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European Journal of Physical and Rehabilitation Medicine 2024 April;60(2):340-8
DOI: 10.23736/S1973-9087.24.08203-0

ORIGINAL ARTICLE

Cognitive assessment to optimize prediction of functional outcome in subacute hip fracture: a short-term prospective study

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ABSTRACT

BACKGROUND: Cognitive impairment is a long-known negative prognostic factor after hip fracture. Cognition is usually screened by a single easy-to-administer bedside tool, but recent studies have shown that screening tests may be not enough to rule out cognitive impairment with an unfavorable prognostic role. Unfortunately, data on outcome prediction by further cognitive assessments is sparse.
AIM: We focused on patients with subacute hip fracture defined cognitively intact or mildly impaired on the screening evaluation performed by the Short Portable Mental Status Questionnaire (SPMSQ). We hypothesized that each of 3 further cognitive tests could independently predict activities of daily living, with optimal prediction of function obtained by performing all three the tests.
DESIGN: Short-term prospective study.
SETTING: Rehabilitation ward.
POPULATION: Inpatients with subacute hip-fracture.
METHODS: Three cognitive tests were performed on admission to rehabilitation in the patients who made ≤4 errors on the SPMSQ: Montreal Cognitive Assessment (MoCA), Rey Auditory Verbal Learning Test (RAVLT, immediate and delayed recall) and Frontal Assessment Battery (FAB). We assessed activities of daily living by the Barthel index. Successful rehabilitation was defined with a Barthel Index Score ≥85.
RESULTS: Each of the three cognitive tests assessed before rehabilitation significantly predicted the Barthel index scores measured at the end of the rehabilitation course in our sample of 280 inpatients. However, only the MoCA score retained its significant predictive role when the scores from the three tests were included together as independent variables in a multiple regression model, with adjustments for a panel of potential confounders (P=0.007). The adjusted odds ratio to achieve successful rehabilitation for a seven-point change in MoCA score was 1.98 (CI 95% from 1.02 to 3.83; P=0.042).
CONCLUSIONS: Contrary to our hypothesis, MoCA but not RAVLT and FAB retained the prognostic role when the scores from the three tests were evaluated together as potential predictors of functional ability in activities of daily living.
CLINICAL REHABILITATION IMPACT: In the presence of a normal (or mildly altered) score on the SPMSQ in subacute hip fracture, MoCA scores improve prediction of activities of daily living and should be routinely performed.

(*Cite this article as:* Di Monaco M, Sgarbanti M, Trombetta S, Gullone L, Bonardo A, Gindri P, *et al.* Cognitive assessment to optimize prediction of functional outcome in subacute hip fracture: a short-term prospective study. Eur J Phys Rehabil Med 2024;60:340-8. DOI: 10.23736/S1973-9087.24.08203-0)

KEY WORDS: Activities of daily living; Cognitive dysfunction; Hip fractures.

Recent prospective studies have emphasized the long known unfavorable prognostic role exerted by cognitive impairment after hip fracture in older people. Impaired cognition has been significantly associated with high mortality rates,[1, 2] increased risk of recurrent fractures and prosthetic hip dislocations,[3, 4] blunted ability to function in activities of daily living,[5, 6] impaired mobility,[7] low likelihood of discharge home and reduced number of days alive and at home, a combined patient-centered outcome measure.[8, 9] The recent results are in agreement with a lot of previous original studies and various systematic reviews: on the whole, the wider literature has consistently reported poor outcomes in cognitively impaired subjects with a fragility fracture of the hip.[10-12] Notably, the presence of cognitive impairment has been associated with poor outcomes independently of many potential confounders.[13]

The most common way to assess cognition is the bedside administration of a single short test with simple and dichotomous interpretation rules: screening tests as the Mini Mental State Examination (MMSE) and the Short Portable Mental Status Questionnaire (SPMSQ) are easy-to-administer and categorize the patients as either intact or impaired.[14-17] The screening tests have 2 major strengths: high feasibility and demonstrated prediction of relevant outcome measures.[18-23] However, 2 important issues regarding cognitive assessment have been scarcely investigated in patients recovering from a fracture of the hip. First, the capability of a "normal" score on a screening test to rule out all the cognitive deficiencies with a prognostic disadvantage is questionable: several cognitive domains which may theoretically have relevant prognostic implications are not assessed by the screening tools. Secondly, the best cognitive tests that may optimize prediction of relevant outcomes beyond screening tools have not been identified.

A very recent study has investigated the prognostic role of 3 further tests in women with subacute hip fracture with no more than 4 errors on the SPMSQ: each of the three tests, Montreal Cognitive Assessment (MoCA), Frontal Assessment Battery (FAB) and Rey Auditory Verbal Learning Test (RAVLT) has proven to predict functional ability in activities of daily living in the women with no obvious cognitive impairment on the screening test.[24] Unfortunately, the independence of the three tests from each other and/or the best test of the 3 to predict function have not been investigated.

We focused on inpatients with subacute hip fractures classified as "cognitively intact" or "mildly impaired" on the SPMSQ. Our aim was to investigate the capability of MoCA, FAB and RAVLT to predict activities of daily living. We hypothesized that each of the three tests could independently exert a prognostic role with optimal prediction of function gained by performing all three the tests.

Materials and methods

Patients

We assessed for eligibility inpatients with subacute hip fracture admitted consecutively to our rehabilitation division during a 24-month period. The patients who made more than four errors on the SPMSQ performed within 24 hours after admission to our rehabilitation ward were excluded from the study, because of overt cognitive impairment. All the patients underwent surgery (either hip arthroplasty or internal fixation) and were referred for inpatient rehabilitation during their stay in the orthopedic ward by consultant physiatrists. The agreed upon criteria for referring the patients to undergo subacute inpatient rehabilitation were as follows: a presumptive high recovery of function in basic activities of daily living and an expected good adherence to an individual rehabilitation project including a total of three hours of physical therapy and/or occupational therapy daily. The median (interquartile range) length of stay in the rehabilitation ward was 36 (from 29 to 41) days. We excluded the patients whose fractures were caused by either major trauma (trauma energy higher than the one due to a fall from a standing position) or bone cancer and those with no weight bearing on the surgical treated lower limb. The study was conducted in accordance with the principles set forth in the Helsinki Declaration. All the patients included in the final sample gave their written informed consent to participate in the study. IRB approval was obtained for the study protocol (Ethical Committee from City of Health and Science from our city).

Assessments

Skilled physiatrists performed the Barthel Index (original version) to assess functional ability in basic activities of daily living both at admission to rehabilitation and at discharge from the rehabilitation division. The Barthel Index was also used to estimate the anamnestic pre-fracture level of functional autonomy by interviewing patients and caregivers. The Barthel Index score ranges from 0 (full dependence) to 100 (full independence). In the absence of a threshold universally agreed on to identify functional autonomy, we defined successful rehabilitation with a Bar-

thel Index score ≥85 in agreement with several reports.[25-27] At the time of Barthel Index assessment the physiatrists were not aware of the results of the cognitive evaluation.

The SPMSQ was performed as the screening test to assess cognition. It consists of 10 questions on orientation for place and time, personal information, long-term memory and serial subtraction. We adjusted the SPMSQ score for school education levels. All the patients with ≤4 errors on the SPMSQ completed the cognitive assessment by performing three further tests: Montreal Cognitive Assessment (MoCA), immediate and delayed recall of the Rey Auditory Verbal Learning Test (RAVLT) and Frontal Assessment Battery (FAB). MoCA is thought to shortly perform a global cognitive evaluation including trials for visual-spatial skills and executive functions (trail making, clock drawing, copy of a figure), picture naming, short-term memory, attention (both selective and sustained attention, serial calculation), language (sentence repetition and verbal fluency), abstraction, deferred recall and orientation (time and space). MoCA score ranges from 0 (worst) to 30.[28] FAB is thought to evaluate frontal lobe functions and the presence and the severity of a dysexecutive syndrome affecting both cognition and motor behavior. The short battery consists of six subtests, exploring different executive domains: conceptualization and abstract reasoning (similarities test), cognitive flexibility (phonological verbal fluency), motor programming and executive control of action (Luria's Fist-Edge-Palm Test), sensitivity to interference (conflicting instructions), inhibitory control (go-no-go test) and environmental autonomy (prehension behavior test). FAB scores range from 0 (worst) to 18.[29] RAVLT is thought to assess the ability to encode, combine, store and recover verbal information in different stages of immediate memory. RAVLT is a list-learning paradigm including 15 nouns the patient hears for five times. Each time the patient is asked to recall as many words from the list as possible (immediate recall). The scores range from 0 (worst) to 75. After a 15-minute delay, the patient is asked to recall the words again (delayed recall). The scores range from 0 (worst) to 15.[30] Trained psychologists administered all the cognitive tests on admission to rehabilitation. All the cognitive scores were adjusted for both school education level and age.

A blood sample was collected in the morning after an overnight fasting, within 24 hours after admission to the rehabilitation ward in order to assess the blood levels of 25-hydroxyvitamin D by an immunoenzymatic test (IDS Inc., Fountain Hills, AZ, USA; coefficient of variation intraassay <8%, interassay <10%). The vitamin D status was investigated because it significantly affects the functional outcome following hip fracture: low levels of 25-hydroxivitamin D have been consistently shown to predict poor outcomes, likely because of their unfavorable effects on muscle strength, physical performance, body balance, and propensity to falls.[22, 31-33]

Statistical analysis

We assessed for normality all the continuous variables by using a Shapiro-Wilk Test. Descriptive statistics were shown as mean and standard deviation for normally distributed variables, median and interquartile range for non-normally distributed variables. Dichotomous variables were reported as percentages. We performed a univariate linear regression analysis to assess the association between the scores on the cognitive tests evaluated before rehabilitation and the Barthel index scores measured at the end of the rehabilitation course. A univariate linear regression test was also performed to evaluate the association between eight potential confounders and the Barthel Index scores after rehabilitation. Five of the eight potential confounders (age, Barthel Index scores assessed by anamnesis before fracture, hip fracture type classified as either medial or lateral, 25-hydroxyvitamin D and neurologic impairment due to prevalent diseases) were significantly associated with the Barthel Index scores at univariate analysis, whereas three (sex, time interval between fracture and admission to rehabilitation and infections requiring antibiotic therapy during the stay length) were not. The five potential confounders significantly associated with the functional score at univariate analysis were included in a linear multiple regression model as independent variables together with the scores from the cognitive tests. The dependent variable in the regression model was the Barthel Index score assessed at the end of the rehabilitation course. Given non-normal distribution, the dependent variable underwent an area transformation, using the formula (r-1/2)/w, where w is the number of observations and r is the rank.[34] After transforming the dependent variable, the residuals were normally distributed in the regression models. Homoscedasticity was verified by plotting the residuals against the predicted values: the variance of the residuals looked homogeneous across levels of the predicted values.

We investigated the association between the scores of the cognitive tests and successful rehabilitation (Barthel Index score ≥85) by binary logistic regression, after adjustment for the same panel of potential confounders included in the linear regression model. To compute clinically meaningful odds ratios, we divided the scores of the cognitive tests by

the difference between the 75° and the 25° percentiles of the score distribution in our sample. Multicollinearity was assessed by examining the tolerance for each independent variable, which was greater than 0.52 in the regression model (no redundant predictors were found). No missing data were found in the 280 patients included in the study. The statistical package used was SPSS, Version 17 (SPSS Inc., Chicago, IL, USA). For all the analyses, the significance threshold was set at $P<0.05$.

Results

Figure 1 shows the flow diagram for the study: data were available for 280 inpatients whose descriptive statistics are shown in Table I.

At univariate analysis, the scores from SPMSQ, MoCA, FAB and RAVLT (both immediate and delayed recall) assessed on admission to rehabilitation were significantly associated with the Barthel index scores assessed at the end of the rehabilitation course ($P<0.001$), as shown in Table II. After multiple adjustments, MoCA scores were the only cognitive scores significantly associated with both Barthel index rating ($P=0.007$, Table III), and successful rehabilitation ($P=0.042$; Table IV). The adjusted odds ratio to achieve successful rehabilitation for a seven-point change in MoCA score was 1.98 (CI 95% from 1.02 to 3.83).

Ninety-seven of the 280 patients did not make any mistakes on the SPMSQ assessed on admission to rehabilitation, 89 made one error, 57 made two errors, 25 patients and 12 patients made three and four errors, respectively.

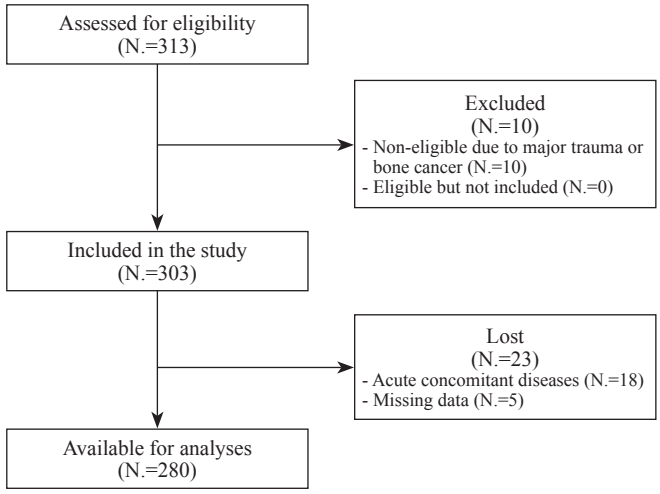

Figure 1.—Flow diagram for the study.

Figure 2 shows the Barthel Index scores on discharge from rehabilitation in the 280 patients categorized according to the number of errors made on the SPMSQ (range from 0 to 4) assessed at admission. We found significant differences in final Barthel index scores among the five groups ($c^2=23.8$; $P<0.001$). By comparing pairs of categories, we found that Barthel Index scores were not significantly different between the patients without errors (median 95, interquartile range from 80 to 100) and those with one error on the SPMSQ (median 90, interquartile range from 75 to 95): $c^2=1.8$; $P=0.180$. Conversely, the class of patients with two errors on the SPMSQ had lower Barthel Index

TABLE I.—*Descriptive statistics for the 280 inpatients included in the study.*

Age (years), mean (SD)	79.6 (8.2)
Sex (women/men), %	82%/18%
Hip fracture type (lateral/medial), %	56%/44%
25-hydroxyvitamin D (ng/mL), mean (SD)	18.5 (12.5)
At least one infection during the rehabilitation course, %	37%
Prevalent neurologic impairment, %	18%
Time interval between fracture and admission to rehabilitation (days), mean (SD)	14.1 (8.1)
Barthel Index Score before fracture (assessed by anamnesis)	100 (from 95 to 100)
Barthel Index Score at admission to rehabilitation	55 (from 45 to 65)
Barthel Index Score at discharge from rehabilitation	90 (from 75 to 95)
Barthel Index Score ≥85 at discharge from rehabilitation, %	62%
Number of errors on SPMSQ	1 (from 0 to 2)
MoCA Score	21 (from 17 to 24)
RAVLT Score (immediate recall)	38 (from 33 to 46)
RAVLT Score (delayed recall)	9 (from 6 to 11)
FAB Score	14 (from 11 to 16)

Data is shown as median (interquartile range) where not indicated otherwise.
SD: standard deviation; SPMSQ; Short Portable Mental Status Questionnaire; MoCA: Montreal Cognitive Assessment; RAVLT: Rey Auditory Verbal Learning Test; FAB: Frontal Assessment Battery.

TABLE II.—*Univariate association between the cognitive tests assessed before rehabilitation and the Barthel index scores assessed at the end of the rehabilitation course in the 280 inpatients.*

Cognitive test	SPMSQ	MoCA	FAB	RAVLT (immediate)	RAVLT (delayed)
Beta	0.28*	0.34*	0.28*	0.30*	0.24*

SPMSQ: Short Portable Mental Status Questionnaire; MoCA: Montreal Cognitive Assessment; FAB: Frontal Assessment Battery; RAVLT: Rey Auditory Verbal Learning Test. Beta: standardized coefficient. *P<0.001.

TABLE III.—*Linear multiple regression analysis model assessing the association between the scores on all the cognitive tests evaluated before rehabilitation and the Barthel index scores assessed at the end of the rehabilitation course.*

Independent variables	B (95%CI)	Beta	P
(Constant)	-2.57 (-4.32; -0.82)		0.004
Age (years)§	-0.03 (-0.04; -0.02)	-0.27	<0.001
Barthel index before fracture§	0.04 (0.03; 0.05)	0.29	<0.001
Hip fracture type§	-0.21 (-0.39; -0.03)	-0.11	0.025
25-hydroxyvitamin D (ng/mL)§	0.008 (0.001; 0.015)	0.11	0.025
Neurologic disease§	-0.42 (-0.66; -0.17)	-0.17	0.001
Number of errors on the SPMSQ	-0.03 (-0.12; 0.06)	-0.03	0.563
MoCA Score§	0.04 (0.01; 0.07)	0.18	0.007
FAB Score	0.02 (-0.02; 0.06)	0.07	0.253
RAVLT Score (immediate recall)	0.005 (-0.006; 0.02)	0.06	0.365
RAVLT Score (delayed recall)	0.006 (-0.02; 0.03)	0.03	0.614

The dependent variable was the Barthel Index Score at discharge from the rehabilitation ward (after normalization by area transformation). The independent variables were those listed in the Table. Trochanteric fractures and presence of neurologic diseases were conventionally attributed a value of one, whereas fractures of the cervical region and absence of neurologic diseases were conventionally attributed a value of 0. For the whole model, F value was 16.8 (R^2: 0.38, P<0.001).
SPMSQ: Short Portable Mental Status Questionnaire; MoCA: Montreal Cognitive Assessment; FAB: Frontal Assessment Battery; RAVLT: Rey Auditory Verbal Learning Test.
§Dependent variables significantly associated with the Barthel Index scores.

TABLE IV.—*Binary logistic regression analysis assessing the association between the scores on all the cognitive tests evaluated before rehabilitation and successful rehabilitation in the 280 inpatients.*

Independent variables	B (SE)	Odds Ratio (95% CI)	P
(Constant)§	-14.82 (5.47)		0.007
Age (years)	-0.09 (0.02)	0.91 (0.87; 0.96)	<0.001
Barthel Index before fracture	0.20 (0.05)	1.22 (1.10; 1.35)	<0.001
Hip fracture type	-0.88 (0.32)	0.41 (0.22; 0.78)	0.006
25-hydroxyvitamin D (ng/mL)	0.03 (0.01)	1.03 (1.005; 1.01)	0.019
Neurologic disease§	-1.39 (0.44)	0.25 (0.11; 0.59)	0.002
Number of errors on the SPMSQ/2§	0.07 (0.30)	1.07 (0.59; 1.92)	0.826
MoCA Score/7§	0.68 (0.34)	1.98 (1.02; 3.83)	0.042
FAB Score/5	0.15 (0.31)	1.17 (0.63; 2.16)	0.626
RAVLT Score (immediate recall)/13	0.32 (0.24)	1.38 (0.86; 2.22)	0.181
RAVLT score (delayed recall)/5	-0.07 (0.18)	0.93 (0.66; 1.31)	0.673

The dependent variable was the presence of a Barthel Index scores ≥85 at the end of the rehabilitation course. The independent variables included in the regression model are listed in the table. Trochanteric fractures and presence of neurologic diseases were conventionally attributed a value of one, whereas fractures of the cervical region and absence of neurologic diseases were conventionally attributed a value of 0. For the whole model, χ^2: 109.1, Nagelkerke R^2: 0.44, P<0.001).
SPMSQ: Short Portable Mental Status Questionnaire; MoCA: Montreal Cognitive Assessment; FAB: Frontal Assessment Battery; RAVLT: Rey Auditory Verbal Learning Test. To compute clinically meaningful odds ratios, we divided the scores of the cognitive tests by the difference between the 75° and the 25° percentiles of the score distribution in our sample.
§Dependent variables significantly associated with the Barthel Index scores.

scores (median 80, interquartile range from 70 to 95) than the class with one error: c^2=5.91; P=0.015.

We identified the 186 patients with ≤1 error on the SPMSQ as cognitively intact according to the capability of the SPMSQ to predict functional ability in activities of daily living. In the 186 patients, MoCA scores were the only cognitive scores significantly associated with both Barthel Index rating (P=0.009, Table V), and successful rehabilitation (P=0.037; Table VI) after multiple adjustments. The adjusted odds ratio to achieve successful rehabilitation for a seven-point change in MoCA score was 2.61 (CI 95% from 1.06 to 6.43).

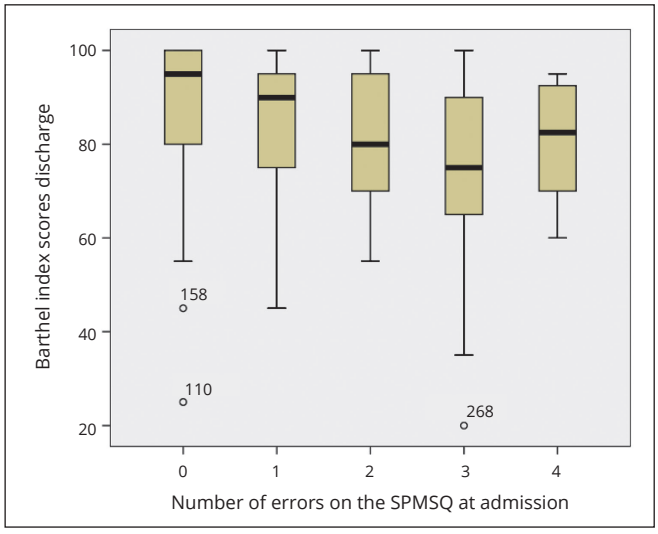

Figure 2.—Boxplot showing Barthel index scores at the end of the rehabilitation course in the 280 inpatients categorized on the basis of the number of errors on the Short Portable Mental Status Questionnaire (SPMSQ) performed at admission to the rehabilitation ward. For each group of patients, the Barthel index score is shown as interquartile range (box limits), median (horizontal line inside the box), total range (vertical lines) and outliers (dots).

Discussion

In the hip-fracture inpatients classified as "intact" or "mildly impaired" on the SPMSQ, each of the 3 cognitive tests we performed (MoCA, FAB and RAVLT) significantly predicted the short-term functional ability. However, only the MoCA score retained its significant prognostic role when the scores from the three tests were included together as independent variables in the same multiple regression model. Contrary to our hypothesis, performing the three tests was not better than performing MoCa alone to predict activities of daily living. To our knowledge, no previous studies investigated the independence of the prognostic role exerted by different cognitive tests after hip fracture in older people with no obvious altered cognition on a screening evaluation. The rationale of our hypothesis rested on the specific features of the cognitive tests we performed: MoCA is a short battery aimed to globally assess cognition, whereas FAB and RAVLT are designed to deepen the investigation of specific areas. In particular, the six subtests of the FAB selectively address frontal lobe functions,[29] whereas RAVLT (with both immediate and delayed recall of a 15-noun list) assesses verbal memory in different stages.[30] Our results suggest that performing all the three tests may be redundant, at least to evaluate the functional prognosis. The reasons underling redundancy are not obvious. We hypothesize that information on frontal lobe functions and verbal memory carried by the MoCA score may be enough to capture their prognostic contribution. Alternatively, frontal lobe functioning and verbal memory may have no relevant prognostic roles, but this supposition is inconsistent with the capability of both FAB and RAVLT to predict the functional outcome when used as the only tool for cognitive assessment. Several potential mechanisms involving various cognitive domains have been advocated to justify the association between impaired cognition and unfavorable outcomes.[35-37] One potential mechanism rests on the impossibility of recalling and following instructions to optimize function, including behavior strategies and proper use of aids.[38, 39] A

TABLE V.—*Linear multiple regression analysis model assessing the association between the scores on the cognitive tests evaluated before rehabilitation and the Barthel Index scores assessed at the end of the rehabilitation course in the 186 inpatients with ≤1 error on the SPMSQ.*

Independent variables	B (95%CI)	Beta	P
(Constant)	-3.64 (-6.33; -0.96)		0.008
Age (years)§	-0.03 (-0.04; -0.02)	-0.28	<0.001
Barthel Index before fracture§	0.05 (0.03; 0.08)	0.27	<0.001
Hip fracture type§	-0.33 (-0.56; -0.10)	-0.18	0.005
25-hydroxyvitamin D (ng/mL)§	0.008 (-0.001; 0.017)	0.12	0.066
Neurologic disease§	-0.36 (-0.68; -0.03)	-0.14	0.032
MoCA Score§	0.05 (0.01; 0.08)	0.22	0.009
FAB Score	0.008 (-0.04; 0.06)	0.06	0.761
RAVLT Score (immediate recall)	0.003 (-0.01; 0.02)	0.03	0.679
RAVLT Score (delayed recall)	0.008 (-0.02; 0.04)	0.04	0.557

The dependent variable was the Barthel Index Score at discharge from the rehabilitation ward (after normalization by area transformation). The independent variables were those listed in the Table. Trochanteric fractures and presence of neurologic diseases were conventionally attributed a value of one, whereas fractures of the cervical region and absence of neurologic diseases were conventionally attributed a value of 0. For the whole model, F value was 9.4 (R^2: 0.33, P<0.001).
SPMSQ: Short Portable Mental Status Questionnaire; MoCA: Montreal Cognitive Assessment; FAB: Frontal Assessment Battery; RAVLT: Rey Auditory Verbal Learning Test.
§Dependent variables significantly associated with the Barthel Index scores.

TABLE VI.—*Binary logistic regression analysis assessing the association between the scores on the cognitive tests evaluated before rehabilitation and successful rehabilitation in the 186 inpatients with ≤1 error on the SPMSQ.*

Independent variables	B (SE)	Odds Ratio (95% CI)	P
(Constant)	-25.71 (8.66)		0.003
Age (years)§	-0.08 (0.03)	0.92 (0.87; 0.98)	0.006
Barthel Index before fracture§	0.30 (0.08)	1.35 (1.15; 1.59)	<0.001
Hip fracture type§	-1.20 (0.43)	0.30 (0.13; 0.70)	0.006
25-hydroxyvitamin D (ng/mL)§	0.04 (0.02)	1.04 (1.008; 1.08)	0.014
Neurologic disease§	-1.64 (0.57)	0.19 (0.06; 0.59)	0.004
MoCA Score/7§	0.96 (0.46)	2.61 (1.06; 6.43)	0.037
FAB Score/5	0.11 (0.45)	1.12 (0.46; 2.70)	0.801
RAVLT Score (immediate recall)/13	0.09 (0.32)	1.10 (0.58; 2.06)	0.779
RAVLT Score (delayed recall)/5	0.05 (0.27)	1.05 (0.62; 1.77)	0.867

The dependent variable was the presence of a Barthel index scores ≥85 at the end of the rehabilitation course. The independent variables included in the regression model are listed in the table. Trochanteric fractures and presence of neurologic diseases were conventionally attributed a value of one, whereas fractures of the cervical region and absence of neurologic diseases were conventionally attributed a value of 0. For the whole model, Chi-squared: 71.8, Nagelkerke R^2: 0.45, P<0.001).
SPMSQ: Short Portable Mental Status Questionnaire. MoCA: Montreal Cognitive Assessment. FAB: Frontal Assessment Battery. RAVLT: Rey Auditory Verbal Learning Test. To compute clinically meaningful odds ratios, we divided the scores of the cognitive tests by the difference between the 75° and the 25° percentiles of the score distribution in our sample.
§Dependent variables significantly associated with successful rehabilitation.

second mechanism is low adherence to rehabilitation.[40, 41] Thirdly, blunted health literacy, with inadequate ability to find, understand and use information and services to inform health-related decisions and actions may link impaired cognition and poor outcomes.[42, 43] Finally, cerebral injuries may cause both impaired cognition and loss of function by causing motor damages and behavior changes, according to a biomedical model.[44, 45] It is likely that different mechanisms act together to link impaired cognition and poor outcomes. A "multi-mechanism-hypothesis" is consistent with the good predictive capability of the MoCA score that supplies a global (although short) evaluation of different areas.

Our data shows that the screening evaluation by using the SPMSQ was not able to identify all the patients whose cognitive impairment carried a prognostic disadvantage in activities of daily living. Even in the patients classified as "intact" on the SPMSQ, a further cognitive assessment could unmask deficiencies predicting unfavorable outcomes. The results confirm two recent reports and strongly suggest additional evaluations in the patients who seem undamaged on a screening test.[24, 46] In particular, a MoCA test in the patients with a normal (or mildly altered) score on the SPMSQ emerges as a good tool to better the predictive capability of the cognitive assessment in the patients with subacute hip fracture. A seven-point difference in MoCA scores (corresponding to the difference between 25° and 75° percentiles in MoCA score distribution in the sample) was associated with an adjusted odds ratio of around 2 to achieve successful rehabilitation. The result is similar to the one recently reported by Bardesono *et al.* in 127 women with subacute hip-fracture.[24] Further studies are needed to assess the prognostic role of the MoCA score after screening cognition by other tests that may work better than the SPMSQ to predict activities of daily living.

Defining the functional prognosis in people with hip fracture has relevant implications, because poor outcomes are common even after successful surgery: around 60% of the hip-fracture survivors lose the functional level they had before fracture, 40% do not walk independently and 30% are dependent in several basic activities of daily living and are candidates to nursing homes.[11] Early prediction of poor outcomes helps patient-centered rehabilitation teams to define proper rehabilitation objectives, to plan discharge destination, to supply information on home aids and need of assistance and community support and to adapt rehabilitation interventions.[47]

In agreement with several previous reports, we found that a poor functional outcome was significantly predicted by several variables beyond impaired cognition. In our sample, the negative prognostic factors were older age, low functional ability before fracture, fracture of the trochanteric (lateral) region, prevalent neurologic diseases and low levels of 25-hydroxyvitamin D at admission to the rehabilitation ward.[13, 22] It is noteworthy that the prognostic role of low MoCA scores persisted after adjustment for the panel of predictors that were included in the multiple regression models.

Strengths and limitations of the study

Six strengths of our study are: longitudinal, prospective design; blindness of the assessors; inclusion of a homogeneous sample of inpatients with subacute hip fracture due

to fragility; adjustment of the results for multiple potential confounders; assessment of multicollinearity in the regression models; focus on activities of daily living, *i.e.*, a pivotal outcome measure.

The study has also various limitations. Several potential confounders, including fear of falling, depression, prevalent vertebral fractures, concurrent humeral fractures, social support, nutritional status, delirium and pain were not available.[13, 22, 48, 49] Generalizability is limited because we investigated selected patients: community-dwelling persons who were admitted to a single rehabilitation ward in Italy after post-surgery referral for inpatient rehabilitation. We had no long-term outcome data on activities of daily living and we had no data on other outcome measures, namely physical performance, participation and quality of life.

Conclusions

MoCA scores significantly contributed to predict the functional outcome in the hip-fracture inpatients who made ≤4 errors on the SPMSQ. Conversely, further evaluations by using RAVLT and FAB did not improve the prognostic evaluation. We suggest that MoCA should be routinely performed in the patients defined cognitively intact or mildly impaired on the SPMSQ. Further studies should clarify the generalizability of our results and MoCA predictive role in the presence of cognitive screening tests different from the SPMSQ. Furthermore, comparisons between MoCA and other tools should be made to define the best cognitive evaluation for prognosis estimation.

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions
Marco Di Monaco conceived the first idea of the study and planned it. He interpreted data and wrote the first draft of the manuscript and its final version; Maria Sgarbanti, Carlotta Castiglioni and Francesca Bardesono co-conceived the idea of the study; they were implicated with the management of the patients and collected clinical data and helped to write the first draft of the manuscript and commented on the following drafts; Silvia Trombetta, Laura Gullone, Alessandra Bonardo and Patrizia Gindri conceived, performed and interpreted the neuropsychologic assessment; they commented on manuscript drafts; Edoardo Milano contributed to collect clinical data (he was the chief of the Division where the study was conducted); he commented on the first draft of the manuscript and on the successive versions; Giuseppe Massazza co-conceived the idea of the study; he contributed to write the final version. All the authors read and approved the final version of the manuscript.

History
Article first published online: March 14, 2024. - Manuscript accepted: January 18, 2024. - Manuscript revised: December 11, 2023. - Manuscript received: August 27, 2023.