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THE EFFECT OF POST STROKE DEPRESSION ON FUNCTIONAL OUTCOME AND QUALITY OF LIFE

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SUMMARY – In spite of being a common and important complication of stroke, post stroke depression is often overlooked, so its impact on stroke outcome remains under recognized. The aim of the study was to determine the effect of depression on functional outcome and quality of life in stroke patients. The study included 60 patients treated for their first clinical stroke, 30 of them diagnosed with depression and 30 patients without depression. Testing was done in all patients two and six weeks after stroke. Depression was diagnosed according to the Mini International Neuropsychiatry Interview, DSM-IV diagnostic criteria, and depression severity was quantified by the Hamilton Depression Rating Scale; functional impairment was determined by the Barthel Index; and post stroke quality of life was assessed by the Short Form 36 (SF-36) questionnaires. The patients with depression had significantly more severe functional disability both at baseline and after rehabilitation treatment, although the potential for functional recovery in depressed patients was less than in non-depressed ones. The quality of life in patients with post stroke depression was impaired more severely in all SF-36 domains compared with non-depressed stroke patients, with the domains of the role of emotional functioning and social relations being most severely affected.

Key words: *Stroke – complications; Depression; Treatment outcome, assessment; Quality of life*

Introduction

Post stroke depression (PSD) is a common and serious complication of stroke[1,2]. A form of depression occurs in at least one fourth of patients within the first year after stroke, and the risk of depression is highest within the first few months after stroke onset[3]. In addition, PSD is considered to be the main negative prognostic factor as regards the patient's return to work after stroke[4], and depression severity has been found to be an independent predictor of post stroke mortality[5,6]. Nevertheless, PSD is rarely diagnosed, mood disorders are most frequently overlooked, and their significance in relation to stroke outcome is neglected and underestimated[7].

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Over the last two decades, there are an increasing number of studies investigating various aspects of PSD: its prevalence, phenomenology, course, etiopathogenesis, risk factors, prevention, and treatment[8-11]. However, systematic reviews of literature show inconsistent findings in almost all of these aspects. The prevalence of major PSD varies widely among the studies and, furthermore, there are no definite conclusions regarding its etiology and predictors and, consequently, regarding prevention and treatment procedures[12,13]. In addition, the association of depression with cognitive, neurological and functional status of stroke patients, as well as the significance of depressive disorder for stroke outcome remains unclear[14].

The conflicting character of previous research results indicates the need of further research in this important field of medicine. The aims of the present study were to determine the effect of PSD on disease

outcome, i.e. the degree of impairment and quality of life after stroke.

Patients and Methods

The prospective study included 60 patients of both sexes over 18 years of age, who were treated for their first clinical stroke at the Department of Neurology, Clinical Center of Vojvodina, Novi Sad, Serbia. One group comprised patients not diagnosed with depression in the acute phase of stroke (n=30), whereas the other group comprised patients who were diagnosed with depression two weeks after stroke onset (n=30). The inclusion criteria were: first symptomatic stroke (ischemic or hemorrhagic) verified by brain computed tomography (CT) and/or brain magnetic resonance imaging (MRI), and the Mini Mental State Examination (MMSE) score over 10. The exclusion criteria were: presence of previous physical disability due to other neurological, orthopedic or rheumatic diseases, impaired consciousness, sensorimotor aphasia, severe somatic disease that would prevent patient follow up, and suicidal ideas.

During hospitalization, in the acute phase of stroke, all patients underwent Doppler and/or duplex examination of carotid arteries, transcranial Doppler examination of the vertebrobasilar territory, brain CT and/or brain MRI. Neurological, neuropsychiatric and neuropsychological tests were performed in all patients two weeks after stroke onset (to fulfill the ICD-10 diagnostic criteria for a depressive episode) and six weeks after stroke onset, which in most cases coincided with completion of in-hospital rehabilitation treatment.

Depression was diagnosed using the Mini International Neuropsychiatric Interview (MINI) (Serbian version/DSM-IV 4.4), which is designed as a concise structured interview adapted to the diagnosis of depressive disorder in both the DSM-IV and ICD-10 classifications. Depression severity was quantified using the Hamilton Depression Rating Scale (HDRS). Cognitive impairment was assessed by the (MMSE). Functional status was expressed using Barthel Index (BI). Quality of life was assessed six weeks after stroke onset using the Short Form 36 (SF-36) questionnaire, and the results were analyzed from the aspects of eight quality of life domains, summary physical score and summary mental score. Responses were coded and domain scores and summary scores were calculated by the method described in the SF-36 version 2.0[15,16].

Statistical analysis was performed using the SPSS version 13 software. Data were analyzed using basic descriptive statistics, such as absolute and relative numbers, arithmetic mean, standard deviation, and range. Statistical significance of differences in the results obtained was assessed using Mann Whitney U test, Kruskal-Wallis H, Wilcoxon test, Student's t-test and χ^2-test. Association of variables, scales, scores and domains was analyzed using Pearson's and Spearman's correlation coefficients.

Results

In the group of depressed patients, minor depression (HDRS score 8-15) was found in 86.7% and major depression (HDRS score ≥16) in 13.3% of patients. The mean HDRS score was statistically significantly higher in depressed patients than in non-depressed patients both at two and at six weeks post stroke ($p<0.001$). At six weeks, 26.7% of the patients initially diagnosed with depression experienced spontaneous recovery (HDRS score <8), which was statistically significant ($p=0.008$). However, none of the patients diagnosed with major depression in the acute phase of stroke had spontaneous remission of depression.

The mean BI scores were significantly higher in patients without PSD than in those with PSD both at two and six weeks after stroke ($p<0.001$). In both groups of patients, there was a significant increase in BI scores six weeks after stroke compared to the scores two weeks after stroke; the mean increase was 31.9 in patients with PSD and 10.8 in patients without PSD ($p<0.001$) (Fig. 1). There was no statistically significant difference in the degree of functional impairment between men and women with PSD; the BI score was 47.9±22.0 in women and 61.6±26.4 in men ($p=0.130$).

In the group without PSD, most patients had minimal disability (56.7%). In the group with PSD, moderate disability (33.3%) and significant disability (30%) were most frequent, whereas maximum disability was found in 13.3%. The difference in disability between the two groups of patients was statistically highly significant ($p<0.001$). The difference in ambu-

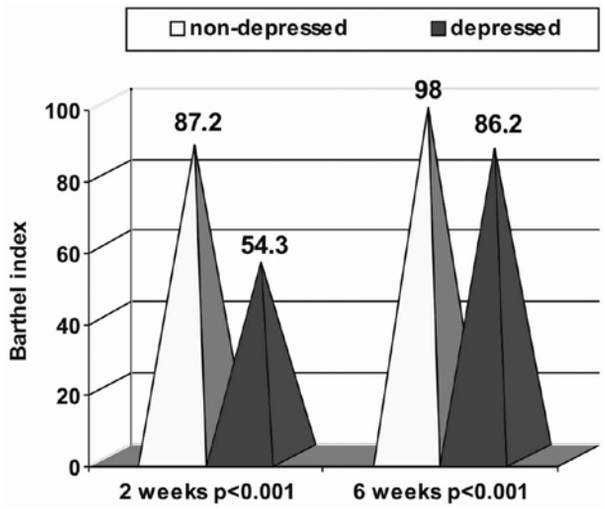

Fig. 1. Barthel index in non-depressed and depressed patients 2 and 6 weeks after stroke.

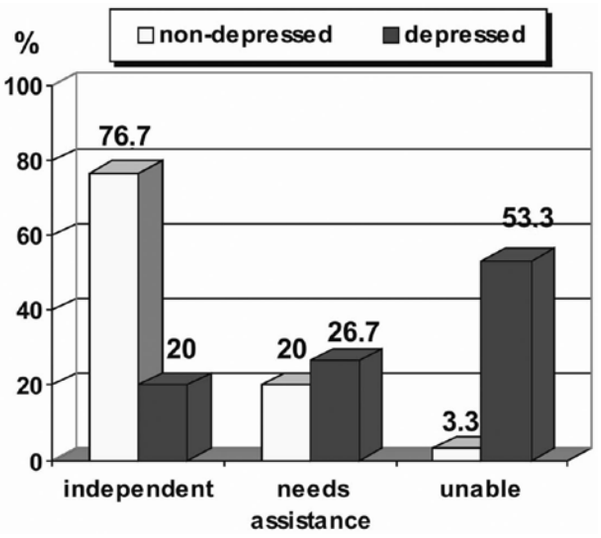

Fig. 2. Ambulation in non-depressed and depressed patients.

lation between the two groups was also statistically highly significant (p<0.001) (Fig. 2).

Correlation between the HDRS and BI scores two weeks after stroke in patients without and with PSD was r=-0.459 (p=0.011) and r=-0.215 (p=0.253), respectively. Correlation between the HDRS and BI scores six weeks after stroke in patients without and with PSD was r=-0.004 (p=0.979) and r=-0.341 (p=0.065), respectively. Correlation between the BI score two weeks after stroke and the HDRS score six weeks after stroke in patients with PSD was r=-0.052 (p=0.784), indicating that it is not possible to predict the HDRS score on later testing on the basis of the BI score on initial testing. Correlation between the HDRS score two weeks after stroke and the BI score six weeks after stroke in patients with PSD was r=-0.359 (p=0.051), indicating that the BI score on later testing cannot be predicted with a high degree of certainty on the basis of the HDRS score on initial testing.

Depressed patients had statistically significantly impaired all the quality of life domains compared with the general population, whereas non-depressed patients differed from the general population in the

Table 1. Short Form 36 (SF-36) domain scores in non-depressed and depressed patients compared with the general population (50±10)

SF-36 domains	Non-depressed patients	Depressed patients
	p	p
General health	0.044	<0.001
Physical functioning	0.327	<0.001
Role-physical	0.020	<0.001
Bodily pain	<0.001	0.015
Mental health	0.732	<0.001
Vitality	0.107	<0.001
Role-emotional	0.708	<0.001
Social functioning	0.216	<0.001
Summary physical score	0.702	<0.001
Summary mental score	0.608	<0.001

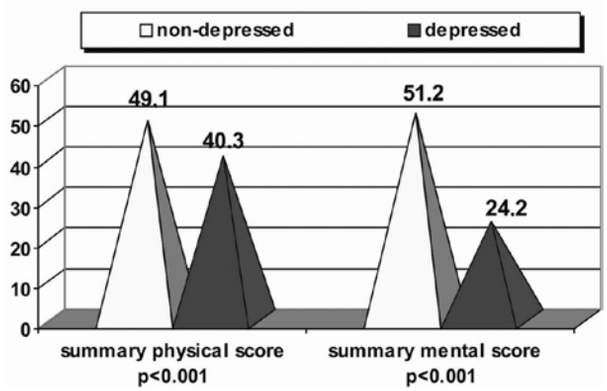

Fig. 3. Short Form 36 summary physical and mental scores in non-depressed and depressed patients.

domains of the role of physical functioning, bodily pain and general health (Table 1).

There were statistically significant differences in both summary physical score and summary mental score between the patients with and without PSD (p<0.001). Patients without PSD did not differ significantly from the general population, while the difference between patients with PSD and the general population was significant, especially in summary mental score (Fig. 3).

The mean scores on all SF-36 domains were higher in patients without PSD than in those with PSD. These differences were statistically highly significant in all SF-36 domains (p<0.001) except for the domain of bodily pain (p=0.011) (Figs. 4 and 5).

The lowest scores on individual SF-36 domains in non-depressed patients were found for the role of physical functioning, followed by general health. In depressed patients, the lowest scores were found for the role of emotional functioning and social functioning.

The social functioning score indicated that social relationships were 'extremely' or 'very' impaired in 70% (n=21) of depressed patients and in none of non-depressed patients; the difference was statistically significant (p<0.001).

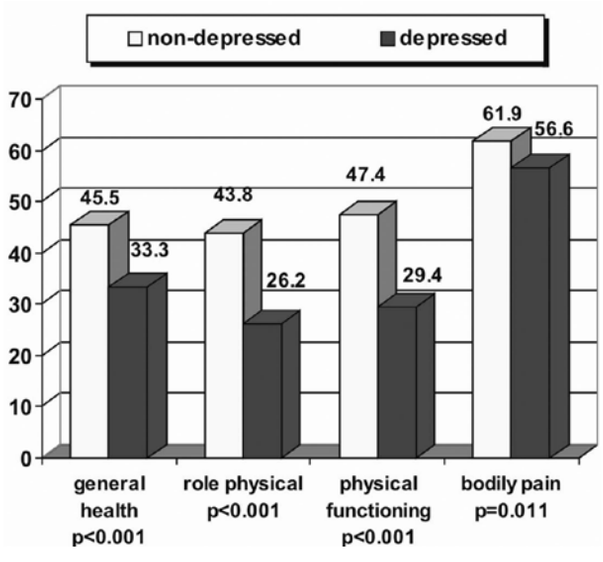

Fig. 4. Standardized mean Short Form 36 domain scores.

Discussion

The most useful way to assess the relationship between physical impairment and PSD is not to evaluate the severity of neurological deficits, but to express the impairment as functional disability for activities of daily living (ADL). What all instruments measuring functional disability have in common is that they classify patients into several categories based on the level of disability, i.e. independence or need of assistance.

Previous research results have shown that functional disability is most frequently associated with PSD as a psychological reaction to physical impairment; however, it is by no means its only determinant. There are findings that orthopedic patients with comparable disability are less frequently depressed than stroke patients[17].

Most studies have shown that functional disability is significantly more severe in depressed patients compared with non-depressed patients. In addition, some studies demonstrated the significance of disability as a predictor of PSD[18,19], while other studies found the association between depression and impaired ADL to be independent of the severity of cognitive impairment, social functioning, age and education[20] and that moderate or severe disability increased the risk of PSD by about 20%[21]. However, there are inconsistent data; some studies found no association between ADL impairment and depression severity[22,23].

In the present study, we found significantly more severe functional disability (p<0.001) in depressed patients (54.3) compared with non-depressed pa-

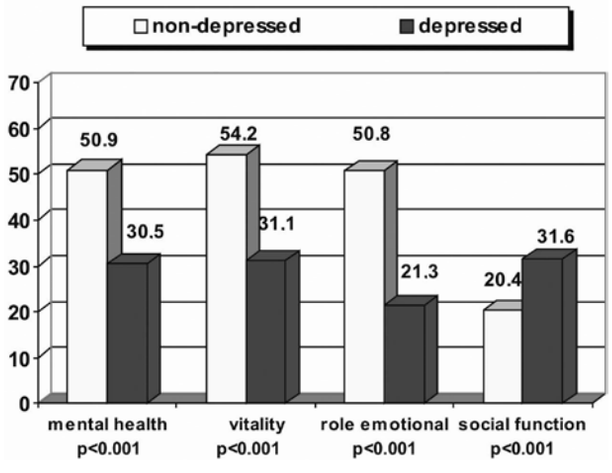

Fig. 5. Standardized mean Short Form 36 domain scores.

tients (87.2) during in-hospital assessment, which is in agreement with most previous studies. Even six weeks after stroke, after completed rehabilitation treatment, the mean BI was significantly higher in non-depressed patients (98) than in depressed patients (86.2) ($p<0.001$). In non-depressed patients, the BI score corresponded to mild disability on initial testing and minimal disability on repeat testing. Conversely, depressed patients had moderate disability on initial testing and mild disability after completed rehabilitation.

We found a highly significant difference in functional disability between the patients with and without PSD ($p<0.001$). Furthermore, with regard to ambulation alone, there was a statistically highly significant difference between the two groups ($p<0.001$). These findings confirm the association between depression and functional disability in stroke patients and suggest the possible significance of ambulation in differentiating between depressed and non-depressed stroke patients.

In our patients with PSD, we did not find significant correlation between the severity of depressive symptoms (HDRS score) and severity of functional disability (BI) either during hospitalization or during follow up. These results suggest that comorbidity of depression should be considered in all stroke patients, regardless of the degree of their functional impairment.

Another important issue is a potential predictive relationship between functional status and depression severity in the first years after stroke. If functional disability causes depression *via* a psychological mechanism, it may be assumed that the severity of in-hospital ADL impairment may predict depression in further course of disease. Similarly, if the severity of depression affects functional recovery, it may be assumed that in-hospital depression will predict subsequent ADL impairment. Both assumptions have been proved by previous research[8], although there are also opposing literature data suggesting that the risk of depression is still increased many years after stroke, regardless of functional disability and other potential risk factors[24].

In the present study, the baseline functional status was the best predictor of functional outcome at six weeks ($r=-0.844$, $p<0.001$). In addition, there was weak correlation between the HDRS score on initial testing and the BI score on repeat testing in depressed patients ($r=-0.359$, $p=0.051$). This implies that it is possible to predict functional disability six weeks after stroke on the basis of initial depression score, although not with high certainty; the patients that were most depressed during hospitalization were among those that were most disabled after completed rehabilitation treatment. However, considering the nonsignificant correlation between the initial BI score and the HDRS score at six weeks, it can be concluded that the patients who initially had the most severe disability were not most depressed after six-week follow up ($r=0.052$, $p=0.784$).

Assessment of the effect of depression on functional recovery is a complex task, considering numerous variables shown to affect functional recovery after stroke. If we take into account that PSD has adverse effects on motivation and cognitive functions in these patients, it would be logical to expect it to have negative effects on functional recovery as well. However, literature data are contradictory; whereas some results show that PSD affects negatively functional recovery[25,26], others demonstrate no association between PSD and functional recovery in stroke patients[22,27]. It has been shown that depression does not affect recovery of motor function and that its negative effect on functional recovery starts only after discharge from the hospital[28]. This may be so because during intensive rehabilitation treatment patients perceive significant motor recovery and find stimulating circumstances that may be different from those at home. Returning home is certainly a difficult experience for disabled patients and their caregivers; therefore, the risk of depression is increased, especially when the patient is not able to apply the acquired motor abilities in his or her daily activities[29]. Therefore, the time of discharge from the hospital should be the moment to start treatment of depression[28].

Our findings support the assumption that depression is associated with increased disability in stroke patients. However, if the results are presented as functional improvement, i.e. difference in the mean BI scores on the initial and repeat testing, both groups showed significant recovery ($p<0.001$). It is likely that our depressed patients recovered relatively well also because of the intensive rehabilitation treatment they

received. Anyhow, our results and the comparable results of previous studies show that depressed patients have an equal potential for functional recovery, although outcome in their case is worse.

Although quality of life has been researched for almost two decades, few studies have dealt with stroke patients and there are virtually no research reports comparing quality of life in depressed and non-depressed stroke patients.

An Australian population study aiming at identifying determinants of the quality of life after stroke has shown that a significant number of patients had a very low quality of life two years after stroke, and that depression is one of the independent risk factors affecting the quality of life. Similar results have been reported from other studies including different populations and observing different periods following stroke[30,31]. In a prospective study in a Turkish population, the quality of life within six months after stroke was significantly lower than in healthy controls ($p<0.0001$) and significantly associated with depression, functional status and level of education[32]. In a Swedish study, the most important determinants of the quality of life 16 months after stroke were found to be depression, functional status, age, and sex[33].

In our study, comparison of non-depressed patients and the general population showed that the quality of life after stroke in patients without affective disorder was significantly impaired only in the domains of the role of physical functioning and general health.

Although our results suggest that the quality of life is significantly more impaired in depressed patients in all SF-36 domains, certain domains may be identified as particularly impaired. Thus, while in the group without PSD the most impaired domains were the role of physical functioning (43.8) and general health (45.5), in the group with PSD the most impaired domains were the role of emotional functioning (21.3) and social functioning (25.2). In this way, a specific profile of impaired quality of life in PSD patients may be distinguished; our results suggest that the quality of life in depressed patients, regardless of their more severe functional disability compared with non-depressed patients, seems to be affected primarily by impaired affective function, consequently affecting the role of emotional functioning domain.

In addition, the summary physical and mental scores were significantly different between the depressed and non-depressed patients ($p<0.001$). Whereas non-depressed patients did not differ significantly from the general population, depressed patients did, especially in the summary mental score.

An unexpected finding in our study was the high mean score in the domain of bodily pain in both non-depressed (and even more surprisingly) in depressed patients, considering the well-known association and interaction between primary depression and somatic pains, which has biological grounds, since pain and depression share the same central nervous system pathways[34]. However, these results can, at least partly, be explained by sociocultural differences between the American and our population in the perception and interpretation of pain. In addition, it is likely that the results were influenced by the fact that we excluded from the study all patients with a history of physical disability due to rheumatic, orthopedic or other neurological diseases and severe somatic dysfunctions, which is certainly a population with frequent pain conditions.

As in the case of functional impairment, the association between depression and social functioning is complex and interrelated; on the one hand, patients with poor social support seem to become depressed more frequently and, on the other hand, depressed patients seem to impair more frequently their social functioning. In addition, depression and social functioning may be associated with a third factor, such as cognitive impairment.

Research on the association between PSD and social functioning has shown that social withdrawal and deterioration of social function following a stroke may be a consequence of depression[35]. Other in-hospital factors that significantly correlate with social functioning are cognitive status and functional status. It is understandable that limitations in physical and intellectual abilities also lead to social withdrawal and dissatisfaction with social relationships[36]. Åstrom *et al.* (1993) have reported that three years after stroke, only 7% of depressed patients and 66% of non-depressed patients socialized with friends and relatives[37]. The latter findings, however, did not clarify whether the limited social interactions after stroke are a cause or consequence of depression, or associated with some other factors.

In our patients, social functioning was analyzed through the SF-36 domain of social relationships. The results showed that social relationships were 'extremely' or 'very' impaired in 70% of depressed patients and in none of non-depressed patients ($p<0.001$).

Conclusion

There was no significant correlation between the severity of depression and severity of functional disability, either during hospitalization or during follow up. The absence of this correlation prompts consideration of the comorbidity of depression in all stroke patients, regardless of the degree of their functional impairment. Functional disability was significantly more severe in depressed patients compared with non-depressed patients, with a highly significant difference in ambulation. The potential for functional recovery was no less strong in depressed patients, although they had worse functional abilities at the end of rehabilitation treatment, compared with non-depressed patients. The quality of life of depressed patients was significantly more impaired in all SF-36 domains, with the role of emotional functioning and social functioning being most affected.

In conclusion, stroke outcome, expressed as functional disability and quality of life, is significantly more unfavorable in stroke patients who develop a depressive disorder. Therefore, treatment of this complex sequel of stroke should be timely, appropriate and comprehensive, including a multidisciplinary approach and support by the family and society at large.

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Sažetak

UTJECAJ DEPRESIJE NAKON MOŽDANOG UDARA NA FUNKCIONALNI ISHOD I KVALITETU ŽIVOTA

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Dijagnoza depresije nakon moždanog udara često se previdi, iako se radi o čestoj i važnoj komplikaciji moždanog udara, tako da je i njezin utjecaj na ishod moždanog udara zanemaren i podcijenjen. Cilj ovoga istraživanja je bio utvrditi utjecaj depresije na funkcionalni ishod i kvalitetu života bolesnika s moždanim udarom. Prospektivno istraživanje obuhvatilo je 60 bolesnika liječenih zbog klinički dijagnosticiranog prvog moždanog udara, od toga 30 bolesnika s dijagnosticiranom depresijom i 30 bolesnika bez depresije. Testiranja su provedena dva i šest tjedana nakon moždanog udara. Depresija je dijagnosticirana prema mini međunarodnom neuropsihijatrijskom intervjuu, DSM-IV dijagnostičkim kriterijima (MINI), a težina depresije kvantificirana je Hamiltonovom ljestvicom za procjenu depresivnosti. Funkcionalni status je procjenjivan pomoću Barthelova indeksa, a kvaliteta života nakon moždanog udara upitnikom Short Form 36 (SF-36). Značajno teža funkcionalna onesposobljenost zabilježena je u skupini bolesnika s depresijom, i to na početku kao i nakon završenog rehabilitacijskog tretmana. Potencijal za funkcionalni oporavak kod depresivnih bolesnika nije manji, iako je na kraju rehabilitacijskog tretmana stupanj funkcionalnih sposobnosti u ovoj skupini bio niži. Kvaliteta života depresivnih bolesnika značajno je smanjena u svim domenama upitnika SF-36 u odnosu na nedepresivne bolesnike, pri čemu je najteže oštećena uloga emocionalnog funkcioniranja te socijalni odnosi.

Ključne riječi: *Moždani udar – komplikacije; Depresija; Ishod liječenja, procjena; Kvaliteta života*