16], relationship with each factor and the quantification of the importance and priority of factors[17], therefore this analysis is used for diagnosis judgment of disease and prediction of occurrence[15,18,19], planning of preventive strategies[18], and effect judgment[20]. In this study, decision tree analysis was used to evaluate and examine factors related to cognitive decline in a comprehensive way. This type of analysis may be able to more accurately predict cognitive decline.

Therefore, the purpose of this study was to examine the relationship between cognitive

decline and physical and executive function in community-dwelling older adults using classification and regression tree (CART) analysis, and to reveal the combination, importance, and priority of the many related factors of cognitive decline.

METHODS

Participants of Measurement Events

Physical and cognitive assessments were performed on community-dwelling older adults in Kobe from September to November 2015. There is no single definition of 'older adults' so in this study the minimum age was set at 65 years. To recruit participants, information leaflets and posters were given to neighborhood association leaders to post at community centers approximately two months before the testing session. The total number of participants was Two hundred eighty one community-dwelling adults. If a family member or caregiver accompanying a participating older adult also wanted to join the measurement events, he/she was accepted for measurements as a token of goodwill, even if their age was younger than 65 years. Therefore, the participants were aged from 25 to 92. Exclusion criteria for analysis were as follows: 1) less than 65 years old, 2) consent was not obtained, 3) all measurements were not performed completely, or 4) analysis data was missing. Two hundred and nineteen people met the criteria and were included in the analysis.

Information about this study was provided in writing to all the participants prior to starting the assessment, and all participants provided their informed consent. This study was approved by the XXXX University Graduate School of Health Sciences Health Ethical Committee.

Demographic Data

We assessed demographic data including age, gender, height, weight, educational history (number of years from elementary school to last institution of education), number of people living with the participant, alcohol consumption status (do not drink, rarely, sometimes, every day), history of falling, and comorbidities, using a self-administered questionnaire. A history of falling in the past 1 year was defined as "unintentionally coming to the ground or some lower level and other than as a consequence of sustaining a violent blow, loss of consciousness, sudden onset of paralysis as in stroke or an epileptic

seizure during the past 1 year"[23]. Comorbidities were evaluated by self-reported answers (hypertension, diabetes, stroke, hip osteoarthritis, knee osteoarthritis, spinal canal stenosis). These demographic data were written by the participants on their assessment-sheet.

Physical Measurements

We performed four physical tests: SMI, grip strength, the Timed Up and Go test (TUG), and the Short Physical Performance Battery (SPPB). Skeletal muscle of the trunk and the limbs was measured using the Inbody 430 medical-grade body composition analyzer (Biospace Co., Ltd., Seoul, Korea). Participants stood barefoot on two metal electrodes and held the left and right metal grip electrodes with both upper limbs. SMI was calculated using the following formula[24]: SMI (kg/m^2) = appendicular skeletal muscle mass index (kg) / height $(m)^2$. Grip strength was measured by a Smedley-Type Hand Dynamometer Grip D (Takei Kiki Kogyo, Tokyo, Japan). Measurements were carried out twice on the dominant hand and the maximum value of 2 trials was used for analysis. During the TUG[25], the time was measured from standing up from a chair with a height of approximately 45 cm with a backrest, walking around a cone 3 m away, and sitting down again. The measurement was taken, from the signal of the "Ready go" to the patient sits back down in the chair, and at a comfortable walking speed. The SPPB[26] is composed of three tasks: a hierarchical standing balance task (side-by-side stand, semi-tandem stand, tandem stand), a short walk at a comfortable speed, and five repetitive chair stands (5CS). In standing balance, the holding times of a side-by-side stand, semi-tandem stand, and tandem stand were measured. A side-by-side stand is a standing position with the inside of both feet in contact, a semi-tandem stand is a standing position where the inner side of the heel on the arbitrary side is in contact with the inner side of the toe on the opposite side. A tandem stand is a standing position with the heel on the arbitrary side and the toe on the opposite side in contact. The subjects started from the measurement of the semi-tandem stand, and if it was possible for subjects to hold the semi-tandem stand for 10 seconds, the position was shifted to a tandem stand measurement. If a subject could not hold the semi-tandem stand position for 10 seconds, we changed to a side-by-side stand measurement. To measure posture, the subjects gripped the measuring device and held the correct position until they were stable, then were asked to release their grip and

measurement began from the time the subject released their grip. For walking speed, each participant's comfortable walking speed was measured. The measurement section was set to 2.44 m (8-feet), and spare paths of 2 m were provided before and after the measurement section. An average time of 2 measurements was calculated and converted into a speed (m/s). In 5CS, we measured the time of five consecutive sit-to-stand actions from a chair sitting position, as quickly as possible with a chair with a seat height of approximately 45 cm with a backrest. If it was confirmed that the knee joint did not fully extend on standing or that the gluteal did not contact the seat surface during the sitting action, remeasurement was performed. The score of the SPPB was calculated according to the method of Guralnik et al[26] (12 points perfect score).

Cognitive and Executive Function Measurements

We measured a Mini Mental State Examination (MMSE), the Trail Making Test part A (TMT-A), and part B (TMT-B) as cognitive functions. The MMSE consists of 0 to 30 points by short-term memory registration and recall, attention, naming, following verbal commands, judgment, and copying a double pentagon. The subjects were divided into two groups by MMSE score. Participants with an MMSE score of ≥ 24 were defined as the 'no cognitive decline older adults' group (N-CD group) and MMSE scores of < 24 were defined as the 'cognitive decline older adults' group (CD group)[27,28]. The TMT was conducted in accordance with the report of Wagner et al[29]. The TMT consists of two parts: A and B. In the first part (TMT-A), subjects traced scattered numbers from 1 to 25 written in circle, as quickly as possible without lifting the pencil off the paper. In the second part of the test (TMT-B), subjects traced scattered circles with numbers and letters. The TMT-B contains 13 circles with numbering from 1 to 13, and 12 circles with letters A through L. Tracing the sequence proceeds from the first number to the first letter followed by the second number and the second letter. In this study, we used the Japanese version of the TMT-B by changing letters from the Roman alphabet to simple Japanese 'kana' characters. In both parts, we measured the time to trace all circles correctly. If participants made an error, the examiner indicated the error and directed the participant to correct the mistake and continue the task.

Statistical Analysis

Participants' assessment variables were analyzed using the student's t-test and χ^2 test.

CART analysis was used to divide participants on the dependent variable (N-CD group vs CD group) based on predictors identified from the univariate analyses. The significance level was set at $P < .05$. Univariate analysis was performed using IBM SPSS version 20, CART was performed using R Ver. 3. 0. 2, minimum size of end node = 5, depth = 3. CART methodology creates a hierarchical order of selecting predictors and determines their optimal cut-points that best classify participants into the dichotomous outcome groups. The analysis results in classification criteria and is represented as a hierarchical tree which facilitates simple interpretation and application in clinical settings.

RESULTS

One hundred and ninety three older participants were included in the N-CD group (88.1%) and 26 older participants were included in the CD group (11.9%). (The average MMSE score, N-CD group: 27.9 ± 1.8 score, CD group: 22.2 ± 2.1 score). The CD group had a significantly older age ($p = 0.003$), shorter education history ($p = .022$), many persons living together ($p = .028$), lower SMI ($p = .009$), and a higher prevalence of diabetes and hip OA (diabetes; $p < .001$, hip OA; $p < .05$) than the N-CD group. In physical measurements, the CD group had lower grip strength ($p = .0064$), slower speed of TUG, 5CS, walking speed, TMT-A and B ($p < .001$), shorter time of standing balance ($p < .001$), and lower score of SPPB ($p < .001$). Both the TMT-A and B scores were significantly lower in the CD group than in the N-CD group (Table 1).

CART identified 4 end nodes with 3 levels of partition and 3 partitioning variables. Selected variables were walking speed, the TMT-A, and the TUG test. Walking speed was the first determinant with a cut-point of 1.01 m/s (the proportion of walking speed < 1.01: N-CD group 40.7%, CD group 59.3%; the proportion of walking speed ≥ 1.01: N-CD group 94.8%, CD group 5.2%). Among participants in a less than 1.01 m/s subgroup, the TMT-A was the second determinant with a cut-point score of 107.47 seconds (the proportion of TMT-A ≥ 107.47: N-CD group 0%, CD group 100.0%; the proportion of TMT-A < 107.47: N-CD group 55.0%, CD group 45.0%). Among the participants with a TMT-A of less than 107.47 seconds, the TUG test was the third determinant with a cut-point score of 12.29 seconds (the proportion of TUG ≥ 12.29: N-CD group 41.7%, CD group 58.3%; the proportion of TUG < 12.29: N-CD group 75.0%, CD group 25.0%) (Fig

1). The classification accuracy was 92.2% table by CART (Table 2).

DISCUSSION

The purpose of this study was to investigate the importance and combination of each factor on the executive function and performance function related to cognitive decline in community-dwelling older adults using CART analysis. We entered related factors that were significantly correlated with cognitive decline into the analysis. The results showed that walking speed, the time of the TMT-A test and the time of TUG were more strongly related to cognitive decline in this order than other demographic, physical, or executive measurements. To our knowledge, this is the first study to examine the combination, importance, and priority of factors related to cognitive decline. This result could provide useful data to facilitate measurements for predicting cognitive decline.

Firstly, walking speed was chosen as the strongest factor related to cognitive decline. Many studies have reported the association between walking speed and cognitive decline. Tabbarah et al [12] reported a significant association with walking speed and cognitive function in a 7-year longitudinal examination of 70-79 year old persons. Michelle et al[30] investigated changes of cognitive functions and walking speed in community-dwelling elderly aged 70-89 years and showed that both cognitive function score and walking speed decreased with time. Furthermore, this study indicated that cognitive function declines as the walking speed becomes slower[30]. These results support our results, whereas few previous studies stated the priorities of exercise performance measurements associated with cognitive decline. The current study is the first to suggest that walking speed is the strongest factor to identify cognitive decline than other exercise performance measurements.

Secondly, the completion time of the TMT-A test was selected as a strong factor related to cognitive decline, whereas the TMT-B was not. Previous studies[31,32] which reported the association between cognitive decline and executive function showed that only the TMT-A, not B, was associated with cognitive decline. Patrick et al[31] examined the number and type of dysfunctions and related factors in elderly people with amnestic mild cognitive impairment (MCI), mild Alzheimer disease (AD), and non-dementia. As a result, cognitive decline is accompanied by a decrease of hippocampus volume and a decrease

of the TMT-A which is an evaluation index of processing speed. Sönke et al[32] conducted morphological cranial MRI scans and neuropsychological examinations on amnesic MCI, mild AD and non-demented persons aged 45-95 years, followed by tracking for approximately 2 years, and there was a significant decrease in the MMSE and the TMT-A in only mild AD. Regarding the association between cognitive decline and the TMT-A, the current study was consistent with previous studies[31,32]. On the other hand, Chen et al[33] reported that the TMT-B had a higher rate ratio to predict the detection of early AD than the TMT-A. Our results are inconsistent with that study. However, the difference of rate ratio between the TMT-A and B was slight (rate ratio: TMT-A 3.00 vs TMT-B 3.72). Therefore, further study might be needed to reveal which TMT is more useful to predict cognitive decline depending on the characteristics of subjects.

Finally, the time of the TUG test was selected as another strong factor related to cognitive decline. McGough et al[34] reported that physical performances such as time of the TUG test and walking speed were related to executive functions. A study[35] investigating the relationship of short-term memory ability and a movement test in community-dwelling elderly showed that a fast speed of walking and the TUG were related to cognitive impairment as defined by a three-word recall task of the MMSE. The current study is consistent with these previous reports. Regarding the priority between walking speed and TUG speed, Eggermont et al[36] investigated walking speed and the TUG test in older persons with MCI, AD and no cognitive impairment older persons, and showed that a 4 m walking speed was significantly lower in the MCI and AD groups than in no cognitive impairment persons, while the TUG result was significantly lower in the AD group than in the no cognitive impairment persons, but not in the MCI group. This result suggested that walking speed was more effective than the TUG test to identify cognitive impairment in the elderly. This study explains the difference of utility between the TUG test and walking speed to identify cognitive decline, therefore, the TUG test may be selected as a lower determinant than walking speed in this study.

The classification accuracy in this study was higher than the previous research[16,20,37], which was a very useful result. Compared to N-CD, CD group has older and lower educational background[3,4,6], living with living with many, diabetes[38] suffering a high proportion, SPPB (balance and grip strength) decrease[39] It was. As a reason for living

together, family caregiver is considered[40].
Although these results are consistent with previous studies, they were not identified as a cause of cognitive decline in analysis by CART.

The purpose of this study was to investigate the importance and combination of each factor on the executive function and performance function related to cognitive decline in community-dwelling older adults using CART analysis. We entered related factors that were significantly correlated with cognitive decline into a CART analysis. The results showed that walking speed, the time of the TMT-A test and the time of the TUG test were more strongly related to cognitive decline in this order than other demographic, physical, or executive measurements. To our knowledge, this is the first study to examine the combination, importance, and priority of factors related to cognitive decline. This result could provide useful data to facilitate measurements for predicting cognitive decline.

Limitations

This study identified factors related to cognitive decline and analyzed the combination (relevance) of each factor. The results of the current study may be useful as a screening tool for identifying cognitive decline in community-dwelling older adults. However, this study has some limitations. First, subjects of this study were voluntary participants, thus the results might be different in other older subjects such as patients in hospitals or facilities who could not voluntarily participate in measurements in this study. Second, because demographic data was written by the participants themselves, demographic data, in particular their medical history, might not be accurate. Third, this study was a cross-sectional study. Thus, we could not demonstrate the causal relationship of results. Fourth, although we selected only time of the TMT as an executive function, other executive function tests were not used. Therefore, longitudinal studies for this association may be necessary to develop this result. In addition, further studies examining participants in other place such as hospitals, facilities and so on, and adding other executive function tests such as the Digit Symbol Substitution Test, Letter Verbal Fluency Test, Category Verbal Fluency Test might be needed to generalize this result.

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Table 1. Characteristics of cognitive decline in community-dwelling older adults.

Variables	Mean (SD) or Number (%)		*P* value
	N-CD group (n = 193)	CD group (n = 26)	
MMSE, score	27.9 (1.8)	22.2 (2.1)	<.001[a]
Age, yr	72.4 (6.6)	76.6 (7.6)	.003[a]
Gender, male	56 (29.0)	6 (23.1)	.646[b]
Height, cm	155.9 (7.7)	152.8 (8.2)	.055[a]
Weight, kg	53.4 (9.0)	53.7 (9.7)	.871[a]
BMI, kg/m^2	22.0 (3.2)	22.7 (3.4)	.286[a]
Educational history, yr	12.2 (2.2)	11.1 (2.5)	.022[a]
Alcohol consumption status			.462[b]
not drink	99 (51.3)	13 (50.0)	
rarely	31 (16.1)	7 (26.9)	
sometimes	30 (15.5)	2 (7.7)	
every day	33 (17.1)	4 (15.4)	
History of falling, yes	36 (18.7)	9 (34.6)	.073[b]
No. of people living together	1.2 (0.9)	1.7 (1.1)	.028[a]
SMI, kg/m^2	7.6 (1.7)	6.5 (1.8)	.001[a]
Hypertension, yes	64 (33.2)	13 (50.0)	.124[b]
Diabetes, yes	14 (7.3)	6 (23.1)	.019[b]
Stroke, yes	3 (1.6)	2 (7.7)	.108[b]
Hip OA, yes	10 (5.2)	5 (19.2)	.021[b]
Knee OA, yes	26 (13.5)	4 (15.4)	.763[b]
Spinal canal stenosis, yes	13 (6.7)	4 (15.4)	.126[b]
Grip strength, kg	26.4 (6.9)	22.5 (6.8)	.006[a]
TUG, s	8.1 (2.0)	12.0 (4.2)	<.001[a]
5CS, s	8.2 (3.2)	10.9 (4.4)	<.001[a]
Tandem Standing Balance, possib	170 (88.1)	15 (57.7)	<.001[b]
Walking speed, m/s	1.4 (0.2)	1.0 (0.3)	<.001[a]
SPPB, score	11.6 (1.0)	10.5 (1.8)	<.001[a]
TMT-A, s	75.3 (25.6)	100.6 (43.3)	<.001[a]
TMT-B, s	110.7 (51.6)	157.7 (62.6)	<.001[a]

Abbreviations: N-CD group, no cognitive decline older adults group; CD group, cognitive decline older adults group; MMSE, Mini Mental State Examination; BMI, Body Mass Index; SMI, Skeletal muscle Mass Index; OA, osteoarthritis; TUG, Timed Up and Go Test; 5CS, 5 Chair Stand; SPPB, Short Physical Performance Battery; TMT-A, Trail Making Test partA; TMT-B, Trail Making Test partB.

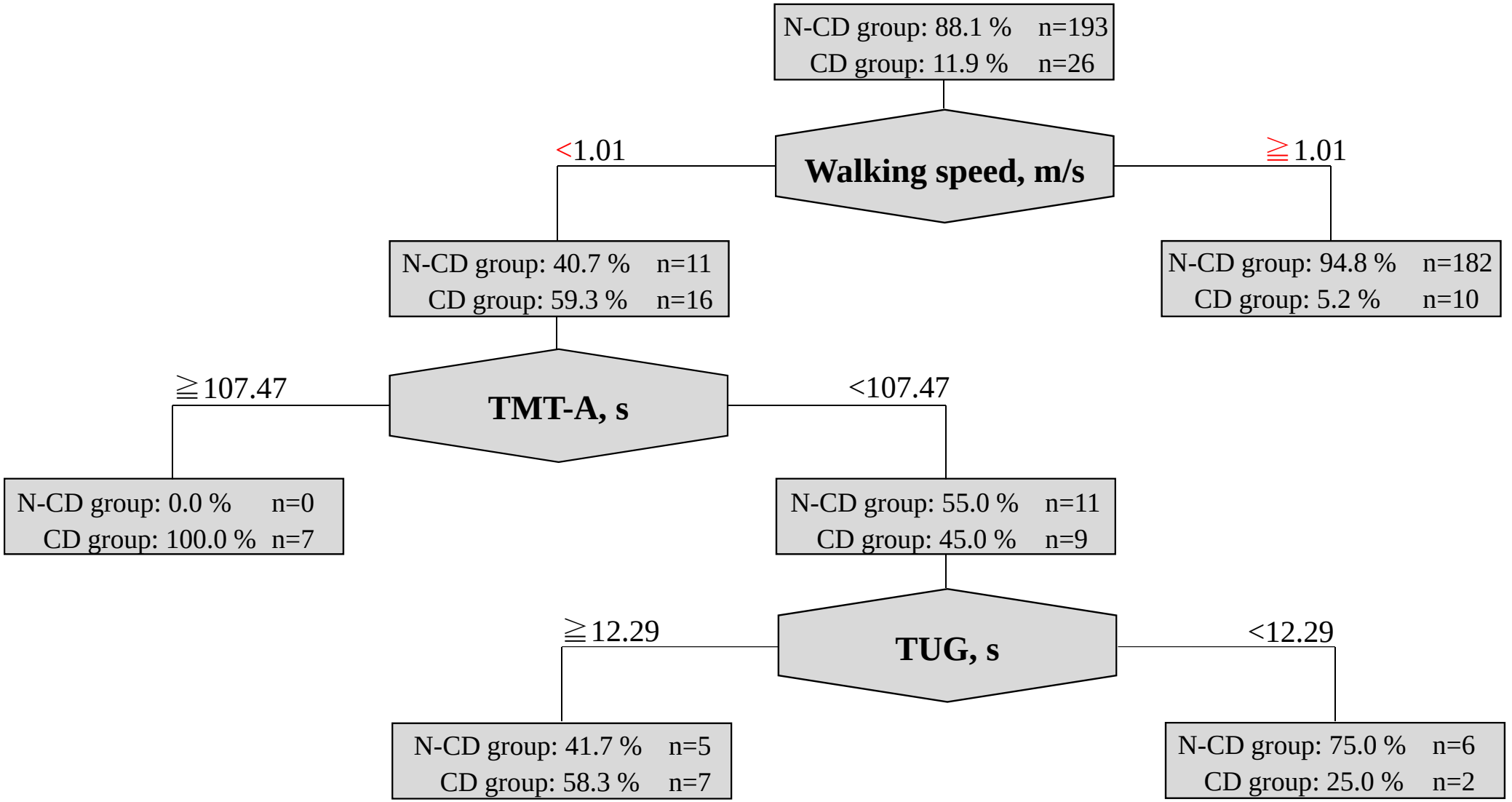
[a]student's t-test

[b]χ^2 test

Table 2. Misclassification Table for Persons with Impaired Cognitive Decline

		Actual no. of Participants		
		MMSE < 24	**MMSE ≧24**	**Total**
Predicted no. of Participants	**MMSE < 24**	14	5	19
	MMSE ≧24	12	188	200
	Total	26	193	219

Abbreviations: MMSE, Mini Mental State Examination.
risk estimate = 0.078 (classification accuracy = 0.922)
standard error of risk estimate = 0.19



Abbreviationsno: N-CD group, cognitive decline older adults group; CD group, cognitive decline older adults group; TUG, Timed Up and Go Test; TMT-A, Trail Making Test partA

Figure 1. Extraction of factors related to cognitive decline by classification and regression tree.