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Original Scientific Paper

IMPAIRED QUALITY OF LIFE IN SURVIVORS OF CRANIOCERVICAL ARTERY DISSECTION

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SUMMARY – The functional outcome of cervical artery dissection (CAD) survivors is usually good, but patients report impaired quality of life (QOL).

The aim of the study was to compare QOL and changes in headaches between CAD patients and patients of similar age and outcomes who suffered ischemic stroke of other determined etiology (ISOE).

The study included 20 CAD patients (10 female, age 44.55 ± 10.71 years), and 20 ISOE patients (3 female, age 48.00 ± 8.7 years). Functional outcome was measured with the modified Rankin scale (mRS) and QOL with the European Quality of Life Health Questionnaire (EQ-5D). We assessed changes in the frequency and severity of migraines and other headaches and performed a student's t-test for intergroup comparison.

The mean mRS was 0.5 ± 0.83 in CAD and 0.35 ± 0.75 in ISOE patients. CAD patients had fewer comorbidities and more frequent migraines. No problems in any of the 5 EQ-5D domains were reported in 30% of CAD and 80% of ISOE patients (P = 0.02). The visual analog scale (VAS) of mean health was 71.25 ± 19.52 in CAD patients and 87.25 ± 16.18 in ISOE patients (P = 0.01). A 100% VAS score was obtained in 10% of CAD patients and 40% of ISOE patients (P = 0.02).

Although CAD patients had fewer comorbidities, they had more impaired QOL compared to ISOE patients of similar age and outcome. They also reported a worsening of their migraines.

Keywords: *Quality of life; Arterial dissection; Stroke; Migraine*

Introduction

Craniocervical artery dissection is the most common single etiology of ischemic stroke in young adults, with a wide spectrum of clinical presentations[1,2,3,4]. Mortality rates in the acute phase of CAD are generally low, although they may be underestimated for

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patients with higher mortality before imaging was performed, or overestimated for patients with a benign clinical presentation that may have gone undiagnosed[1]. The reported recurrence rate of ischemic symptoms is low; up to 13.3%[1]. The rate of recurrent dissection is higher, but with asymptomatic or oligosymptomatic presentations[5]. Functional outcome is described as good in about three quarters of patients with CAD[1,2,6], and the overall functional prognosis of patients with stroke due to CAD does not differ from that of young patients with stroke due to other causes[6]. The modified Rankin scale (mRS) captures only functional disability and is therefore not sensitive enough to assess the sequelae in patients with only mild symptoms and a good functional outcome. Since young adults are mostly affected, the effect of functional outcome in terms of QOL and socio-professional integration is important[2,7]. A search of Medline, Scopus, Google scholar and Web of science revealed only two publications regarding the outcome of cervical artery dissection on QOL[7,8], and one on the development of posttraumatic stress disorder (PTSD) and its impact on QOL[9]. The studies have demonstrated that QOL is impaired in almost half of long-term CAD survivors, even in patients with local or transient symptoms or without functional disability, as in posterior circulation stroke due to vertebral artery dissection[7]. Almost half of CAD survivors meet the criteria for PTSD[9].

Studies have demonstrated that psychiatric symptoms are common after stroke[10]. A sudden onset of neurological deficits may contribute to distress and anxiety beyond levels seen with other acute medical illnesses[11,12]. A single-center study showed that anxiety, depression and PTSD are common after stroke, have a high degree of co-occurrence and are associated with worse outcomes, including QOL and functional status[13]. However, a study comparing QOL between stroke patients caused by CAD and other etiologies has never been performed and differences in the development of psychiatric symptoms between these two groups have not been assessed.

In the Cervical Artery Dissection and Ischemic Stroke Project (CADISP) consortium and the Italian Project on Stroke in Young Adults (IPSYA), migraine, especially migraine without aura, was more common in CAD patients than in non-CAD ischemic stroke patients[14,15].

In CAD survivors, in addition to sequelae related to cerebral ischemia, residual headache or neck pain has been described in some patients, but published data are scarce[16,17]. Although an improvement of migraine after dissection was initially presumed to be the result of aspirin treatment[16], recently it was confirmed to occur regardless of aspirin treatment[18,19]. Such findings reinforced the link between migraine and CAD.

Aims

The aim of the study was to assess the difference in QOL between CAD patients and ISOE patients. Also, changes of migraine and headache compared to pre-stroke levels between these two groups were assessed.

Patients and methods

The study included 20 consecutive CAD patients and 20 consecutive age-matched ISOE patients during outpatient follow-up visits. In the group of CAD patients, the diagnosis was previously confirmed on the basis of clinical presentation and imaging findings showing an intramural hematoma on axial cervical MRI cuts, or a string sign, intimal flap or pseudoaneurysm on angiography. Patients with CAD after major trauma were not included in the study. In non-CAD patients, stroke etiology was assessed. Comorbidities were listed (hypertension, diabetes mellitus, hyperlipidemia, history of cardiac disease, obliterative atherosclerotic disease of the lower extremities, treated or untreated coronary artery disease, previous stroke, carotid endarterectomy and seizures) and then quantified.

Time from the index event was measured and assessed, and then dichotomized as more or less than 1 year. Clinical presentations, imaging findings and treatment of CAD or non-CAD stroke patients were retrieved from patient charts. All patients underwent a neurological assessment and their functional outcome was estimated using mRS.

Health outcome was measured with the EQ-5D questionnaire. EQ-5D is a standardized measure of health status developed to provide a simple, generic

measure of health. It consists of EQ-5D measurements of mobility, self-care, usual activity, pain/discomfort and anxiety/depression, as well as an EQ-VAS of the best imaginable health state. Each item in EQ-5D has 3 levels; level 1 indicating no problem, level 2 indicating some problems and level 3 indicating extreme problems. The percentage of patients with no problems in any of the 5 EQ-5D domains was calculated for each cohort. EQ-VAS indicates the best imaginable health state, with 100% representing the maximum health state. Mean EQ-VAS was calculated for each group, and the percentage of patients obtaining 100% maximum health state was calculated for each cohort.

The study assessed the presence of migraine for both cohorts, as well as changes in the frequency and severity of migraines and other headaches compared to pre-stroke levels.

The study was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Sestre milosrdnice University Hospital Center. Patients signed the informed consent before entering the study. Permission for the use of EQ-5D was obtained from the EuroQol Group.

Statistical analysis

The data are presented as mean values and standard deviations for each group. The presented health outcomes for each domain were measured with the EQ-5D questionnaire. The percentage of no problems in any of the 5 domains of EQ-5D and the maximum health state between groups was compared by means of the Student's t-test at a level of significance of 95%.

Results

Patients' demographic data are presented in Table 1. Patients in the ISOE cohort were 4 years older and mostly male (85%), while in the CAD cohort 50% of the patients were female. Patients with CAD had fewer comorbidities than ISOE patients. In CAD patients, 8/20 had 1 comorbidity, mostly hypertension, and 1 patient had 2 comorbidities. In ISOE patients, 13/20 had 2-6 comorbidities. Most patients, 75% of CAD patients and 55% of ISOE patients, were assessed one year after the index event.

There was no significant difference in functional outcome measured by mRS (Table 2). Mean mRS was

Table 1. Patients' demographic data

	Cervical artery dissection N=20	**Ischemic stroke of other etiology N=20**
Age (mean±SD) years	44.55±10.71 years	48.00±8.7 years
Gender	10 female (50%)	3 female (15%)
Number of patients with comorbidities Number of comorbidities (range)	9 (45%) 1-2	13 (65%) 2-6
Number of patients assessed one year after the index event	15 (75%)	11 (55%)

Table 2. Functional outcome data measured by the modified Rankin scale (mRS)

	Cervical artery dissection	**Ischemic stroke of other etiology**
Modified Rankin Scale (mRS) Score: mean±SD	0.5±0.83	0.35±0.75
Number of patients with mRS 0	13	15
Number of patients with mRS 1	5	4
Number of patients with mRS 2	1	0
Number of patients with mRS 3	1	1

Table 3. Health outcome measured with the European Quality of Life Health Questionnaire (EQ-5D)

EQ-5D		**Cervical artery dissection (No. and percentage of pts)**	**Ischemic stroke of other etiology (No. and percentage of pts)**
EQ – Mobility	Level 1 Level 2 Level 3	15 (75%) 5 (25%) 0	18 (90%) 2 (10%) 0
EQ – Self care	Level 1 Level 2 Level 3	18 (90%) 2 (10%) 0	19 (95%) 0 1 (5%)
EQ – Usual activity	Level 1 Level 2 Level 3	12 (60%) 7 (35%) 1 (5%)	18 (90%) 1 (5%) 1 (5%)
EQ – Pain/discomfort	Level 1 Level 2 Level 3	13 (65%) 7 (35%) 0	19 (9%) 1 (5%) 0
EQ – Anxiety/ depression	Level 1 Level 2 Level 3	13 (65%) 7 (35%) 0	17 (85%) 3 (15%) 0
Number of patients with no problems in all EQ – 5D domains		6 (30%)	16 (80%)*
EQ-5D Visual analogue scale (VAS)	Mean±SD Number of patients with 100% VAS	71.25±19.52 2 (10%)	87.25±16.18 8 (40%)**

*P=0.002; **P=0.04

0.5 ± 0.83 in CAD patients and 0.35 ± 0.75 in ISOE patients (P=0.55). A total of 19/20 patients in both groups achieved a good outcome (mRS ≤ 2). Only one patient had an mRS score of 3 in both groups.

Health outcomes measured with the EQ-5D questionnaire are presented in Table 3. Both groups of patients witnessed some derangement of normal function, which was more prominent in CAD patients than in ISOE patients (6.55 ± 1.61 vs. 5.55 ± 1.60, P=0.028). No problems in any of the 5 domains (mobility, self-care, usual activity, pain/discomfort and anxiety/ depression) of EQ-5D measurements were reported in 30% of CAD patients and 80% of ISOE patients (P=0.002). The mean perception of health state measured by EQ-5D VAS (max. 100%) was 71.25 ± 19.52 in CAD patients and 87.25 ± 16.18 in ISOE patients (P=0.007). A total of 10% of CAD patients and 40% of ISOE patients (P=0.02) achieved the maximum health state (EQ-5D VAS 100%).

Data on migraine incidence and changes of migraine and headache compared to pre-stroke level are presented in Table 4. Migraine was present more frequently in CAD patients compared to ISOE patients (P=0.04) (Table 4). In the CAD group, new onset migraine was found in one patient, a worsening of migraine was reported in 4/7 migraines and a worsening of headache in 3/20 patients. Only 1/7 patients reported an improvement of migraine. In the ISOE cohort, an improvement of migraine was reported in 2/3 migraine patients and an improvement of headache

Table 4. Data on the incidence of migraine and changes of migraine and headache compared to pre-stroke level

		Cervical artery dissection	**Ischemic stroke of other etiology**
Migraine	Before stroke After stroke	7/20 (35%) 8/20	3/20 (5%)* 2/20
Changes of migraine	Amelioration Worsening	1/7 4/7	2/3 0
Changes of headache	Amelioration Worsening	0 3/20	4/20 2/20

*P=0.04

in 2/20, while a worsening of headache was reported in 2/20 patients. Most CAD patients reported a worsening of migraine and headache, while ISOE patients reported an improvement of migraine and headache.

Discussion

In this study, we compared QOL and headache burden in a cohort of patients suffering from CAD with a cohort of ISOE patients. Despite a good functional outcome (mRS 0-2) and a lack of or a low burden of other comorbidities, CAD patients reported lower QOL compared to ISOE patients of similar age but with a higher burden of comorbidities. In this age group, female patients were more frequently affected by CAD compared to ISOE.

Long-term QOL impairment was reported in the CAD cohort; not only in disabled patients, but also in patients without significant disability and in survivors without an ischemic stroke[8]. In this study, low mRS was associated with better overall QOL[8]. In a previous study investigating the impact of stroke type and lesion location on QOL, survivors of hemorrhagic strokes did not experience more QOL impairment than survivors of ischemic strokes[20]. However, patients with infratentorial strokes reported better overall functioning than patients with supratentorial strokes. The same is true of patients with lacunar strokes with less dysfunction compared to patients with cortical or subcortical infarction[20]. Severely impaired QOL was related to older age, comorbidity and stroke severity[8,20]. In only one study, long-term impairment of QOL was reported in patients after vertebral artery dissection, with a good clinical outcome in two thirds of the patients[7]. In both studies of QOL in patients with dissection, Stroke Specific Quality of Life (SS-QOL) was applied to include psychological and cognitive function, and not just disability[7,8]. Despite a good functional outcome, impaired QOL was reported in 30% of the patients[8]. Analyzing the affected domains in patients without significant disabilities, impaired QOL was observed in "thinking", "energy" and "language", whereas the smallest changes were in "self-care", "personality" and "mood"[8]. In our study, CAD patients reported lower QOL, measured with EQ-5D, compared to ISOE patients of similar age and a similar, mostly positive, outcomes (mRS $\leq$ 2 in 19/20 patients in both groups), but with a higher burden of comorbidities. No problems in any of the 5 domains (mobility, self-care, usual activity, pain/discomfort and anxiety/depression) of the EQ-5D questionnaire were reported in 30% of CAD patients and 80% of ISOE patients ($P=0.002$). The most frequently affected domains were: usual activity, pain/discomfort and anxiety/depression. The perception of maximum health state (EQ-5D VAS 100%) was obtained in 10% of CAD patients and 40% of ISOE patients ($P=0.04$). The mean perception of health state (EQ-5D VAS) was 71.25 ± 19.52 in CAD patients and 87.25 ± 16.18 ($P=0.007$) in ISOE patients. Most patients in the CAD cohort were assessed after 1 year (75%). These results confirm a long-term impairment in QOL despite a lower comorbidity burden in CAD patients compared to other strokes in patients of similar age and functional outcome. Since CAD mostly affects younger adults, resulting mostly in a good functional outcome, this is the first study showing more impairment in QOL in CAD patients compared to patients of similar age and functional outcome who suffered other strokes.

The CAD cohort demonstrated a higher burden of migraine compared to the ISOE cohort. A high migraine burden was also observed in studies comparing ischemic stroke due to CAD and ischemic stroke of other causes in young patients, as in the CADISP study and IPSYA[3,14,15], and a lower rate of migraine in young patients with ischemic stroke of other causes[3,14]. In our cohorts, 50% of CAD patients and 15% of ISOE patients were female. As expected, patients with ISOE had more comorbidities, like vascular risk factors. Similar findings of a higher incidence of vascular risk factors in young patients with ischemic stroke not caused by CAD were described in studies of ischemic strokes in young adults, like CADISP and IPSYA[3,14,15].

In our study, a worsening or new onset of migraine was observed in CAD patients, as opposed to ISOE patients. However, our sample was small. Completely opposite results were observed in IPSYA[19], the largest prospective study on ischemic stroke in young patients. Previous observations of migraine improvement after CAD in small series were attributed to aspirin treatment[2,18,21]. An improvement of migraine was observed in half of the 36 patients with ischemic stroke[21], and a total disappearance of migraine or migraine relief was more frequently found in the group of CAD patients[18].

Although the sample size in our study was rather small, a similar higher migraine burden in CAD patients was observed, and a completely different pattern of changes of migraine and headache between CAD and ISOE patients was recorded. Together with the finding of a decreased QOL despite a lower burden of comorbidities in CAD compared to ISOE patients, the results reinforce the hypothesis of a possible biological mechanism underlying migraine and CAD. However, further prospective studies aiming to investigate this relationship are needed.

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Sažetak

SMANJENA KVALITETA ŽIVOTA KOD BOLESNIKA KOJI SU PREŽIVJELI DISEKCIJU CERVIKALNE ARTERIJE

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Funkcionalni ishod bolesnika koji su preživjeli disekciju cervikalne arterije (DCA) obično je dobar, ali se bolesnici žale na smanjenu kvalitetu života (QOL).

Cilj istraživanje bio je usporediti QOL i promjene glavobolje u bolesnika s DCA s bolesnicima slične dobi i ishoda koji su preboljeli ishemijski moždani udar druge etiologije (IMUE).

Istraživanje je obuhvatilo 20 bolesnika s DCA (10 žena, dob 44,55 ± 10,71 godina) i 20 drugih bolesnika s IMUE (3 žene, dob 48,00 ± 8,7 godina). Funkcionalni ishod mjeren je modificiranom Rankinovom ljestvicom (mRS). Kvaliteta života mjerena je europskim zdravstvenim upitnikom o kvaliteti života (EQ-5D). Procijenjena je promjena u učestalosti i težini migrene i druge glavobolje. Za međugrupnu usporedbu izveden je Studentov t-test.

U bolesnika s DCA srednja vrijednost mRS iznosila je 0,5 ± 0,83, a u bolesnika s IMUE 0,35 ± 0,75. Pacijenti s DCA imali su manje komorbiditeta i češće migrene. Rezultat bez problema u svih 5 EQ-5D domena registiran je u 30 % bolesnika s DCA i 80 % bolesnika s IMUE (P = 0,02). Vizualna analogna ljestvica srednjeg zdravstvenog stanja (VAS) iznosila je 71,25 ± 19,52 u bolesnika s DCA i 87,25 ± 16,18 u bolesnika s IMUE (P = 0,01). VAS 100% postiglo je 10 % bolesnika s DCA i 40 % bolesnika s IMUE (P = 0,02).

Iako su bolesnici s DCA imali manje popratnih bolesti, imali su smanjenu kvalitetu života u usporedbi s bolesnicima s IMUE slične dobi i ishoda. Također su imali pogoršanje migrene.

Ključne riječi: *Kvaliteta života; Arterijska disekcija; Moždani udar; Migrena*