Early Recovery of Aphasia through Thrombolysis: The Significance of Spontaneous Speech

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Background: Aphasia is one of the most devastating stroke-related consequences for social interaction and daily activities. Aphasia recovery in acute stroke depends on the degree of reperfusion after thrombolysis or thrombectomy. As aphasia assessment tests are often time-consuming for patients with acute stroke, physicians have been developing rapid and simple tests. The aim of our study is to evaluate the improvement of language functions in the earliest stage in patients treated with thrombolysis and in nontreated patients using our rapid screening test. *Materials and Methods:* Our study is a single-center prospective observational study conducted at the Stroke Unit of the University Medical Hospital of Trieste (January-December 2016). Patients treated with thrombolysis and nontreated patients underwent 3 aphasia assessments through our rapid screening test (at baseline, 24 hours, and 72 hours). The screening test assesses spontaneous speech, oral comprehension of words, reading aloud and comprehension of written words, oral comprehension of sentences, naming, repetition of words and a sentence, and writing words. *Results:* The study included 40 patients: 18 patients treated with thrombolysis and 22 nontreated patients. Both groups improved over time. Among all language parameters, spontaneous speech was statistically significant between 24 and 72 hours (*P* value = .012), and between baseline and 72 hours (*P* value = .017). *Conclusions:* Our study demonstrates that patients treated with thrombolysis experience greater improvement in language than the nontreated patients. The difference between the 2 groups is increasingly evident over time. Moreover, spontaneous speech is the parameter marked by the greatest improvement. **Key Words:** Ischemic stroke—aphasia—thrombolysis—spontaneous speech—screening test.

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Introduction

Stroke is the third cause of death and is the first cause of disability worldwide.[1] Its prevalence in patients over 65 years of age ranges from 46 to 73 per 1000 persons.[2] Owing to the aging general population, the number of patients with stroke is likely to increase over the next years.

Recombinant tissue plasmin activator (rtPA) is adopted to perform intravenous thrombolysis to facilitate reperfusion in patients with acute ischemic stroke. The total dose administrated is .9 mg/kg within 4.5 hours after symptom onset.[1] Benefits of thrombolysis emerged from a meta-analysis of individual patient data from randomized controlled trials.[3]

Stroke-related disabilities often have a large impact on quality of life and activities of daily living. Aphasia is one of the most devastating consequences of stroke that occurs in 20%-40% of cases.[4-6] It is an acquired language disorder affecting verbal production or verbal comprehension (e.g., spontaneous speech, oral and written naming, repetition, reading aloud and spelling, and oral and written comprehension), whereas cognitive functions remain unaffected.[6]

As language is pivotal for social interaction, patients with stroke-related aphasia experience difficulties in social relations and activities, mood, or return to work, leading to a further decrease in quality of life.[6,7] Aphasia is also related to higher health-care costs due to longer speech therapy interventions and hospitalizations.[8,9] The most significant prognostic factors for language recovery are type of aphasia and initial severity of language impairment.[6,10] For instance, global aphasia (a disorder affecting all components of language processing) often results in worse recovery outcomes.[5,6,11,12] Type of stroke, localization, and size of brain lesion after stroke are all reported to play a pivotal role in language recovery and rehabilitation. Further decisive factors are age, gender, handedness, medical history, years of education, family support, and motivation.[4,6,13]

The National Institutes of Health Stroke Scale (NIHSS) is a well-established bedside tool to rapidly assess the severity of neurologic deficit caused by stroke.[14-16] NIHSS is adopted in emergency settings to assess the severity of stroke, to determine patients' eligibility for specific treatments, such as thrombolysis and thrombectomy, and to evaluate the outcome of interventions.[17,18] It is also a powerful predictor of clinical outcome.[19,20] NIHSS consists of 11 items assessing the main neurologic functions, such as eye movement, visual fields, coordination, motor strength, sensation, neglect, and language. NIHSS score ranges from 0 to 42, with 7 points attributed to language functions (2 points for orientation, 2 points for command execution, 3 points for aphasia). High NIHSS score is associated with unfavorable aphasic outcome. However, this tool is not detailed enough when it comes to language processing evaluation.

Although evidence supports the positive effect of speech therapy on recovery of aphasia,[21] there is an ongoing debate on the right moment to start the intervention. Some authors suggest the benefits of starting it as soon as possible.[9,22] Therefore, testing aphasia in acute stroke phase can be useful to plan a well-timed language therapy.

Only few tests are used to determine the type and severity of aphasia, which often are time-consuming (15-40 minutes) and excessively tiring for patients with acute stroke. Moreover, the administration of most tests requires trained speech therapists, who are usually unavailable in emergency settings. Physicians agree on the need of a simple and rapid test, ideally only few minutes long. Therefore, these physicians have tried to develop a tool in their own language. However, no Italian version is currently available.[9] The test should consist of naming, comprehension, repetition, word fluency, reading, and writing tasks. The recovery of aphasia in acute stroke also depends on the degree of reperfusion after thrombolysis or thrombectomy.[23,24]

Recombinant tissue plasminogen activator (rtPA) may affect ischemic stroke-related size, pattern, nature of infarcts, and recovery of aphasia.[25,26] However, only few studies have been conducted on aphasia in acute phase since the early thrombolytic era. Therefore, re-evaluating the relevant factors of aphasia recovery is crucial as intravenous thrombolysis has become a standard of care in patients with acute stroke.[27]

The aim of our study is to evaluate the improvement of language functions in the earliest stage in patients with stroke-related aphasia. The study compared patients treated with thrombolysis and nontreated patients using a rapid screening test in an emergency setting.

Materials and Methods

Any researcher interested in our study is invited to contact the corresponding author per e-mail. The authors will be pleased to share analytical methods and study materials of this study.

Study Design and Population

Our study adopted a single-center prospective observational design and was conducted in the Stroke Unit of the University Medical Hospital of Trieste, Italy, from January to December 2016. The study population was composed of consecutive patients of both genders, above 18 years of age, with aphasia resulted from acute ischemic stroke. Aphasia is defined as the loss of linguistic or communicative skills, marked by difficulties in understanding or producing words, naming objects (anomia) or recalling words during conversation, phonemic distortion, or exchange of words (phonemic or semantic paraphasia).[28] Aphasic patients were divided into 2 groups: patients treated with thrombolysis and nontreated patients.

Patients eligible for thrombolysis were treated with intravenous rtPA (.9 mg/kg of body weight, maximum of 90 mg, infused over 60 minutes with 10% of the total dose administered as an initial intravenous bolus over 1 minute) within 4.5 hours from symptom onset.

We developed a rapid screening test suitable for emergency settings, the ApsAA (Aphasia Post-Stroke Acute Assessment). Both groups underwent 3 aphasia assessments by trained local physicians. Patients were tested at baseline (treated patients before thrombolysis, nontreated patients at arrival in the stroke unit) and after 24 and 72 hours. All assessments were video-recorded, subsequently transcribed, and scored independently by 3 trained evaluators (2 clinical neuropsychologists specialized in language assessment and 1 physician) not involved in the data collection. Inter-rater agreement was very high, and the same score was reached in 87.5% of cases. In case of diverging opinions, the videos were reanalyzed to achieve a satisfactory level of agreement.

Patients were enrolled in the study if they met the following criteria: (1) ischemic stroke with aphasia arriving to hospital within 24 hours from symptom onset; (2) all type and severity of aphasia; (3) right handedness; (4) adult Italian native speaker; and (5) at least 5 years of formal education. Patients with the following criteria were not included: (1) prestroke dementia (suspected or confirmed); (2) severe impairment of vision or hearing (based on medical history or clinical examination); (3) pre-existing psychiatric or neurologic disorder (e.g., previous stroke, cerebral neoplasia, severe depression); (4) disorders of vigilance; and (5) history of alcoholism or chronic occupational exposure to neurotoxic substances.

Participants underwent common stroke workup, assessment of stroke risk factors, carotid ultrasound, and electrocardiography, in most cases transthoracic echocardiography (some patients had transesophageal echocardiography) and Holter electrocardiography. All patients were examined with a nonenhanced computed tomography (CT) at baseline and before discharge. Moreover, patients treated with thrombolysis underwent CT angiography at baseline and nonenhanced CT at 24 hours.

The Trial of Org 1072 in Acute Stroke Treatment (TOAST) classification was adopted to classify stroke etiology, lesion size, and type.[29] We divided stroke's etiology into 5 categories: large-artery atherosclerosis, cardioembolism, small-vessel occlusion, stroke of other determined etiology, and stroke of undetermined etiology.

In addition, the following data were collected: (1) demographic details (age, sex); (2) stroke risk factors (hypertension, diabetes, dyslipidemia, smoke, atrial fibrillation); (3) time of stroke onset; (4) time span between symptom onset and administration of first screen aphasia test; (5) NIHSS score at baseline and at 24 and 72 hours; (6) prestroke and discharge modified Rankin Scale (mRS) score; and (7) complications (symptomatic hemorrhage, successive strokes).

Symptomatic hemorrhage is an intracerebral hemorrhage on CT scan within 72 hours from symptom onset with a 4-point increase in NIHSS. Modified Rankin Scale and NIHSS scores were determined by 2 independent observers.

The study was conducted according to the principles of the Declaration of Helsinki. Informed consent was given by the patients themselves or obtained by a proxy in accordance with the European and national regulations. The method adopted to obtain the informed consent depended on the severity of their neurologic deficits at hospital admission (determined by higher values on the NIHSS, level of consciousness, severity of aphasia, and particularly verbal comprehension). To facilitate patients' understanding and decision-making, the language was carefully adapted, additional writing or drawing was used when necessary. Quality of consent was tested with online assessment of comprehension. However, despite these procedures, 61% of patients were unable to provide full consent. Therefore, consent was provided by a relative. Approval for the study was obtained from the local ethics committee.

Screening Test

We developed a very brief language evaluation test suitable for emergency settings, the ApsAA. It includes a set of tasks to assess language impairment through input and output subtests: spontaneous speech through a description of a complex picture,[30] oral comprehension of words, reading aloud and comprehension of written words, oral comprehension of sentences, naming, repetition of words and a sentence, and writing words. Most of the stimuli were selected from a well-validated Italian aphasia test[31] and checked for linguistic variables that have proved to influence language production and comprehension. All visual and linguistic parameters are based on an empirically derived Italian lexical database.[32,33]

The ApsAA is composed of 8 language subtests, which include

- Spontaneous speech. Patients are given a colored picture printed on a board representing a simple scene that they are invited to describe. Patients are instructed to look at the picture, tell what they see, and try to talk in sentences. The Cookie Theft picture description task from the *Boston Diagnostic Aphasia Examination* was chosen because it is considered an ecologically valid approximation to spontaneous discourse.[30]
- Oral comprehension of words. Patients are invited to point at the right figure among 3 alternatives shown on a board. All words are concrete names. The wrong options are either phonologically or semantically related to the right one. This subtest comprises 2 items.
- Reading and comprehension of written words. This subtest comprises 2 items. Two consecutive boards featuring 1 written word and 3 pictures are shown to the patients. Patients are instructed to read aloud the written word. Then, they are asked to choose the right picture representing the written word among the three. The wrong options are either orthographically or semantically related to the right one.

- Oral comprehension of sentences. The examiner read a sentence and patients are requested to point at the right figure among 2 alternative figures shown on a board. The sentences examined comprehension of verbs antonyms (i.e., buy/sell), grammatical processing (morphologic endings, active and passive sentences). This subtest comprises 4 items.
- Naming. This subtest comprises 4 items. Patients should name 4 images presented by the examiner, that is, *ciliegie* (cherries), *bicchiere* (glass), *forbici* (scissors), *giraffa* (giraffe). Stimuli are 3 syllables long and were balanced for both word frequency (2 high, 2 low frequency) and semantic category (2 living, 2 nonliving entities).
- Repetition of words. This subtest comprises the repetition of 2 words of different length, frequency, concreteness, and phonological complexity. Patients are invited to repeat the words *scopa* (broom) and *esperienza* (experience).
- Repetition of a sentence. Patients are invited to repeat a 7-word active sentence: *Il ragazzo accompagna il nonno dal dottore* (the boy accompanies his grandfather to the doctor).
- Writing to dictation of words. The subtest comprises 2 items. Patients are asked to write the words *scopa* (broom) and *esperienza* (experience).

The estimated length of the ApsAA is 3-5 minutes. Patients' posture need to enable them to see the boards. If patients wear glasses or use hearing aids, so do they during the screening test. Patients were invited to use only their left arm to perform the ApsAA tasks to avoid problems related to right palsy, which is sometimes concomitant to aphasia.

ApsAA maximum score amounts to 65 points distributed among the subtests as follows:

- Spontaneous speech. The duration of the task is fixed to 1 minute. This assignment imposes predictable speech output, as the description should contain 16 key elements, information, or semantic units (subjects, objects, actions, places) represented in the picture. Consequently, speech can be scored according to the number of the identified information units. Alternative ways of identifying the 16 elements can be accepted as described by Forbes and Venneri.[34]

The scoring method for evaluation of spontaneous speech was adopted from Allibrio et al.[35]: 1 point for each named element; .5 extra point (up to a maximum of 3 points) for each relevant named element not listed among the 16 elements, which is semantically close, a semantic paraphasia, semantic conduite d'approche or rephrasing close in meaning.

A maximum of –2 points for phonemic mistakes and up to further –2 points for syntactic mistakes:

- Phonemic mistakes: –1 point for phonemic paraphasia, pause of more than 2 seconds before answering and conduite d'approche; –2 points for numerous paraphasia and some neologisms;
- Syntactic mistakes: –1 point for production of sentences with omissions or conjugation or function word mistakes or occasional mistakes in the argumentative structure; –2 points for the production of sentences with frequent omissions of function word or substitution of conjugated formed through direct speech (agrammatism) or severe deficiency in conjugation and function word choice or frequent mistake in the argumentative structure (paragrammatism).
- Oral comprehension of words: 2 points for immediate right answer; 1 point for self-correction, right answer after repetition of question or pause of more than 2 seconds before answering; 0 point for mistake or no answer.
- Comprehension of written words: 2 points for immediate right answer; 1 point for self-correction, right answer after repetition of question or pause of more than 2 seconds before answering; 0 point for mistake or no answer.
- Oral comprehension of sentences: 2 points for immediate right answer; 1 point for self-correction, right answer after repetition of question or pause of more than 2 seconds before answering; 0 point for mistake or no answer.

The following are scored as in Allibrio et al.[35]:

- Reading of written words: maximum 3 points for each word read correctly.
- Naming, repetition of words, repetition of sentence, writing words: 3 points for immediate (within 2 seconds) correct answer (in Italian or dialect); 2 points for self-correction, anomic pause, rephrasing or semantic paraphasia with high correspondence, phonemic paraphasia with less than 1/3 of sounds being substituted; 1 point for rephrasing or semantic paraphasia with low correspondence, phonemic paraphasia with substituted sounds between 1/3 and 2/3; 0 point for no answer, neologism, perseveration, use of gestures.

To explore the applicability and sensibility of the ApsAA, the scale was previously administered to 20 (male = 13, female = 7) consecutive patients with postacute and chronic stroke-induced aphasia and to 27 (male = 15, female = 12) patients without aphasia. The first group's average score amounted 62 (standard deviation [SD] 2.12), whereas the second group score amounted 29 (SD 21.88). Postacute aphasia patents' mean time of assessment was 63 days (SD 36) after stroke onset. Mean age was 66 years (SD 10.5), whereas mean years of education was 9 (SD 3.3). Nonaphasic patients' mean age was 72 years (SD 8.4) and mean years of education was 9.5 (SD 3.1). Furthermore, postacute and chronic aphasic patients were assessed with a well-validated aphasia battery[36] to establish ApsAA external validity.

Statistical Analysis

Chi-square or Fisher's exact test and Student's *t* test or Mann–Whitney test were used to compare between groups the baseline categorical and the continuous variables, respectively, as appropriate. Student's *t* test and Mann–Whitney test were also used to compare the change of clinical and linguistic parameters between groups.

Moreover, we compared the baseline and the follow-up speech parameters within each group using Wilcoxon signed-rank test for 2 related samples. We performed the analysis using SPSS v.22.0 (IBM Corp, Armonk, NY, USA).

Results

The study included 40 subjects: 18 patients treated with thrombolysis and 22 nontreated patients. Table 1 shows a comparison between the demographic and the clinical features of the 2 groups. No significant difference was observed between the 2 groups in terms of gender and mean years of education. The groups do not differ as far as comorbidity is concerned, except for dyslipidemia, which was more frequent in the nontreated group. Seven patients from the treated group (37.8%) and 5 patients from the nontreated group (22.7%) had a carotid artery stenosis not significant from a hemodynamic point of view. Four patients of the treated group (22.2%) and 5 patients of the nontreated group (22.7%) had a hemodynamically significant carotid artery stenosis. No difference in these variables was found between the 2 groups. The distribution of the aphasic syndromes in the 2 groups is described in Table 2, with global aphasia as the most frequent in both groups. Table 3 shows the suspected location of artery occlusion, lesion areas, and size of lesion of the 2 groups. At follow-up CT, 7 patients of the treated group showed a lesion in 1 area (38.9%), 6 patients in 2 areas (33.3%), 1 patient in 3 or more areas (5.6%), and 4 patients (22.2%) did not show any cerebral lesion.

As far as the nontreated group is concerned, at follow-up CT, 6 patients showed brain lesion in 1 area (27.3%), 5 patients in 2 areas (22.7%), 3 patients in 3 or more areas

Table 1. *Comparison between demographic and clinical features of the 2 groups*

	Thrombolysis (n = 18)	No thrombolysis (n = 22)	*P*
Mean age (SD)	73.17 (±9.19)	78.82 (±6.69)	.030*
Gender			
Male, n (%)	9 (50%)	14 (63.6%)	.385†
Female, n (%)	9 (50%)	8 (36.4%)	
Mean years of education (SD)	10.9 (±4.56)	9.14 (±3.56)	.226†
Risk factors			
Arterial hypertension, n (%)	14 (77.8%)	21 (95.5 %)	.155§
Glucose intolerance, n (%)	3 (16.7 %)	6 (27.3%)	.476§
Diabetes mellitus type 2, n (%)	3 (16.7%)	4 (18.2%)	1.000§
Dyslipidemia, n (%)	8 (44.4 %)	18 (81.8%)	.014‡
Smoke, n (%)	9 (50%)	8 (36.4 %)	.385‡
Ischemic cardiopathy, n (%)	4 (22.2%)	5 (22.7%)	1.000§
Atrial fibrillation, n (%)	5 (27.8%)	12 (54.5%)	.088‡

Abbreviation: SD, standard deviation.
*Student's *t* test.
†Mann–Whitney test.
‡Chi-square test, as appropriate.
§Fisher's exact test, as appropriate.

Table 2. *Subtypes of aphasia in patients treated with thrombolysis and patients not treated at hospital admission*

Aphasia subtypes	Thrombolysis (n = 18 patients)	No thrombolysis (n = 22 patients)	Total
Global	10 (55.5%)	10 (45.4%)	20 (50%)
Broca's	3 (16.7%)	2 (9.1%)	5 (12.5%)
Wernicke's	1 (5.5%)	4 (18.2%)	5 (12.5%)
Conduction	0 (0%)	1 (4.5%)	1 (2.5%)
Transcortical motor	1 (5.5%)	1 (4.5%)	2 (5%)
Not classifiable	3 (16.7%)	4 (18.2%)	7 (17.5%)

Patients were assessed with our ApsAA (Aphasia Post-Stroke Acute Assessment) battery.

Table 3. *Suspected location of artery occlusion, lesion areas, and size of lesion in the 2 groups*

		Thrombolysis, n (%)	No thrombolysis, n (%)	*P**
Location of artery occlusion	Internal carotid artery	3 (16.7%)	1 (4.5%)	.310†
	Middle cerebral artery M1	2 (11.1%)	4 (18.2%)	.673†
	Middle cerebral artery M2/3/4	11 (61.1%)	16 (72.7%)	.435†
	Small vessels	2 (11.1%).	1 (4.5%)	.579†
Lesion area at follow-up CT	Basal ganglia	5 (27.8%)	7 (31.8%)	.781*
	Frontal	9 (50%)	4 (18.2 %)	.033*
	Parietal	3 (16.7%)	9 (40.9%)	.096*
	Temporal	5 (27.8%)	6 (27.3%)	1.000†
	Occipital	1 (5.6%)	2 (9.1%)	1.000†

Abbreviation: CT, computed tomography.
*Chi-square test, as appropriate.
†Fisher's exact test, as appropriate.

(13.6%), and 8 patients (36.4%) did not show any cerebral lesion.

Table 4 illustrates the clinical outcome for the treated and nontreated groups. In both groups, 1 patient died. No significant hemorrhagic complication was experienced in the 2 groups. NIHSS score at baseline was not significantly different between the groups. Both treated and nontreated groups experienced NIHSS improvement over time.

As far as stroke etiopathogenic classification is concerned, according to the TOAST criteria, the treated group showed large-artery atherosclerosis, n = 4 (22.2%); lacune, n = 2 (11.1%); cardioembolism, n = 6 (33.3%); stroke of undetermined etiology, n = 6 (33.3%); and stroke of other determined etiology, n = 0 (0%). The nontreated group showed large-artery atherosclerosis, n = 5 (22.7%); lacune, n = 0 (0%); cardioembolism, n = 10 (45.5%); stroke of undetermined etiology, n = 7 (31.8%); and stroke of other determined etiology, n = 0 (0%).

Table 5 shows mean subtest scores of the 2 groups at first, second, and third speech evaluation. Patients in both groups improved significantly between baseline and 24 hours, and between 24 hours and 72 hours. In terms of spontaneous speech, the treated group improved significantly during all intervals, whereas the nontreated group improved only within the first 24 hours.

Table 6 represents a comparison of speech parameters changes over time in the 2 groups. The difference was statistically significant in spontaneous speech between 24 and 72 hours (P value = .012), and between baseline and 72 hours (P value = .017). The improvement of the 2 groups in all other parameters does not differ significantly.

Figure 1A highlights the evolution of the 2 groups' aphasia screening test total score over time, whereas Figure 1B shows the evolution of spontaneous speech score. Although both groups improved over time, the treated group showed greater improvement than the nontreated group, especially between 24 and 72 hours. Figure 1C

Table 4. *Treated and nontreated groups' outcome*

	Thrombolysis (n = 18)	No thrombolysis (n = 22)	*P*
Mortality, n (%)	1 (5.6%)	1 (4.5%)	1.000†
NIHSS baseline, mean (SD)	8.0 (±4.1)	8.1 (±7.2)	.440*
NIHSS 72 h, mean (SD)	2.9 (±3)	6.8 (±7.7)	.183*
NIHSS discharge, mean (SD)	2.0 (±3.2)	4.6 (±6.4)	.105*
mRS before admission, mean (SD)	.17 (±.7)	.36 (±.95)	.256*
mRS at discharge, mean (SD)	1.8 (± 1.8)	2.4 (±1.9)	.254*
Clinically significant hemorrhagic complications	0	0	na
Clinically nonsignificant hemorrhagic complications	0	0	na
Other complications, n (%)	1 (5.6%)	3 (13.6%)	.613†
Days of hospital stay, mean (SD)	11.5 (±6)	19.1 (±14.8)	.210†

Abbreviations: mRS, modified Rankin Scale; na, not applicable; NIHSS, National Institutes of Health Stroke Scale; SD, standard deviation.
*Mann–Whitney test, as appropriate.
†Fisher's exact test, as appropriate.

Table 5. *ApsAA scores in the 2 groups*

	Thrombolysis						No thrombolysis					
	T1, mean (SD)	T2, mean (SD)	T3, mean (SD)	P*, T1 versus T2	P*, T2 versus T3	P*, T1 versus T3	T1, mean (SD)	T2, mean (SD)	T3, mean (SD)	P*, T1 versus T2	P*, T2 versus T3	P*, T1 versus T3
Total score	20.61 (±16.76)	34.00 (±21.94)	43.82 (±21.03)	.011	.003	.003	19.18 (±19.46)	29.52 (±22.36)	31.500 (±21.31)	.015	.019	.013
Spontaneous speech	.72 (±1.73)	3.35 (±3.63)	6.68 (±5.68)	.009	.008	.005	1.64 (±2.68)	3.05 (±3.12)	3.00 (±4.07)	.023	.400	.114
Oral comprehension of words	2.00 (±1.78)	2.82 (±1.78)	3.14 (±1.70)	.017	1.000	.041	1.73 (±1.91)	2.57 (±1.83)	2.75 (±1.65)	.026	.102	.011
Comprehension of written words	1.06 (±1.39)	2.23 (±1.85)	2.79 (±1.67)	.003	.450	.007	1.55 (±1.87)	2.05 (±1.86)	2.25 (±1.73)	.180	.197	.061
Reading	2.77 (±2.60)	4.00 (±2.57)	4.64 (±2.20)	.049	.581	.046	2.41 (±2.63)	3.57 (±2.46)	3.88 (±2.36)	.049	.053	.018
Oral comprehension of sentences	3.11 (±3.02)	4.94 (±3.34)	6.21 (±2.89)	.014	.066	.012	2.36 (±3.02)	4.14 (±3.44)	4.50 (±3.16)	.019	.200	.011
Naming	4.33 (±4.55)	7.35 (±5.57)	9.21 (±4.06)	.033	.041	.011	4.64 (±4.22)	6.62 (±5.06)	7.50 (±4.77)	.033	.058	.011
Repetition	4.60 (±3.45)	5.88 (±3.29)	7.07 (±2.70)	.140	.197	.018	3.27 (±3.18)	4.76 (±3.59	5.06 (±3.28)	.035	.246	.044
Writing	2.00 (±2.45)	3.41 (±2.78)	4.07 (±2.46)	.040	.357	.020	1.59 (±2.13)	2.76 (±2.90)	2.56 (±2.80)	.250	.317	.091

Abbreviations: ApsAA, Aphasia Post-Stroke Acute Assessment; T1, aphasia screening test at baseline; T2, aphasia screening test at 24 hours; T3, aphasia screening test at 72 hours.
*Wilcoxon signed-rank test for 2 related samples.

Table 6. *Comparison between the 2 groups' speech parameters over time*

	ΔT1–T2			ΔT2–T3			ΔT1–T3		
	Thrombolysis, mean (SD)	No thrombolysis, mean (SD)	P*	Thrombolysis, mean (SD)	No thrombolysis, mean (SD)	P*	Thrombolysis, mean (SD)	No thrombolysis, mean (SD)	P*
Total score	13.76 (±20.07)	9.62 (±16.72)	.492†	6.04 (±4.39)	4.07 (±6.08)	.341	20.04 (±18.72)	13.34 (±17.09)	.315†
Spontaneous speech	2.59 (±3.68)	1.33 (±2.76)	.565	2.96 (±3.23)	.47 (±1.87)	.012	5.75 (±5.28)	1.47 (±3.41)	.012†
Oral comprehension of words	.88 (±1.27)	.81 (±1.50)	.566	.00 (±.00)	.33 (±.72)	.094	.71 (±1.20)	1.13 (±1.45)	.406
Comprehension of written words	1.24 (±1.30)	.52 (±1.69)	.067	.23 (±1.01)	.33 (±.98)	.977	1.43 (±1.50)	.88 (±1.67)	.243
Reading aloud	1.29 (±2.69)	1.05 (±2.16)	.897	.23 (±1.36)	.47 (±.83)	.512	1.43 (±2.38)	1.50 (±2.13)	.738
Oral comprehension of sentences	1.88 (±2.69)	1.67 (±3.06)	.762	.69 (±1.44)	.47 (±1.36)	.753	2.57 (±2.85)	2.31 (±3.09)	.783
Naming	3.24 (±6.04)	1.76 (±3.48)	.376	1.23 (±2.20)	1.33 (±2.44)	.754	3.86 (±4.52)	3.13 (±4.08)	.645†
Repetition	1.35 (±4.05)	1.38 (±2.75)	.880	.39 (±1.04)	.47 (±1.51)	.628	2.50 (±3.32)	1.81 (±2.90)	.967
Writing to dication	1.29 (±2.31)	1.10 (±2.21)	.937	.31 (±1.18)	.20 (±.77)	.581	1.79 (±2.52)	1.13 (±2.28)	.660

Abbreviations: SD, standard deviation; T1, aphasia screening test at baseline; T2, aphasia screening test at 24 hours; T3, aphasia screening test at 72 hours.
*Mann–Whitney test (with the exception of Student's *t* test).
†Student's *t* test.

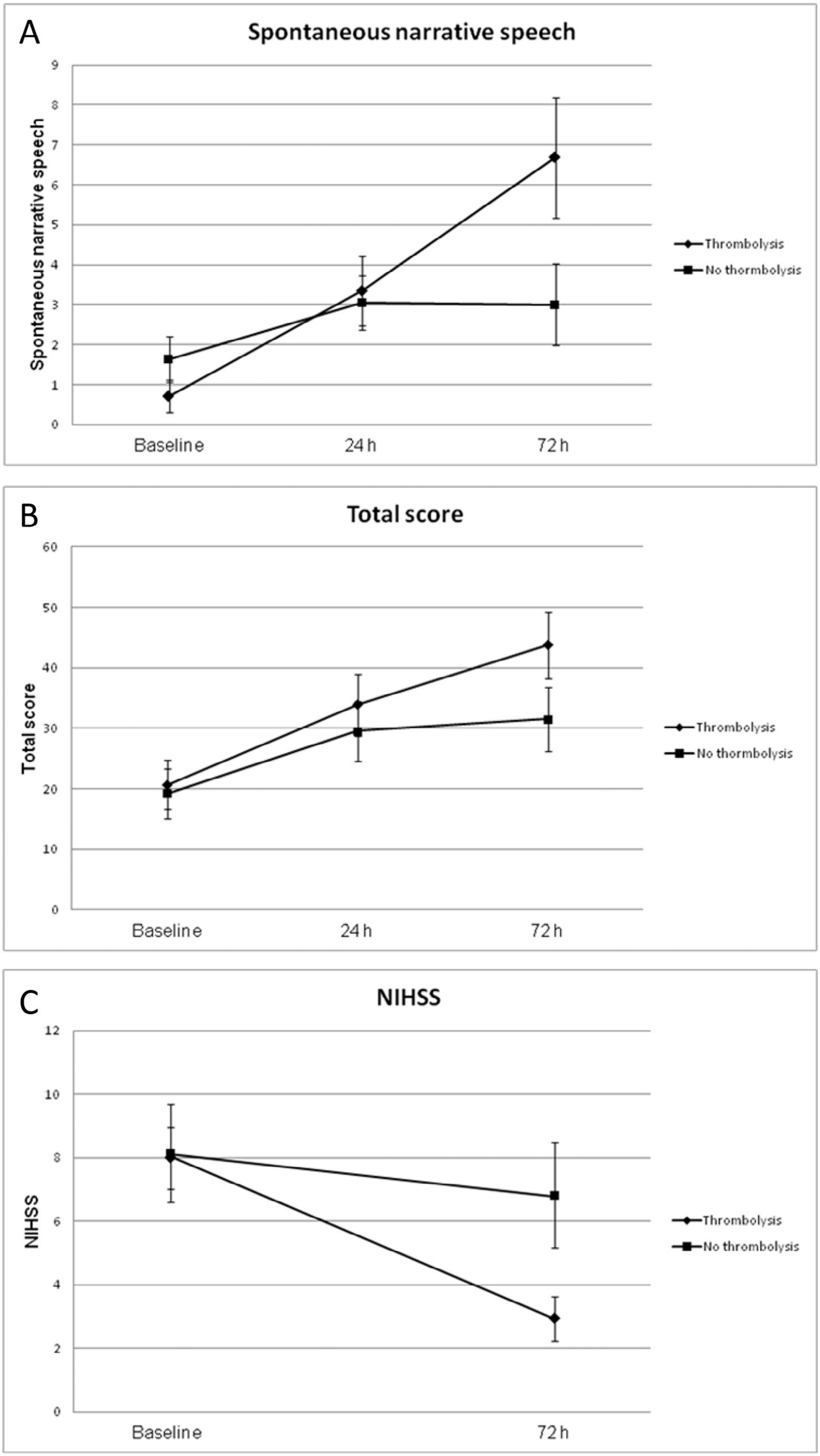

Figure 1. *(A) Evolution of the 2 groups' aphasia screening test total score over time. (B) Spontaneous speech score. (C) Evolution of the 2 groups' NIHSS score from baseline to 72 hours.*

illustrates the evolution of the 2 groups' NIHSS score from baseline to 72 hours.

Discussion

The main finding of this study is that patients treated with thrombolysis showed greater improvement in speech processing than the nontreated group. Spontaneous speech was the parameter marked by the greatest difference. Moreover, the 2 groups showed greater difference over time.

The recovery from aphasia after stroke acute phase depends on the degree of reperfusion after thrombolysis or thrombectomy. The preservation of the ischemic tissue in language regions is the main mechanism to support early recovery of speech.[23,24]

Most studies on this topic have examined the improvement of speech and language impairments in stroke subacute and chronic phases with a complete speech evaluation test, which is time-consuming and requires a speech therapist or neuropsychologist to be administered. Only few studies have evaluated the recovery of language impairments in the hyperacute phase. A complete language assessment battery in the hyperacute phase cannot be administered because of the critical conditions of patients and the time constraint in emergency settings. Studies that have evaluated aphasia in hyperacute phase were retrospective and used part of NIHSS.[27]

NIHSS is an established tool to evaluate rapidly neurologic impairment caused by stroke.[14-16] NIHSS consists of 11 items. It ranges from 0 to 42 points, of which 7 points are attributed to language functions: 2 points for orientation, 2 points for command execution, 3 points for aphasia. Most of studies assessing aphasia in acute phase have focused on these last 3 items.[37]

Spontaneous speech evaluation is composed of item 9 ("Aphasia—Best language"), which has a limited influence on the total score (3 points). Compounded by the difficulty and length of evaluating spontaneous speech mistakes, spontaneous speech is often underestimated and omitted.

Evaluating aphasia by NIHSS may be criticized as lacking in sensibility.[38] Moreover, because of its semiquantitative nature, it cannot discriminate aphasia subtypes, such as sensory and motor.[39]

The low sensitivity of NIHSS has not only diagnostic consequences but also operative. Physicians tend to use NIHSS to decide whether thrombolysis should to be carried out or not. In case of low score, physicians often choose not to expose the patient to the risks of thrombolysis. Patients with isolated aphasia have a low NIHSS score (maximum of 7 points) and may not be treated with thrombolysis. For instance, in the study of Leira et al,[40] 194 patients with NIHSS score of 6 or less accessing the Emergency department within 4.5 hours from stroke onset were enrolled in TOAST. However, these patients with isolated mild neurologic deficit did not receive any thrombolytic treatment.

However, evidence shows that patients with aphasia at onset have worse outcome compared with nonaphasic patients.[41] Isolated aphasia may not be considered a sufficient neurologic defect to proceed with thrombolytic treatment. Therefore, this clinical practice does not allow patients with potential bad outcome to receive a suitable treatment.

Only few published reports have addressed stroke changes in the severity of aphasia in the earliest poststroke phase. In a cohort of 41 patients with stroke-related aphasia tested on naming, reading and repetition tasks at 24 hours, 48 hours, and 7 days, 61% of the patients showed overall improvement.[42] In 3 other studies that have adopted the 3 items of the NIHSS for speech evaluation, 36%-57% of the patients experienced early improvement.[10,43,44]

There are no available data concerning the amount of time needed for aphasia recovery after thrombolysis.[39]

Poststroke aphasia recovery is related to numerous mechanisms at different phases of the recovery. Indeed, speech is a neurologic function based on complex neural networks.

Hemodynamic changes might be the main factor contributing to the recovery mechanisms in the acute phase. They are crucial for the extension of ischemic lesion.[23,24] Reperfusion therapies influence hemodynamic factors and may therefore facilitate early recovery.

The major mechanism underlying speech improvement in the subacute and chronic stages is functional reorganization.[45,46] Speech and language therapy may enhance the effectiveness of functional reorganization and improve brain plasticity.[47,48]

Some studies have analyzed the development of aphasia in acute phase. However, a short follow-up did not allow determining significant changes in speech performance.[39]

Numerous language screening examination batteries have been developed by researchers. A recently published review compared several tests: Frenchay Aphasia Screening Test (English), Language Screening Test (French), Mississippi Aphasia Screening Test (Korean, Czech and Spanish), Screeling (Dutch), Sheffield Screening Test for Acquired Language Disorders (English), Semantic verbal fluency (Korean), Ullevaal Aphasia Screening (Norwegian). Some of these tools were not adequately validated and all of them have advantages and disadvantages.[9] Currently, there is the need for a validated rapid screening speech test in Italian language to evaluate poststroke aphasia in the earliest stage.

Our test was developed to evaluate the severity of stroke-related aphasia in less than 5 minutes. We evaluated several language skills: spontaneous speech, oral and written comprehension, oral naming, repetition, writing to dictation, and reading aloud. The included tasks provide for short administration time, which fits the needs of the emergency context: enabling physicians to administer thrombolysis as soon as possible in case patients meet the criteria.

Furthermore, patients' conditions are often so severe that administering a long test would be difficult. Our screening test can be performed bedside (as the NIHSS) and by any trained member of the medical staff.

The ApsAA evaluates numerous parameters of language and, unlike NIHSS, it attributes greater importance to spontaneous speech, with a dedicated subscore of 16 points out of the total 65 points. Spontaneous speech was the parameter marked by the greatest difference between treated and nontreated patients.

The size of brain lesion and the severity of aphasia at onset are negative predictive factors.[27] In our test, spontaneous speech is the item marked by the greatest improvement in treated patients. Spontaneous speech ability may involve more and distant neurologic networks. Thrombolysis may limit the extension of the ischemic lesion and improve the complex function of spontaneous speech.

Despite the above-mentioned limitations, our spontaneous speech analysis was rather effective in identifying aphasic patients and in evaluating the effectiveness of thrombolysis on language. This may be due to the greater importance we attributed to this item in terms of score compared with NIHSS score. Discourse is a complex linguistic activity involving different levels of the linguistic system (phonological, morphosyntactic, semantic-lexical, and semantic-pragmatic). Moreover, it concerns other cognitive aspects, including executive functions, theory of mind, processing speed, and sustained attention.[49,50] Several studies have shown that people with aphasia have difficulties in dealing with both micro- (lexicon, morphology, syntax) and macrolinguistic (local and global discourse coherence, informativeness, and pragmatics) aspects of speech production.[51,52] Our method investigates microlinguistic parameters of spontaneous speech that can be easily identified by physician not specialized in linguistic analyses. Indeed, spontaneous speech often allows for quicker assessment compared with other linguistic abilities. Moreover, it might be less affected by several test repetitions. These characteristics suggest that spontaneous speech may represent a valuable alternative in contexts requiring shorter and quicker assessment tools, such as emergency departments and stroke units. Nonetheless, further investigations are warranted to confirm both its short and long-term validity compared with more time-consuming forms of language assessment.

A more thorough analysis of all narrative discourse parameters at micro- and macrolinguistic levels in aphasic patients may better discriminate the 2 subgroups' improvement and provide further information. However, such analysis would require more time and an expert speech therapist.

One limitation of our study was the small number of subjects for each group, which is a statistical shortcoming. However, the sample was representative of a pool of patients within a clinical emergency setting and showed the difficulties in evaluating aphasia patients in acute phase, especially before thrombolysis. The limited number of subjects did not enable us to obtain robust data on other possible subgroups, such as stroke etiology, types of aphasia, and location of cerebral lesion.

In our study, only spontaneous speech proved to be significantly higher in treated patients than in nontreated patients. As shown in Table 5, patients of both groups improved their score in numerous subtests, but no significant difference was found between the 2 groups. This may be due to a number of underlying reasons. First, patients were exposed only to a few stimuli to reduce the test duration. Second, the population in both groups was limited.

Our study analyzed changes in language during the first 3 days. Further data may arise with follow-up at 1 and 3 months. However, because our stroke unit is a hub center, such analysis could not be performed: after the acute phase, most of our patients are transferred to other spoke hospitals or dismissed, and they often live far from our hub center.

We overcame the lack of an adequate rapid screening speech test in Italian by developing our own test, which may be further improved in the future.

The novelty of our study is an analysis of the evolution of speech impairment in acute phase through a test which is more detailed compared with NIHSS. We also analyzed the improvement in different speech skills, with a special focus on spontaneous speech.

The limited case number warrants a more comprehensive study and a longer follow-up to confirm our findings and the role of reperfusion therapies on speech impairment.

Conclusions

Our study showed that patients treated with thrombolysis experienced greater improvement in language than the nontreated group. The difference between the 2 groups was increasingly evident over time. Moreover, spontaneous speech was the parameter marked by the greatest improvement.

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