Quality of life three months post-stroke among stroke patients and their caregivers in a single center study from Romania during the COVID-19 pandemic: A prospective study

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Abstract. The aim of the present study was to determine the health-related quality of life of stroke patients and their caregivers during the fifth wave of the COVID-19 pandemic. A total of 70 patients who had been diagnosed with stroke between October 2021 and March 2022 and 70 caregivers were included in the present study. A prospective follow-up study assessing the quality of life at baseline was conducted after 3 months for both patients and their caregivers. A linear regression analysis was performed to evaluate potential associations between quality of life and assessed factors. The results revealed that age, sex, employment status, hospitalization period, type of stroke, Barthel index for activities of daily living (ADL) and discharge Modified Rankin Scale (mRS), were significant determinants of the 90-day Health-Related Quality of Life (HRQoL). An important clinical change in the QoL score was estimated for both post-stroke patients and their caregivers. The decrease of the HRQoL of patients was statistically influenced by a higher value of ADL (P=0.014), whereas, in the case of their caregivers, the decrease of HRQoL was primarily influenced by the QoL of patients after 3 months (P=0.043). The present study identified some important key

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factors with direct consequences on HRQoL regarding stroke survivors and their caregivers.

Introduction

Stroke is a leading cause of long-term disability, morbidity and mortality globally (1). Worldwide, stroke is the second leading cause of mortality (2,3), and has continued to increase in recent years. A major economic and social burden is the high prevalence of stroke because the psychological, social and physical consequences of strokes on patients are devastating (4). Stroke influences personal autonomy and quality of life (QOL). QOL is an important healthcare issue in patients with stroke which is influenced by various factors such as sex, age, comorbidity, mood and disability (5,6). In addition, patients with silent strokes remain poorly treated because the symptoms are clinically undetectable and difficult to discover (7-9).

The majority of stroke patients suffer from ischemic stroke and are older than 65 years. Post-stroke survivors are affected in multiple ways. First, motor impairment is the main factor that contributes to a decrease of social activities and gives rise to emotional and behavioural changes in post-stroke patients. Cognitive impairments are also important sequelae after stroke. Mental and emotional instability due to brain signalling pathway disruption early after stroke is a key factor that affects the post-stroke recovery and decreases QoL. However, long-term emotional and behavioural changes are challenging issues to be addressed (7-9).

In addition, post-stroke depression (PSD) is an important aspect to deal with in stroke survivors and their families. PSD is one of the main contributors to a diminished QoL after stroke and an increase in mortality (10,11). Notably, one third of post-stroke survivors are affected by PSD in the early stage after stroke but also, after several years after stroke onset.

Despite the research effort made in the field of strokes, clinical studies in the Romanian population are scarce. Management of stroke remains frequently limited by state of the art rehabilitation facilities and by financial considerations hindering access to thrombolytic therapy (12).

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Coronavirus disease-19 (COVID-19) first occurred in Wuhan, China; it was declared a pandemic in March 2020 and subsequently became a major global health threat. Since 2021, over 100 million individuals from 210 countries have been confirmed to have been infected with the COVID-19 virus (13).

In Romania, the first case of infection with the new coronavirus was confirmed on February 26, 2020 and the first three deaths were recorded on March 22, 2020 reaching a maximum of 591 deaths per day on November 2, 2021. The virus is expected to remain active until 2024 even after adequate control measures, particularly with the emergence of numerous mutants called variants of concern, including B.1.1.7 (alpha), B.1.617.2 (delta), and B.1.1.529 (omicron) (14).

PSD is frequently under-detected and under-treated due to social stigma and cognitive deficits that mask the post-stroke depression symptoms. Mental and physical health assessments are crucial in the determination of post-stroke cognitive complications including PSD and long-term outcomes in stroke patients. The QoL indicator is useful to assess beneficial or detrimental changes in patients with stroke after treatment. However, the functional outcome after stroke depends on multiple factors. The hypothesis of the authors is that assessment of the Health-Related Quality of Life (HRQoL) is a powerful tool that can improve the diagnosis of post-stroke comorbidities, including PSD and predict the long-term outcome of stroke survivors (10,11).

However, an important factor that influences PSD development is the absence of family support. The incidence of post-stroke mental complications is increased in individuals without family support. On the other hand, the caregivers of stroke patients are often neglected. There is a lack of tools, that enable the investigation of the impact of stroke on the QoL of caregivers. Since, QoL of caregivers is directly associated with the long-term outcome of post-stroke survivors, there is an urgent need to correctly identify the effects of stroke from a social point of view. This gap of knowledge is even more deep regarding informal caregivers, which are the main support system in low and middle-income countries. This is due to limited access and limited resources in the transitional period from hospital to home-care services (10,11).

Since post-stroke recovery is strongly dependent by socio-cultural, genetic and personal factors, the aim of the present study was to identify socio-demographic key factors that play a role in the impairment of the HRQoL of patients or their caregivers, in the southern part of Romania. The findings of the present study may provide an improved understanding of the socio-cultural differences in stroke-related complications, and in the identification of the optimal specific interventions, in the multimodal approach therapy of post-stroke survivors. In addition, the present study may aid in attracting attention on the critically decreasing QoL of stroke-survivors and their caregivers, thus, leading to significant improvements through the development of adapted health policy strategies.

Materials and methods

Ethical issues. The present study was approved (Registration no. 156/2021) by the Academic and Scientific Ethics and Deontology Committee of the University of Medicine and

Pharmacy in Craiova (Craiova, Romania) according to the European Union Guidelines (Declaration of Helsinki). All the patients signed an information and acceptance form to be included in the present study.

Study design. A total of 70 patients out of 95, diagnosed with ischemic stroke (mild and severe) between October 2021 and March 2022, were included in the present study. The inclusion criteria were as follows: i) Only patients who had a caregiver also willing to participate in the present study, >18 years of age; ii) consecutive patients; and iii) patients that returned home after the discharge. The exclusion criteria were as follows: i) Patients not adherent to the questionnaire; ii) patients in a coma or non-cooperative; and iii) patients with a caregiver that did not adhere to the questionnaire. The present study constitutes a prospective follow-up study.

In order to assess the most difficult period according to a previous study (15), namely, the transitional period from hospital care to home care, assessment was performed at two time points: i) A baseline time point at the end of the hospitalization period and ii) after three months of home care.

Examination and tools. The demographic variables included were sex, age, marital status, employment status, urban/rural environment, level of education, smoking, obesity, number of comorbidities and family support. The communication deficiency (no deficiency, with aphasia, dysarthria, aphasia and dysarthria), lesion location (right, left, base), hospitalization days, Trial of Org 101072 in Acute Stroke Treatment (TOAST), activities of daily living (ADL), Barthel Index, discharge Modified Rankin Scale (mRS) score and HRQoL, were included. In order to appreciate the functional outcome, available scale assessment was performed by a trained specialist.

ADL is a scale that was first used for functional assessment status of elderly individuals associated with daily living activities. This tool can be used as a self-report or by indirect/direct observation. The ADL scale includes 5 parameters: Personal hygiene, dressing, toilet hygiene, mobility and self-feeding. The ADL score is between 0-7, where 0 indicates total dependance and 7 indicates independance. The ADL scale is currently used for chronically ill patients (4).

The Barthel index is a stroke severity scale consisting of 10 activities including feeding, personal toileting, bladder and bowel control, movement from chair or bed, and walking or use of stairs. Similar to the ADL scale, it can be conducted as a self-report or through indirect/direct observation. Each parameter is rated according to the ability of whether the patient can or cannot perform a task. The index rating is in the 0-100 range, where 0-20 is considered total dependency and 100 is independency (5).

TOAST is a tool used as a stroke classification system that establishes five stroke subtypes and the stratification of stroke patient in clinical studies (16).

The 15-dimensional (15D) HRQoL measure is a generic and validated questionnaire that explores 15 dimensions (mobility, vision, hearing, breathing, sleeping, eating, speech, excretion, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity), through a 15D score representing the overall HRQoL on a 0-1 scale (0=being dead and 1=full health). The translated version for the Romanian population (17) that was successfully applied on stroke patients (17-19), was used.

Statistical analysis. Statistical analysis was performed using SPSS version 20 (IBM Corp.). Descriptive statistics included calculation of the mean, median, standard deviation (SD) and interquartile range. Matched samples were compared using Wilcoxon's signed-rank test. Violin plots were drawn to visualize the distribution of HRQoL across the two assessed periods of time in such a manner that those distributions could be compared. Spearman's correlation analysis was performed to illustrate the correlations between the variables. The heatmap matrix was drawn in order to visualize the strength and direction of the correlations. Colours ranged from bright blue (strong positive correlation; r=1.0) to bright orange (strong negative correlation; r=-1.0). P<0.05 was considered to indicate a statistically significant difference.

Results

Characteristics of patients and their caregivers. From October 2021 to March 2022, 70 patients with stroke were treated at the Department of Neurology of the Neuropsychiatry Hospital of Craiova (Craiova, Romania) and were included in the present study.

The characteristics of the patients are revealed in Table I. The mean age of patients was 67.91 (SD, 12.39; range, 32-86) years. Females (41/70; 58.6%) were slightly more than males and the majority of the patients (38/70; 54.3%) were married. The most common comorbidities were hypertension (15.7%) and chronic obstructive pulmonary disease (15.7%).

The characteristics of the caregivers of the patients are revealed in Table II. Their mean age was 50.67 (SD, 12.72; range 25-75) years. Most of the caregivers were employed (51.4%), female (62.9%), and were the children of the patients (44.3%).

The response rate to the 15D questionnaire was 100% for both patients and the caregivers of the patients. The progression of the 15D scores at baseline and the follow-up visit are revealed in Fig. 1. A statistically significant decreased HRQoL was observed in the follow-up visit, after 3 months of home care, than at the end of the hospitalization period (P<0.0001).

Descriptive data of the HRQoL. The 15D scores of patients with stroke were low at baseline and further decreased at the follow-up visit, after 3 months (Fig. 1): Mobility (0.49 ± 0.15 vs. 0.4 ± 0.14), vision (0.55 ± 0.21 vs. 0.42 ± 0.15), hearing (0.6 ± 0.21 vs. 0.44 ± 0.23), breathing (0.52 ± 0.19 vs. 0.46 ± 0.16), sleeping (0.57 ± 0.22 vs. 0.5 ± 0.19), eating (0.49 ± 0.16 vs. 0.32 ± 0.14), speech (0.49 ± 0.17 vs. 0.39 ± 0.12), excretion (0.44 ± 0.13 vs. 0.35 ± 0.13), usual activities (0.45 ± 0.16 vs. 0.37 ± 0.15), mental function (0.41 ± 0.12 vs. 0.29 ± 0.1), discomfort/symptoms (0.45 ± 0.17 vs. 0.39 ± 0.16), depression (0.57 ± 0.17 vs. 0.4 ± 0.1), distress (0.55 ± 0.16 vs. 0.35 ± 0.11), vitality (0.57 ± 0.15 vs. 0.46 ± 0.13), sexual activity (0.51 ± 0.17 vs. 0.39 ± 0.15), total 15D score (0.51 ± 0.13 vs. 0.4 ± 0.12).

All 15 dimensions were statistically lower than baseline, as revealed in Table III. The difference regarding the values was >0.015 for all indicators, thus, the change was also considered clinically important.

Table I. Characteristics of the patients enrolled in the study.

Demographics	Total no. of patients (N=70)
Male sex, no. (%)	29 (41.4%)
Age (years), mean (SD) and	67.91 (12.39)
median (IQR)	68.5 (60-79)
Marital status	
Married	38 (54.3%)
Single	2 (2.9%)
Divorced	10 (14.3%)
Widowed	20 (28.6%)
Employment status	
Employed, no. (%)	15 (21.4%)
Unemployed, no. (%)	14 (20%)
Retired, no. (%)	41 (58.6%)
Education level	
Middle School	19 (27.1%)
High School	46 (65.7%)
College or University	5 (7.1%)
Environment	
Urban	37 (52.9%)
Rural	33 (47.1%)
Smoking	
Never	35 (50%)
Former smoker	35 (50%)
Obesity	
No obesity	47 (67.1%)
Ι	19 (27.1%)
II	4 (5.7%)
Familial support, yes (%)	46 (65.71%)
No. of comorbidities (%)	
0	3 (4.29%)
1	63 (90.0%)
2	4 (5.71%)
Comorbidities	
Hypertension, no. (%)	11 (15.7%)
Diabetes, no. (%)	9 (12.9%)
Bronchial asthma, COPD	11 (15.7%)
Heart failure	4 (5.7%)
Glaucoma	3 (4.2%)
TOAST	
Large-artery atherosclerosis	15 (21.4%)
Cardioembolism	11 (15.7%)
Small-vessel occlusion	17 (24.3%)
Stroke of other determined etiology	17 (24.3%)
Stoke of undetermined etiology	10 (14.3%)
ADL	2.80 (0.88%)
Barthel index	32.29 (8.63%)

SD, standard deviation; IQR, interquartile range; COPD, chronic obstructive pulmonary disease; TOAST, Trial of Org 101072 in Acute Stroke Treatment; ADL, activities of daily living.

Table II. Characteristics of the caregivers of stroke patients enrolled in the study.

Demographics	Total no. of caregivers (N=70)
Male sex, no. (%)	26 (37.1%)
Age (years), mean (SD) and median (IQR)	50.67 (12.72)
Туре	
Parents	1 (1.4%)
Brother/sister	5 (7.1%)
Wife/husband	23 (32.9%)
Children	31 (44.3%)
Grandchildren	10 (14.2%)
Employment status	
Employed, no. (%)	36 (51.4%)
Unemployed, no. (%)	20 (30%)
Retired, no. (%)	13 (18.6%)
Level of education	
Middle School	9 (12.9%)
High School	42 (60%)
College or University	19 (27.1%)

SD, standard deviation; IQR, interquartile range.

Table III. Comparison of the 15D assessment of stroke patients between two time points (baseline and after 3 months).

D	Mean	Standard	QC
Dimension	difference	deviation	Significance
Mobility	-0,098073	0,1142439	<0.0001
Vision	-0,125993	0,1237864	< 0.0001
Hearing	-0,152793	0,1158872	< 0.0001
Breathing	-0,058933	0,1083690	< 0.0001
Sleeping	-0,066443	0,1131272	< 0.0001
Eating	-0,176349	0,1107134	< 0.0001
Speech	-0,094429	0,1239735	< 0.0001
Excretion	-0,087267	0,1196142	< 0.0001
Usual activities	-0,075794	0,1260933	< 0.0001
Mental function	-0,122897	0,1058255	< 0.0001
Discomfort and	-0,050396	0,1009079	< 0.0001
symptoms			
Depression	-0,164797	0,1260221	< 0.0001
Distress	-0,196131	0,0989375	< 0.0001
Vitality	-0,116026	0,1209333	< 0.0001
Sexual activity	-0,115749	0,1194684	< 0.0001
15D score	-0,107696	0,0373576	<0.0001
15D, 15 dimensions			

Similarly, the HRQoL was also decreased for the caregivers of the patients, as revealed in Fig. 2. The 15D scores of the caregivers of the patients were low at baseline and further



Figure 1. Mean 15D score and health-related quality of life dimensions for stroke patients before and after stroke treatment. 1, Mobility; 2, Vision; 3, Hearing; 4, Breathing; 5, Sleeping; 6, Eating; 7, Speech; 8, Excretion; 9, Usual activities; 10, Mental function; 11, Discomfort and symptoms; 12, Depression; 13, Distress; 14, Vitality; 15, Sexual activity; Score, 15D Score. Time=0.0 (baseline), at the end of the hospitalization period; Time=1.0, after 3 months of home care. 15D, 15 dimensions.



Figure 2. Mean 15D score and health-related quality of life dimensions for the caregivers of stroke patients at baseline and follow-up visit. 1, Mobility; 2, Vision; 3, Hearing; 4, Breathing; 5, Sleeping; 6, Eating; 7, Speech; 8, Excretion; 9, Usual activities; 10, Mental function; 11, Discomfort and symptoms; 12, Depression; 13, Distress; 14, Vitality; 15, Sexual activity; Score, 15D Score. Time=0 (baseline), at the end of the hospitalization period; Time=1, after 3 months of home care. 15D, 15 dimensions.

decreased after the follow-up visit that occured 3 months later: Mobility (0.93 ± 0.14 vs. 0.90 ± 0.17), vision (0.86 ± 0.15 vs. 0.77 ± 0.13), hearing (0.92 ± 0.14 vs. 0.82 ± 0.16), breathing (0.88 ± 0.15 vs. 0.82 ± 0.16), sleeping (0.90 ± 0.13 vs. 0.80 ± 0.16), eating (0.94 ± 0.13 vs. 0.92 ± 0.16), speech (0.92 ± 0.13 vs. 0.89 ± 0.14), excretion (0.91 ± 0.16 vs. 0.76 ± 0.17), usual activities (0.86 ± 0.16 vs. 0.86 ± 0.16), mental function (0.91 ± 0.17 vs. 0.81 ± 0.23), discomfort/symptoms (0.91 ± 0.14 vs. 0.80 ± 0.23), depression (0.92 ± 0.11 vs. 0.74 ± 0.13), distress (0.92 ± 0.13 vs. 0.72 ± 0.11), vitality (0.92 ± 0.11 vs. 0.80 ± 0.14), sexual activity (0.93 ± 0.16 vs. 0.84 ± 0.19), score total 15D (0.91 ± 0.11 vs. 0.83 ± 0.12).

According to the responses provided in the 15D assessment, the caregivers of the patients did not declare significant modifications for mobility and usual activities. Clinically and statistically significant differences were observed among the other 13 dimensions and for the total score of the HRQoL, as presented in Table IV.

 Table IV. Comparison of the 15D assessment of the caregivers of stroke patients between two time points (baseline and after 3 months).

Dimension	Mean difference	Standard deviation	Significance
Mobility	0,844640	0,1908114	0.073
Vision	0,830527	0,1178299	< 0.0001
Hearing	-0,030120	0,1094324	< 0.0001
Breathing	-0,089739	0,1117594	< 0.0001
Sleeping	-0,098733	0,1257868	< 0.0001
Eating	-0,066780	0,1242550	0.038
Speech	-0,093053	0,1183144	0.008
Excretion	-0,021434	0,0798299	< 0.0001
Usual activities	-0,029670	0,0896527	< 0.0001
Mental function	-0,152094	0,1577240	< 0.0001
Discomfort and	0,000000	0,0822726	< 0.0001
symptoms			
Depression	-0,098160	0,1527564	< 0.0001
Distress	-0,110663	0,1450031	< 0.0001
Vitality	-0,184069	0,1010856	< 0.0001
Sexual activity	-0,197444	0,1216742	< 0.0001
15D score	-,120749	,1184799	<0.0001

15D, 15 dimensions.

The correlations between all of the assessed factors and the HRQoL of the patients and their caregivers was evaluated, and some of the correlations established are revealed in Fig. 3.

At baseline, the HRQoL of the patients was influenced by age (r=-0.320; P=0.007; the younger survivors had an improved QoL), employment status (r=-0.368; P=0.002; the lack of employment decreased the QoL), the number of hospitalization days (r=-0.288; P=0.016), the ADL (r=0.469; P<0.0001), the Barthel index (r=0.368; P=0.002), the age of the caregiver (r=-0.356; P=0.003), the employment status of the caregiver (r=-0.414; P<0.0001), and the mRS1 (r=-0.423; P<0.0001) (Fig. 3).

After 3 months, during the follow-up visit, the HRQoL of the patients was influenced by age (r=-0.388; P=0.001; the younger survivors had an improved QoL), employment status (r=-0.407; P=0.002; the lack of employment decreased the QoL), obesity (r=0.259; P=0.031), the number of hospitalization days (r=-0.365; P=0.002), TOAST (r=-0.264; P=0.027), ADL (r=0.467; P<0.0001), the Barthel index (r=0.414; P<0.0001), the age of the caregiver (r=-0.355; P=0.003), the employment status of the caregiver (r=-0.449; P<0.0001), mRS1 (r=-0.444; P<0.001), and mRS2 (r=-0.329; P=0.005) (Fig. 3).

At baseline, the HRQoL of the caregivers was influenced by age (r=-0.335; P=0.005; the younger individuals had an improved QoL), employment status (r=-0.305; P=0.010; the lack of employment decreased the QoL), the number of hospitalization days (r=-0.288; P=0.016), the age of the caregiver (r=-0.840, P<0.0001), the employment status of the caregiver (r=-0.410; P<0.0001), the QoL of the patient at baseline (r=0.438; P<0.0001) and after 3 months (r=0.413; P<0.0001). No correlation was observed between the HRQoL and mRS of the caregivers at baseline (r=-0.101; P=0.078) (Fig. 3).

After 3 months, the HRQoL of the patients was influenced by age (r=-0.293; P=0.014; the younger survivors had an improved QoL), employment status (r=-0.262; P=0.028; the lack of employment decreased the QoL), environmental (r=-0.373; P=0.001; improved QoL for urban life), obesity (r=0.259; P=0.031), the number of hospitalization days (r=-0.365; P=0.002), the age of the caregiver (r=-0.827, P<0.0001), the employment status of the caregiver (r=-0.450, P<0.0001), the QoL of patient at baseline (r=0.547; P<0.0001) and after 3 months (r=0.552; P<0.0001). No correlation was identified between the HRQoL and mRS of caregivers at baseline (r=-0.188; P=0.120) or after 3 months (r=-0.101; P=0.404) (Fig. 3).

With regard to the decreased HRQoL of the survivors, ADL was the only factor that significantly influenced it (r=-0.336; P=0.004), which is logical due to the limitation of daily living activities and social interaction. Among caregivers, the intensity of their HRQoL decrease was significantly correlated with their age (r=-0.265; P=0.027), sex (r=-0.239; P=0.046; females had a worse QoL than males), initial QoL of the patient (r=0.444; P<0.0001) and post 3-month QoL (r=0.493, P<0.0001) (Fig. 3).

Given the number of significantly influencing factors, multiple linear regression was performed. ADL (P=0.014) and QoL after 3 months (P=0.043) were the factors most significantly correlated to the decreased HRQoL of the survivors and to the decreased HRQoL of the caregivers (Fig. 3).

Following examination of the influence of lesion location on the scores for the QoL of patients, a significant difference across categories was not identified. In the present study, stroke location was not associated with the magnitude of the decreased QoL of patients (Table V). A possible explanation for this result is the low number of patients included in this study. Further study on a large cohort is required in order to establish which location is strongly associated with QoL in stroke survivors. Furthermore, these findings can be partially explained by the delay in the post-stroke intervention due to delayed presentation to emergency care during the pandemic period.

Discussion

The present study investigated for the first time, the impairment in QoL among patients who suffered stroke and their caregivers in a single center located in Romania during the COVID-19 pandemic, after a three-month post-stroke period, without any intervention to support the transition from hospital to home. For this purpose, demographic variables, the 15D assessment tool, TOAST, ADL, Barthel index and discharge mRS score, that were studied separately in the literature, were used, without comparative evaluation before and during the COVID-19 pandemic (20-23).

Muresanu *et al* highlighted the significant decrease in hospital discharges in Romania among patients who suffered stroke during the COVID-19 pandemic (21). The pandemic led to global chaos, particularly in the healthcare system where it caused sudden interruptions in the provision of healthcare to all patients across the country, induced by the relocation

Difference in scores for QoL for stroke patients	Location of the stroke			
	Right (n=26)	Left (n=26)	Basal (n=18)	P-value
Mean ± SD	-0.103±0.026	-0.116±0.05	-0.1±0.028	0.727
Median (IQR)	-0.1 (-0.12 to -0.08)	-0.11 (-0.15 to -0.07)	-0.09 (-0.13 to -0.09)	

Table V. Association between stroke location and QoL.



Figure 3. Heatmap matrix. Colors range from bright blue (strong positive correlation; r=1.0) to bright orange (strong negative correlation; r=-1.0). Score15D_P_0, the total score of 15D for patients at baseline; Score15D_P_1, the total score of 15D for patients at follow-up visit; Score15D_C_0, the total score of 15D for the caregivers of patients at baseline; Score15D_C_1, the total score of 15D for the caregivers of patients at follow-up visit. 15D, 15 dimensions.

of workforces from healthcare facilities to treating patients with COVID-19 (24) or by the panic instilled in the population that led to a decrease in trust in the medical act with a therapeutic (25) or preventive purpose such as vaccination (23). The number of non-COVID-19 acute emergency cases decreased, a fact reflected by the low number of emergency presentations and the number of CT scans performed (25,26). Moreover, a negative impact of COVID-19 was identified in patients who had risk factors for diseases or already suffered from life-threatening diseases such as stroke, with some hesitation from the patient to initially visit a doctor due to the associated risk of exposure to the virus (27,28).

The present study revealed that the HRQoL of survivors and their caregivers was decreased. The stroke survivors and their family proxies modestly agreed to undergo assessment of QoL following a stroke, as well as functionality assessment at 1 to 2 months post-stroke (29). In the present study, at baseline and after 3 months, the HRQoL of survivors was influenced by age, employment status, number of hospitalization days, ADL, Barthel index, and age as well as employment status of the caregiver. Younger survivors had improved QoL and the lack of employment decreased it. Obesity and TOAST influenced HRQoL after 3 months.

In addition, at baseline and after 3 months, the HRQoL of the caregiver was influenced by age, employment status, ADL, Barthel index, and their employment status. Life satisfaction of family caregivers was associated with feelings and emotions of the patients only. It was strongly linked with the four WHOQOL-BREF domains (physical health, psychological health, environment, and social relationships) of the caregiver (30). Strong psychological repercussions may be generated for both patients and family caregivers (31). The family proxy rated QoL worse than stroke survivors rated that domain, however, the rates were similar in more objective domains such as physical functioning but not analogous in more subjective domains such as mood. What is difficult to determine is whether the patient or the proxy is closer to the 'truth'. For example, depressed patients report a lower HRQoL and these scores are more consistent with proxy HRQoL ratings, but whether the reported lower HROoL of the patient is accurate or whether it is lower than their 'actual' HRQoL, resulting from the overlying depression, is not clear.

The findings of the present study are not consistent with those of a previous study regarding sex differences in HRQoL in patients who suffered stroke, where it was reported that females had a lower QoL than males (32). Worse HRQoL in female patients with stroke was not identified and the interventions including those increasing rehabilitation efforts could be assessed in the future regardless of sex in Romania.

A previous study identified differences in the levels HRQoL with regard to employment status. Unlike individuals at home with no activity and despite their handicap, stoke patients who are retired may have less stress or unhappiness and may maintain a social position/identity, which is based not only on age and social characteristics but also on the sense of self of the individual (33). As expected, it was demonstrated that, both at baseline and after 3 months of home post-stroke stay, the lack of employment decreased HRQoL.

In the present study, the length of hospitalization and mRS at discharge were negatively correlated with HRQoL and the tendency towards depressive mood was likely to influence the HRQoL, concurrently as the other assessed dimensions including mobility, usual activities, mental function, distress, or sexual activity. The same results were detected by Pedersen *et al* for post-stroke Scandinavian patients (33).

Following the pandemic period, significant changes in the QoL of patients were reported, including stroke survivors. In a previous study, a significant decrease in stroke hospitalization time was reported during and after Covid-19 (34). This had a high impact on the outcome of the disease as well as on the QoL of patients and their caregivers.

During Covid-19, an increased number of cases with clinical signs of severe and moderate stroke were recorded. According to the American Heart Association, patients with Covid-19 are more exposed to stroke by a different mechanism than atherosclerosis (35). As a result, this can change the impact of the disease and requires further investigation in order to identify pre- and post-Covid 19 changes in the QoL-related stroke pattern. The delay of thrombolytic therapy for patients who have suffered a stroke has a high impact on post-stroke recovery and functional outcome. It is associated with long term disability and increased healthcare costs.

Notably, a recent study reported an increased risk of stroke in middle-aged individuals, independent of age (35). In the post-Covid-19 era, the consequences of the pandemic have to be carefully monitored (36). The QoL of caregivers is an important topic to be addressed. The post-Covid-19 public health policy has to be wary of the impact of Covid-19 on both stroke survivors and their caregivers.

The present study had several limitations. The statistical assessment of QoL in a relatively small population during the pandemic was extremely difficult, as outliers can alter the results. The trend that was identified in the present study, should be further validated on large cohorts in a multicentric clinical study. Thus, the results are consistent, but some other covariates could influence the QoL, including medication adherence or fatigue, assessed by evaluating post-stroke QoL (37). In order to quantify the HRQoL, a valid tool for the Romanian population is required, based on a precise and valid measurement algorithm for stroke patients. There is still a lack of tools for the assessment of HRQoL in stroke patients in Romania, and this difficulty must be resolved in the future.

The aim of the present study was to identify the multidimensional effects of post-stroke HRQoL among patients and caregivers, in order to propose and implement suitable intervention approaches, to support the transition from hospital to home after stroke, in Romania (36-38).

In conclusion, HRQoL is an important issue to be addressed in the multimodal management of stroke survivors following the acute period. As revealed in the present study, the HRQoL of post-stroke patients and their caregivers was decreased in a significant clinical percentage, in Romania. The aim of the present study was to raise awareness on this issue, identifying certain important key factors with direct consequences on the HRQoL of stroke survivors and their caregivers. The clinical reduction of the QoL of both patients and their caregivers was observed during the pandemic, and changes in health policies in Romania are warranted regarding this issue, particularly in a pandemic.

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Availability of data and materials

The datasets used during the present study are available from the corresponding author upon reasonable request.

Authors' contributions

VP, CVA, AMB, DCC, RP, VB, MMF, MSS and ATS equally contributed to the acquisition, analysis and systematization of data, manuscript writing and critical revision for its important intellectual content. VP and RP confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was performed in line with the principles of the Declaration of Helsinki. Ethical approval (Registration no. 156/2021) was obtained from the Academic and Scientific Ethics and Deontology Committee of the University of Medicine and Pharmacy of Craiova (Craiova, Romania). Informed consent was obtained from all participants involved in the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

- Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, *et al*: Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: A systematic analysis for the global burden of disease study 2010. Lancet 380: 2197-2223, 2012.
- Albu CV, Padureanu V, Boldeanu MV, Bumbea AM, Enescu AS, Albulescu DM, Silosi CA and Enescu A: Vascular neurocognitive disorders and the vascular risk factors. J Mind Med Sci 5: 7-15, 2018.
- Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, Abraham J, Adair T, Aggarwal R, Ahn SY, *et al*: Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the global burden of disease study 2010. Lancet 380: 2095-2128, 2012.
- 4. Gill TM and Feinstein AR: A critical appraisal of the quality of quality-of-life measurements. JAMA 272: 619-626, 1994.
- Hopman WM and Verner J: Quality of life during and after inpatient stroke rehabilitation. Stroke 34: 801-805, 2003.
- White JH, Alston MK, Marquez JL, Sweetapple AL, Pollack MR, Attia J, Levi CR, Sturm J and Whyte S: Community-dwelling stroke survivors: Function is not the whole story with quality of life. Arch Phys Med Rehabil 88: 1140-1146, 2007.
- Howard G, Safford MM, Meschia JF, Moy CS, Howard VJ, Pulley L, Gomez CR and Crowther M: Stroke symptoms in individuals reporting no prior stroke or transient ischemic attack are associated with a decrease in indices of mental and physical functioning. Stroke 38: 2446-2452, 2007.

- 8. Howard VJ, McClure LA, Meschia JF, Pulley L, Orr SC and Friday GH: High prevalence of stroke symptoms among persons without a diagnosis of stroke or transient ischemic attack in a general population: The REasons for geographic and racial differences in stroke (REGARDS) study. Arch Intern Med 166: 1952-1958, 2006.
- 9. Kleindorfer D, Judd S, Howard VJ, McClure L, Safford MM, Cushman M, Rhodes D and Howard G: Self-reported stroke symptoms without a prior diagnosis of stroke or transient ischemic attack: A powerful new risk factor for stroke. Stroke 42: 3122-3126, 2011.
- 10. Wu QE, Zhou AM, Han YP, Liu YM, Yang Y, Wang XM and Shi X: Poststroke depression and risk of recurrent stroke: A meta-analysis of prospective studies. Medicine (Baltimore) 98: e17235, 2019.
- 11. Cojocaru GR, Popa-Wagner A, Stanciulescu EC, Babadan L and Buga AM: Post-stroke depression and the aging brain. J Mol Psychiatry 1: 14, 2013.
- 12. Boudokhane S, Migaou H, Kalai A, Jellad A, Borgi O, Bouden A, Sriha Belguith A and Ben Salah Frih Z: Predictors of quality of life in stroke survivors: A 1-year follow-up study of a tunisian sample. J Stroke Cerebrovasc Dis 30: 105600, 2021.
- Wang C, Wang Z, Wang G, Lau JY, Zhang K and Li W: COVID-19 in early 2021: Current status and looking forward. Signal Transduct Target Ther 6: 114, 2021.
- 14. Kissler SM, Tedijanto C, Goldstein E, Grad YH and Lipsitch M: Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. Science 368: 860-868, 2020.
- Lindblom S, Tistad M, Flink M, Laska AC, von Koch L and Ytterberg C: Referral-based transition to subsequent rehabilitation at home after stroke: One-year outcomes and use of healthcare services. BMC Health Serv Res 22: 594, 2022.
- 16. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL and Marsh EE III: Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in acute stroke treatment. Stroke 24: 35-41, 1993.
- 17. Subtirelu MS, Turcu-Stiolica A and Sintonen H: PMU133 translation and cultural adaptation of 15D quality of life questionnaire from English to Romanian language. Value Health 22: S731, 2019
- 18. Turcu-Stiolica A, Subtirelu MS and Bumbea AM: Can incobotulinumtoxin-A treatment improve quality of life better than conventional therapy in spastic muscle post-stroke patients? Results from a pilot study from a single center. Brain Sci 11: 934, 2021.
- 19. Turcu-Stiolica A, Subtirelu MS and Bumbea AM: Cost-utility analysis of incobotulinumtoxin-A compared with conventional therapy in the management of post-stroke spasticity in Romania. Front Pharmacol 10: 1516, 2020.
- 20. Hayati F, Lah NASN, Zakaria AD, Rahim SSSA and Azizan N: Issues and impact of COVID-19 on surgical services in Northern Borneo, Sabaĥ. BJMS 16: 1-4, 2022.
- 21. Muresanu DF, Strilciuc S, Lorenzovici L, Sófalvi A and Grad D: COVID-19 indirectly hits stroke patients, as hospital discharges in Romania see a dramatic decrease during the pandemic. Eur J Neurol 28 (Suppl 1): S757, 2021.22. Grad DA, Chereches RM, Strilciuc S and Muresanu D: Scars of
- stroke care emerge as COVID-19 shifts to an endemic in many countries. J Med Life 15: 589-591, 2022
- 23. Mărcău FC, Purec S and Niculescu G: Study on the refusal of vaccination against covid-19 in Romania. Vaccines (Basel) 10: 261,2022
- 24. Mărcău FC, Peptan C, Nedelcuță RM, Băleanu VD, Băleanu AR and Niculescu B: Parental COVID-19 vaccine hesitancy for children in Romania: National survey. Vaccines (Basel) 10: 547, 2022.

- 25. O'Brien CM, Jung K, Dang W, Jang HJ and Kielar AZ: Collateral damage: The impact of the covid-19 pandemic on acute abdominal emergency presentations. J Am Coll Radiol 17: 1443-1449, 2020.
- 26. Nodora JN, Gupta S, Howard N, Motadel K, Propst T, Rodriguez J, Schultz J, Velasquez S, Castañeda SF, Rabin B and Martínez ME: The COVID-19 pandemic: Identifying adaptive solutions for colorectal cancer screening in underserved commu-nities. J Natl Cancer Inst 113: 962-968, 2021.
- 27. Baumann M, Le Bihan E, Chau K and Chau N: Associations between quality of life and socioeconomic factors, functional impairments and dissatisfaction with received information and home-care services among survivors living at home two years after stroke onset. BMC Neurol 14: 92, 2014
- 28. Alanne S, Roine RP, Räsänen P, Vainiola T and Sintonen H: Estimating the minimum important change in the 15D scores. Qual Life Res 24: 599-606, 2015.
- 29 Williams LS, Bakas T, Brizendine E, Plue L, Tu W, Hendrie H and Kroenke K: How valid are family proxy assessments of stroke patients' health-related quality of life? Stroke 37: 2081-2085, 2006.
- 30. Cardoso AL, Silva-Junior GO, Bastos LF, Cesar ALM, Serrano LG, Dziedzic A and Picciani BLS: Preliminary assessment of the quality of life and daily burden of caregivers of persons with special needs: A questionnaire-based, cross-sectional survey. Int J Environ Res Public Health 20: 2012, 2023.
- 31. Gargano JW and Reeves MJ; Paul Coverdell National Acute Stroke Registry Michigan Prototype Investigators: Sex differences in stroke recovery and stroke-specific quality of life: Results from a statewide stroke registry. Stroke 38: 2541-2548, 2007.
- 32. Minichiello V, Browne J and Kendig H: Perceptions and consequences of ageism: Views of older people. Ageing Soc 20: 253-278, 2000.
- 33. Pedersen SG, Friborg O, Heiberg GA, Arntzen C, Stabel HH, Thrane G, Nielsen JF and Anke A: Stroke-specific quality of life one-year post-stroke in two Scandinavian country-regions with different organisation of rehabilitation services: A prospective study. Disabil Rehabil 43: 3810-3820, 2021.
- 34. De Bruijn MAAM, Synhaeve NE, van Rijsbergen MWA, de Leeuw FE, Mark RE, Jansen BPW and de Kort PL: Quality of life after young ischemic stroke of mild severity is mainly influenced by psychological factors. J Stroke Cerebrovasc Dis 24: 2183-2188, 2015
- 35. Yang Q, Tong X, Coleman King S, Olivari BS and Merritt RK: Stroke hospitalizations before and during COVID-19 pandemic among medicare beneficiaries in the United States. Stroke 52: 3586-3601, 2021.
- 36. Shakil SS, Emmons-Bell S, Rutan C, Walchok J, Navi B, Sharma R, Sheth K, Roth GA and Elkind MSV: Stroke among patients hospitalized with COVID-19: Results from the american heart association COVID-19 cardiovascular disease registry. Stroke 53: 800-807, 2022.
- Coman AE, Ceasovschih A, Petroaie AD, Popa E, Lionte C, Bologa C, Haliga RE, Cosmescu A, Slănină AM, Bacuscă AI, et al: The significance of low magnesium levels in COVID-19 patients. Medicina (Kaunas) 59: 279, 2023.
- 38. O'Callaghan G, Fahy M, Murphy P, Langhorne P, Galvin R and Horgan F: Effectiveness of interventions to support the transition home after acute stroke: A systematic review and meta-analysis. BMC Health Serv Res 22: 1095, 2022.



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