

# Investigation of the relationship between upper limb apraxia and neuropsychological profile in Alzheimer's disease dementia and mild cognitive impairment

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## ABSTRACT

**Objectives:** This study aimed to examine the differences in upper limb apraxia assessments and neuropsychological profiles of patients diagnosed with Alzheimer's disease (AD) dementia and mild cognitive impairment (MCI) and healthy controls.

**Patients and methods:** A total of 53 participants were included in the retrospective study, including nine patients with MCI, 23 patients diagnosed with AD, and 21 healthy patients equivalent in age and education level. The participants' data were collected between July 2021 and December 2022. A 12-question mini-test taken from the Test of Upper Limb Apraxia (TULIA) was used in the apraxia evaluation. Individuals' upper limb apraxia evaluations were compared according to diagnostic groups, and their neuropsychological profiles were also examined.

**Results:** Apraxia was found to be associated with impairments in memory retrieval function, executive dysfunction, and decrease in object naming performance. Significant differences were observed between diagnostic groups in both apraxia assessment and neuropsychological tests.

**Conclusion:** The findings indicate that the cognitive profile that emerges with the combined use of upper extremity apraxia assessment and related neuropsychological tests may serve as a marker and guide in the planning and correct execution of treatment in the transition to Alzheimer-type dementia, similar to other neuropsychological tests.

**Keywords:** Alzheimer disease, apraxia, dementia, mild cognitive impairment, neuropsychology.

The term apraxia, used to describe problems in planning and executing movements resulting from neurological dysfunction, was first introduced by Steinthal in 1881.<sup>[1]</sup> Today, it is commonly defined as an impairment in the ability to move that does not arise from weakened motor performance due to weakness, sensory loss, ataxia, akinesia, bradykinesia, hypometria, tremor, dystonia, chorea, ballismus, athetosis, or myoclonus.<sup>[2]</sup> Apraxia has many classifications and specific types, including well-known forms such as ideational apraxia, conceptual apraxia, ideomotor apraxia, limb-kinetic apraxia, constructional apraxia, and

conduction apraxia.<sup>[3]</sup> Limb apraxia refers to the impairment in the ability to perform learned skilled movements resulting from neurological damage, which cannot be explained by primary motor and sensory deficits, problems in understanding tasks, or object recognition disorders.<sup>[1,3,4-7]</sup> There are four main forms of upper limb apraxia: ideomotor, limb-kinetic, conceptual, and ideational apraxia.<sup>[8]</sup> The measurement tools recently used to assess apraxia are as follows: the Test of Upper Limb Apraxia (TULIA);<sup>[9]</sup> its short version, Apraxia Screen of TULIA (AST); DEKODa apraxia test;<sup>[10]</sup> Evaluation of Upper Limb Apraxia (EULA);<sup>[11]</sup> and

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Dementia Apraxia Test (DATE).<sup>[12]</sup> Test of Upper Limb Apraxia and AST have been adapted for Turkish.<sup>[13,14]</sup>

Limb apraxia can occur following neurological damage, stroke, or neurodegenerative diseases, and it can also manifest from the early stages of neurodegenerative diseases.<sup>[15]</sup> A substantial portion of the research on apraxia has been conducted on patients with stroke.<sup>[16]</sup> Although it is stated that apraxia can emerge in the early phases of neurodegenerative diseases, apraxia remains an underresearched area in neurodegenerative diseases compared to other cognitive functions.<sup>[17]</sup> Therefore, examining the presentation of apraxia in neurodegenerative diseases where cognitive function losses are observed is considered to be crucial.

Alzheimer's disease (AD) is a neurodegenerative disease that leads to a progressive impairment of cognitive functions with amnesia in the forefront, behavioral issues, and presenting as dementia with the loss of daily functionality in patients.<sup>[17]</sup> In addition to amnesic losses, other cognitive issues such as executive function disorders, agnosia, aphasia, and apraxia also emerge during the course of the disease.<sup>[18,19]</sup> While there are numerous studies on the cognitive losses accompanying AD, research on apraxia is limited.

The National Institute on Aging–Alzheimer's Association (NIA-AA) updated the diagnostic criteria for AD in 2011, incorporating neuropsychological tests, advanced imaging methods, and cerebrospinal fluid analysis.<sup>[20]</sup> Apraxia, which has an insidious onset, gradually worsening over months or even years and accompanied by significant memory losses, was included in the diagnostic criteria established by the NIA-AA in 1981 and updated in 2011.<sup>[18,21]</sup>

In the literature, it has been observed that scores from apraxia screening tests, when compared with healthy controls, successfully detect the early stages of neurodegenerative diseases such as AD and that there are significant impairments in the patients' ability to mimic hand and finger postures.<sup>[21]</sup> Although some apraxia tests were originally designed for patients with stroke, they were also applied to patients with dementia, yielding reliable results for mild cognitive impairment (MCI) and AD.<sup>[22]</sup> A limb and facial praxis tool developed to support the differential diagnosis of dementia demonstrated high diagnostic accuracy in detecting early-stage AD in elderly patients.<sup>[16]</sup>

Examining the relationship between neuropsychological test scores that play a crucial

role in the diagnostic process and apraxia scores is vital in understanding how neuropsychological manifestations and apraxia scores differ according to diagnoses. As studies have shown, both neuropsychological tests and the mentioned apraxia tests aid the diagnostic process in pathological conditions accompanied by cognitive problems. However, studies exploring the relationship between apraxia and neuropsychological tests are limited.

In light of this information, studies that explore the relationship between AD, including memory and other cognitive function issues, and apraxia could contribute to the literature by clarifying this relationship. Hence, this study aimed to examine and reveal the differences in upper limb apraxia assessments and neuropsychological profiles of patients diagnosed with AD and MCI and healthy controls.

## PATIENTS AND METHODS

The retrospective study utilized data from patients diagnosed with MCI and AD and healthy individuals who applied to the neurology outpatient clinic of the SABITA (Health Science and Technology Research Institute)-fiNCAN Laboratory and underwent neuropsychological assessments in the hospital's neuropsychology laboratory between July 2021 and December 2022. The analysis of the collected data was conducted between January 2023 and February 2023. The MCI patients were the amnesic type. The study included nine patients with MCI, 23 patients with AD, and 21 healthy volunteers matched for age and education level, for a total of 53 participants. Participants with alcohol/substance dependence or intellectual disability were not included in this study. The diagnosis of MCI was based on the criteria proposed by Petersen et al.,<sup>[23]</sup> whereas the AD diagnosis was made in accordance with the recommendations of the NIA-AA Workgroups<sup>[20]</sup> by the neuropsychological and clinical assessments of an expert neurologist. The data for the neuropsychological tests and apraxia assessments were collected by three psychologists.

Participants' demographic information was collected from the hospital's patient tracking system, while neuropsychological data were gathered from the neuropsychological test battery registered in the neuropsychology laboratory. The neuropsychological tests administered to participants and used in the study include the following: Wechsler Memory Scale (WMS)-

Revised forward and backward digit span, category naming verbal fluency, and K-A-S verbal fluency, fruit-name counting, Boston Naming Test (BNT) spontaneous naming, Standardized Mini-Mental State Examination (SMMT), Geriatric Depression Scale, Beck Depression Inventory, WMS immediate and long-term visual memory, WMS immediate and long-term logical memory, Verbal Test of Memory Processes (VTMP)-Immediate Memory, VTMP-Total Learning, VTMP-Delayed Recall, and VTMP-Retention, Stroop test, clock drawing test, face recognition test, and the judgement of line orientation test.

In this study, the mini-test used for apraxia assessment consists of 12 questions taken from the TULIA, which was validated and shown to be reliable in Turkish.<sup>[13]</sup> The test was divided into three categories, each containing four questions covering nonsymbolic movements, symbolic movements, and imitation of object use. The reason for selecting these categories and questions is based on clinical observations, believing that they can effectively reflect upper limb apraxia during neuropsychological evaluation and provide a practical assessment. This tool lacked a cutoff value or normative table and was intended for practical clinical observation, and the total scores obtained were considered in the evaluation.

### Statistical analysis

The required sample size was determined through power analysis with the G\*Power version 3.1 (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany), considering a one-way analysis of variance for three groups. The power analysis established that the current study required at least a total of 42 participants, with a power of

0.80, an alpha error value of 0.05, and an effect size of 0.5. Data from 53 individuals was used in the study.

Data were analyzed using IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). All data were reviewed for missing and outlier values, and descriptive statistics were expressed as mean  $\pm$  standard deviation (SD) or frequency. The adherence of variables to normal distribution was assessed with the Kolmogorov-Smirnov test, and nonparametric tests were employed due to the absence of normal distribution. The Kruskal-Wallis test was used for variance analysis. Complementary comparison techniques were implemented to determine the groups with significant differences, and the Mann-Whitney U test was preferred for pairwise comparisons. Spearman correlation analysis was utilized to examine correlations.

### RESULTS

Apraxia scores statistically significantly differed according to diagnostic subcategories ( $\chi^2=12.650$ ,  $p=0.002$ ). Significant statistical differences were found between the AD and MCI groups ( $p=0.027$ ), as well as the AD and healthy control groups ( $p=0.001$ ). Examining the rank means, it was observed that the AD group scored significantly lower than both the MCI and healthy control groups. No significant difference was observed between the MCI and healthy control groups ( $p=0.748$ , Table 1).

In the neuropsychological assessment of the sample, statistically significant differences were found according to the diagnosis variable in the following evaluations: backward digit span, category naming, K-A-S, fruit-name counting, BNT spontaneous naming, SMMT, WMS immediate

**TABLE 1**  
The comparison of apraxia assessments according to diagnosis subcategories

Groups	n	Mean rank	Kruskal-Wallis-H test	SD	<i>p</i>
AD	23	18.48	12.650	4.55	<b>0.002*</b>
MCI	9	32.06			
Control	21	34.17			
Diagnosis	Groups	Mean rank	Mann-Whitney U test	<i>z</i>	<i>p</i>
AD × MCI	AD × MCI	AD=14.22 MCI=22.33	51.000	-2.209	<b>0.027*</b>
	AD × Control	AD=16.26 Control=29.33	98.000	-3.395	<b>0.001*</b>
	MCI × Control	MCI=14.72 Control=15.83	87.500	-0.322	0.748

SD: Standard deviation; AD: Alzheimer's disease; MCI: Mild cognitive impairment; \*  $p<0.05$ .

**TABLE 2**  
The comparison of neuropsychological assessments according to diagnosis subcategories

Neuropsychological test	Groups	n	Mean rank	Kruskal-Wallis-H test	SD	<i>p</i>
Forward digit span	AD	23	26.61	0.132	1.17	0.936
	MCI	9	26.00			
	Control	21	27.86			
Backward digit span	AD	23	19.04	12.082	1.08	0.002*
	MCI	9	32.06			
	Control	21	33.55			
Category naming	AD	23	18.39	14.748	6.77	<b>0.001**</b>
	MCI	9	27.39			
	Control	21	36.26			
K-A-S	AD	23	17.67	15.516	13.6	<b>0.000**</b>
	MCI	9	30.61			
	Control	21	35.67			
Fruit-name counting	AD	23	15.33	23.746	3.03	<b>0.000**</b>
	MCI	9	33.94			
	Control	21	36.81			
BNT spontaneous	AD	23	17.20	16.808	5.66	<b>0.000**</b>
	MCI	9	32.17			
	Control	21	35.52			
SMMT	AD	23	13.46	31.823	4.66	<b>0.000**</b>
	MCI	9	34.89			
	Control	21	38.45			
Geriatric Depression Scale	AD	23	24.55	2.158	5.58	0.340
	MCI	9	17.44			
	Control	21	20.50			
Beck Depression Inventory	AD	23	1.00	3.559	10.6	0.169
	MCI	9	3.00			
	Control	21	6.38			
WMS immediate visual	AD	23	13.65	31.201	4.26	<b>0.000**</b>
	MCI	9	33.94			
	Control	21	38.64			
WMS long-term visual	AD	23	14.98	25.463	4.73	<b>0.000*</b>
	MCI	9	35.28			
	Control	21	36.62			
WMS immediate logical	AD	23	16.04	21.014	4.95	<b>0.000***</b>
	MCI	9	32.56			
	Control	21	36.62			
WMS long-term logical	AD	23	15.30	26.271	5.68	<b>0.000**</b>
	MCI	9	28.72			
	Control	21	39.07			
VTMP-immediate memory	AD	23	18.78	14.717	1.90	<b>0.001**</b>
	MCI	9	26.11			
	Control	21	36.38			

**TABLE 2**  
Continued

Neuropsychological test	Groups	n	Mean rank	Kruskal-Wallis-H test	SD	<i>p</i>
VTMP-total learning	AD	23	15.09	28.694	27.4	0.000**
	MCI	9	27.00			
	Control	21	40.05			
VTMP-delayed recall	AD	23	15.87	26.809	5.15	0.000**
	MCI	9	25.50			
	Control	21	39.83			
VTMP-retention	AD	23	13.78	31.863	3.77	<b>0.000**</b>
	MCI	9	34.22			
	Control	21	38.38			
Stroop error score	AD	10	24.20	4.4062	5.59296	<b>0.004*</b>
	MCI	8	15.75			
	Control	14	11.43			
Clock drawing	AD	17	11.24	2.8889	1.17207	<b>0.000**</b>
	MCI	11	29.41			
	Control	17	30.62			
Face recognition	AD	17	21.06	12.0930	16.44879	0.553
	MCI	10	25.75			
	Control	16	20.66			
Line orientation	AD	13	12.58	13.2368	9.29526	<b>0.016*</b>
	MCI	9	20.78			
	Control	16	24.41			

SD: Standard deviation; AD: Alzheimer's disease; MCI: Mild cognitive impairment; BNT: Boston Naming test; SMMT: Standardized Mini-Mental State Examination; WMS: Wechsler Memory Scale; VTMP: Verbal Test of Memory Processes; \*  $p < 0.05$ .

visual, long-term visual, immediate logical, and long-term logical memory, VTMP-Immediate Memory, VTMP-Total Learning, VTMP-Delayed Recall, and VTMP-Retention, Stroop error score, clock drawing, and line orientation tests ( $p < 0.05$ ). The forward digit span, face recognition, Geriatric Depression Scale, and Beck Depression Inventory did not demonstrate differences based on the diagnostic variable ( $p > 0.05$ , Table 2).

Significant differences ( $p < 0.05$ ) were found between the AD and MCI groups in backward digit span ( $p = 0.008$ ), K-A-S ( $p = 0.022$ ), fruit-name counting ( $p = 0.001$ ), BNT spontaneous naming ( $p = 0.007$ ), WMS immediate logical ( $p = 0.002$ ) and long-term logical ( $p = 0.005$ ) memory, VTMP-Total Learning ( $p = 0.004$ ), and VTMP-Delayed Recall ( $p = 0.022$ ). Furthermore, highly significant differences ( $p < 0.001$ ) were observed in clock drawing ( $p = 0.000$ ), SMMT ( $p = 0.000$ ), WMS immediate visual ( $p = 0.000$ ) and long-term visual ( $p = 0.000$ ) memory, and VTMP-Retention ( $p = 0.000$ ).

No significant differences ( $p > 0.05$ ) were observed in category naming ( $p = 0.067$ ), VTMP-Immediate Memory ( $p = 0.108$ ), Stroop error score ( $p = 0.061$ ), face recognition ( $p = 0.363$ ), and line orientation ( $p = 0.061$ ). Across all tests, patients with AD scored lower than those with MCI.

Significant differences were found in neuropsychological test scores between AD patients and healthy controls in the backward digit span ( $p = 0.002$ ). Highly significant differences ( $p < 0.001$ ) were also found in K-A-S, fruit-name counting, BNT spontaneous naming, WMS immediate and long-term logical memory, VTMP-Total Learning, VTMP-Delayed Recall, clock drawing, SMMT, WMS immediate and long-term visual memory, and VTMP-Retention (all  $p = 0.000$ ). No significant difference ( $p > 0.05$ ) was observed in the face recognition test ( $p = 0.942$ ). Patients with AD scored lower than healthy controls across all tests in which significant differences were found.

**TABLE 3**  
Correlation between apraxia scores and neuropsychological tests

	Correlation coefficient	Significant
Forward digit span	-0.050	0.724
Backward digit span	0.193	0.166
Verbal fluency-category naming	0.334*	0.014
Verbal fluency-K-A-S	0.409**	0.002
Verbal fluency-fruit-name counting	0.522**	0.000
BNT spontaneous	0.327*	0.017
SMMT	0.481**	0.000
Geriatric Depression Scale	0.040	0.801
Beck Depression Inventory	0.342	0.334
WMS immediate visual	0.631**	0.000
WMS long-term visual	0.494**	0.000
WMS immediate logical	0.237	0.087
WMS long-term logical	0.310*	0.024
VTMP-Immediate memory	0.170	0.222
VTMP-total learning	0.342*	0.012
VTMP-delayed recall	0.415**	0.002
VTMP-retention	0.459**	0.001
Stroop error score	0.535**	0.002
Clock drawing	0.406**	0.006
Face recognition	0.079	0.613
Line orientation	0.102	0.543

BNT: Boston Naming test; SMMT: Standardized Mini-Mental State Examination; WMS: Wechsler Memory Scale; VTMP: Verbal Test of Memory Processes; \* p<0.05; \*\* p<0.01.

Significant differences ( $p<0.05$ ) were found in neuropsychological test scores between patients with MCI and healthy controls in the WMS long-term logical memory ( $p=0.018$ ), VTMP-Immediate Memory ( $p=0.036$ ), VTMP-Total Learning ( $p=0.002$ ), and VTMP-Delayed Recall ( $p=0.002$ ). No significant differences were observed in other tests ( $p>0.05$ ). Patients with MCI scored lower than healthy controls in the tests where differences were observed.

The correlation between apraxia scores and neuropsychological test results was examined, and significant correlations ( $p<0.05$ ) were found in verbal fluency-category naming, BNT spontaneous naming, WMS long-term logical memory, and VTMP-Total Learning. Furthermore, highly significant correlations ( $p<0.01$ ) were observed in verbal fluency-K-A-S, fruit-name counting, SMMT, WMS immediate visual and long-term visual memory, VTMP-Delayed Recall, VTMP-Retention, Stroop error score, and clock

drawing. The correlation between the Stroop error score and apraxia score was negative (Table 3).

## DISCUSSION

In this study, a comparison of upper limb apraxia assessments among individuals diagnosed with AD, MCI, and healthy controls was conducted, and the relationships between upper limb apraxia and neuropsychological tests were examined. The results demonstrated that apraxia scores significantly differed among the three groups. The difference was more pronounced between the AD and healthy control groups. However, no significant difference was observed between the MCI and healthy control groups. The results are consistent with other studies that revealed significant differences in apraxia assessments between AD, MCI, and healthy controls.<sup>[10,12,16,21,22,24,25]</sup>

Studies in the literature report that apraxia can be observed from the early stages of MCI and AD,<sup>[26]</sup>

that one out of 10 patients with MCI and more than one out of three patients with AD present with apraxia, and that as the severity of dementia increases, the risk of apraxia rises.<sup>[22]</sup> Furthermore, results from tasks related to tool use suggest that both the sensorimotor knowledge required for tool manipulation and the semantic knowledge about the tool's function are impaired from the early stages of AD.<sup>[27]</sup> Mechanical knowledge, production systems, and topographic information may be preserved in the early and middle stages of AD.<sup>[28]</sup> Although various studies exist in this area, more research is needed on the apraxia profiles observed in AD and MCI.

The present study found significant differences in apraxia scores between the AD and MCI groups, as well as the AD and healthy control groups, while no significant difference was observed between patients with MCI and healthy controls. This suggests that apraxia could be a neuropsychological parameter that appears in the transition to Alzheimer-type dementia, or it may arise alongside the global deterioration observed in AD.

Analyses conducted to determine how neuropsychological evaluations differed according to diagnostic subgroups revealed significant differences in all tests, except for the digit span, face recognition, Geriatric Depression Scale, and Beck Depression Inventory. This differentiation was significant in all tests, except for category naming, VTMP-Immediate Memory, error score, face recognition, and line orientation tests, and highly significant for clock drawing, SMMT, WMS immediate visual and long-term visual memory, and VTMP-Retention scores between the AD and MCI groups. Neuropsychological test scores were significantly different in all tests between the AD and healthy control groups, except for the face recognition test. This differentiation was significant in the backward digit span and highly significant in all other tests. Significant differences were observed only in the WMS long-term logical, VTMP-Immediate Memory, VTMP-Total Learning, and VTMP-Delayed Recall scores between the MCI and healthy control groups.

A review of the literature reveals no recent study examining the neuropsychological profile accompanying upper limb apraxia, particularly in conjunction with other cognitive functions. Additionally, in a study involving patients with corticobasal degeneration (CBD), both with and without apraxia, no significant differences were found

between the two groups in apraxia performance scores and executive functions.<sup>[29]</sup> Furthermore, no significant differences were observed between the two groups in other neuropsychological tests such as the Wisconsin Card Sorting Test, trail making test, Stroop test, digit span, and verbal fluency tests. In our study, the correlation between apraxia scores and neuropsychological tests was examined. The findings are partially consistent with a study demonstrating that apraxia is associated with cognitive functions such as aphasia, memory, and mental slowing.<sup>[30]</sup> However, research in this area is limited, and more studies are required for more definitive interpretations.

In dementia, reduced gray matter volume at the right temporo-occipito-parietal junction is associated with problems in pantomiming.<sup>[31]</sup> The errors observed in pantomime tasks among dementia patients are predominantly movement-orientation errors, which occur in conjunction with a decline in visuospatial performance.<sup>[15]</sup> Errors in praxis due to movement-orientation arise when the movement is not synchronized with the spatial position of the limb. However, in our study, no significant correlation was found between apraxia scores and the scores from the line orientation and face recognition tests. These findings contradict the information available in the literature.

When the correlation between the measured apraxia scores and other neuropsychological tests were examined, significant correlations were found in verbal fluency-category naming, BNT spontaneous naming, WMS long-term logical memory, and VTMP-Total Learning, with highly significant correlations in K-A-S verbal fluency, fruit-name counting, SMMT, WMS immediate visual and long-term visual memory, VTMP-Delayed Recall, VTMP-Retention, Stroop error score, and clock drawing. The correlation between the Stroop error score and apraxia score was negative. Patients with AD predominantly experience losses in memory, as well as in attention, executive functions, constructional skills, and performance in object naming and understanding, and these losses are associated with limb apraxia.<sup>[32]</sup> The losses in these cognitive areas are related to the ability to perform movements with the correct sequence, manipulation, and comprehension, as well as losses in action semantics or impairments in object naming if a tool-based praxis performance is to be demonstrated.

The limitations of the study include its retrospective nature, the absence of staging in AD



patients, the limited sample size, and the failure to consider coexisting cerebrovascular diseases and intracranial lesions that could cause apraxia as exclusion criteria. In addition, the use of a mini-test derived from the TULIA test for measuring apraxia and the lack of neuroimaging findings are among the limitations. Future studies are recommended to establish more rigorous exclusion criteria, work with a larger sample group, include various measurement tools, and incorporate neuroimaging findings. Additionally, longitudinal studies examining the apraxia profile in AD alongside neuropsychological tests are considered important.

In conclusion, this study found apraxia to be associated with impairments in memory retrieval, executive function disorders, and a decline in object naming performance. Additionally, significant differences were observed in apraxia and neuropsychological tests in both of the patient groups compared to healthy controls. This suggests that while it may not be helpful in the early stages, the cognitive profile revealed through the combined use of upper limb apraxia assessments and related neuropsychological tests can serve as a marker and guide in distinguishing diagnoses, planning treatment, and guiding its proper execution similar to other neuropsychological tests. This study contributes to the literature by examining upper limb apraxia alongside the neuropsychological profiles of patients within the context of AD and MCI. Future studies examining apraxia together with neuropsychological tests in other types of dementia where cognitive functions are impaired are crucial in understanding impairments in praxis skills and the development of potential treatment methods.

**Ethics Committee Approval:** The study protocol was approved by the İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee (date: 05.01.2023, no: 06). The study was conducted in accordance with the principles of the Declaration of Helsinki.

**Patient Consent for Publication:** A written informed consent was obtained from each patient.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Author Contributions:** Idea/concept, design, control/supervision, data collection and/or processing, analysis and/or interpretation, literature review, writing the article, critical review, references and fundings, materials: S.Ş., İ.D.; Statistical analysis: L.H., E.Y.

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