DIETARY INTAKE IN ADULT FEMALE COELIAC DISEASE PATIENTS IN SLOVENIA

PREHRANSKI VNOS ODRASLIH BOLNIC S CELIAKIJO V SLOVENIJI

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ABSTRACT

Keywords:
coeliac disease,
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gluten-free diet

Objectives. The aim of the study was to assess dietary intake of coeliac disease (CD) patients and to determine if they are meeting the dietary reference values for a balanced diet.

Subjects/Methods. 40 women with CD, aged from 23 to 76 participated in our study. Total daily intake was assessed by a three-day food diary. Resting metabolic rate (RMR) was calculated using Harris-Benedict equation. Considering physical activity level (PAL) 1.4, the recommended total energy expenditure (TEE) value was determined. The data was evaluated with professional evaluation software Prodi and statistically analysed.

Results. 40 participants returned the food diary. The average energy intake was significantly too low to ensure the meeting of all-day energy needs (p<0.05). The meals contained a recommended proportion of protein, but a statistically significantly higher proportion of fat (p<0.05), lower proportion of carbohydrates and a significantly lower intake of dietary fibre (p<0.05). Regarding macro-, micro- elements and vitamins, there was a significant lack in the intake of calcium and iodine, folic acid, vitamin D and vitamin A (p<0.05), meanwhile iron intake was at the lower limit of the recommended intake, whereas zinc, potassium and vitamin K intake were significantly higher according to the recommended values, but were comparable with the intake of the general population in the Central European area.

Conclusion. Even in subjects with adequate or low daily energy intake, their meals contained too much fat, too few carbohydrates and dietary fibre as well as inorganic substances. The patients with CD should get regular nutritional monitoring and education on the quality and balance of a gluten-free diet.

IZVLEČEK

Ključne besede:
celiakija,
prehranski vnos,
gluten, dieta
brez glutena

Izhodišče. Celiakija je sistemska imunsko pogojena bolezen, ki nastane kot posledica uživanja glutena pri genetsko disponiranih osebah. Bolnik s celiakijo mora iz prehrane izključiti vsa živila, ki vsebujejo gluten. Za zagotavljanje dnevnih potreb vseh pomembnih hranil ter vitaminov je pomembna prehranska kakovost brezglutenske diete.

Namen. Z raziskavo smo želeli ugotoviti, kakšen je prehranski vnos odraslih bolnic s celiakijo v Sloveniji glede na veljavna priporočila za uravnoteženo prehrano in glede na Prehrambene navade odraslih prebivalcev Slovenije z vidika varovanja zdravja.

Metode. V raziskavo smo vključili 40 žensk s celiakijo, ki so uživale brezglutensko dieto in bile stare od 23 do 76 let. Za zbiranje podatkov o prehranskih navadah smo uporabili metodo prehranskega dnevnika, v katerega so preiskovanke tri poljubne dneve v tednu dosledno zapisovale vse, kar so zaužile tisti dan. Metabolizem v mirovanju (RMR) smo izračunali po Harris-Benedictovi enačbi. Za določitev celodnevnih energetskih potreb (CEP) smo glede na poročanje o dnevnih aktivnostih RMR pomnožili z ustreznim faktorjem za fizično aktivnost (PAL). Podatke smo ovrednotili z računalniškim programom za strokovno načrtovanje prehrane Prodi 5.9, ki upošteva Referenčne vrednosti za vnos hranil D-A-CH. Dobljene podatke smo statistično obdelali.

Rezultati. Prehranski dnevnik je vrnilo 40 udeleženk. Ovrednoteni prehranski dnevniki kažejo, da je bil povprečen energetski vnos hranil statistično pomembno (p<0,05) prenizek za zagotavljanje priporočenih celodnevnih energetskih potreb preiskovank. Bolnice s celiakijo so zaužile primeren delež beljakovin (14,2%), vendar statistično pomembno (p<0,05) prevelik delež maščob (36,4%) ter premajhen delež ogljikovih hidratov (48,2 %) in prehranskih vlaknin (18,9 g/dan).
Med makro-, mikroelementi in vitamini so preiskovanke v povprečju zaužile statistično pomembno (p<0,05) premalo kalcija in joda, folne kisline, vitamina D in vitamina A. Vnos železa je bil na spodnji meji priporočil, vrednosti cinka in kalija pa sta presegli priporočene vrednosti, vendar sta bili primerljivi z vnosom splošne populacije v srednjeevropskem okolju.

Zaključek. Rezultati kažejo, da brezglutenska prehrana bolnic s celiakijo v Sloveniji ne ustreza smernicam zdrave in uravnotežene prehrane glede na Referenčne vrednosti za vnos hranil D-A-CH. Ugotovili smo, da je tudi pri preiskovankah, pri katerih je bil dnevni energetski vnos hranil primeren ali celo prenizek, prehrana vsebovala prevelik delež maščob, premalo ogljikovih hidratov in prehranskih vlaknin ter anorganskih snovi. V prihodnosti bo treba narediti več na področju kvalitete prehrane in rednega prehranskega spremljanja bolnikov s celiakijo. Izobraževanja o brezglutenski prehrani bodo morala vključevati tudi nasvete, kako doseči priporočene dnevne vnose vseh pomembnih hranil in vitaminov.

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1 INTRODUCTION

Coeliac disease (CD) is a chronic disease caused by an inappropriate immune response to the protein found in grains of wheat (gliadin), rye (secalin), barley (hordeins) and possibly oats (avenin), which are collectively known as prolamins. Patients with coeliac disease should eliminate all food containing gluten (wheat, spelt, rye, kamut, barley, oats), and all products containing listed grains or wheat starch from the diet (1). Gluten-free (GF) foods are foods that contain up to 20 mg/kg gluten (20 ppm). This applies to both natural GF products (e.g. corn, rice, buckwheat) and products consisting of one or more ingredients from wheat, rye, barley, oats or their crossbred varieties, which have been specially processed to remove gluten so that the gluten level does not exceed 20 mg/kg in total (2).

The disease can only develop in people with a genetic predisposition (HLA DQ2 and/or DQ8). The disease can present itself in various clinical forms, and it affects people of all ages. The diagnosis of overt coeliac disease is established by the presence of specific antibodies against tissue transglutaminase (t-TG), anti-endomysial antibody (EMA), deamidated gliadin peptide antibodies (DGP antibodies) and characteristic histological changes of the small intestine (3). If immunoglobulin A anti-tissue transglutaminase type 2 antibody titers are high (>10 times the upper limit of normal), then the option is to diagnose CD without duodenal biopsies by applying a strict protocol with further laboratory tests (3).

Various studies have determined that because patients with CD adhere to a strict GF diet, they have an unbalanced input of the main nutrients (proteins, fats, carbohydrates) and the lack of some macro - and microelements and vitamins (4,5). Predominantly, the patients lack a proper intake of dietary fiber, iron, unsaturated fatty acids, calcium, and certain vitamins (B12, A, D, E, K) (6). This is related to decreased mineral bone density and increased potential for obesity (4,7). Vitamin deficiency also increases the risk of developing cardiovascular disease in the same way as hypertension or hypercholesterolaemia (8).

With the advances in knowledge about the possibilities of improving the quality of GF diet in order to achieve the recommended daily intake of nutrients and vitamins, we could significantly influence the health status of CD patients (9).

According to the available data, nutrition instructions for coeliac disease patients in Slovenia focus only on allowed and probated foods.

The aim of this study was to determine whether the GF diet of adult female patients with coeliac disease in Slovenia meets the recommendations for a healthy and balanced diet.

2 METHODS

Adult CD patients were invited to participate in our study. Inclusion criteria were: being at least 21 years of age, having a biopsy proven coeliac disease and following a strict GF diet for at least one year, and being generally healthy individuals, except for having coeliac disease. We used convenience sampling. From the original available group of 48 CD patients, who met the criteria for inclusion, 40 adult female CD patients returned food diaries and were included in the study. All of them were members of the Slovenian Coeliac Disease Society, had a biopsy proven coeliac disease and followed a strict gluten-free diet for at least one year. Participants were between 23 and 76 years old (with the average of 51.5 years). Since they were following a strict gluten free diet and had no additional diseases, the participants were considered healthy women, and therefore the recommended values for a healthy population were taken into account. Participants responded to a questionnaire about their age, education, occupation, physical activity level, whether they were eating breakfast, the duration of CD and the time they followed a strict GF diet, whether they had any other allergies or intolerances to foods and the possible presence of symptoms in the last 6 months.

Patients having any other serious medical condition were excluded from the study. National Medical Ethics Committee of the Republic of Slovenia approved the study. All patients received written and oral information concerning the study before they gave their consent.

Investigators delivered a three day weighed food diary to all participants and provided them with exact instructions on how to complete the diary and how to use household measures. The participants were asked to choose any two days during the week and one day during the weekend. Any discrepancies in the data were resolved by direct communication.

The results were compared to Reference values for nutrient intakes D-A-CH (10) and to the data from the National study (NS): Dietary habits of adults in Slovenia in terms of health (11). This group is considered to be representative of the »general population« in Slovenia.

The Seca medical scale with a measuring rod for height was used to measure the weight and height of the participants. Measurements and interviews were always performed by one and the same investigator.

Body mass index (BMI) was calculated with the metric BMI formula – we divided weight in kilograms with height in meters^2. Rest Metabolic Rate (RMR) was calculated with predictive Harris-Benedict equation, the coefficient of variation is about 8%:

RMR women = 655 + (9.6 x weight kg) + (1.8 x high cm) – (4.7 x age in years) (12).

Calculated RMR was additionally confirmed with bioimpedance measurements. For the bioimpedance measurements we used Bodystat® QuadScan 4000. All measurements were performed in the morning, before the subjects consumed any food. For the statistical analysis we used calculated RMR.

Additionally, the recommended total energy expenditure (TEE) value with considering physical activity level PAL 1.4,which indicates sedentary lifestyle or low activity level, was used (10). The proportion of total daily energy intake according to RMR was determined.

Three-day food diaries were evaluated with computer program for professional evaluation of diets, Prodi 5.9. A database of this program also includes gluten-free products from different manufacturers. All the results were statistically analyzed with SPSS (Statistical Package for the Social Science 20).

For each subject, all measured data, including their background information (gender, age, height, weight, education, physical activity level, body mass index, rest metabolic rate, total daily energy intake for each day, intakes of macro - and microelements and vitamins), were imported in one database and statistically analysed using the SPSS.

Descriptive statistics, the analysis of variance and tests of differences between variables (t-test for independent samples and chi-square) were calculated by standard SPSS procedures, with significance of p<0.05. Recommended values for body mass index, rest metabolic rate, total daily energy intake for each day, intakes of macro - and microelements and vitamins were added to the database as new variable values to the variables for each subject and tests of significance were performed on this extended database.

3 RESULTS

31% of participants had tertiary or university education, whilst the remaining 69% had primary or secondary education. 45% were employed, and the majority performed easy physical, intellectual, or secretarial work. 48% were retired and 7% were unemployed. 7% of all had an additional allergy or intolerance to food, mostly lactose intolerance. Most of the participants enjoyed breakfast and 3-5 meals a day, and reported sedentary lifestyle or low physically activity level.

3.1 Daily Energy Intake

The characteristics of participants and the calculated RMR, TEE and energy content of meals consumed in an average day are shown in Table 1. Calculated RMR was additionally confirmed with bioimpedance measurements. The minimal (4773 kJ/day), maximal (7137 kJ/day) and average (6004 kJ/day) values were comparable with calculated values.

Table 1. The characteristics of participants and the calculated RMR, TEE and energy content of meals consumed in an average day.

	Age [years]	Body weight [kg]	Body height [cm]	BMI [kg/m²]	RMR [kJ/day]	Total daily energy intake [kJ/day]	% total daily energy intake according to RMR [%]
Average	51.6	66.4	165	24.3	5669	6823	121.7
(min – max)	(23 – 76)	(41 – 109)	(152 – 174)	(17.3 – 38.2)	(4703 – 7492)	(3868 – 11093)	(64.1 – 220.8)
*Recommended intake or the estimated value				18.5-24.9	5442*	7535-7953 *	140**
***Sig. (p<0.05)					0.017	0.024	

BMI – Body Mass Index, RMR– Rest Metabolic Rate, TEE - Total Energy Expenditure
* Recommended values according to the Reference values for nutrient intake (D-A-CH) for the Basal metabolic rate - BMR and TEE of the average values according to the age structure of participants in the survey (10).
** For the recommended TEE, factors for physical activity PAL 1.4 were taken into account.
*** The difference of the average value of the recommended intake. The difference was considered statistically significant if p<0.05.

Evaluated food diaries show that average total energy intake was 6823 kJ, or 1630 kcal significantly (p<0.05) too low to ensure the meeting of recommended daily energy needs (TEE) of the participants (kJ 7535-7953 or 1800-1900 kcal). Results from the proportion of total daily energy intake according to RMR show that the range of the proportion is from only 64.1% to 220.8%, in an average of 121.7%. These results indicate that the average of total daily energy intake was too low to ensure meeting total daily energy needs. The proportion of total daily energy intake in an average day, depending on the calculated RMR and TEE, is shown in the Figure 1.

Figure 1. The proportion of total daily energy intake in an average day, depending on the calculated RMR and TEE.
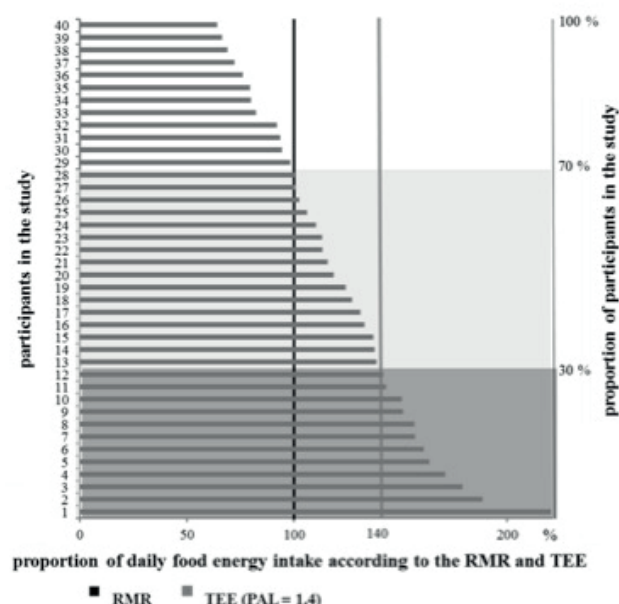
RMR: Rest Metabolic Rate, TEE: Total Energy Expenditure, PAL: Physical Activity Level
(We considered the factor of 1.4, because the majority of participants reported low/medium physical activity.)

Taking into account the average PAL of 1.4, results show that as much as 70% of the participants did not meet recommended daily energy needs, 30% of participants exceed the TEE and 30% of participants did not meet the calculated energy needs for RMR (Figure 1).

3.2 The Daily Intake of Protein, Fat, Carbohydrate and Dietary Fibre in Women with Coeliac Disease

The average intake of the main nutrients in women with CD included a large, but adequate, proportion of protein (14.2%), a significantly higher proportion of fat (36.4%; p<0.05), and a too low proportion of carbohydrates (48.2%) and dietary fibre (18.9 g/day) in relation to the recommendations for a balanced diet (2). Only one CD patient in our study consumed a sufficient amount of dietary fibre.

The proportion of participants achieving the recommended daily intake of each main nutrient is presented in Figure 2.
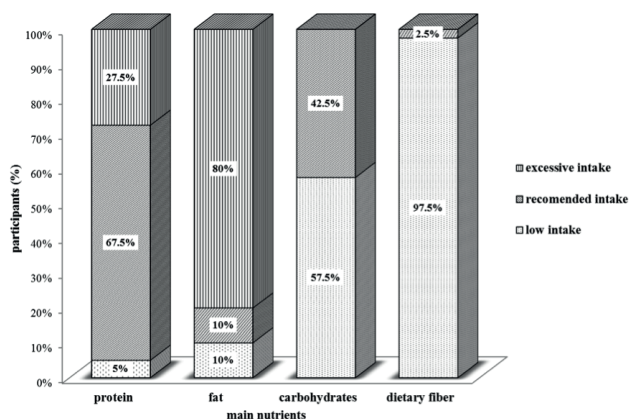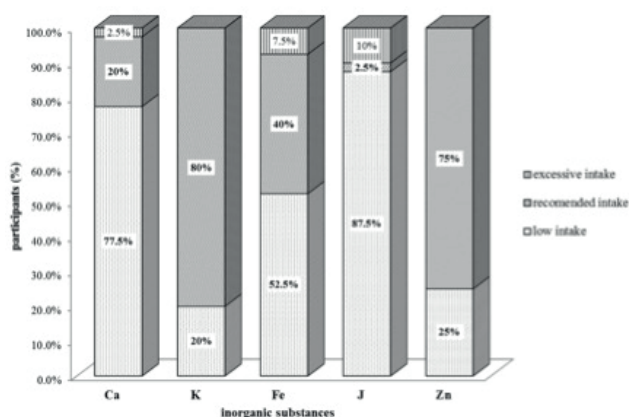

Figure 2. The proportion of participants achieving the recommended daily intake of each of the main nutrients.

3.3 The Daily Intake of Inorganic Macro-and Micronutrients in Women with Coeliac Disease

On average, the participants consumed significantly lower amounts (p<0.05) of calcium (760.7 mg/day) and iodine (96.2 mg/day), meanwhile the amount of iron (10.2 mg/day) was at the lower limit of the recommended intake, whereas the amounts of zinc (8.6 mg/day) and potassium (2716.6 mg/day) were beyond the recommended intake, but were comparable with the intake of the general population in Central Europe.

The proportion of participants achieving the recommended daily intake of each of the inorganic substance is shown in Figure 3.
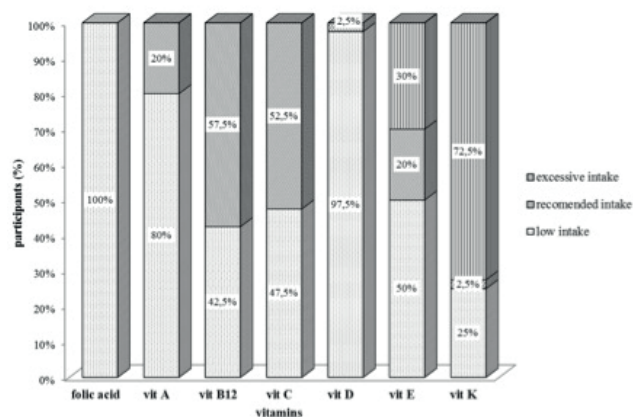
Figure 3. The proportion of participants achieving the recommended daily intake of each of the inorganic substance.

Figure 4. The proportion of participants achieving recommended daily intake of each of the vitamins.

3.4 The Daily Intake of Vitamins in Women with Coeliac Disease

Among the vitamins analysed in our study, significant (p<0.05) and most prominent were folate (the average intake of 221.3 mg per day), because none of the participants on a strict GF diet did not reach the recommended value of folic acid (400 mg/day). On average, the entire group of participants had a significantly low intake of vitamin D (2.6 mg/day; p<0.05), according to the recommended intake. Considering the normal daily intake of vitamin D in adult diet, which is 2-4 mg, the results show that 30% of the participants in the survey reached normal daily intake of vitamin D, whereas 57.5% of the participants had a lower daily intake of vitamin D, and 12.5% of women with coeliac disease had a daily intake of vitamin D higher than 4 mg.

A large proportion of the participants had a low intake of vitamins A, C, B12 and E. Most participants had a higher intake of vitamin K than recommended (the average intake of 115.5 mg/day; p<0.05).

The proportion of participants achieving recommended daily intake of each of the vitamins is shown in Figure 4.

4 DISCUSSIONS

The results of our study were interpreted with respect to the recommended values of individual nutrients and vitamins for women (10). Similar studies showed that results may be influenced by dietary changes during the management of a food diary as well as inaccurate or false reporting of all entered nutrients (11). This is particularly evident in the relationship between the reported daily energy intake and calculated RMR (8).

The average RMR was 5669 kJ (1354 kcal) and it is comparable to, or slightly higher than, RMR in comparable age and sex matched group Reference values for nutrient intake (D-A-CH) (10). According to individual reports of daily physical activity level, PAL 1.4 that describes sedentary lifestyle with moderate activity was used to determine the recommended TEE (12). Taking this into account, the CD patients in this study would need to consume between 7535 and 7953 kJ (from 1800 to 1900 kcal) daily. The results show that the average total daily intake of our CD patients (6823 kJ or 1630 kcal) was significantly too low (in an average of10-14 %) to ensure the meeting of daily energy needs. In addition, in 70% of CD patients, daily energy intake was too low to meet their recommended TEE.

It is also important to note that 40% of the CD patients had BMI equal to, or greater than, 25 kg/m²; similar results were published by Kopec et al.'s study (2009),

according to which 43,6% of CD patients had BMI equal to, or greater than, 25 kg/m^2 (13). It can be concluded that the reporting of food intake in certain CD patients is not realistic, which is consistent with the data from literature, where people with a higher BMI often reported lower food intake than the one actually consumed (8, 11). Upon evaluation of food diaries and identifying the main nutrient intake, we found that the GF diet is unbalanced in our population. The average daily intake included a large but adequate proportion of protein, a significantly higher proportion of fat, and a too low proportion of carbohydrates and dietary fiber in relation to the recommendations for a balanced diet (10). As previously observed in the study conducted at the Mayo Clinic (14), we also concluded that the reason for the unbalanced diet is improper food choice. Compared to the general population, patients with coeliac disease consume less pasta, bread and pizza but more eggs, meat and cheese to satisfy their desire and need for food (14). The average daily intake of protein in our study (14.2 %) coincides with the average protein intake in women (also accounted for 14.2%) from the survey data on the dietary habits of Slovenes (11). Of the 40 CD patients in our study, 17 (42.5%) consumed less than 0.8 g protein/kg body weight, which implies that, in the full-day diet (regardless if the proportion of protein in a ratio of fats and carbohydrates is suitable), the total daily energy intake of nutrients is low and thus confirms our results regarding the lack of all-day energy intake of nutrients.

An increased proportion of the daily intake of fats in our study (36.4%) coincides with the survey data on the dietary habits of Slovenes, according to which the average fat intake represents 38.8% of the daily energy intake in women (11), while Kinsey et al. (15), in their study, found that fat represented 31% of all-day energy intake in British patients with CD. The results indicate that the proportion of ingested fat in the diet is too high and the meals of CD patients in Slovenia were not balanced. A greater amount of fat in the diet increases the risk of obesity, and an excessive proportion of saturated fats and trans fats increases the risk of cardiovascular disease and certain types of cancer (16).

With regards to the data about the daily intake of carbohydrates, CD patients on average consume 193 grams of carbohydrates per day, which represents 48.2% of the energy intake. This is comparable with the results of an English study, according to which patients with coeliac disease consumed 213 grams of carbohydrates, or 49% of daily energy intake (15). This is slightly higher than the data about the dietary habits in Slovenia, where an average proportion of daily energy intake with carbohydrates, consumed by a Slovenian female, was 47% (11). More than half of the CD patients use the proportion of carbohydrates which is less than the recommended

amount. This coincides with an increased intake of fat in the overall dietary intake and with the data from the literature, according to which an insufficient intake of carbohydrates correlates with an increased consumption of fat and, thereby, increases the risk of chronic diseases (e.g. cardiovascular disease) (10, 11).

Only one CD patient in our study consumed a sufficient amount of dietary fibre. In a gender-comparable English study, dietary fibre intake among patients with coeliac disease was even lower, 12 g per day (in our study 18.8 g per day) (15).

Among macro-and microelements that were discussed in our study, calcium and iodine are particularly important. These are the two substances that our CD patients do not consume in big enough quantities. On average, CD patients consumed 760 mg of calcium per day (the recommended amount is 1000 mg/day (10, 12)), which meets only 76% of the daily calcium intake needs. The results are comparable with an English study, according to which the patients with coeliac disease consumed 797 g of calcium daily. An insufficient intake of calcium can lead to long-term health problems, such as osteoporosis, which is one of the most common diseases accompanying patients with CD (8,15). Intake of iodine is also a concern. On average, the CD patients consumed 96 mg of iodine daily, which satisfies only 53-64 % of the daily needs.

In contrast to the English study, according to which the CD patients consumed higher levels of iron than the recommended value (15), the average daily amount of ingested iron in our study and in a U.S. study is lower: 10.2 and 11 mg, respectively (10, 17). This was also found in Finland, where CD patients had significantly lower values of iron (18).

The average intake of zinc was 8.6 mg and was 22.8% higher than the recommended value of 7 mg/day (10). Regarding Central European diet, an average daily intake of potassium for adults is 2-3 g, which was confirmed in our study as well (10).

Upon evaluation of food diaries, we came to the conclusion that a large proportion of CD patients on a strict GF diet do not consume the recommended values of individual vitamins, which was also described in the study conducted by Hallert et al. (8).

Among the vitamins that were discussed in our study, folates are the most important, because none of the CD patients reached the recommended daily intake of folic acid. A Finnish study also confirmed a significantly low folate content (18). The second vitamin with a proven insufficient intake in almost all CD patients is the vitamin D. Normal daily intake of vitamin D in general population is ten to five times lower than the recommended intake, thus the recommended intake of vitamin D can only be achieved with dietary supplements (19). Pertaining to the

normal daily intake of vitamin D, we found that more than half of our CD patients had an insufficient intake, which is in line with the findings of other authors (8, 15, 20, 21). Good sources of vitamin D for patients with coeliac disease are oily fish, eggs and nutrients fortified with vitamin D, such as margarine, gluten free yogurts and gluten free cereal flakes. Because some yogurts and most cereals contain gluten, the CD patients consequentially consume less vitamin D than the general population (8).

Our study also proved an insufficient intake of vitamin B12, which is consistent with the findings of other authors (8, 15). This indicates that the lack of vitamin B12 in the diet is prevalent for CD patients. Vitamin B12 is absorbed in the upper part of the small intestine, where, in the case of non-compliance with a strict gluten-free diet, damage to the villi occurs, which leads to the reduced absorption of nutrients and vitamins (8). CD patients, who enjoyed mussels, had an intake of 83.7 mg of the vitamin B12, but, due to the large deviations, these results were not included.

The only exception is vitamin K, with most of the CD patients consuming higher amounts than recommended. Depending on the selection of foods mentioned in food diaries, the patients with coeliac disease in Slovenia are knowledgeable of the allowed and prohibited food. As already mentioned, the food diaries evaluation may not fully reflect the real situation, especially in people who are overweight (8, 11). In our study, 40% of CD patients had BMI equal to or greater than 25 kg/m^2, which could have the influence on the results and which, at the same time, proves that the obesity epidemic described in other studies has reached the patients with coeliac disease in Slovenia (13).

5 CONCLUSION

The research gives us a rough insight into the diet of adult coeliac disease patients in Slovenia. Gluten free diet of coeliac disease patients in Slovenia does not meet the guidelines for a healthy and balanced diet according to the Reference values for nutrient intakes D-A-CH. Because of an improper composition of the meals, the nutrition of patients with coeliac disease is unbalanced: it consists of an increased proportion of fat, and contains an insufficient intake of carbohydrates and dietary fibre, as well as inorganic substances, such as iron, calcium, iodine and folate, vitamin B12 and fat-soluble vitamins A, D and E.

As far as the selection of foodstuffs in the food diaries is concerned, we concluded that coeliac disease patients in Slovenia know very well which foods they can consume (gluten-free) and which foods they should not consume. In the future, more emphasis should be given to the balanced composition of foods, improving the quality of

a gluten-free diet in tandem with a regular nutritional monitoring of coeliac disease patients.

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THE IMPACT OF SPORTS ACTIVITIES ON QUALITY OF LIFE OF PERSONS WITH A SPINAL CORD INJURY

VPLIV ŠPORTNIH AKTIVNOSTI NA KAKOVOST ŽIVLJENJA OSEB S POŠKODBO HRBTENJAČE

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ABSTRACT

Keywords:
spinal cord injury,
sports activities,
quality of life,
secondary health
conditions

Objectives. Studying the quality of life of people with a spinal cord injury is of great importance as it allows the monitoring of both functioning and adaptation to disability. The aim of this study was to determine the difference between persons with a spinal cord injury involved in sports activities and those not involved in sports activities in relation to their quality of life and the presence of secondary health conditions (pressure ulcers, urinary infections, muscle spasms, osteoporosis, pain, kidney problems-infections, calculosis and poor circulation).

Methods. The study included a total of 44 participants with spinal cord injury-paraplegia of both genders; 26 of them were athletes and 18 were not athletes. The athletes were training actively for the last two years, minimally 2-3 times per week. A specially designed questionnaire, medical documentation and the Spinal Cord Injury Quality of Life Questionnaire (SCI QL-23) were used for research purposes. Chi-square test was used to analyze the differences between the groups, while multiple analysis of variance (MANOVA) was used to determine the differences between the sets of variables.

Results. Among the participants, the athletes perceived higher quality of life than the non-athletes (male gender p<0.001 and female gender p<0.05). Regarding secondary health conditions, the athletes reported the presence of less pain (p=0.034) and a subjective feeling of better circulation (p=0.023).

Conclusion. The implementation of sports activities significantly improves quality of life in the population of people with spinal cord injury-paraplegia. However, sports activities only partially affect secondary health conditions.

IZVLEČEK

Ključne besede:
poškodbe hrbtenjače,
športne aktivnosti,
kakovost življenja,
sekundarna
zdravstvena stanja

Izhodišče. Študij kakovosti življenja oseb s poškodbo hrbtenjače je pomemben, ker omogoča spremljanje delovanja in prilagajanje na invalidnost. Cilj te raziskave je bil ugotoviti razlike v kakovosti življenja in prisotnost sekundarnih zdravstvenih stanj (preležanin, okužb sečil, mišičnih krčev, osteoporoze, bolečin, težav z ledvicami – okužbe, calculosis in slabe prekrvavitve) med osebami s poškodbo hrbtenjače, vključenimi v športne aktivnosti, in tistimi, ki v športne aktivnosti niso vključene.

Metode. V raziskavi je sodelovalo 44 udeležencev s poškodbo hrbtenjače – s paraplegijo – obeh spolov; od tega je bilo 26 športnikov, 18 pa ne. Športniki so aktivno vadili v zadnjih dveh letih minimalno dva- do trikrat na teden. Posebej oblikovan vprašalnik, medicinska dokumentacija in vprašalnik 'Spinal Cord Injury Quality of Life Questionnaire' (SCI QL-23) so bili uporabljeni v raziskovalne namene. Test hi-kvadrat smo uporabili za analizo razlik med skupinami, medtem ko je bila uporabljena multipla analiza variance (MANOVA), da se določijo razlike med kompleti spremenljivk.

Rezultati. Udeleženci športniki dosegajo višjo kakovost življenja kot nešportniki (moškega spola p<0,001 in ženskega spola p<0,05). Ko gre za sekundarna zdravstvena stanja, imajo športniki manj bolečin (p=0,034) in subjektivni občutek boljšega obtoka (p=0,023).

Zaključek. Izvajanje športne dejavnosti pomembno vpliva na zvišanje kakovosti življenja v populaciji ljudi s poškodbo hrbtenjače – s paraplegijo, vendar športne aktivnosti le delno vplivajo na sekundarna zdravstvena stanja.

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1 INTRODUCTION

Spinal cord injury (SCI) is one of the most severe forms of disability, both from the physical aspect as well as from the psychological, social and professional aspects (1). From 10.4 to 83.0 new SCI cases per million inhabitants are recorded each year worldwide (2). Based on the available data, the incidence in Western Europe amounts to 6 new cases per million per year for non-traumatic SCI (3) and 16 new cases per million for traumatic SCI (4). During rehabilitation, in addition to a number of therapeutic procedures, it is important to educate patients on the need for a lifelong care of their activity limitations and the maintainance of the optimal state of health (5, 6).

Secondary health conditions have been defined as: physical or psychological health conditions that are influenced directly or indirectly by the presence of a disability or an underlying physical impairment (7-9). The most common secondary health conditions in SCI are: pain, bowel and bladder regulation problems, muscle spasms, fatigue, esophageal symptom and osteoporosis (9). In addition, pressure ulcers, urinary infections, kidney problems (infections, calculosis) and poor circulation are often present in persons with SCI (1, 10).

The inclusion of persons with SCI in social and recreational activities is one of the aspects of a long-term rehabilitation plan (11, 12). Sports activities are implemented both during (13, 14) and after rehabilitation (15) in order to improve strength, aerobic fitness, and physical functioning (16); in addition, sports activities have positive effects on psychological well-being (17).

Studying the quality of life (QoL) in persons with a spinal cord injury is very important as it allows the monitoring of functioning and adaptation to disability. Persons with a spinal cord injury have a lower QoL than the general population (18, 19). There are two main concepts in the assessment of QoL. The objective approach is based on one's characteristics that can be objectively measured by an external appraiser, whereas the focal point of the subjective approach is on the person's emotional or cognitive assessment of the congruence (20). The quality of life of persons with SCI can be evaluated with the Quality of Life Profile: Physical and Sensory Disabilities Version (QOLP-PSD) (20, 21), the Perceived Quality of Life Scale (PQOL) (22-24), the Quality of Life Scale (QOLS) (25). Moreover, the tools designed for the assessment of QoL in general population can be used, such as the World Health Organization Quality of Life-BREF scale (WHOQOL-BREF) (18, 26, 27), the Short Form (SF-36) (28, 29), the Satisfaction with Life Scale (SWLS) (30, 31), the Quality of Well-being Scale (QWB) (20, 30) and others (32, 33). The existing research suggests that the completeness of injury and social interaction (hobbies, spending time with friends, sports) can affect the level of quality of life of

persons with SCI (34), as well as the level of SCI, education and employment (27, 35). The impact of sports activities on quality of life is assessed in the healthy population (36, 37) as well as in persons with SCI (32, 38).

We hypothesized that persons with SCI involved in sport activities would report higher quality of life according to The Spinal Cord Injury Quality of Life Questionnaire (SCI QL-23) (39), and less secondary health conditions (pressure ulcers, urinary infections, muscle spasms, osteoporosis, pain, kidney problems-infections, calculosis and poor circulation) in comparison to the non-sporting SCI population. The aim of the research is to determine the difference between athletes and non-athletes in relation to the given research variables.

2 MATERIALS AND METHODS

The research was conducted in 2013 at the Home for Adult Persons with Disabilities in Belgrade, Association of paraplegics and quadriplegics "Dunav" in Belgrade, Athletic club "Pogledi" from Belgrade, Wheelchairs basketball club "Dunav" from Belgrade, Table tennis club of persons with disabilities Belgrade "STIB" and Sports and Recreational Association "Sve je moguće" from Belgrade.

2.1 Participants

From the total of 80 available participants with SCI of both genders, aged 20-60 years, who have signed the agreement to participate in this study, only 44 participants fulfilled the criteria of the study. The criteria were: a minimum of 2 years since the spinal cord lesions, spinal cord injury at the level of the thoracic, lumbar or sacral region (paraplegia), and, if athletes, training actively for the last two years, minimally 2-3 times per week. The sample was divided into two groups. The first group included 26 participants actively involved in sports (athletes), whereas the second group consisted of 18 participants not involved in sports (non-athletes).

2.2 Instruments

Two questionnaires were used in this study, one for the collection of general information and characteristics related to SCI, and one for quality of life assessment – The Spinal Cord Injury Quality of Life Questionnaire (SCI QL-23) (39). The first was designed for this survey in order to collect data on the gender, age, time since spinal cord injury, type of sports that a person does and the frequency of training. The participants were also given a list of common secondary health conditions associated with SCI in this questionnaire (pressure ulcers, urinary infections, muscle spasms, osteoporosis, pain, kidney problems-infections, calculosis and poor circulation), and were asked to confirm their presence or absence.

The completeness of spinal cord injury according to ASIA impairment scale (American Association Impairment scale) (40, 41) was taken from the medical records of the participants.

2.2.1 The SCI QL-23

The SCI QL-23 is a self-report questionnaire derived from a battery of general and specific questionnaires applied in the studies of the quality of life of persons with a spinal cord injury (39). SCI QL-23 consists of 23 statements/questions, which include: functioning (FUNC), mood (MOOD, DEPR. scale), loss of independence experience (PROB-problems reinjury), and overall rating of life situations (GQOL-global quality of life).

Functioning (FUNC) refers to functional limitations in mobility, body care, movement and social interaction. It contains ten items in the form of statements that describe the possible conditions of persons with SCI within these areas. Questions are pre-designed and of proper weight (in accordance with the weighting of Sickness Impact Profile-SIP) system (42). A participant needs to mark only those items with which she or he agrees. Each confirmed item carries a certain value. The key test-results are ranged on the scale from 0-100; a lower score represents a better result.

The mood (MOOD, DEPR. scale) includes 6 items related to the presence of depressive feelings and bad mood. Each item has four levels of answers provided. A participant marks the answer that best describes him or her. The key test-results are ranged on the scale from 0 to 100; a lower score represents a better result.

The experience of independence loss (PROB-problems reinjury) refers to the assessment of the perception of physical dependence, complications and social stigma related to the specificity of injury. It includes 6 items with four levels of answers offered. The participants were asked to circle the answer to each specific item (given in the form of questions) that best describes how they feel. The key test-results are ranged on the scale 0-100; a lower score represents a better result.

The overall rating of life situations (GQOL-global quality of life) contained a single question, and the participants had to choose an answer on the scale 1-7. The key test-result is graduated on the scale 0-100; a higher score represents a better result (34, 35, 43-45).

2.2.2 Translation

After receiving a permission and the original test in the English language, it was necessary to make a cultural adaptation into the Serbian language. First, the given version was translated by two independent translators. Following the adjustment of both versions, the questionnaire was translated from Serbian back to

English by a person whose native language is English and who was not familiar with the questionnaire. After the bilingual adaptation by the expert, the final version was used on the sample of 20 persons with SCI not included in the present study. This pilot study was realized in order to test the understanding of questions and to clarify potential dilemmas (46).

2.3 Statistical Analysis

The basic methodological principle of this research is based on the comparison of results between the participants with SCI-paraplegia who are involved in sports activities and the participants who are not involved in sports activities, with the aim of determining the differences between the given research variables. Basic measures of central tendency of the results were represented by arithmetic mean ($\bar{x}$) and standard deviation (SD). The differences between the individual groups were tested by the χ^2- test. Multiple analysis of variance (MANOVA) was used to determine the differences between the sets of the variables between the experimental and control group, while Bonferroni criterion was used to test the differences between the pairs of individual variables. We used Pearson correlationto determine the power of predictors on global quality of life (GQOL). Statistical analysis was carried out by software package Excel 2003 (Microsoft®Office Excel 2003) and SPSS Win 17.0.

2.4 Ethical Notes

The research was realized in accordance with the terms of the "Declaration of Helsinki for recommendations guiding physicians in biomedical research involving human subjects" (http://www.cirp.org/library/ethics/helsinki/), with the approval and consent of the Ethics Committee of the Faculty of Sport and Physical Education, University of Belgrade.

3 RESULTS

This study included a total sample of 44 participants. Of these, 59.1% were involved in sports, and 40.9% of participants were not involved in sports activities. All subjects had paraplegia; 25 of them had the injury of the thoracic spine, whereas 19 participants had the lumbar spine injury. There was no difference between groups in relation to the completeness of the spinal cord injury (χ^2=2.27, p=0.132) and in relation to gender (χ^2=1.45, p=0.228). Male participants from the group of athletes and the group of non-athletes differed by age (35.9±6.5 vs. 48.8±7 years respectively, p=0.000) and by the time after injury (14.2±6.7 vs. 22.5±8.8 years respectively, p=0.005). There was no difference between female participants from the group of athletes and the

group of non-athletes in relation to their age (43.2±8.5 vs. 43.4±13.2 years respectively), or in relation to the time after injury (19.8±0.5 vs. 24.5±16.7 years respectively, p=0.461) (Table 1).

Table 1. The characteristics of the participants, both athletes and non-athletes.

Parameters	Athletes	Non-athletes	
Level of injury, n (%)			
Thoracic	15 (57.7%)	10 (55.6%)	
Lumbar	11 (42.3%)	8 (44.4%)	
ASIA*, n (%)			
A (complete)	16 (61.5%)	11 (61.1%)	χ^2 test
B (incomplete)	4 (15.4%)	3 (16.7%)	χ^2=2.27
C (incomplete)	6 (23.1%)	4 (22.2%)	p=0.132
Sex, n (%)			
Male	19 (73.1%)	13 (72.2%)	χ^2 test
Female	7 (26.9%)	5 (27.8%)	χ^2=1.45
Total	26 (100%)	18 (100%)	p=0.228
Age, x̄±SD (years)			MANOVA
Male	35.9±6.5	48.8±7	**p=0.000**
Female	43.2±8.5	43.4±13.2	p=0.978
Time after injury x̄±SD (years)			
Male	14.2±6.7	22.5±8.8	**p=0.005**
Female	19.8±0.5	24.5±16.7	p=0.461

*ASIA – American Spinal Injury Association

The participants involved in sports (athletes) have been practising sports activities for 9.4±4.5 years (Table 2), with shorter or longer breaks; however, they were training minimally 2-3 times per week during the last two years continuously, and that we considered relevant for this research. When it comes to the secondary health conditions (Table 3), most of the participants from both groups reported urinary tract infections (69.2% vs. 66.7% respectively), but athletes had significantly less pain (p=0.034) and a subjective feeling of poor circulation (p=0.023), while the presence of pressure ulcers was at the border of statistical significance (p=0.057).

Table 4 shows the SCI QL-23 results. The participation in sports activities had a significant impact on the results of all four subtests, both in relation to male (p=0.000) and female gender (FUNC p=0.000, MOOD p=0.000, PROB p=0.006 and GQOL p=0.000). The participants who were athletes had achieved their best results in the area of mood (MOOD), both in relation to male and female gender (7.72±9.47 vs. 7.41±7.63 respectively), but they had also achieved high values on the subtest of Global Quality of Life-GQOL (80.56±15.96 vs. 83.33±16.67 respectively).

Table 2. The type of sport, number of training sessions on a weekly basis and years of training of athletes with SCI.

Parameters	Male	Female	Total
Type of sport, n (%)			
Athletics	7 (26.9%)	-	7 (26.9%)
Basketball wheelchair	9 (34.6%)	-	9 (34.6%)
Shooting	-	3 (11.5%)	3 (11.5%)
Bicycling	1 (3.8%)	-	1 (3.8%)
Archery	1 (3.8%)	2 (7.7%)	3 (11.5%)
Table tennis	-	2 (7.7%)	2 (7.7%)
Body building	1 (3.8%)	-	1 (3.8%)
Total	19 (73.1%)	7 (26.9%)	26 (100%)
Number of training sessions/weekly, n (%)			
2-3 x (basketball wheelchair, table tennis, bicycling)	10 (38.4%)	2 (7.7%)	12 (46.1%)
4-5 x (archery, shooting)	1 (3.8%)	5 (19.2%)	6 (23.1%)
6-7 x (body building)	1 (3.8%)	-	1 (3.8%)
8-12 x (athletics)	7 (26.9%)	-	7 (26.9%)
Total	19 (73.1%)	7 (26.9%)	26 (100%)
Years of training (Total)	9.2±5	9.9±3.1	9.4±4.5

Table 3. The presence of secondary health conditions in persons with SCI who are involved in sports acticities in comparison to those who are not involved in sports activities.

Parameters	Athletes	Non-athletes	MANOVA
SHC*, n (%)			
Pressure ulcers	7 (26.9%)	10 (55.6%)	**p=0.057**
Urinary infections	18 (69.2%)	12 (66.7%)	p=0.862
Muscle spasms	8 (30.8%)	5 (27.8%)	p=0.835
Osteoporosis	1 (3.8%)	2 (11.1%)	p=0.359
Pain	3 (11.5%)	7 (38.9%)	**p=0.034**
Kidney problems (infections, calculosis)	3 (11.5%)	4 (22.2%)	p=0.352
Poor circulation	1 (3.8%)	5 (27.8%)	**p=0.023**

*Secondary health conditions

The greatest difference between the ranges of values of athletes compared to non-athletes was on the test PROB (31.79±18.87 vs. 67.59±18.68 respectively) for male participants and on the test FUNC (10.95±10.03 vs. 61.28±5.12 respectively) for female participants. As there

Table 4. SCI QL-23 results of the participants who are involved in sports activities, compared to those who are not involved in sports activities.

Parameters	Athletes	Non-athletes	MANOVA
FUNC, x̄±SD (the lower the better)			
Male	10.40±10.84	45±15.79	p=0.000
Female	10.95±10.03	61.28±5.12	p=0.000
MOOD, x̄±SD (the lower the better)			
Male	7.72±9.47	36.57±26.67	p=0.000
Female	7.41±7.63	58.33±12.73	p=0.000
PROB, x̄±SD (the lower the better)			
Male	31.79±18.87	67.59±18.68	p=0.000
Female	30.56±22.85	73.61±18.16	p=0.006
GQOL, x̄±SD (the lower the better)			
Male	80.56±15.96	48.61±19.79	p=0.000
Female	83.33±16.67	33.33±11.78	p=0.000

Table 5. GQOL in relation to variables: age, time after injury and secondary health conditions.

	Athletes				Non-athletes			
	Male		Female		Male		Female	
Variables	r	P-level	r	P-level	r	P-level	r	P-level
Age	-0.325	NS	-0.702	NS	-0.028	NS	-0.043	NS
Time of injury	-0.342	NS	-0.219	NS	-0.008	NS	0.151	NS
Pressure ulcers	-0.186	NS	-0.447	NS	0.070	NS	0.707	NS
Urinary infections	-0.377	NS	-0.447	NS	-0.211	NS	-	.
Muscle spasms	0.246	NS	0.707	NS	-0.284	NS	-	-
Osteo-porosis	-	-	-0.447	NS	-	-	0.000	NS
Pain	-0.211	NS	-	-	0.041	NS	0.707	NS
Kidney problems (infections, calculosis)	**-0.545**	**0.019***	-	-	-0.122	NS	0.000	NS
Poor circulation	0.042	0.042	-	-	0.220	NS	0.000	NS

r=Pearson's correlation coefficient
*P<0.05
NS=not significant

is a significant difference between male participants from the group of athletes and the group of non-athletes in relation to their age and the time after injury, using Pearson's correlation coefficient, we have presented their impact on GQOL, as well as the impact of the secondary health conditionson GQOL (Table 5).

4 DISCUSSION

In our study, a significantly higher quality of life of persons with SCI engaged in sports activities, as compared to those who did not do any sports, was found, which is consistent with other research (13, 29, 47, 48). In another study, in which the test SCI QL-23 was used as well (19), persons with paraplegia had an average value score of 44.07±29.11 in the given area of functioning (FUNC), while our participants who were non-athletes had a lower score (a lower score means a better performance), in terms of both genders (45±15.79 vs. 61.28±5.12 respectively). However, the participants who were doing sport in our research had a significantly lower score in the given area, for both genders (10.40±10.84 vs. 10.95±10.03 respectively). This means that the involvement in sports activities had a significant effect on the improvement in the area of functioning.

It is known that persons with SCI suffer from depression and have negative mood (9, 49), as also evidenced in

our study, on the subtest MOOD (Table 4). However, the biggest difference between SCI athletes and non-athletes is found exactly in this subtest, as expected, since it is known that physical activity affects the improvement of mood in this population as well (17, 23, 50). However, it should be noted that male non-athletes in our study had similar results to the ones in recently published studies (19, 45), but female non-athletes had significantly worse results. Kreuter et al. (35) indicated the relation of some socio-demographic characteristics and depressive feelings in persons with SCI, which could be potentially important factors and a possible explanation for this result.

The results of the third subtest (PROB) indicate a level of difficulty, i.e. problems of persons with SCI which concern the feelings of inability to walk free and the necessary assistance, as well as problems integrating into the environment and problems with defecation and pain (Table 4). Previously published studies from 2012 (34) and 2014 (19, 45) presented a better score compared to our results pertaining to the non-athletic participants (the average of 13.1-46.1% for male participants and 23.3-59.6% for female participants). However, sports,

whether practiced individually (eg. athletics, shooting, archery and body building in our research) or in groups (wheelchair basketball and table tennis), significantly reduces the above mentioned problems and difficulties that accompany SCI. This can be seen from the results of athletes on this subtest that are nearly two times better than the ones from the aforementioned research.

Comparing the results of the fourth subscales (GQOL) with the results from other studies (35, 45), we have found that our participants not involved in sports had GQOL lower for an average 27.9%-37.4% in comparison to the participants from Australia and Sweden, as well as in comparison to the participants from Iran. When complemented by the fact that the groups from those countries were heterogeneous (persons with paraplegia and persons with tetraplegia), this result shows that the personal feeling of quality of life of our participants is at a significantly lower level. In Sweden and Australia, according to a given study, one of the strongest predictors of quality of life was participation in social activities and productive life in the community. However, our participants who are athletes perceived quality of life as significantly higher than the participants from the afore mentioned research (that is, 56.4% more than participants from Australia and 45.5% more than participants from Sweden), which means that the inclusion of persons with spinal cord injuries into society through sport contributes significantly to better quality of life in our country, too. In addition, other studies show a variation in the results of quality of life in relation to the given state (27).

In relation to secondary health conditions, the implementation of sports activities contributed to the decrease of pain and subjective feeling better circulation. Studies conducted by Norrbrink et al. (51), Martin Ginis et al. (23) and van der Scheer et al. (52) also indicated a positive effect of exerciseon the reduction of musculoskeletal and neuropathic pain. The majority of our participants (a total of 68.2%) had an urinary infection, which is consistent with the data from other studies (10, 53). Pressure ulcers, in our study, as the second most common secondary health conditions, occurred in 38.6% of the participants, while in other studies this frequency varied between 21.1 and 41.8% (54, 55). The SCI athletes in our study reported less presence of pressure ulcers, which is not negligible, since the difference was at the border of statistical significance (Table 3). It is known that inactivity affects the formation of pressure ulcers in persons with SCI (56), which supports the results of our research.

Numerous studies show that persons who are older and have a longer period after injury (duration effect) suffer more from secondary conditions or symptoms (chronic pain, pressure ulcers, bladder problems, spasms, etc.) that may affect their perception of quality of life (9).

However, we found that among our participants almost no predictor had no power effect on GQOL, including the age, time of injury and secondary health conditions. A study from 2012 (31) showed that persons with SCI, regardless of their age and the time passed after injury, had the potential to improve their overall QoL, or some domains of QoL. It is interesting that the only association between the predictor and GQOL was found in male athletes, and was related to kidney problems. Possible reasons should be sought in the fact that athletes have a higher degree of perspiration during training and competing, which leads to a greater flow of fluid through the kidneys after hydration. This information should be the subject of future research in the area of sports for persons with SCI. The first limitation of our study is that all the data were obtained exclusively by means of self-reporting (secondary health conditions and QoL), which means that they could be biased and under the influence of forgetting. Next, the sample of the participants was relatively small, further limiting a detailed analysis of the differences between the groups. The limiting factor of our study is certainly the nonhomogeneousness of the group of the participants involved in sports activities in relation to the type, intensity and frequency of sports training. First of all, we were guided by the well-known fact that doing sports affects the motivation and the 'fighting spirit,' the important factors for both overcoming of disability and perception of QoL. However, some studies indicate that a higher frequency of training (29) and certain combination of aerobic and strength exercises (24) affect the QoL, pain, stress and depression. Thus, our study indicates the need for further research on the effects of certain types of sports activities (systematized in relation to the exercise type, intensity and frequency of training) on different QoL domains and secondary health conditions. In addition, future studies should include other factors that may affect the quality of life of athletes and non-athletes with SCI, such as the marital status, financial status, occupation, place of residence, social assistance, employment, physical and social barriers, and more.

5 CONCLUSION

Athletes with SCI perceive a significantly higher quality of life, according to SCI QL-23, in terms of the functioning, mood, problems related to the loss of independence and the overall rating in life situations, when compared to non-athletes with SCI. Pertaining to the secondary health conditions, sports activities affect the presence or absence of pain and the subjective feeling of poor circulation.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

ETHICAL APPROVAL

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FACTORS INFLUENCING THE SIX-MONTH MORTALITY RATE IN PATIENTS WITH A HIP FRACTURE

DEJAVNIKI, KI VPLIVAJO NA ŠESTMESEČNO STOPNJO UMRLJIVOSTI PRI BOLNIKIH Z ZLOMOM KOLKA

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ABSTRACT

Keywords:
cognitive status,
comorbidity, poor
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six-month mortality

Background. There are several potential risk factors in patients with a hip fracture for a higher rate of mortality that include: comorbid disorders, poor general health, age, male gender, poor mobility prior to injury, type of fracture, poor cognitive status, place of residence. The aim of this study was to assess the influence of potential risk factors for six-month mortality in hip fracture patients.

Methods. The study included all patients with a hip fracture older than 65 who had been admitted to the Clinic for orthopaedic surgery during one year. One hundred and ninety-two patients were included in the study.

Results. Six months after admission due to a hip fracture, 48 patients had died (6-month mortality rate was 25%). The deceased were statistically older than the patients who had survived. Univariate regression analysis indicated that six variables had a significant effect on hip fracture patients' survival: age, mobility prior to the fracture, poor cognitive status, activity of daily living, comorbidities and the place where they had fallen. Multivariate regression modelling showed that the following factors were independently associated with mortality at 6 months post fracture: poor cognitive status, poor mobility prior to the fracture, comorbid disease.

Conclusion. Poor cognitive status appeared to be the strongest mortality predictor. The employment of brief tests for cognitive status evaluation would enable orthopaedists to have good criteria for the choice of treatment for each patient screened.

IZVLEČEK

Ključne besede:
kognitivni status,
komorbidnost,
slabo kognitivno
stanje, zlom kolka,
šestmesečna
umrljivost

Izhodišča. Obstaja več možnih dejavnikov tveganja za višjo stopnjo umrljivosti, kot so spremljajoče bolezni, slabo splošno zdravstveno stanje, starost, moški spol, zmanjšana mobilnost pred poškodbo, tip zloma, slab kognitivni status, kraj bivanja. Cilj te študije je bil oceniti vpliv možnih dejavnikov tveganja na šestmesečno smrtnost pri bolnikih z zlomom kolka.

Metode. Študija je vključevala vse bolnike z zlomom kolka, starejše od 65 let, ki so bili sprejeti na Kliniko za ortopedsko kirurgijo in travmatologijo v enem letu. V raziskavo je bilo vključenih 192 bolnikov.

Rezultati. Šest mesecev po sprejemu zaradi zloma kolka je umrlo 48 bolnikov (šestmesečna smrtnost je bila 25%). Umrli so bili statistično starejši od bolnikov, ki so preživeli (p<0,001). Univariantna regresijska analiza je pokazala, da je šest spremenljivk pomembno vplivalo na preživetje bolnikov z zlomom kolka: starost, mobilnost pred zlomom, slab kognitivni status, vsakodnevne aktivnosti, komorbidnost in kraj, kjer so padli. Multivariantno regresijsko modeliranje je pokazalo, da so naslednji dejavniki bili neodvisno povezani z umrljivostjo šest mesecev po zlomu: slab kognitivni status, slaba mobilnost pred zlomom in komorbidne bolezni.

Zaključek. Zdi se, da je slabo kognitivno stanje najmočnejši napovedni dejavnik umrljivosti pri bolnikih z zlomom kolka. Uporaba kratkih testov za oceno kognitivnega stanja bi ortopedom omogočila dober kriterij za izbiro načina zdravljenja pri obravnavanem bolniku.

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1 INTRODUCTION

Mortality among patients with hip fractures is two or three times higher than that seen in the general population (1-3). Despite improvements in the treatment of hip fracture patients, only 60% recover all their previous functions. Between 7.9% and 26.9% die within three to six months, and 25% have levels of disability that require constant care (4-6).

A number of studies have looked at possible determinants or predictors of hip fracture mortality (7-10). Potential risk factors for a higher rate of mortality are comorbid disorders (11, 12), poor general health (11, 13), age (13-16), male gender (11, 12), poor mobility prior to the injury (13, 17), diabetes mellitus (13, 17), type of fracture (17), poor cognitive status (14) and place of residence (11). However, the exact roles and relative contributions of these factors have not been clearly determined.

It is indicated that a prognosis for survival of hip fracture patients may be given on the basis of the ability to walk and maintain an activity of daily living prior to the injury (7, 18), whereas the type of fracture, type of treatment and age of the patient seem not to be the main predictors of the ultimate outcome of treatment (8, 11). Studies have further indicated that the influence of poor cognitive status together with a chronic disease results in low survival rates (19).

The number of poor cognitive status patients with a hip fracture proportionally increases with age, and cognitive disorders are pre-morbid conditions which are very frequently associated with an unsatisfactory outcome (1, 6, 8, 14, 20-24). A patient's mental function and mobility before the injury may be considered a good indicator of their general condition and may be useful in predicting the outcome.

The aim of this paper was to assess the influence of risk factors on six-month mortality in patients with a hip fracture.

2 MATERIALS AND METHODS

This study was conducted at the University hospital, which treats all patients with hip fractures in Sumadija Region (Central Serbia). The study included all patients with a hip fracture who were aged over 65 years and who were admitted to the Trauma and Orthopaedics Clinic between March 2008 and March 2009. All study parameters were assessed and recorded during the first 24 hours after admission.

Data were collected by way of a specifically designed questionnaire which recorded patients' personal details (gender, age, occupation and place of residence), circumstances and location of the injury as well as the status of the patient prior to the injury in terms of their ability to walk, their use of assistive devices and details of all previous injuries and fractures in the past few years.

Data relating to the injury were recorded by an orthopaedist when a patient was admitted. The assessment of the patient's general health was completed by an internist at the time of the admission. According to data thus obtained, all patients were divided into three groups, namely:

1. patients with mild comorbid diseases, such as mild hypertension, diabetes mellitus with good control by oral antidiabetic medication, benign prostatic hypertrophy;
2. patients with moderate comorbid deseases, such as compensated cardiomyopathy, insulin dependent diabetes mellitus with initial vascular complication (retinopathy, nephropathy), chronic obstructive pulmonary disease, occasional supraventricular arrhythmias; and
3. patients with severe comorbid deseases, such as acute myocardial infarctus, decompensated cardiomyopathy, poorly controlled insulin-dependent diabetes mellitus with a marked angiopathy (angina pectoris, gangrene of the extremities).

Mental status was assessed using the Short Portable Mental Status Questionnaire (SPMSQ), which is a modified version of the Blessed test (25, 26) and is administered quickly and easily (1, 8). The SPMSQ is a ten-item questionnaire for the assessment of cognitive function. It was administered within 24 hours of admission by the patient's orthopaedist. Ten parameters were recorded with a score of 0, 1, 2 or 3. The level of cognitive function was categorized according to the results of SPMSQ test: >7 correct answers (cognitive function was intact); 6 or 7 correct answers (cognitive function was mildly impaired); 3-5 correct answers (cognitive function was moderately impaired); <3 correct answers (cognitive function was severely impaired). In order to compare the outcome for patients with severe cognitive dysfunction (<3) and patients with cognitively intact, mild or moderate impairment (≥3), we have used the cut-off level fewer than 3 correct answers (26). An overall score of 3 or below indicates extremely poor cognitive function and corresponds with poor cognitive status (1, 8, 21, 25). All patients with the score of 3 or below were also examined by a psychiatrist.

The ADL index was used to evaluate the functional independence or dependence of patients with regard to bathing, dressing, going to the toilet, transferring, continence, and feeding. A score of '0' indicates that the patient is "dependent in all daily activities". Score 6 means that the patient is fully capable of maintaining all the mentioned activities by him/herself (27, 28).

All the patients were treated according to conventional protocols. Comorbidities were treated prior to surgery. Patients with a fracture of the neck of the femur received a partial hip replacement by prosthesis. Patients with a trochanteric fracture were treated with reduction and internal fixation of the fracture.

Follow-up of the cohort of hip-fracture patients was performed six months after the injury to determine survival status. The Central Death Register was used for all status checks when the status could not be confirmed by means of post-mortem records.

Statistical analyses were performed using IBMSPSS-Statistics, version 19. Continous variables were presented as mean values ± standard deviation. Categorical variables were presented as frequencies of exposure as a percentage. Univariate associations between potential risk factors and an outcome were tested using the chi-square test for categorical variables, and Student's t test for independent samples for continuous variables. The link between potential risk factors and the fatal outcome were tested by linear and multiple logistic regressions, whereas the strength of the link was expressed in values of odds ratio with 95% confidence interval. All analyses were assessed at the statistical significance level p<0.05. Informed consent was obtained from all the patients or their careers. The research has been approved by the Ethical Committee of the Clinical Centre "Kragujevac". Ethical approval: Principles of ICH Good Clinical Practice were strictly followed for the study protocol.

3 RESULTS

There were 192 hip fracture patients in total (59 (30.7%) males and 133 (69.3%) females). The mean age was 76.9 (age range from 65 to 91). Forty-seven (35.6%) patients were older than 80 years of age. There were no deaths during surgery.

Six months after admission for a hip fracture 48 patients died, accounting for the six-month mortality rate 25%. The deceased patients were significantly older than the patients who survived (p<0.001) (Table 1). Fourteen of the deceased patients were male and thirty-four female. There was no statistical difference between the rate of mortality in women (25.56%) and men (23.76%) (p=0.786).

Forty patients had a cognitive status score of 3 or lower (20.8%). The remaining 152 patients (79.2%) had scores higher than 3. The surviving patients were significantly more likely to have a SPMSQ value above 3 (p<0.001). One hundred and ten patients (57.3%) had fallen at home and eighty-two (42.7%) outside their home. It was found that there was a considerably higher rate of mortality in patients who had suffered a fracture at home (p=0.0024). Prior to the hip fracture, 170 patients (88.5%) could walk

Table 1. Basic characteristics of the patients with hip fractures.

Variable	Deaths (n=48)	Surviving (n=144)	Statistically significant
Age	80.23±6.60	75.43±6.00	p<0.001
Gender			
Male	14 (29.2%)	45 (31.3%)	p=0.786
Female	34 (70.8%)	99 (68.7%)	
SPMSQ			
≤3	28 (58.3%)	12 (8.3%)	p<0.001
>3	20 (41.7%)	132 (91.7%)	
Ability to walk			
tied to bed	18 (37.5%)	4 (2.8%)	
use of assistive devices	21 (43.7%)	64 (44.4%)	p<0.001
without assistive devices	9 (18.8%)	76 (52.8%)	
Place of the injury			
in the home	37 (77.1%)	73 (50.7%)	p=0.0024
out of the home	11 (22.9%)	71 (49.3%)	
ADL	2.25±0.54	2.84±0.39	p<0.001
Comorbidities			
mild diseases	15 (31.3%)	80 (55.5%)	
moderate diseases	17 (35.4%)	56 (38.9%)	p<0.001
severe diseases	16 (33.3%)	8 (5.6%)	

SPMSQ- The Short Portable Mental Status Questionnaire
ADL- Activities of Daily Living index

independently, whereas twenty-two patients (11.5%) could not. Only four bedridden patients survived the period of six months after the fracture. A considerably higher rate of mortality was found in patients who could not walk independently before the injury (p<0.001).

Out of twenty-four patients with very severe comorbidities, eight (33.3%) survived the period of six months after the fracture. A considerably lower rate of survival was found in patients with a serious comorbidity in contrast to those without one (p<0.001).

The analysis of the seven variables listed in Table 2, by univariate regression analysis, showed that six of them significantly influenced the survival in the patients with a hip fracture: age, mobility prior to the fracture (walking), poor cognitive status (SPMSQ), ADL, comorbidities and the place where the fall occurred.

These six variables were entered into a multivariate regression model. Poor cognitive status, mobility prior

to the fracture and comorbidities were found to be independently associated with survival at 6 months following the hip fracture (Table 2).

Table 2. The univariate and multivariate logistic regression with the outcome (deaths/ surviving) as the dependent variable.

Variable	Crude OR (95% CI)	p	Adjusted OR (95% CI)	p
Age	0.88 (0.84-0.94)	<0.001*	0.95 (0.88-1.02)	0.153
Gender	1.10 (0.54-2.26)	0.786	-	-
SPMSQ (≤3)	15.40 (6.76-35.10)	<0.001*	4.88 (1.74-13.66)	0.003*
Ability to walk	5.36 (2.93-9.82)	<0.001*	2.73 (1.32-5.66)	0.007*
Place of the injury	3.27 (1.55-6.91)	0.002*	1.14 (0.43-3.02)	0.797
ADL	1.24 (1.12-1.37)	<0.001*	1.08 (0.93-1.24)	0.315
Comorbidities	0.34 (0.21-0.56)	<0.001*	0.51 (0.26-0.98)	0.043*

SPMSQ- The Short Portable Mental Status Questionnaire
ADL- Activities of Daily Living index
OR- odds ratio
CI- confidence interval
p- statistically significant
*- significant difference (p<0.05)

4 DISCUSSION

The six-month mortality rate recorded in this study is similar to that recorded in previous studies (4-6, 20). We found that the mortality rate was considerably higher in female patients, which is in contrast to some previous work (11, 15, 19, 22, 29, 30). Nevertheless, gender did not prove to be a significant prognostic indicator of mortality in hip fracture patients, which is in line with the results of some studies (11), but in contrast to other research (6, 11, 14, 19, 22, 29). The type of a fracture suffered did not influence mortality rate in our sample.

As in previous studies (17), poor mobility levels prior to the injury had an important impact on the six-month mortality rate in patients with a hip fracture; it was independently associated with mortality. This is not surprising, as mobility prior to the injury reflects both the patients' general health as well as their cognitive

status (22). Comorbidities in our research, as in many previous studies (11, 19, 22, 31), have been shown to be an important prognostic factor for mortality following a hip fracture. Whilst it is true that all methods of categorization of comorbidities have insufficiently clear criteria, subjectivity and/or insufficiently high sensitivity, certain conditions are important prognostic indicators in their own right (e.g. metastatic disease, de-compensated heart failure, chronic lung diseases and others) (19).

We could not demonstrate that the age of the patient played a significant role in the prediction of mortality after a hip fracture, which was the case with other studies (11, 32). However, we did find that a poor cognitive status was a significant predictive factor and this has also been shown in previous work (22, 29, 33). We found that older, mentally stable patients had a better ultimate outcome after a fracture, regardless of other observed factors, than younger patients with serious cognitive disorders. Younger patients with a hip fracture and severe cognitive disorders had a poor prognosis. This presents an important new perspective on the influence of age on the outcome in patients with a hip fracture. Cognitive functioning may therefore be regarded as the most sensitive indicator of physiological ageing. Based on this study, it seems reasonable to conclude that taking age as an isolated predicting factor may lead to wrong treatment and rehabilitation of elderly patients after a hip fracture.

There are inherent study limitations when looking into the relationship between existing cognitive function and mortality among hip fracture patients. These include recognising symptoms similar to poor cognitive status, keeping a detailed record of cognitive disorders in medical records, and recognising initial and mild symptoms of poor cognitive status. We were particularly interested in hip fracture patients' evaluation of cognitive status immediately after the injury, when an orthopaedist makes an important decision about the treatment (1, 21, 24, 34). Orthopaedists obtain many pieces of information about cognition through an interview (35), and special instruments for the detection of cognitive disorders are useful for, and complementary to, the general evaluation of the patient after a hip fracture. The scale for detection of poor cognitive status, according to Blessed (25), is widely used and recognised as a tool for assessing cognitive status among hip fracture patients. Nevertheless, both orthopaedists and psychiatrists have explored other instruments in an attempt to find a more suitable tool for this evaluation (1, 8, 14, 21, 22, 25).

In spite of the fact that poor cognitive functioning has already been highlighted as an important prognostic factor of mortality in hip fracture patients (1, 6, 8, 11, 21, 22, 30), it was not featured in treatment protocols for patients with a hip fracture. Poor cognitive status in

elderly hip fracture patients could be determined by an orthopaedist within the first 24 hours after admission, and then this information could be used to define the course of treatment irrespective of the patient's calendar age. Psychiatrists can be invited in as temporary members of a multidisciplinary team who will look after the patients with a complex hip fracture (36). Regardless of the recorded results, scales for quick assessment of cognitive status are still rarely employed in the routine work of an orthopaedist.

In the course of the study it was found that the majority of the observed risk factors did not operate independently of one another. In contrast to age and place where a fracture occurred, which have an impact only as clustered factors, it has been shown that poor cognitive status, comorbidity and mobility prior to the fracture have a significant and independent role in predicting six-month mortality in elderly patients with a hip fracture (37).

This study makes a good prognostic tool for the estimation of survival of patients after hip fracture.

4.1 Limitations of the Study

Not all risk factors that may be associated with the cause of mortality were taken into consideration (type of fracture, type of fixation, osteoporosis, waiting time for surgery, etc.). The follow up period may have been short, so in a future study, we could prolong that period.

5 CONCLUSIONS

Cognitive disorders are the strongest predictors of mortality in hip fracture patients. The employment of brief tests for the evaluation of cognitive status enables an orthopaedist to have a good 24-hour direction as regards the choice of the treatment for each patient screened. The methodological issues concerning the evaluation of patients' mobility prior to the fracture and complex evaluations about the severity of somatic conditions (comorbidities) also warrant further work.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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ETHICAL APPROVAL

The research has been approved by the Ethical Committee of the Clinical Centre "Kragujevac".

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DEMOGRAPHIC AND HISTOPATHOLOGICAL CHARACTERISTICS OF COLORECTAL POLYPS: A DESCRIPTIVE STUDY BASED ON SAMPLES OBTAINED FROM SYMPTOMATIC PATIENTS

DEMOGRAFSKE IN HISTOPATOLOŠKE ZNAČILNOSTI KOLOREKTALNIH POLIPOV: DESKRIPTIVNA RAZISKAVA NA OSNOVI VZORCEV, PRIDOBLJENIH OD SIMPTOMATSKIH PACIENTOV

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ABSTRACT

Keywords:
colorectal polyp, epidemiology, colonoscopy examination, Albania

Background. Colorectal polyps (CP) are common among individuals older than 50 years. Some polyp types can precede colorectal cancer (CRC). This study aimed at describing histopathological characteristics of colorectal polyps in relation to age and gender among symptomatic patients referred for a colonoscopy examination during 2011-2014 in Tirana, Albania.

Methods. Study population included 267 individuals aged ≥ 20 years and diagnosed with ≥ 1 polyp during a colonoscopy examination. A total of 346 polyps were identified, excised and measured, and underwent histopathological examination.

Results. Adenomas accounted for 79.8% of all polyps and tubular type was the most frequent one (74.4%). The majority of polyps (42.5%) were small (<1 cm), 38.7% of a medium size (1-2 cm) and 18.8% large (>2 cm). Adenomas were larger than non-adenomatous polyps (p<0.01)
There was no gender difference with regard to patient age (p=0.22) or polyp size (p=0.84) Adenomas were more frequent among men compared to women (p=0.02). Age was strongly related to polyp characteristics. The proportion of adenomas increased significantly with age (p<0.01). Within adenomas, the proportion of villous types - a precursor of colorectal cancer - increased remarkably with age (p=0.01). Older age was positively associated with potentially malignant adenomas (defined as adenomas > 1 cm and showing high-grade dysplasia) (p<0.01).

Conclusion. Adenomas accounted for the majority of polyps. Their morphology, size and malignant potential were related to patient age.

IZVLEČEK

Ključne besede:
kolorektalni polipi, epidemiologija, kolonoskopija, Albanija

Uvod. Kolorektalni polipi (CP) so pogost pojav pri posameznikih po 50 letu starosti. Nekatere vrste polipov se lahko razvijejo v kolorektalnega raka (CRC). Ta raziskava skuša opisati histopatološke značilnosti kolorektalnih polipov v povezavi s starostjo in spolom med simptomatskimi pacienti, ki so bili napoteni na kolonoskopsko preiskavo v obdobju od leta 2011 do 2014 v Tirani, Albanija.

Metode. Raziskava je vključevala 267 posameznikov, starih 20 ali več let, ki jim je bil med kolonoskopijo diagnosticiran najmanj en polip. Skupno je bilo identificiranih, odstranjenih, izmerjenih in podvrženih histopatološki preiskavi 346 polipov.

Rezultati. Adenomi so predstavljali 79,8% vseh polipov, med njimi pa je prevladoval tubulni tip (74,4%). Večina polipov (42,5%) je bilo majhnih (<1 cm), 38,7% je bilo srednje velikosti (1-2 cm), 18,8% pa je bilo velikih (>2 cm). Adenomi so bili večji kot ne-adenomatozni polipi (p<0,01).
Z vidika starosti pacientov (p=0,22) oziroma velikosti polipa (p=0,84) ni bilo bistvene razlike med spoloma. Adenomi so bili bolj pogosti pri moških kot pri ženskah (p=0,02). Starost je močno povezana z značilnostmi polipa. Delež adenomov se je s starostjo bistveno povečal (p<0,01). V smislu adenomov se je delež viloznih tipov – prekurzorjev kolorektalnega raka – s starostjo izjemno povečal (p=0,01). Višja starost je potrjeno povezana s potencialno malignimi adenomi (opredeljeno kot adenomi >1 cm, ki izkazujejo visoko stopnjo displazije) (p<0,01).

Zaključek. Adenomi predstavljajo večino polipov. Njihova morfologija, velikost in potencial rakavosti je povezan s starostjo pacienta.

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1 BACKGROUND

Colorectal cancer (CRC) poses a great burden on population health. It represents the 4th and 3rd most common type of cancer among men and women, respectively (1). The estimated lifetime risk of developing the disease is 5% (2). Its incidence is increasing in the majority of countries, including South-Eastern European countries (3). Such increase is influenced (among other things) by the adoption of a Western-type diet and lifestyle (4). Costs related to CRC care account for 12% of cancer costs, making it the 2nd most expensive cancer to treat. CRC represents the 2nd cause of cancer-related deaths among men aged from 40 to 79 and women older than 80 years (2).

Colorectal polyps are very common among middle-aged individuals, with a prevalence being as high as up to 30%. The epithelial type (either adenomatous or hyperplastic) represents the most common form of colorectal polyps, followed by non-epithelial (inflammatory and juvenile) polyps (5). Some polyp types, especially adenomas, are considered to be precursors of CRC (6, 7). Despite the evidence on the beneficial role of screening in reducing the burden of CRC (8), in Albania no screening programs or prevention measures have been implemented due to limited financial and human resources. No studies have explored the burden of CRC and its precursors in general population either. Therefore, available information on CRC incidence and mortality in Albania is based on calculated extrapolations using the data from neighboring countries and not taking into account genetic, cultural, environmental, social and racial differences across the countries (9). In such conditions, a less expensive alternative is to analyze polyp characteristics among symptomatic individuals in order to identify the burden of precancerous types among them.

The aim of this study was to explore for the first time in Albania, the morphologic and histopathological characteristics of colorectal polyps, and describe their distribution with regard to age and gender, using samples from 267 consecutive patients referred to the gastroenterologist for a colonoscopy examination.

2 SUBJECTS AND METHODS

2.1 Study Population

During 2011-2014, 1100 the patients aged ≥ 20 years were referred by a family doctor or gastroenterologist to undergo a colonoscopy examination in relation to their symptoms (hematochezia, melena, positive fecal occult blood, abdominal pain, constipation or chronic diarrhea). A total of 67 patients (69.8% men) were excluded due to the presence of CRC and another 766 patients (48.9% men) were excluded due to the negative findings (lack of popyls) during the examination. The study population comprised 267 individuals (64.8% men) with at least one diagnosed and resected polyp. The patients with colorectal cancer were the oldest (mean age 62.7 years) and those with negative findings were the youngest (mean age 49.9 years).

2.2 Endoscopy Procedure

Colonoscopy examinations were performed by two doctors. Any time a polyp was identified, a polypectomy procedure followed. In case of suspected malignancy, a cold forceps biopsy was obtained. The procedure was performed with Narrow band Imaging (NBI, EVIS EXERA II CV-180 Olympus™), high definition endoscopes and without the use of chromo-endoscopy during the identification procedure. Opened biopsy forceps of 7 mm and opened polypectomy snare with known diameter were used for measuring the polyps before piecemeal resection. Cold forceps and cold snare have been the polypectomy methods of choice for smaller polyps, and hot snare has been the method of choice for larger polyps.

2.3 Histopathological Examination

All specimens were histologically examined by a pathologist and, when in doubt (26 cases), a second, experienced pathologist was called to help reaching a decision. First, we measured the height and diameter of each specimen. After that, we put them in formalin solution. Once fixed, the specimen was sectioned in such a way that the relationship of the stalk to the head of the polyp was clear. To avoid missing a small focus of carcinoma, the entire specimen was submitted for histologic evaluation. The sections were stained with hematoxylin eosin (HE). All slides were examined under a light microscope (4X, 10X and 40X dry objectives).

2.4 Classification of Polyps

The 2010 World Health Organization (WHO) criteria were applied to assess the grade of dysplasia and architecture of the polyps (10). Adenomatous polyps were divided into low-grade or high-grade dysplasia. Depending on the presence and volume of villous tissue, adenomatous polyps were further classified as tubular, tubulovillous or villous.

The presence of hypercellular stroma, large mucin-filled cysts, the lack of smooth muscle core and flattened epithelium were used as criteria to diagnose a juvenile polyp. Finally, the presence of various degrees of inflammatory infiltrate, ulceration, edema and granulation tissue were the criteria on the basis of which the diagnosis of an inflammatory polyp was made.

2.5 Statistical Analysis

Continuous variables are presented as mean and standard deviation (SD), while categorical variables are presented as numbers and proportions. Independent sample t-tests were used for comparisons of continuous, normally distributed variables. Categorical variables were compared using the chi square test. Two-sided tests with a 0.05 significance level were used. All statistical analyses were performed using STATA 13 (Stata Corp LP, 4905 Lakeway Drive, College Station, Texas, USA).

3 RESULTS

A total of 267 patients, aged ≥ 20 years, with at least one resected polyp during the colonoscopy examination, were included in the study. The minimum number of polyps per person was one (in 211 patients) and the maximum five (in 2 patients). This yielded a total of 346 polyps (the unit of analyses).

Adenomas accounted for 79.8% of all cases. The majority of polyps (42.5%) were small (<1 cm); 38.7% were of medium size (1-2 cm) and the rest (18.8%) large (>2 cm) (Table 1).

Table 1. Characteristics of the study participants.

Characteristics of the study population	All n=346	Men n=229	Women n=117	P value*
Age (years), mean (SD)	54.1 (13.3)	54.8 (13.1)	52.8 (13.6)	0.22
Polyp type, n (%)				0.02
Non-adenomatous	70 (20.2)	38 (16.6)	32 (27.1)	
Adenomatous	276 (79.8)	191 (83.4)	85 (72.9)	
Polyp size (cm), n (%)				0.84
<1	147 (42.5)	95 (41.5)	52 (44.4)	
1-2	134 (38.7)	91 (39.7)	43 (36.8)	
>2	65 (18.8)	43 (18.8)	22 (18.8)	

*Obtained from chi square tests (for categorical variables) or two-sample t-test (continuous variables) comparing men and women

Hyperplastic and tubular types accounted for the majority (71.4% and 74.4%) of non-adenomatous and adenomatous polyps respectively (Table 2).

Table 2. Distribution of non-adenomatous and adenomatous polyps by gender.

Polyp types	Total	Men	Women	P value
Non-adenomatous polyps, n (%)	70	38	32	0.92
Hyperplastic	50 (71.4)	28 (73.6)	22 (68.8)	
Inflamatory	14 (20.0)	7 (18.5)	7 (21.8)	
Juvenile	6 (8.6)	3 (7.9)	3 (9.4)	
Adenomatous polyps, n (%)	276	191	85	<0.01
Tubular	205 (74.4)	151 (79.1)	54 (46.6)	
Tubulovillous	59 (21.3)	31 (13.5)	28 (23.7)	
Villous	12 (4.3)	9 (3.9)	3 (2.5)	

3.1 Gender-specific Analyses

There were no statistically significant gender difference with regard to age (p=0.22) and polyp size (p=0.84). Adenomatous polyps were more frequent among men compared to women (p=0.02) (Table 1). When analyzed separately, we did not observe gender differences in the distribution of non-adenomatous polyps (p=0.92), while adenomas were distributed differently between men and women (p<0.01). The tubular type accounted for 79.1% of all adenomas among men and only for 46.6% of them among women (Table 2).

3.2 Polyp Size

Overall, non-adenomatous polyps were smaller than adenomas (p<0.01). Small polyps (< 1 cm) comprised the absolute majority (82.8%) of non-adenomatous polyps, while the distribution of adenomas with regard to size was more proportional. Middle-sized polyps (1-2 cm) accounted for 44.5% of cases, followed by small (32.3%) and large (> 2 cm) ones (23.2%) (Table 3).

Table 3. Distribution of polyps by size.

Polyp types	Polyp Size		
	< 1 cm	1-2 cm	> 2 cm
Non-adenomatous polyps, n (%)	58 (82.8)	11 (15.7)	1 (1.5)
Hyperplastic	47 (94.0)	3 (6.0)	-
Inflamatory	11 (78.6)	3 (21.4)	-
Juvenile	-	5 (83.3)	1 (16.7)
Adenomatous polyps, n (%)	89 (32.3)	123 (44.5)	64 (23.2)
Tubular	82 (40.0)	99 (43.3)	24 (11.7)
Tubulovillous	7 (11.9)	19 (32.2)	33 (55.9)
Villous	-	5 (41.7)	7 (58.3)

We did not observe any gender differences with regard to size when analyses were conducted separately among non-adenomatous polyps (p=0.52) and adenomas (p=0.71) (Figure 1).
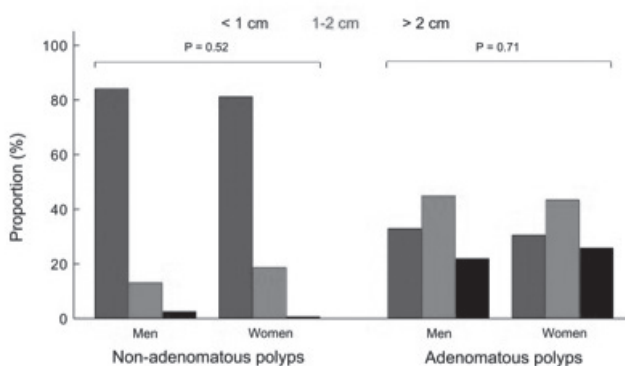

Figure 1. Gender differences pertaining to polyp size.

3.3 Influence of Age on Polyp Characteristics

A linear relationship was observed between patient age and type of polyp. Adenomas were more frequent than non-adenomatous polyps among all age groups, but this difference tended to increase with age (p<0.01) (Figure 2).
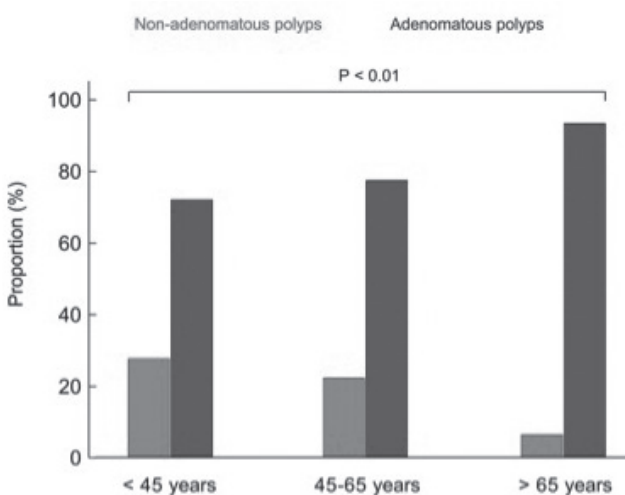

Figure 2. The distribution of polyps by age.

Age was also associated with subtype distribution among adenomas; tubular subtype accounted for 89.2% of all adenomas among patients < 45 years, but this proportion dropped with increasing age to 74.8% among patients 45-65 years and further to 59.7% among those > 65 years. On the contrary, the proportion of villous subtype - the most important CRC precursor - increased from 1.5% among patients < 45 years to 13.9% among those older than 65 years (p=0.01) (Figure 3).
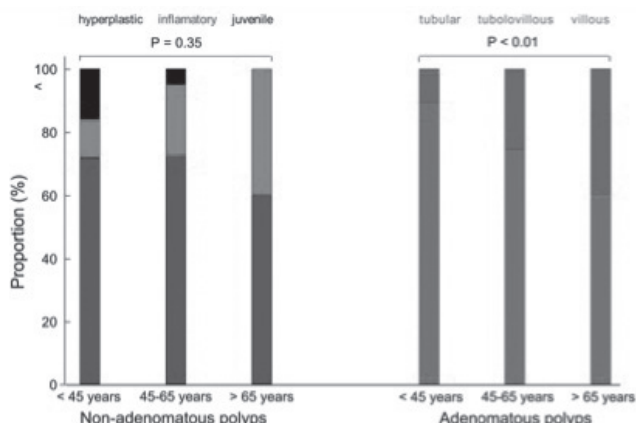
Figure 3. Age differences in the distribution of polyps.

Lastly, we explored the association between grade of dysplasia and patient age, and observed that older patients showed more often adenomas with high-grade dysplasia compared to their younger counterparts (p=0.008). However, high-grade dysplasia was not uncommon among young and middle-aged patients, and accounted, respectively, for 29.2% and 43.2% of all adenomas in these groups (Table 4).

Table 4. Distribution of polyps by size.

Grade of dysplasia	Age group			P value
	< 45 years	45-65 years	> 65 years	
Low-grade dysplasia	46 (70.8)	79 (56.8)	32 (44.4)	
High-grade dysplasia	19 (29.2)	60 (43.2)	40 (55.6)	0.008
< 1 cm	-	4 (2.9)	-	
≥ 1 cm	19 (29.2)	56 (40.3)	40 (55.6)	

4 DISCUSSION

This study showed that adenomas accounted for 79.8% of all polyps and they were more frequent among elderly and male patients. Within adenomas, the proportion of villous type - a direct precursor of CRC - increased remarkably with age. Further, adenomas found in older patients had in ~56% of cases high-grade dysplasia and were > 1 cm large (both indicators of a high malignant potential) (11). A direct comparison of our findings with previous studies is challenging due to differences with regard to study period and population (in terms of age, gender and ethnicity). In addition, it has been shown that the prevalence of adenomas based on autopsy studies is higher than that reported from studies based on endoscopy findings (12).

A study conducted in Denmark during 1986-1987 reported that adenomas accounted for the majority (60%) of the 305 examined polyps (13). A more recent analysis conducted in Western Australia reported that adenomas accounted for 70% of all polyps (14). In a study conducted in Canada in 2002, Khan et al. (15) reported that adenomas accounted for 83% of all polyps, followed by hyperplastic (12.3%) and inflammatory (2.8%) types. Among studies conducted outside Europe and North America, Tony et al. (16) reported that among 124 patients diagnosed with a polyp, 79.5% were adenomas, 10% juvenile, 9% hyperplastic and 1.5% inflammatory. The most recent published study (to our knowledge) was conducted in Iran in 2010 (17). Of the 856 polyps examined, 85% were adenomas. Of those, 56% were tubular, 17% villous and 27% tubulovillous. Findings from our study are in line with these previously conducted analyses.

4.1 Public Health Implications

To date, there is a general consensus on the beneficial role of screening average-risk individuals in their 50s every 10 years. Different suggested approaches (opportunistic or programmatic screening) help preventing CRC by removing polyps with high malignant potential (3) or detect CRC at an early stage, improving its prognosis. To illustrate, the 5-year survival is 90% if CRC is diagnosed early (while still localized) and only 10% in advanced stages when distant metastases develop (18).

We showed that the proportion of patients with high-grade dysplasia and size > 1 cm accounted for ~ 56% of patients older than 65 years. However, such adenomas with high malignant potential were not exclusively observed among older adults. They accounted for nearly 1/3 of adenomas observed among younger (< 45 years) and 40.3% of those observed among middle-aged (45-65 years) patients. Further, adenomas with a villous component (either tubulovillous or villous) accounted for ~ 10% of adenomas among patients < 45 years and 1/4 of those among patients 45-65 years. These results show clearly a potentially beneficial role of conducting screening programs among individuals in their fourth to fifth decade of life in order to identify polyps with high malignant potential and reduce the burden of CRC in Albanian population.

4.2 Strengths and Limitations

Our study is the first national study and one of the few recent analyses worldwide (16, 17) exploring histopathological characteristics of colorectal polyps and their distribution. However, it carries certain limitations, among which it is worth mentioning that the study population comprises consecutive symptomatic patients and not a representative national sample. Moreover, additional information on the disease stage would

provide additional valid evidence. Further, we do not know the type and distribution of such polyps among the severe cases that died before undergoing colonoscopy examination.

5 CONCLUSIONS

This study provides evidence that precancerous lesions are very frequent among symptomatic patients undergoing a colonoscopy examination. Although such lesions are more frequent among elderly people, a relatively high proportion of adenomas with malignant potential were found among younger individuals. These findings support the need for prevention strategies and screening programs in order to reduce the risk of future CRC in the Albanian population.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

ETHICAL APPROVAL

The information used in this study was collected at the examination clinic and variables allowing direct identification of participants removed prior to data analyses. The study was conducted in accordance with the code of Ethics of the World Medical Association (Declaration of Helsinki).

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MATERNAL PERCEPTIONS OF AND RESPONSES TO CHILD SEXUAL ABUSE
MATERIN POGLED IN ODZIV NA SPOLNO ZLORABO OTROKA

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ABSTRACT

Keywords:
child sexual abuse,
disclosure,
maternal response

Background. Several researches indicate that most child victims delay disclosing of sexual abuse for significant periods of time. There are numerous reasons as to why children are avoiding the disclosure of the abuse. The aim of this study was to determine how a mother's response to a child's allegations impacts the child's willingness to disclose sexual abuse.

Methods. We conducted a retrospective quantitative and qualitative analysis of 73 court-referred cases of child sexual abuse which have been disclosed in Slovenia in the last ten years. All the child victims included in the study were female and the perpetrators adult male persons. The expert opinions were made by the same expert.

Results. We realized that, at the occurrence of abuse, the child victims were from 4 to 15 years old and their mean age was at 11. 5 years. About two-thirds of children were victims of the intra-familial type (61.6%) and a little more than one third of extra-familial type of sexual abuse (38.4%). The group of victims with the support of their mothers needed about 9 months to disclose the secret, while the delay of the disclosure in the cases without the support of mothers was much longer (M=6.9 years).

Conclusions. For female child victims of sexual abuse the perceived protective attitude of their mothers is very important. Especially when the sexual abuse happened in the family, the mother's support can attribute to stop the ongoing abuse, eliminate its immediate effects and decrease its likely negative long-term outcome.

IZVLEČEK

Ključne besede:
spolna zloraba otrok,
razkritje,
odziv matere

Izhodišča. Raziskave kažejo, da otroci, ki so žrtve spolne zlorabe, dolgo časa ne spregovorijo o svojih doživetjih. Za to obstajajo številni razlogi. Naš namen je bil ugotoviti, kako se razkritje kaže na Slovenskem, predvsem pa, kako na razkritje vpliva materin odziv na otrokove obtožbe.

Metode. Retrospektivno smo izvedli kvantitativno in kvalitativno analizo 73 sodnih mnenj o sumih storjenih spolnih zlorab, opravljenih v zadnjih 10 letih. V raziskavo smo vključili žrtve ženskega spola, storilec pa je bil v vseh primerih odrasel moški. Izvedenec, ki je o sodnih primerih podal mnenje, je bil v vseh primerih ista oseba.

Rezultati. Pokazalo se je, da so žrtve spolne zlorabe stare od 4 do 15 let, v povprečju pa 11,5 leta. Okrog dve tretjini teh deklic sta zlorabo doživeli v družini (61,6%), nekaj več kot tretjina pa zunaj družine (38,4%). Žrtve, ki so bile deležne materine opore in pomoči, so potrebovale okrog 9 mesecev, da so razkrile zlorabo, tiste, ki podpore matere niso bile deležne, pa so imele večje težave in so o zlorabi spregovorile šele po nekaj letih (M=6,9 leta).

Zaključek. Za deklico, ki je žrtev spolne zlorabe, je izrednega pomena, da v materi prepozna zaupanja vredno osebo. Posebno, če se zloraba pojavi v družini, lahko materina podpora pripomore k prekinitvi zlorabe, omili njene travmatske učinke in zmanjša njene dolgotrajne negativne posledice.

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1 INTRODUCTION

A child's self-disclosure of sexual abuse contributes to the cessation of abuse, as well as to the restriction of posttraumatic stress disorders, negative long-term consequences on the victim's psychological/physical health, and alterations in social functioning. But it was estimated that from 30% to even 80% of victims do not purposefully disclose their misuse before adulthood. This suggests that many children may endure sexual trauma throughout the course of their childhood and adolescence without receiving important support or without necessary interventions (1).

Telling someone is the primary mechanism by which child victims are identified, since typically no one else is witness to the abuse, and offenders rarely come forward on their own (2). As the disclosure of abuse is, due to the nature and dynamics of child sexual abuse (hereinafter in text referred to as CSA), for children exceedingly difficult, the occurrence of sexual abuse in childhood is still a greatly underreported offense (1, 3).

Disclosures are often tentative, involve some telling and then retracting, can be partial or full, and occur over time. Age, gender, the type and duration of abuse, relationship to the perpetrator, family dynamics, availability of support, especially from one's mother, importantly impact a child's ability to self-disclose sexual abuse (4). Children under the age of 6 appear more likely to disclose abuse accidentally, but their reports tend to be vague (1). Sorenson and Snow (1) found that among children aged from 3 to 9 abuse was usually discovered through the child's inappropriate statement or sexualized behaviour (28% and 17%, respectively). Kogan found that purposeful disclosure increases with age, with female victims aged between 7 and 13 more likely to tell an adult, and with older adolescents aged from 14 to 17 years more likely to tell a peer. From a cognitive perspective, older children are, due to increased cognitive abilities and social experience, better able to report abuse; at the same time, they are also more aware of costs and benefits of the disclosure (1).

With regard to gender, it has been proposed that boys are less likely to disclose abuse than girls for varied reasons, including the increased risk of stigmatization. As they were abused by males, the fears of being labelled homosexual are blocking them (1).

Arata found an inverse relationship between the disclosure and severity of abuse. Subjects reporting contact sexual abuse were significantly less likely to disclose it than those reporting non-contact sexual abuse (5).

The duration of sexual abuse has a significant impact on its disclosure – the longer children are abused, the more hesitant they may be to disclose their abuse (1, 6-8).

Victim-perpetrator relationship is another reason why some child victims do not disclose. Wyatt and Newcomb found that the more closely victims are related to the perpetrator the less likely they are to disclose (3). Burgess and Holmstrom noted that children abused by a close family member are less likely to report their abuse than those abused by a stranger (3). Because perpetrator's strategies are oriented towards the maintenance of child's compliance and silence, child is inhibited to disclose abuse (1, 8). As child's relationship with perpetrator is often an emotionally significant one, in which important needs are met for the child, many victims report ambivalent feelings for their perpetrators and do not disclose them (1). It was also found that the delay of disclosure is nearly twice as long when perpetrator is physically violent toward victim or other members of family (1).

An important factor which can impair child's willingness to disclose sexual abuse is the perceived mother's support (9). In this case mother's support can be defined as her willingness to accept the possibility that her child was sexually victimized, and the absence of evidence of punishing or pressuring the child to deny abuse (1). It was established that sexually abused children whose caretakers were supportive disclosed at a rate of 3.5 times more frequently than those whose caretakers were non-supportive (63% and 17%, respectively). According to Elliott and Briere (1), children whose mothers were non-supportive were significantly more likely to recant their initial disclosure of abuse than children whose mothers were supportive (15.4% and 3.3%, respectively).

Researches consistently indicated that most child victims delay disclosing for significant periods of time and that many child victims do not disclose their abuse when it is discovered in some manner (1). It was found that less than one in four victims of CSA disclose immediately. Most children delay reporting their sexual victimization for months and years. According to some studies, latency of disclosure can range from 3 to 18 years, or even much longer (1).

Due to various reasons children sometimes withdraw their accusations. Sorenson and Snow found that children recanted their allegations in proximately 22% of the cases. However, 92% of those who recanted subsequently reaffirmed their allegations. While some children moved from denial to tentative and then active disclosure in one session, this process took months to occur for others (1).

We aimed to verify the occurrence of sexual abuse of children in Slovenia. We set up the following hypotheses:

H1: Children with learning-related disabilities are significantly more frequently victims of CSA, and are also frequently re-victimized;

H2: Victims of CSA come from specific living environments;

H3: CSA is more likely to occur in the family than outside it;

H4: Most victims of CSA entrust their experience of abuse to their mothers;

H5: If CSA occurs within the family, the victim has greater difficulties to disclose his or her experience;

H6: The duration of CSA is prolonged if the victim perceived that she or he does not have mother's support.

2 METHODS

2.1 Participants

There were 73 judicially processed cases of CSA that had occurred in Slovenia in last ten years included in the study. All victims were female and the offenders were adult males. Boys as victims of CSA (3%) and false allegations of CSA (8.75%) were excluded from the study, as defined according to the professional criteria and judicial proceedings (10, 11).

2.2 Procedure

We analysed a sample of forensic psychological opinions, done by the same expert soon after the victim's disclosure, or at the beginning of judicial processing of suspected sexual abuse offenses. Some concepts, such as the family functioning and the mother' support, were preliminary defined according to the generally accepted theoretical approach (4, 5, 12, 13).

2.3 Instruments

Semi-structured interviews; psycho-diagnostic assessment instruments; child developmental, behavioural, familial and social data (obtained from kinder-garden, school, social and law enforcement institutions).

2.4 Data Analysis

The data were processed with statistical program IBM SPSS. Descriptive statistics was used to gain a basic insight in the sample of CSA. Then the hypotheses were verified with Pearson's chi-square test, ANOVA test, Chi-Square Test of Independence (14).

3 RESULTS

The results of the analysis of our sample of CSA are presented in Tables 1, 2, and 3.

From Table 1 can be seen basic characteristics of victims of CSA: their age, learning capacity, living environment, and their relationship with their offender. Victims aged from 4 to 15 years (the average of 11.5 years), among them 4% of children, have demonstrated learning difficulties, and

half of them were sexual re-abused. Most of CSA, almost two-thirds – 61.6% of all CSA – occurred within family and nearly one-third occurred outside family – in 38.4% of all. Intra-familial abuse appeared most often in step-parent families – 34.2%; functional family – 27.4%, dis-functional family – 19.2%; and in a single-parent family –19.2%.

Table 1.   The basic characteristics of the CSA victims (N=73).

Victim's age	range = 4-15 years	M±SD = 11.5 ±2.79
Victim's learning capacity	**f**	**%**
Appropriate	62	83.6
Learning difficulties	12	16.4
Victim's living environment	**f**	**%**
Step-father family	25	34.2
Normal functional family	20	27.4
Dis-functional family	14	19.2
Single-parent family	14	19.2
Offender of CSA	**f**	**%**
Intra-familial abuser	45	61.6
Incestuous abuser	19	26
Relative, close family friend	14	19.2
Incest	12	16.4
Extra familial abuser	28	38.4

f= frequency; %= percentage; M=mean; SD=Standard Deviation

Most offenders in the intra-familial type of CSA were discovered among stepfathers or current mother's partners – 26% of all offenders. They are followed by victim's relatives or family close friends – 19.2% and 16.4%, respectively, and by biologically most closely related, biological fathers or brothers (13.7 % and 2.7%, respectively).

Table 2 shows the delay of victim's disclosure, also in the relation to the type of CSA and mother's response to child's allegations. First, we can see that only 15% of all CSA victims were able to disclose their abuse immediately. Qualitative analysis showed that immediate reports appeared only in the cases when abuse was a unique child's experience, when the perpetrator was a stranger, and, in particular, when mother's support was evident. Other victims, 85% of them, had major difficulties to disclose sexual abuse: in 35.62% of victims the latency of disclosure was within one year; in 34.2% of victims the latency of disclosure was from 1 to 6 years; 15.01% of victims needed from 7 to 20 years to disclose abuse, in one case the latency of disclosure was even 25 years.

Interviews with victims revealed that those with major trouble to disclose interrupted the silence mostly

accidentally. Adolescents, particularly those who were victims of incest or an incestuous form of sexual abuse, interrupted silence after a severe conflict with father, step-father or mother's current partner as a perpetrator. Most victims, 35.6%, disclosed abuse to their mothers, 30.1% of victims trusted a class teacher, social worker, or other professional person at school. Moreover, 13.7% of CSA victims disclosed sexual abuse to friends; while 13% of them reported abuse to a sibling, grandmother, father, or to a foster parent; 7% of older victims, menwhile, disclosed abuse to their boyfriends.

Almost half of mothers, 47.9%, believed, supported and protected their children from further abuse. But more than half of them, 52.1%, did not give support to their children. They were ambivalent in believing and supporting their children, or even put pressure on a child to withdraw her allegations (32.9% and 19.2 %, respectively). We can see that those victims whose mothers supported their partners, or reacted ambivalently to child's allegations, mostly delayed the disclosure of CSA. In the case of complete opposition, the average of latency was more than three times longer than in the case of victims with mother's support (M±SD=3.65±2.13 years); in the case where mothers showed an ambivalent attitude to child's allegations, the average of latency of disclosure is even nearly seven times longer in comparison to victims with support, and nearly twice as long as in the case when mothers were in the complete opposition (M±SD=6.93±7.82 years).

Problems occur when abuse happens within the family. Table 3 shows that 75.6% of victims who have experienced abuse within the family were looking for understanding and support somewhere outside the family. Conversely, the victims who have experienced sexual abuse outside the family disclosed the abuse in almost equal measure to mothers and other persons (53.6% and 46.4% respectively).

Thus, the first four hypotheses were partially or fully confirmed.

Our first hypothesis (H1) that children with learning difficulties are significantly frequently victims of CSA is not completely confirmed. It holds only partially in the assumption of a high risk for re-abuse.

Both the second hypothesis (H2) – that most victims of CSA come from a specific living environment – and the third hypothesis (H3) – that CSA is more likely to occur in the family than outside of it – are confirmed. In fact, abuse most frequently occurred within the family, either in a step-parent family, a dysfunctional family, or a single parent family.

The fourth hypothesis (H4) that most victims of CSA entrust their experience of abuse to their mothers is not fully confirmed. Mother is a confidential person to her child, especially when abuse happened outside the family.

Table 2. The delay of CSA victims' disclosure.

Latency (month/year)	f	%	M±SD = 3.43±5.34
Immediately report	11	15.01	0±0
1-12 months	26	35.62	0.4±0.35
1- 6 year	25	34.25	3.4±1.35
7- 25 years	11	15.01	14.1±6.28
Type of CSA	**f**	**%**	**Delay M±SD (year)**
Extra-familial type	28	38.4	1.9±5.18
Intra-familial type	14	19.2	3±4.15
Incest and incestuous type	31	42.5	5±5.65
The trustworthy person	**f**	**%**	
Mother	26	35.6	
Professionals at school	22	30.1	
Schoolfellow/friend	10	13.7	
Familial member	10	13	
Boyfriend	5	7	
Maternal response/ disclosure	**f**	**%**	**Delay M±SD (year)**
Support	35	47.9	0.75±1.11
Ambivalence	24	32.9	6.93± 7.82
Resistance	14	19.2	3.65± 2.13
No support	38	52.1	

f= frequency; %= percentage; M=mean; SD=Standard Deviation

Table 3. The venue of CSA occurrence and the victim's choice of a trustworthy person.

	Victim's choice of a trustworthy person			
	Mother		Other person	
	f	%	f	%
Extra-familial type	15	53.6	13	46.4
Intra-familial type	11	24.4	34	75.6

f= frequency; %=percentages

When abuse occurred in the family, children more often looked for a trustworthy person outside the family.

The fifth hypothesis (H5) that the victims of the intra-familial type of CSA have greater difficulties to disclose their experiences than victims of the extra-familial type of CSA is confirmed with Pearson's chi-square test. The results confirmed a significant correlation between these two variables [χ^2 (1)=6.386, p<0.005]. The delay of disclosure in the extra-familial type of CSA is shorter than

in the intra-familial type, and especially, in the form of incest and incestuous CSA.

The sixth hypothesis (H6) that the duration of CSA is prolonged when the victims of CSA do not perceive the support of their mothers was confirmed with ANOVA test. The comparison of groups with different kinds of mothers' responses (supportive response, ambivalent response and strict resistance) and their latency of disclosure shows that the differences between the victims are statistically significant [$F_{(2.70)}$=12.714; p=0.000]. The shortest delay of disclosure was found in the group of victims whose mothers believed and supported them. Table 3 shows that victims with perceived mother's support need about 9 months to disclose the abuse, while those with mother's ambivalent response need 6 years and 11 months, which is even longer than those with mother's strict resistance, who need 3 years and 8 months.

With Chi-Square Test of Independence we examined the relationship between the type of mother's respond and victim's relationship with the perpetrator of CSA, and we found that it is statistically significant [χ^2 (2.73)=34.11, p<.05]. The test results indicate that mother's response to child's allegations was significantly different when perpetrator was the victim's biological father, brother, stepfather or mother's current partner, than when perpetrator was a distant relative or close family friend, in which case mother's support was significantly frequently present (74% and 13%, respectively). An even greater difference in mother's response was registered in the case in which perpetrator was child's biological father, brother, stepfather, or current partner, and in the case in which perpetrator was someone outside the family (0% and 45%, respectively). In the case when the perpetrator was a neighbor, an acquaintance, or a stranger, mother more often believed and supported abused child.

4 DISCUSSION

Since the sample analysis of forensic psychological opinions has given us an insight into the occurrence of CSA in Slovenia, it can be concluded that the aim of the study has been achieved. In general, the data on victims' age, living environment, form and type of CSA, victim-perpetrator relationship, mother's response to disclosure and the delay of disclosure are, with only two derogations, well comparable with the data of already pubished surveys (15-18). First, we have anticipated that children with learning disabilities are more likely to become victims of sexual abuse (19, 20). However, in our study, significant differences in the incidence of CSA between children with learning disability and those without them were not found. That can be explained in terms of the difference in the used methodology of data recording and registration, as well as in terms of barriers in the

sense that the question is whether such cases of CSA ever achieved a judicial treatment, as disabled children are less likely to disclose, it is less likely that someone will carefully listen to their allegations and more likely that the abuse will be minimised or brushed aside.

As we expected, nearly two-thirds of our sample of CSA happened within the family and only a little over a third outside the family. Regardless, if CSA happened in a step-parent family, dysfunctional familial environment or in single-parent family, common to all those types of families with CSA occurrences were signs of family boundary dissolution, especially as loss of boundaries and family roles-reversal (e.g., who is a parent and who is a child). In this respect, especially in dysfunctional family, we observe that the presence of psychopathological disorders was higher in the form of low resistance to stress, non-productive coping strategies, mental disorders, substance use, and spousal violence – in one of the parents, or even in both.

According to other research (15-18), the most common offenders of CSA in domestic environments are victim's stepfather, but surprisingly often – in comparison with other studies – also victim's biological father. A higher incidence of father-daughter incest in our sample is the second derogation, mentioned previosuly. In comparison with other research data, mostly obtained through interviews of adult women, our data were obtained during judicial proceedings and are also much higher than the following data indicating father-daughter incest: Finkelhor, USA, 1978, 1.5% among female students; Russell, USA, 1983, 4.5%; Sariola and Uutela, Finland, 1996, 2%; Yildirim et al., Turkey, 34.9% in forensic sample (21, 22). Of course, we have to ask ourselves what such high incidence of father-daughter incest means and says about the functioning of families for a society as a whole, but it should also be taken into account that getting reliable data on father-daughter incest incidence is still hard, because, worldwide, this type of incest is still most persistently silenced domestic mystery, which is, therefore, very difficult to detect. It is true that incest gets more often reported recently, but it is often not very clear if published data are due to the different methodological approach and, as such, comparable to the other data at all.

Major problems to disclose CSA when it occurred in the family are understandable. Abuse by a stranger or an acquaintance is easier to report because there are fewer "costs" than by disclosing abuse when the perpetrator comes from the domestic environment, and in which case the victim is inhibited with guilt and fear of consequences to oneself and her family. Therefore, for young children it may be also easier to define sexual activity as wrong when perpetrator is a stranger than in the case when child is abused by a close family member.

Victim's barriers to disclose abuse offenses in family can be well understood through Summit's concept of Child Sexual Abuse Accommodation Syndrome (23) and its five stages. Perpetrator, through strategies of intimidation ("If you tell anyone, I'll kill your dog;" "The family will be broken up;"),isolation from the other family members ("Don't tell your mother, she will hate you;"), stigmatization ("Nice children don't talk about things like that;"), and strategies to strengthen child's feelings of helplessness ("Nobody will believe you.") maintained victim's compliance and secrecy. If the child in such situation did not receive immediate protective intervention, there is no further option to stop the abuse and the child is learning to accommodate to the reality. After this, disclosure is possible only at an eventual breakdown of accommodation mechanisms.

Our interviews with victims have confirmed this theoretical concept. A long kept secret was disclosed at the moment of victim's emotional outbreak at adolescence, at the time when a child becomes more capable to comply with the requirements of an independent life and begin to challenge the authority of parents. Usually, it was triggered by a severe conflict with the perpetrator as a parent.

Quantitative analysis has confirmed that the delay of the disclosure of CSA that happened within the family is significantly associated with mother's response to child's allegations, as well as with her relationship with the perpetrator.

Unpredictable maternal behaviour, her ambivalence regarding believing and supporting an abused child had even worse effects on the victim's ability of resistance against the exploitation than mother's constant rejection of child's allegations. It keeps young victim in the state of permanent uncertainty and restrains her in the position of further overlap of abuse. According to victims' storytelling, many of them warned their mothers of what was happening, even though in vain, at least once before the disclosure of abuse.

Like Knott and Fabre who have highlighted that mother's response to child's disclosure of sexual abuse depends on her relationship with the perpetrator (24), we found that mother's support was either missing, or provided, but changeable more frequently when the perpetrator was her spouse or a current sexual partner. There are several possible explanations, but they are all more or less speculative. One of the more likely explanations is that there is an emphasized maternal existential/emotional dependence on the offender.

There are some specificities of the mother-daughter relationship when incest and the incestuous form of CSA is present in the family. In cases of father-daughter incest, the mother-daughter boundary dissolution in the form of role reversal was manifested as parentification: the daughter took on emotional/instrumental caregiving responsibilities which were excessive and developmentally inappropriate, and are typically expected of the mother (We have a sick, depressed, non-autonomous mother and a daughter who leads the household, takes care of the younger siblings, etc.). In the case of the incestuous form of CSA, the role reversal in the parent-child relationship was more complex, but, still, adultification prevailed: the daughter assumed developmentally inappropriate expectations or responsibilities, her relationship with her mother resembled a relationship between peers, friends, and the daughter's role was also that of a protective adult. Forensic psychological opinions carried out on the basis of various sources of information give us a fairly reliable insight into posttraumatic stress disorders and possible consequences of CSA, but they were primary focused on questions concerning victims, while later aims and hypothesis requested a much broader approach, whereby some of the data has not been registered. In the future research, in such a case, it is better to identify the subject of research in advance, and collect data simultaneously (e.g., what maternal characteristics are associated with mother's unconditional belief, disbelief, affective and behavioural support, temporal dimension of her response, her initial and her enduring response, etc.). It saves time, effort and improves the reliability of the data.

5 CONCLUSION

Sexual abuse of children is not only a matter of the perpetrator and victim. When it occurs in the family, especially in the form of incest or incestuous abuse, it reflects the whole complexity of family dynamics, and it is a problem of all its members. From the perspective of potentially serious consequences for victims even in adulthood, it is desirable that the occurrence of CSA is disclosed and stopped as soon as possible.

According to this, maternal attitude and reaction to child's allegations are crucial. Personnel in social institutions, which are, in the moments of disclosure of CSA, in practice, mainly confronted with mother's sometimes rigid system of defence mechanisms, should be able to view and respond to such problems in a professional way. With the aim to foster more supportive maternal responses to the abused child, it is desirable we become more familiar with the basic principles of motivational interviewing, adopt active and empathic listening, and other techniques for engaging "resistant" families.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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ETHICAL APPROVAL

This study of the cases of court opinion CSA was completed according to the Section 19 (The Offenses against Sexual Integrity) of Criminal Code of the Republic of Slovenia (KZ-1, 2008), and to the Council of European Convention on the Protection of Children against Sexual Exploitation and Sexual Abuse, 2007. With the Guidelines of the Committee of Ministers of the Council of Europe on Child-friendly Justice, 2010, the public has been excluded. In all the procedures before a court, the expert witness was bound to secrecy and respect of human rights. With the publication of the present analysis, these principles are not violated in any way.

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INFECTIONS CAUSED BY COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* EUROPEAN CLONE (ST80) IN SLOVENIA BETWEEN 2006 AND 2013

PRIKAZ PRIMEROV OKUŽB, POVZROČENIH S PROTI METICILINU ODPORNO BAKTERIJO *STAPHYLOCOCCUS AUREUS*, DOMAČEGA OKOLJA, KI PRIPADA EVROPSKEMU KLONU (ST80) V SLOVENIJI V OBDOBJU MED 2006 IN 2013

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ABSTRACT

Keywords:
CA-MRSA,
ST80 (European clone), invasive infections, death, Slovenia

Introduction. According to the existing literature, a heterogeneous sequence type (ST) or clones of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) circulate in Europe. In Europe, the European clone that belongs to sequence type ST80 is predominant.

Methods. The aim of the study was to investigate the phenotypic and genotypic characteristics and epidemiological data of CA-MRSA ST80 and its occurrence in Slovenia. We retrospectively analyzed those CA-MRSA isolates that were isolated during microbiological procedures in microbiological laboratories between 2006 and 2013. Only CA-MRSA isolates from the national collection of CA-MRSA strains that belonged to ST80 (European clone) were analyzed. We determined the Pantone-Valentine leukocidin (PVL), *mec*A genes, exfoliative toxin genes and type of staphylococcal cassette chromosome (SCC*mec*) by polymerase chain reaction (PCR). We determined also spa type and sequence type.

Results. ST80 was confirmed in only 2 (0.5%) out of 385 CA-MRSA isolates, collected in a national collection of CA-MRSA. Both isolates were positive for the PVL genes, *mec*A gene, exfoliative toxin type D gene and SCC*mec* IV. One CA-MRSA isolate was confirmed in a wound swab taken from a 47-year-old male, and the second was isolated from blood cultures of a 69-year-old female. No epidemiological connections between them were found.

Conclusions. In Slovenia CA-MRSA infections caused by ST80 are rare. In the future, it is necessary that a surveillance study of CA-MRSA at the national level continues and CA-MRSA be considered as a public health threat.

IZVLEČEK

Ključne besede:
CA-MRSA,
ST80 (evropski klon), invazivne okužbe, smrt, Slovenija

Izhodišča. Po podatkih iz literature kroži v Evropi zelo heterogena skupina sekvenčnih tipov (ST) in klonov proti meticilinu odporne bakterije Staphylococcus aureus, domačega okolja (CA-MRSA). V Evropi med CA-MRSA prevladuje evropski klon, ki pripada sekvenčnemu tipu ST80.

Metode. V raziskavi smo želeli pridobiti informacijo o fenotipskih in genotipskih lastnostih ter epidemiološke podatke o CA-MRSA, ki pripadajo sekvenčnemu tipu ST80 in njihovo razširjenost v Sloveniji. Retrospektivno smo pregledali izolate CA-MRSA, ki so bili osamljeni med rutinsko mikrobiološko diagnostiko v mikrobioloških laboratorijih v obdobju od 2006 do 2013. Analizirali smo le izolate CA-MRSA, ki so bili vključeni v nacionalno zbirko izolatov CA-MRSA in so pripadali sekvenčnemu tipu ST80 (evropski klon). Za lažjo opredelitev CA-MRSA ST80 smo uporabili tudi verižno reakcijo s polimerazo (PCR), s katero smo določili tip kasete stafilokoknega kromosoma (SCCmec), gene mecA, levkocidina Pantone-Valentine (PVL) in tip stafilokoknega eksfoliativnega toksina. Izolatom CA-MRSA smo določili tudi tip spa in sekvenčni tip.

Rezultati. ST80 smo potrdili pri dveh (0,5%) od 385 izolatov CA-MRSA, zbranih v nacionalni zbirki CA-MRSA. Pri obeh izolatih smo dokazali gene PVL, mecA, eksfoliativni toksin tipa D in tip SCCmec IV. En izolat CA-MRSA smo dokazali iz brisa rane 47-letnega bolnika, drug izolat pa pri 69-letni bolnici iz hemokulture. Oba primera nista bila epidemiološko povezana.

Zaključki. Okužbe, povzročene s CA-MRSA ST80 v Sloveniji, so redke. V prihodnosti je pomembno, da s sledenjem CA-MRSA na nacionalnem nivoju nadaljujemo, saj CA-MRSA po svetu predstavljajo novo grožnjo javnemu zdravju prebivalcev.

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1 INTRODUCTION

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is in Europe associated mainly with the European clone which belongs to the clonal complex (CC) / sequence type (ST) CC80 / ST80 (1-6). This clone was first recognized in Denmark in 1993 (7, 8) and now CA-MRSA ST80 is widely spread throughout Europe. Epidemiological data presume that this clone originated outside Europe, in the Middle East or in North Africa (1, 3, 5-6).

CA-MRSA ST80 is typically resistant to fusidic acid, kanamycin / amikacin and tetracycline (1). In Kuwait, a high-level mupirocin resistant CA-MRSA strain ST80 was found (1, 3, 5). The majority of CA-MRSA ST80 isolates carry Pantone-Valentine leukocidine (PVL) genes, staphylococcal cassette chromosome (SCC*mec*) IV and exfoliative toxin type D gene (*etd*) (3, 5-8). In France and in Croatia, a PVL-negative variant of CA-MRSA ST80 has been described (6). The European clone is associated mainly with skin and soft-tissue infections, but rarely causes other invasive infections such as bacteriemia or meningitis (3, 4).

We have described the first PVL positive CA-MRSA ST80-IV isolates in Slovenia in four patients hospitalized in one Slovenian hospital in 2003 and 2004 (9). These CA-MRSA isolates were associated with skin and soft-tissue infections: one patient developed meningitis. All CA-MRSA isolates were typically resistant to beta-lactam antibiotics, kanamycin, tetracycline and fusidic acid and harboured PVL and *etd* genes (9).

In Slovenia, a national monitoring of CA-MRSA strains began in the year 2006. In a national collection obtained at medical microbiology department of the National Laboratory for Health, Environment and Food only CA-MRSA isolates that were resistant to oxacillin and cefoxitin and susceptible to at least two of the following four antibiotics, ciprofloxacin, erythromycin, clindamycin and gentamicin (screening definition of the presumptive CA-MRSA) were included (10-12). Dominant clones identified were ST5, ST45, ST22 and ST398. The authors, in their previous studies, confirmed that genetically heterogeneous CA-MRSA clones circulate in our country (11, 12).

To our knowledge, no case of death due to CA-MRSA ST80 has been reported in our country. Because ST80 is one of the predominant clones in Europe and because ST80 was confirmed in Slovenia in the years 2003 and 2004, the aim of the current study was to investigate the presence of the CA-MRSA ST80 strain among human samples in our country. The study describes the detailed characterization by epidemiological investigation, antimicrobial resistance pattern, toxin gene and molecular profiling.

2 METHODS

2.1 MRSA Surveillance in October 2013

In October 2013, a blood culture from a 69-year-old female yielded MRSA. She had a transsphenoidal biopsy of a large parasellar meningioma and was prior to surgery without health-care risk factors. Subsequent screening swabs from the nose and tracheal aspirate yielded CA-MRSA. In an attempt to identify the source of the CA-MRSA, an epidemiological investigation was started, and surveillance swabs (throat, nose, groin) were obtained from all her available household members, nose swabs from domestic animals (pigs, goats, poultry) and dust samples from the farm environment.

2.2 Retrospective Analyses of CA-MRSA Isolates Collected in a National Collection of Presumptive CA-MRSA Isolates

We reviewed presumptive CA-MRSA isolates in the strain collection database from 2006 to 2013. Only CA-MRSA that belonged to ST80 were included in further analyses.

2.3 Patients' Data and Case Definition

A trace back epidemiological investigation for each patient with CA-MRSA ST80 isolate was performed. Several features were collected from the medical report: patient characteristics (demographic data, clinical data), treatment and outcome. A CA-MRSA was defined as a strain isolated from ambulatory patients or from inpatients within 48 hours of hospital admission, with no risk factors for nosocomial acquisition in the previous year, such as colonisation or infection with MRSA, hospitalization or residence in long-term care facilities, surgery or use of an indwelling catheter. All other isolates were considered as HA-MRSA.

2.4 Bacterial Isolates and Antimicrobial Susceptibility Testing

All *S. aureus* isolates were identified by mass spectrometry (MALDI-TOF, Biotyper, Bruker Daltonic GmBH, Bremen, Germany). The susceptibility of CA-MRSA isolates was tested against 16 antimicrobial agents using the disk diffusion method according to the guidelines of the Clinical Laboratory Standard Institute (CLSI) (13). The antibiotics tested were penicillin, cefoxitin, vancomycin, gentamicin, tobramycin, kanamycin, erythromycin, clindamycin, tetracycline, ciprofloxacin, trimethoprim-sulfamethoxazole, chloramphenicol, rifampin, linezolid, mupirocin and fusidic acid (BD, Maryland, USA). Minimal inhibitory concentration (MIC) determination of oxacillin was performed using the E-test (bioMerieux, Marcy I'Etoile, France).

2.5 Molecular Characterization

MRSA isolates were screened by PCR (polymerase chain reaction) for the PVL encoding lukS-PV and lukF-PV genes and *mec*A gene using Genotype Staphylococcus (Hain Lifesciences, Germany). The identification of the SCC*mec* types and the presence of exfoliative genes (*eta, etb, etd*) was performed using primers as described previously (14-15). MRSA isolates with a positive phenotypic screening pattern were characterized by *spa* typing according to a method described previously (16). Multilocus sequence typing (MLST) was performed as described by Enright et al (17). ST designations were assigned by the MLST database (available from: http://www.mlst.net).

3 RESULTS

3.1 Isolate Characteristics

Between 2006 and 2013, among the 385 CA-MRSA isolates included in our national collections, only 2 (0.5%) were identified with resistance to penicillin, cefoxitin, kanamycin, tetracycline and fusidic acid and susceptibility to vancomycin, gentamicin, tobramycin, erythromycin, clindamycin, ciprofloxacin, trimethoprim-sulfamethoxazole, chloramphenicol, rifampin, linezolid and mupirocin.

Both CA-MRSA isolates had MIC of oxacillin between 16-64 mg/L and MIC of vancomycin 2 mg/L. PVL and *mec*A genes and SCC*mec* IV were confirmed in both CA-MRSA isolates. Both CA-MRSA isolates were associated to ST80.

3.2 Clinical Characteristics of MRSA Infection

One CA-MRSA isolate was isolated from a wound swab and one from blood culture. No CA-MRSA ST80 were found between 2006 and 2012. Epidemiological investigations showed that both CA-MRSA ST80 isolates were detected in the year 2013, in different regions of Slovenia, and no connection between them was found.

First CA-MRSA ST80 was confirmed in a 47-year-old male. The patient had no health-care associated risk factors for MRSA colonization or infection, and no surveillance swabs for MRSA were taken. He had clinical signs of a wound infection and bacterial sampling was performed in a surgical emergency department. Initial antibiotic therapy was inappropriate (amoxicillin/clavunate) and infection was cured with clindamycin.

Epidemiological investigation showed that the second CA-MRSA ST80 strain was isolated from a 69-year-old female. The patient was previously healthy with no known risk factors for MRSA infection. Upon admission for transsphenodial biopsy of a large parasellar meningioma, no surveillance swabs for MRSA were taken. Infection of purulent meningitis occurred thirteen days after the first admission. A head CT scan showed inflammation in the region where the biopsy had been performed and a lumbar puncture confirmed meningitis. Intravenous therapy with cefepime (2 g/6 hour) and vancomycin (3 g/day) was started. She was intubated and mechanically ventilated. The patient remained febrile despite the treatment and vancomycin was changed to daptomycin (10 mg/kg). Clindamycin was added, because she also developed pneumonia. Cerebrospinal fluid remained sterile but eubacterial PCR yielded *S. aureus*. Transesophageal Echo was negative. Despite several cleanings of the nose and paranasal sinuses the control CT scan revealed local deterioration. New ischaemic brain lesions were also seen. Ethmoidectomy and meatotomy of paranasal sinuses were performed. Patient slowly improved. Upon waking up, she started to bleed massively from both nostrils. Nasal tamponade was inserted and she received a transfusion of red blood cells. The massive bleeding repeated itself and she was unsuccessfully resuscitated. She died 25 days after the first surgery (Table 1).

3.3 MRSA Surveillance in October 2013

All human, animal and farm environmental samples tested in an association with 69-year-old female patient were MRSA negative.

4 DISCUSSION

The frequency of CA-MRSA ST80 varies from < 5% in Spain to 92% in Greece (1). A high frequency of ST80 strain is also documented in Kuwait, Lebanon, Israel, Egypt, Algeria and Tunisia, suggesting their clonal origin (1, 4, 6). According to the authors, CA-MRSA ST80 is also circulating in our neighboring countries (Italy, Austria, Croatia) (6), but surprisingly CA-MRSA ST80 is not very common in Slovenia. To date, infections caused by CA-MRSA ST80 seemed to be sporadic cases. In our previous study that lasted from 2003 to 2004, we confirmed CA-MRSA ST80 isolates in four hospitalized patients following necrotizing soft tissue infection, purulent abscesses and epidural catheter infection and meningitis (9). Between 2006 and 2013, we found only 2 (0.5%) CA-MRSA ST80 strains among 385 presumptive CA-MRSA isolates. Both CA-MRSA ST80 isolates were confirmed in the year 2013, in different regions of Slovenia, and no epidemiological connections between these two infections were found. According to our epidemiological investigation, both of the patients with CA-MRSA infection were in good health prior to their infections. The first patient had a wound infection, without health-care associated risk factors, and no surveillance samples for MRSA carriage were taken. The patient was treated in a surgical emergency department without hospital admission. However, it cannot be excluded that the patient was colonized with CA-MRSA prior to surgical procedure.

Table 1. Phenotypical, genotypical and epidemiological characteristics and clinical data from patients infected with CA-MRSA ST80 strain in Slovenia between 2006 and 2013.

Characteristic		
Gender	M	F
Age (years)	47	69
Diagnosis at hospital admission	Abscessus glutei	Meningeoma
Source of isolates	Wound swab	Blood cultures, tracheal aspirate
Type of infection	SSTI	Sepsis and meningitis
Outcome	recovered	death
Risk factors for MRSA colonization		
History of MRSA infection / colonization	No	No
Surgery in the past year	No	Yes
Hospitalization in the past year	No	Yes
Residence in a day care	No	No
Resistance pattern	P, OX, TE, FA, K	P, OX, TE, FA, K
MIC of oxacillin (mg/L)	16	64
Typing		
SCCmec type	IV	IV
spa type	t044	t044
MLST (ST)	80	80
Toxin gene profile		
PVL	+	+
etd	+	+

Legend:
M male, F female, SSTI skin and soft tissue infection, MIC minimal inhibitory concentration, PVL Panton-Valentine Leukocidin, MLST multi locus sequence typing, ST sequence type, SCCmec staphylococcal cassette chromosome mec, SCCmec type IV, etd exfoliative toxin gene type D, FA fusidic acid, K kanamycin, Te tetracycline, P penicillin, OX oxacillin (cefoxitin)

The second patient developed a serious infection caused by CA-MRSA ST80 after surgery and no surveillance samples for CA-MRSA carriage were taken prior to surgery. CA-MRSA was isolated from the patient's blood culture, tracheal aspirate, nose swab and cerebrospinal fluid. In an attempt to identify the source of the CA-MRSA, surveillance swabs were taken from the patient's husband. Because the patient was living on a farm, nasal swabs were also taken from clinically healthy piglets and dust samples from their environment. All samples tested were MRSA negative. The major limitation of our study was the lack of extensive staff and hospital environment screening. Therefore, the source of the patient's CA-MRSA isolate remained unclear. Based on clinical data, epidemiological investigation and lack of health-care risk factors, we predicted that CA-MRSA in the 69-year-old female was transmitted by the hands of the personnel temporarily colonized with bacteria or contaminated medical equipment during surgery, or the patient was colonized with CA-MRSA in the community. Upon confirmation of CA-MRSA isolate in the patient's specimens, the standard and contact precautions for preventing MRSA transmission in hospital were introduced. Despite appropriate antibiotic therapy, the patient died and, to our knowledge, this was the first documented death caused by CA-MRSA ST80 in Slovenia.

According to our results, we suspect that infections caused by CA-MRSA ST80 in Slovenia remain relatively low and are underestimated. Firstly, the epidemiological investigation of a patient's infections is performed only when atypical MRSA isolate is recovered from patient's specimens, such as resistance to tetracycline, which is associated with LA-MRSA (4). Secondly, phenotypically confirmed MRSA is not routinely tested for genotypic characteristics, such as spa type or ST. Thirdly, no information is available about the occurrence of CA-MRSA among healthy carriers that are a potential source of infections in the community. Finally, clinical samples are not routinely cultured, but only upon inappropriate therapy or progressing infection. In conclusion, we also speculate that migration will likely increase CA-MRSA carriage and infections in the near future also in our country.

In 2014, on behalf of the National Institute of Public Health of Slovenia, two surveillance programs were assigned to monitor CA-MRSA and LA-MRSA incidence on the national level. To date, CA-MRSA infections caused by the ST80 strain are rare in Slovenia, but molecular testing, epidemiological investigations and surveillance studies of CA-MRSA and LA-MRSA are needed to control and monitor these pathogens that are considered a public health threat all over the world.

ETHICAL APPROVAL

All the data analysed in this study were collected at the National Laboratory for Health, Environment and Food without information about the identity of individuals diagnosed with CA-MRSA infections according to the Contagious Diseases Act, Health Care Databases Act and Communicable Diseases Reporting Regulation. The study was conducted in accordance with the code of Ethics of the World Medical Association (Declaration of Helsinki).

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THE ASSESSMENT OF ENERGY AND PROTEIN NEEDS COVERAGE IN HOSPITALIZED PATIENTS

OCENA POKRITOSTI POTREB PO ENERGIJI IN BELJAKOVINAH MED HOSPITALIZIRANIMI BOLNIKI

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ABSTRACT

Keywords:
hospital settings,
energy nutritional
value of the menu,
protein nutritional
value of the menu,
percentage of energy
coverage, percentage
of protein coverage

Aim. Aiming at assessing sufficiency of energy/protein intake in hospitalized patients, the objective was to monitor and analyze actual food intake of patients hospitalized in three clinical wards of one of major Slovenian hospitals.

Methods. 53 patients were included in the study. Food intake was assessed 3 times daily from leftovers. Nutritional status was assessed with Nutritional Risk Screening tool 2002. The observed outcomes were percentage of energy coverage (PEC) and percentage of protein coverage (PPC). In PEC energy nutritional value of the menu (ENVM), and in PPC protein nutritional value of the menu (PNVM) were considered as the main modifiable risk factors. Data were analyzed univariately and multivariately by using logistic regression method.

Results. The patients did not cover energy needs (67.4±24.5%). Multivariate model for PEC was highly significant (R2=0.347; pmodel<0.001) with ENVM showing high strength of association (b=0.040; p=0.004). Patients also did not cover protein needs (84.0±40.2%). Multivariate model for PEC was highly significant (R2=0.477; pmodel<0.001) and PNVM showing high strength of association (b=0.937; p=0.002).

Conclusion. For successful prevention and early detection of malnutrition, food intake in hospitals is vital and should be constantly monitored. A simple method for monitoring is proposed. The menus provided to patients should also be adequate in terms of energy and protein content.

IZVLEČEK

Ključne besede:
hospitalizacija,
energijska vrednost
obroka, beljakovinska
vrednost obroka,
energijska pokritost,
proteinska pokritost

Namen. Namen raziskave je bil ugotoviti zadostnost vnosa energije in beljakovin pri hospitaliziranih bolnikih. Cilj je bilo sistematično spremljanje in analiza dejanskega vnosa hrane pri bolnikih, hospitaliziranih na treh kliničnih oddelkih v eni izmed večjih slovenskih bolnišnic.

Metode. V raziskavo je bilo vključenih 53 bolnikov. Vnos hrane je bil zabeležen in spremljan trikrat dnevno prek vrednotenja ostankov obroka na pladnju. Stanje prehranjenosti je bilo ocenjeno z orodjem Nutritional Risk Screening 2002. Opazovani izidi so bili delež pokritosti potreb po energiji (PEC) in delež pokritosti potreb po beljakovinah (PPC). Pri PEC (delež pokritosti potreb po energiji) je bil glavni dejavnik tveganja, na katerega je mogoče vplivati, energijska vrednost jedilnika (ENVM), pri PPC (delež pokritosti potreb po beljakovinah) je bila to beljakovinska prehranska vrednost jedilnika (PNVM). Podatki so bili analizirani univariantno in multivariantno, z logistično regresijsko metodo.

Rezultati. Bolniki niso pokrili energetskih potreb (67,4±24,5%). Multivariantni model za PEC je bil močno statistično značilen (R2=0,347; pmodel<0,001) in je pokazal visoko stopnjo povezanosti z ENVM (b=0,040; p=0,004).
Prav tako bolniki niso zadostili potrebam po beljakovinah (84,0±40,2). Multivariantni model za PEC je bil ravno tako močno statistično značilen (R2=0,477; pmodel<0,001) in je pokazal visoko stopnjo povezanosti z PNVM (b=0,937; p=0,002).

Zaključek. Uživanje hrane v bolnišnici je ključno za uspešno preprečevanje in zgodnje odkrivanje slabe prehranjenosti, zato bi moralo biti redno spremljano. Predlaga se spremljanje vnosa hrane s preprosto metodo. Bolnišnični jedilniki morajo pokrivati bolnikove potrebe po energiji in beljakovinah.

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1 INTRODUCTION

Malnutrition and cachexia are considered to be serious, life threatening and costly public health problems (1). The prevalence of malnutrition in hospitals worldwide is about 20-50% (2-4); in Slovenia, Trtnik (5) showed that around 40% of patients were at nutritional risk or malnourished.

The nutritional status decline is largely dependent on the nature of disease or injury and consequent stress and inflammatory response, which is exacerbated with low energy and protein intake (6, 7). However, in a large part of studies exploring malnutrition and cachexia, this aspect seems to be left out (8-12).

Insufficient food intake in hospitals is an important factor for the development of malnutrition (3, 13, 14). Food intake <25% of the received food is linked with 2-3-times greater mortality (13, 14). Malnutrition and low food intake are undoubtedly linked with higher costs due to longer hospitalization and frequent re-hospitalizations (1, 14-16). It is also more and more obvious that along the aging of populations, malnutrition (and cachexia) of aged plurimorbid patients, especially hospitalized (this is a highly vulnerable group), is a rising public health problem(17). Unfortunately, only a small number of these patients with very low food intake is recognized and receives nutritional support, artificial nutrition or oral supplements (13). The aim of our pilot study is to demonstrate the actual energy and protein intake of hospitalized patients from three clinical wards, at one of major Slovenian hospitals.

2 PATIENTS AND METHODS

2.1 Study Design

The design of this small pilot study was observational. It was a health examination survey in which quantitative, practical and inexpensive methods that can be easily incorporated into dietetic, medical and nursing practice were used. The study was conducted from 26. 5. 2014 to 20. 6. 2014.

2.2 Patients

In the study, patients from three different clinical wards of one of the major hospitals in Slovenia were enrolled. Two of them were internal medicine wards, while the third ward was a surgical one. 53 patients were included in the study: 15 men and 4 women from clinical ward 1, 15 men and 17 women from internal medicine wards 2, 16 men and 12 women from surgical wards 3.

The criteria for enrolment were, namely: (1) the ability of the patient to understand the course of the study and be able to sign the informed consent form by hand;(2) at least 5 days of expected stay on the ward; (3) terminal patients were excluded; (4) only patients that were eating exclusively per os were included (patients receiving enteral or parenteral nutrition were excluded).

All included patients received unaltered food prepared in the central kitchen. The appropriate menu was selected by a physician or registered nurse at admission. Some patients received oral nutritional supplements and supplemental food prescribed by nurses and/or dietetics.

2.3 The Measurement of Food Intake and Nutrition Status

2.3.1 Food Intake Monitoring

The study was conducted under the auspice of hospital food and dietetics service and in close collaboration with the head nurse of medical clinics, the head nurse of surgical clinics and with nursing staff on the selected wards. A method most useful in practice is simply writing down the ingested share (all, nothing, ¼, ½ and ¾) of all the food on the tray. For greater accuracy we separately assessed every single component of a meal (for example: soup, meat, side dish etc.). Patients received hospital food portioned by kitchen staff. In our calculations we assumed that the portion actually received is the same as stated on menu.

The food intake of the enrolled patients for at least 3 full days and up to 7 days was followed. Food intake was assessed visually from photographs of the leftovers. For the assessment of liquids a simple measuring tool – a plastic knife with marks - was used (Figure 1). For each component of a meal the remaining food from photographs to the nearest quarter (25%, 50%, 75% and 100%) was visually estimated (12). From these data, energy and protein intake was calculated. Food intake data were followed by using "Winpis" software.

Figure 1. Food assessment with improvised measures for liquids (12).

2.3.2 The Measurement of Nutritional Status

We measured the height and weight of the patients, and completed the Nutritional Risk Screening 2002 (NRS 2002), which takes into account the parameters, such as the presence of illnesses or injuries, body mass index (BMI), involuntary weight loss and food intake in the last week (18-20). Its purpose is to detect not only developed malnutrition but also the risk for developing malnutrition in the hospital setting (20).

Energy needs were estimated using Harris-Benedict equation (21) with appropriate stress and activity factors summarized by Ferrie and Ward (22). The protein needs of the patients were estimated and adjusted for illness, injury and renal function, using the recommendations summarized by Ferrie, et al. (23). Energy and protein needs were estimated using actual or corrected (when BMI >30 kg/m2) body weight (15). Ideal body weight by Devine equation (24) was used in 4 patients in which weight was not obtainable. These patients were also underweight.

2.4 Methods

2.4.1 Observed Outcomes

We observed the actual intake (the amount of energy and protein the patients actually ingested) in the form of the actual energy intake (kcal per day) and actual protein intake (g of ingested protein per day).We compared these values with the estimated energy and protein needs (what patients should have ingested). We expressed these values as relative values: percentage of energy coverage (PEC) and percentage of protein coverage (PPC). We also followed the theoretical intake – the energy and protein content of the received meals (ENVM and PNVM) (the amount of energy and protein that patients received on their plates, but were not necessarily eaten).

Finally, two main observed outcomes, percentage of energy coverage (PEC) and percentage of protein coverage (PPC), were determined.

2.4.2 Explanatory Factors

Energy nutritional value of the menu (ENVM) was considered as the main modifiable factor in the analysis of PEC. Protein nutritional value of the menu (PNVM) was considered as the main modifiable risk factor in the analysis of PPC.

2.4.3 Confounding Factors

As potential confounding factors, medical ward (1=internal medicine ward 1, 2=internal medicine ward 2, 3=surgical ward), age (years), and sex (1=male, 2=female) were considered.

2.4.4 Statistical Methods

The association between the outcomes and their main modifiable factors, as well as potential confounders (sex, age, hospital ward), was firstly assessed univariately. A simple linear regression method was used for assessing the relationship between PEC and ENVM, age and sex, and PPC and PNVM, age and sex, while multiple linear regression was used for assessing the relationship between PEC or PPC and a ward. The dummy variables were created using a simple method for coding dummies (one group was assigned as the reference group).

Afterwards, multiple linear regression method was performed to adjust the estimates of the association between PEC and ENVM, and PPC and PNVM, for potential confounders. Again, the dummy variables were created using a simple method for coding dummies (one group was assigned as the reference group).

P-value of 0.05 or less was considered significant. The SPSS statistical package for Windows (Version 21.0, SPSS Inc., Chicago, IL, USA) (License: University of Ljubljana, Slovenia) was used as a tool for the analysis.

2.5 Ethical Considerations

All the enrolled patients handedly signed the informed consent form. The study was approved by The Republic of Slovenia National Medical Ethics Committee and was conducted in accordance with the declaration of Helsinki and Oviedo convention.

3 RESULTS

3.1 Study Group Characteristics

In the study 53 patients were included. 15 patients (28.3%) were coming from internal medicine ward 1, 23 patients (43.4%) from internal medicine ward 2, and 15 patients (28.3%) from surgical ward 3. Among them there were 22 women (41.5%) and 31 men (58.5%). The mean age was 69.7±11.4 years (internal medicine ward 1: 66.7±16.4; internal medicine ward 2: 71.3±9.2; surgical ward: 73.3±9.0). The mean value of BMI was 27.5±6.3 (internal medicine ward 1: 26.1±5.3; internal medicine ward 2: 29.9±6.9; surgical ward: 25.2±4.9). 31/53 (58.5%) of patients had NRS 2002 scores ≥3 (internal medicine ward 1: 11/15, 73.3%; internal medicine ward 2: 6/23, 26.1%; surgical ward: 14/15, 93.3%).

On average, estimated daily energy needs were assessed to 2064±467kcal (internal medicine ward 1: 2179±472 kcal; internal medicine ward 2: 1849±349 kcal, and surgical ward: 2278±506 kcal), and estimated daily protein needs were assessed to 86.4±24.3 g (internal medicine ward 1: 88.6±17.4 g; internal medicine ward 2: 68.6±13.2 g, and surgical ward: 111.4±20.6 g).

3.2 Food Intake Characteristics

On average, 3.8% of patients ate less than 25% of offered food, 18.9% ate 25-50% of offered food, 45.3% ate 50-75% of offered food and 32.1% ate 75-100% of offered food.

3.2.1 Energy Intake Characteristics

Mean daily energy intake on all wards was low. On average, daily energy intake was 1327±418 kcal (internal medicine ward 1: 1430±560 kcal; internal medicine ward 2: 1346±341 kcal, and surgical ward: 1194±348 kcal).

The average value of ENVM daily was 1932±240 kcal (internal medicine ward 1: 2052±315 kcal; internal medicine ward 2: 1818±117 kcal; surgical ward: 1987±230 kcal).

3.2.2 Protein Intake Characteristics

Mean daily protein intake on all wards was low as well. On average, daily protein intake was 65.9±23.2 g (internal medicine ward 1: 64.8±33.4 g; internal medicine ward 2: 71.3±16.4 g, and surgical ward: 58.8±18.7 g).

The average value of PNVM daily was 95.4±15.4 g (internal medicine ward 1: 94.2±25.9 g; internal medicine ward 2: 95.1±3.7 g; surgical ward: 97.2±13.9 g).

3.3 The Analysis of Percentage of Energy Coverage

It was possible to establish PEC in all 53 patients enrolled in the study.

On average patients did not cover their relative energy needs: the average value of PEC was 67.4±24.5% (min: 17.2%; max: 127.3%) (internal medicine ward 1: 67.5±25.4%; internal medicine ward 2: 76.0±24.8%; surgical ward: 53.9±17.7%).

The results of univariate analysis of association between PEC and ENVM showed that, in this model, ENVM did not show statistically significant association with PEC, and only 2.8% of variability of PEC could be explained by the fact that the model consisted solely of ENVM (Table 1). All other results are presented in Table 1.

All data necessary to perform multiple logistic regression analysis of association between PEC and ENVM were present in all 53 patients enrolled in the study as well. The results are presented in Table 2. The model was highly statistically significant (p_{model}< 0.001), and in total 37.4% of variability of PEC could be explained by this model. In comparison to the results of univariate analysis ENVM in multivariate model showed increased strength of association with PEC that was statistically highly significant (Table 1), and also the percentage of variability of PEC that could be explained by ENVM increased to 15.4%. The strength of association increased also between PEC and all considered potential confounding factors, except sex (Table 2).

Table 1. The results of simple linear regression analysis of the association between percentage of energy coverage and risk factors (N=53).

Risk factor	Observed category	Reference category	b	95 % C.I. limits for b		p	R^2
				Lower	Upper		
ENVM (kcal)			0.017	-0.011	0.045	0.230	0.028
Age (years)			0.584	0.001	1.167	0.050	0.073
Sex	Males	Females	-7.765	-21.461	5.931	0.260	0.025
Ward	Internal medicine ward 1	Surgical ward	13.664	-3.347	30.676	0.113	0.141
	Internal medicine ward 2	Surgical ward	22.059	6.597	37.521	0.006	

Legend: b=regression coefficient, C.I.=confidence interval; ENVM=energy nutritional value of the menu (theoretical intake)

Table 2. The results of multiple linear regression analysis of the association between percentage of energy coverage and risk factors (N=53).

Risk factor	Observed category	Reference category	b	95 % C.I. limits for b		p
				Lower	Upper	
ENVM (kcal)			0.040	0.014	0.067	0.004
Age (years)			0.809	0.269	1.348	0.004
Sex	Males	Females	-4.643	-16.450	7.163	0.433
Ward	Internal medicine ward 1	Surgical ward	19.345	3.446	35.244	0.018
	Internal medicine ward 2	Surgical ward	29.918	15.391	44.446	<0.001

Legend: b=regression coefficient, C.I.=confidence interval; ENVM=energy nutritional value of the menu (theoretical intake)

3.4 The Analysis of Percentage of Protein Coverage

It was possible to establish PPC in all 53 patients enrolled in the study.

On average, patients did not cover their relative protein needs: the average value of PPC was 84.0±40.2% (min: 17.8%; max: 165.5%) (internal medicine ward 1: 74.3±36.2%, internal medicine ward 2: 109.2±37.2%; surgical ward: 54.9±21.7%).

The results of univariate analysis of the association between PPC and PNVM showed that in this model PNVM has already shown statistically significant association with PEC (9.5% of variability of PPC could be explained by the fact that the model consisted solely of PNVM) (Table 3). All other results are presented in Table 3.

All data necessary to perform multiple logistic regression analysis of the association between PPC and PNVM were present in all 53 patients enrolled in the study as well. The results are presented in Table 4. The model was highly statistically significant (pmodel = <0.001), and in total 47.7% of variability of PPC could be explained by this model. In comparison to the results of univariate analysis PNVM in multivariate model showed increased strength of association with PEC (Table 2), and also the percentage of variability of PPC that could be explained by PNVM increased to 36.0%.

Table 3. The results of simple linear regression analysis of the association between percentage of protein coverage and risk factors (N=53).

Risk factor	Observed category	Reference category	b	95 % C.I. limits for b		p	R²
				Lower	Upper		
PNVM (g)			0.799	0.104	1.495	0.025	0.095
Age (years)			0.377	-0.610	1.365	0.446	0.011
Sex	Males	Females	-7.819	-30.440	14.802	0.491	0.009
Ward	Internal medicine ward 1	Surgical ward	19.344	-5.066	43.755	0.118	0.341
	Internal medicine ward 2	Surgical ward	54.284	32.097	76.470	<0.001	

Legend: b=regression coefficient, C.I.=confidence interval; ENVM=energy nutritional value of the menu (theoretical intake)

Table 4. The results of multiple linear regression analysis of the association between percentage of protein coverage and risk factors (N=53).

Risk factor	Observed category	Reference category	b	95 % C.I. limits for b		p
				Lower	Upper	
PNVM (g)			0.937	0.375	1.499	0.002
Age (years)			0.573	-0.235	1.382	0.160
Sex	Males	Females	-2.900	-20.664	14.863	0.744
Ward	Internal medicine ward 1	Surgical ward	27.948	4.021	51,876	0.023
	Internal medicine ward 2	Surgical ward	57.057	36.409	77.705	<0.001

Legend: b=regression coefficient, C.I.=confidence interval; ENVM=energy nutritional value of the menu (theoretical intake)

4 DISCUSSION

4.1 The Main Findings of the Study

The main findings of the study showed: a) that, on average, energy needs coverage was not sufficient, and that it could be significantly increased by increasing ENVM, and b) that, on average, protein needs coverage was not sufficient either, although the situation was better than in energy coverage, and that it could be, like in energy needs coverage, significantly increased by increasing PNVM. The main hypothesis – that energy and protein intake in hospitalized patients on average falls below their estimated needs – was confirmed.

4.2 Other Important Findings

Somewhat overlooked contributing factor in the development of hospital malnutrition is that not only food intake but also the amount of the provided food is insufficient. We found a direct association between the provided quantity of energy and protein and the actual intake. Simply and unsurprisingly, if more food is provided, more can possibly be eaten. We observed that too often the provided food was insufficient. 1800-2000 kcal menus were often prescribed universally to both men and women of different heights and weights. A rather high percentage of patients would not cover 100% of the estimated energy needs even if the meals would be fully consumed. This is especially evident in men with higher weight and in patients with conditions characterized by increased metabolism. We also noted patients receiving restrictive menus that are intended for a short time use and have only about 1200 kcal and 40 g of protein. Other researchers also reported that the amount and quality of hospital and nursing home meals often fell below the needs of patients (25, 26). Hankey and Wynne (27) performed a study in an elderly care hospital on 72 elderly patients (>65 years). Mean energy provision (not intake) was only 1472±320 kcal, also the recommendations for fibre and several micronutrients were not met. In another study (28), Wright with colleagues (25) analyzed the energy and nutrient content of hospital diets (regular, soft, low sodium, 1500 kcal, 60 g protein, full liquid and clear liquid) most commonly prescribed to elderly patients in two American hospitals. It would seem that malnutrition is too often treated without regard to what actually caused or contributed to its development. We reached the point where nutrition risk screening is mandatory in all acute care hospitals accredited by Joint Commission (29), but the provision of basic meals that would cover 100% of patient's individual energy, protein and other nutrient needs is not.

The menus with modified texture and restrictive diets are especially prone to being insufficient (25). We also noticed that hospital menus may be "too healthy"; the hospital food has low energy density. Especially for the elderly, small energy and protein dense meals would be more beneficial (30-33). Broths, soups, stewed fruit and similar foods with negligible energy and protein content are abundant in hospital menus and can be problematic. Especially soups have, for their energy content, a disproportionate satiating effect, so the food intake from the successive dishes is greatly reduced (34, 35). A limiting factor in spontaneous food intake is not the energy value, but the volume of the food (33); the amount of ingested food stays the same despite the increased energy density (34, 35). Enrichment of hospital food with a goal to provide increased energy density was proven to be an effective method in increasing energy intake of hospitalized patients (30-33). Hospital food can be easily and cheaply enriched with cream, cheese, ricotta, milk powder, protein powders, maltodextrins, canola oil and butter.

Nutritional risk (1, 4) and low food intake is still widespread in hospital environments worldwide (Table 6).

Food intake in hospitals should be monitored with the same diligence as blood pressure and temperature. Food intake monitoring is simple and does not require special equipment or in depth knowledge (13).

Energy intake (what patients actually ingested) of hospitalized patients in EU is, on average, below 1500 kcal, with protein intake around 60 g (9-11). In one similar Slovenian study (8), the average intake was 1364±326 kcal/d and 61.83±13.78 g of protein.

4.3 The Limitations and Strengths of the Study

The study has some limitations. Firstly, the main limitation of this study is that it was performed on only 53 patients. Secondly, the patients included in the study received normal hospital food, therefore the food was subjected to slight variations in portioning. Finally, it was performed in only one hospital. Here, we also have to stress that, in any case, the results and, consequently, also the study should not be considered representative of the entire hospital.

On the other side, this pilot study has also important strengths. The major one is that it pointed out the possibility of insufficient energy and protein coverage in hospitalized patients. This is an emerging problem in ageing populations and it should be taken into consideration. Another strength is the simple method used for rough but quick assessment of food intake, which is feasible to perform anywhere.

4.4 The Implications of the Study Results for Public Health

As in previous studies we can conclude that hospital malnutrition is still widely present in EU and is still being under-detected (1, 4). The actual food intake is rarely monitored, even when malnutrition is detected (3, 13, 14). From the perspective of public health, early detection of malnutrition and effective nutritional intervention with sufficient energy and protein intakes means better clinical outcomes, shorter hospital stay and lower costs of treatment (13).

4.5 Suggestions for Future Research in the Field

This study should be succeeded by a larger study conducted in several hospitals that would determine the prevalence of malnutrition and nutritional risk in Slovenian hospitals. Moreover, the effect of hospital food fortification on the actual food intake should be examined.

5 CONCLUSION

In this study, we demonstrated energy and protein intake on three clinical wards. When compared to the estimated energy and protein needs, we determined that food intake was in general insufficient. For successful prevention and early detection of malnutrition, food intake in hospitals must be monitored. We recommend using a simple method: after a meal, the nurse writes down if the patient ate all, nothing, ¼, ½, or ¾ of the food on the tray. Although it is simple and approximate, used with NRS 2002, it can detect a nutritional risk earlier than any other method. However, if the provided food was not sufficient (as was demonstrated in many studies, including this one), this could lead to a substantial error. An adequate hospital menu for an individual patient should always be chosen, preferably at admission. All patients need to receive minimally the amount of food that would cover or exceed their needs. Malnutrition is a disease and food is a prevention and therapy. Feeding a patient should be done with equal care and responsibility as their therapy application.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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None.

ETHICAL APPROVAL

The study was approved by The Republic of Slovenia National Medical Ethics Committee and was conducted in accordance with declaration of Helsinki and Oviedo convention.

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CANCER PATIENTS' SURVIVAL: STANDARD CALCULATION METHODS AND SOME CONSIDERATIONS REGARDING THEIR INTERPRETATION

POPULACIJSKO PREŽIVETJE BOLNIKOV Z RAKOM: UPORABA RAZLIČNIH PRISTOPOV IN PROBLEMI INTERPRETACIJE REZULTATOV

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ABSTRACT

Keywords:
cancer survival,
population-based
survival analysis,
cancer registries,
relative survival,
bias

Background. Cancer patients' survival is an extremely important but complex indicator for assessing regional or global inequalities in diagnosis practices and clinical management of cancer patients. The population-based cancer survival comparisons are available through international projects (i.e. CONCORD, EUROCARE, OECD Health Reports) and online systems (SEER, NORDCAN, SLORA). In our research we aimed to show that noticeable differences in cancer patients' survival may not always reflect the real inequalities in cancer care, but can also appear due to variations in the applied methodology for relative survival calculation.

Methods. Four different approaches for relative survival calculation (cohort, complete, period and hybrid) have been implemented on the data set of Slovenian breast cancer patients diagnosed between 2000 and 2009, and the differences in survival estimates have been quantified. The major cancer survival comparison studies have been reviewed according to the selected relative survival calculation approach.

Results. The gap between four survival curves widens with time; after ten years of follow up the difference increases to more than 10 percent points between the highest (hybrid) and the lowest (cohort) estimates. In population-based comparison studies, the choice of the calculation approach is not uniformed; we noticed a tendency of simply using the approach which yields numerically better survival estimates.

Conclusion. The population-based cancer relative survival, which is continually reported by recognised research groups, could not be compared directly as the methodology is different, and, consequently, final country scores differ. A uniform survival measure would be of great benefit in the cancer care surveillance.

IZVLEČEK

Ključne besede:
preživetje bolnikov
z rakom, populacijska
analiza preživetja,
register raka,
relativno preživetje,
pristranskost

Izhodišča. Preživetje bolnikov z rakom je kompleksen kazalnik, ki je izjemno pomemben pri ocenjevanju regijskih in globalnih neenakosti v diagnostiki in zdravljenju onkoloških bolnikov. Med najbolj prepoznavne mednarodne projekte, ki periodično objavljajo primerjave populacijskega preživetja bolnikov z rakom, sodijo CONCORD, EUROCARE in zdravstvena poročila OECD. Za nekatere populacije pa je populacijsko preživetje bolnikov z rakom na voljo tudi na spletnih aplikacijah, kot so SEER (Združene države Amerike), NORDCAN (Skandinavija) in SLORA (Slovenija). Z našo raziskavo smo želeli opozoriti, da nekatere očitne razlike med preživetjem onkoloških bolnikov iz različnih držav niso nujno posledica neenakosti v organizaciji, dostopnosti, kakovosti ali učinkovitosti sistema zdravstvenega varstva, temveč da lahko odstopanja nastanejo tudi le zaradi razlik v metodologiji, uporabljeni pri izračunavanju relativnega preživetja.

Metode. V analizi smo primerjali štiri metode za izračunavanje relativnega preživetja: kohortni, popolni, obdobni in mešani (hibridni) pristop. Razlike smo kvantificirali na primeru relativnega preživetja slovenskih bolnic, ki so zbolele za rakom dojke med letoma 2000 in 2009. V drugem delu raziskave smo naredili pregled izborov pristopov k izračunavanju relativnega preživetja v najpomembnejših mednarodnih raziskavah.

Rezultati. Razkorak med preživetvenimi krivuljami se veča s časom: deset let po diagnozi naraste razlika med najboljšo (hibridni pristop) in najslabšo (kohortni pristop) oceno že na 10 odstotnih točk. Ugotavljamo tudi, da pristop k izračunavanju relativnega preživetja med osrednjimi mednarodnimi projekti ni poenoten. Poleg tega se nakazuje tendenca po uporabi pristopov, pri katerih so ocene preživetja višje.

Zaključek. Populacijsko preživetje onkoloških bolnikov, ki ga v svojih publikacijah prikazujejo ugledne mednarodne raziskovalne skupine, ni neposredno primerljivo. Načini izračunavanja se namreč razlikujejo tako med raziskovalnimi skupinami kot tudi znotraj posamezne skupine. V zadnjih letih smo že bili priča interpretacijam razlik v relativnem preživetju bolnikov z rakom iz različnih držav, ki so bile pristranske prav zaradi neupoštevanja razlik, ki nastanejo pri uporabi različnih metod izračunavanja. Prepričani smo, da bi javnozdravstvena stroka in politika veliko pridobili s poenotenjem izračunavanja preživetja bolnikov z rakom.

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1 INTRODUCTION

Cancer patients' survival is, together with the incidence, prevalence and mortality, one of the basic cancer burden indicators. Population-based survival of cancer patients, as shown by cancer registries for more than 60 years (1), is a valuable indicator, which reflects patients' characteristics as well as the organisation, accessibility, quality and efficiency of the healthcare system. Generally, it greatly differs from the survival of patient groups with a particular disease treated in individual hospitals, as commonly presented by clinicians (2).

Because of the extreme importance of survival indicator for assessing regional, international or global inequalities in the diagnosis practices and clinical management of cancer patients, several comparisons between and within countries are available today: the CONCORD study provides relative survival estimates for 31 countries on five continents (3, 4), the EUROCARE study offers the relative survival data for 23 European countries (5, 6), the OECD health reports present relative survival data for OECD countries (7, 8), the SEER estimates the relative survival for 98% of the U.S. population (9), the NORDCAN provides the relative survival data for 5 North European countries (10), and the SLORA calculates the relative survival measures for Slovenia (11).

The data on cancer patients are collected in cancer registries according to the internationally agreed and comparable procedures. Despite the exemplary quality and comparability of the data, the applied relative survival methods are not consistent between and within the releases of above studies, and, consequently, the published results on the population-based survival for the comparable calendar years and populations vary considerably.

In groups of patients, survival represents the proportion of patients still alive after a certain period of time since the diagnosis. In population-based survival analyses, we tend to estimate only the dying probability of patients with a disease investigated (i.e. the probability of dying from cancer) and thus tend to avoid all non-cancer causes of death. Such survival is called net cancer survival, and it is methodologically most correctly estimated using PoharPerme method, but traditionally one of the relative survival methods is used as an approximation (12, 13).

The basic and, at the same time, the most simple measure of survival is the so-called observed survival, where causes of death are not considered and survival of the patients is not compared to the population survival. Among various methods available for calculating the observed survival, currently, the most frequently used is the Kaplan-Meier's method (14). The observed survival rate accounts for all

deaths, and it is a true reflection of the actual mortality in a patient group. When considering a particular cause of death (i.e. cancer), typically all deaths due to other causes could simply be censored (the so-called cause-specific survival) (15). Such a technique for estimating net survival would seem reasonable also in population studies, however, in practice, it turns out that the number of patients entered into such studies is too large to allow the exact cause of death to be established for each individual patient; the data on the official causes of death, which are usually collected by national mortality registries, are often insufficiently accurate for these purposes (16, 17). Therefore, and because of the incomparability of the observed survival between different populations, in population studies net cancer survival is estimated by relative survival methods, rather than by the cause-specific survival (18).

Relative survival is calculated as a ratio between the observed and the expected survival, i.e. the survival expected with respect to gender and age in a certain time period in the entire population from which the patients come (19). The expected survival is calculated from general mortality data, published routinely in the form of mortality tables within the framework of countries' vital statistics (20). Relative survival of cancer patients is generally reported for one, three, five and ten years after the diagnosis. The study designs in the relative survival analysis can be distinguished according to the definition of persons at risk who contribute to each conditional survival probability and according to the use of follow-up time. Four different study designs are described and implemented in our research – all applied in several recognised relative survival comparison studies or online reports (3-11). We have adopted the same terminology for various study designs (cohort, complete, period and hybrid approach) as suggested by Brenner and Rachet (21), even though this terminology has not been used consistently in the literature (22). The four approaches do not differ in the mathematical point of view, since the calculation procedures for the estimation of relative survival and its confidence intervals are the same in all four study designs. The major difference in four approaches is in the case selection (Figure 1): from the same patients' pool, distinctive individuals are selected for each particular approach, which certainly leads to the difference in end results. All diagnosed patients were included in relative survival estimates with complete approach only. With cohort approach the patients from the earliest incidence year were selected, but with period and hybrid approaches only most recently diagnosed patients are picked up (21, 23).
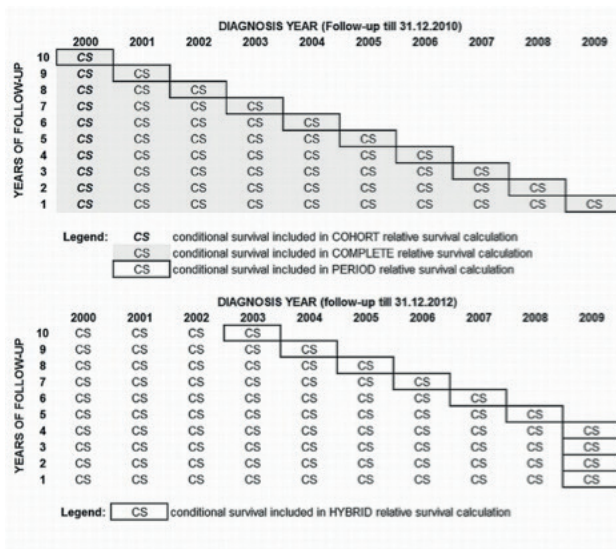
Figure 1. The illustration of the choice of patients diagnosed between the years 2000 and 2009 that contribute to a relative survival calculation with cohort, complete and period approaches (top: a follow up untill the end of 2010) and those that contribute to the hybrid approach (bottom: a follow up untill the end of 2012).

In our paper, we aim to highlight some important methodological issues regarding the design and interpretation of population-based survival comparison studies, and to draw specific attention to the possibility that noticeable differences in cancer patients' survival may not always reflect the real inequalities in the access to cancer care, but can also appear due to variations in the methodology applied in the calculation of survival.

2 METHODS

To demonstrate the quantitative differences in results between cohorts, complete, period and hybrid relative survival, the relative survival estimates for Slovenian female breast cancer patients diagnosed between 2000 and 2009 have been calculated using each of four study designs (Table 1). The sample was derived from the population-based Cancer Registry of the Republic of Slovenia. All cases registered on the basis of a death certificate or autopsy only were excluded prior to analyses, since survival in these cases is equal to zero. The administrative censoring date was December 31, 2010, except for the hybrid relative survival analysis, where the follow-up was extended until December 31, 2012. For the expected survival calculation, the Slovenian life tables (20) and the Ederer II method (24) were used in all examples. The Pohar-Perme estimator (PPE) (25) is added in Table 1 for comparison, since it is the only unbiased estimator for net survival. The analysis was performed

with the STATA software package, using publicly available macros (26).

Distinctive patients sampling has been applied as explained below and summarized in Figure 1: With the cohort approach, the entire group of patients must be followed-up for a certain period of time, in our case for ten years. Thus, every person included in the analysis should have the possibility to survive these ten years. In Slovenian breast cancer patients, where the patients diagnosed from 2000 to 2009 and followed-up until the end of 2010 are available (Figure 1, top), only the patients diagnosed in 2000 can be followed-up for ten years, and thus, only they are included in the cohort analysis of ten-year relative survival. With the complete approach, the patients diagnosed at a later date and followed up for less than ten years are also included (Figure 1, top). The patients followed-up for a shorter period of time are considered in the calculation of complete relative survival only for the time when they were actually followed-up. Thus, the group diagnosed three years before the study was completed (in 2007 in our example case), contributes to one- and three-year complete relative survival, but not to five- or ten-year survival. The period survival approach includes only the patients diagnosed in the most recent calendar year (the year 2009 in Figure 1) in the calculation of one-year survival, while the calculation of two-year survival includes only those patients who were diagnosed two years before (2008) and who have survived the first year; accordingly, the calculation of five-year survival includes only those patients who were diagnosed five years before (2005) and who are still alive at least four years after the diagnosis. The approach that combines the features of the period and cohort relative survival analyses is called hybrid relative survival (21). With hybrid approach, the follow up time is available for a more recent period than records on cancer patients (at the bottom part of Figure 1, patients were diagnosed until 2009, but in the case of the hybrid approach, the follow-up was performed until the end of 2012). For the calculation of conditional survival after one, two and three years, the cohort approach on 2009 patients was applied, as all 2009 patients were followed-up for three years. Moreover, for the calculation of conditional survival after four to ten years, the period analysis of patients diagnosed in the most recent years available (2008–2002) is used.

3 RESULTS

3.1 An Empirical Example

The sample data set included 11,060 females with a median follow-up time of 4.2 years. The up-to-ten-year relative survival curves derived by the cohort, complete, period and hybrid relative survival analyses are plotted in Figure 2 and 95% confidence intervals are presented in Table 1.

Table 1. The one- to ten-year relative survivals with 95% confidence intervals and Pohar Perme relative survival estimators for Slovenian female breast cancer patients diagnosed between 2000 and 2009* derived by cohort, complete, period and hybrid approaches.

Follow-up time	COHORT all patients diagnosed in 2000		COMPLETE all patients diagnosed from 2000 to 2009		PERIOD some patients diagnosed from 2000 to 2009*		HYBRID some patients diagnosed from 2003 to 2009*	
	Relative survival (95% confidence interval)	Pohar Perme estimator	Relative survival (95% confidence interval)	Pohar Perme estimator	Relative survival (95% confidence interval)	Pohar Perme estimator	Relative survival (95% confidence interval)	Pohar Perme estimator
1-year	96 (94-97)	96	95 (95-96)	96	96 (92-99)	97	96 (92-99)	97
2-year	90 (87-92)	91	92 (91-92)	92	93 (89-96)	93	93 (89-96)	93
3-year	85 (82-87)	85	88 (87-89)	88	89 (85-92)	90	89 (86-92)	90
4-year	80 (77-83)	81	85 (84-86)	86	87 (83-91)	88	87 (84-90)	88
5-year	77 (74-80)	77	83 (82-84)	83	85 (81-89)	85	85 (82-88)	86
6-year	73 (70-77)	75	80 (79-81)	81	83 (79-86)	83	84 (80-87)	83
7-year	72 (68-75)	72	79 (77-80)	80	80 (76-84)	82	82 (78-85)	82
8-year	71 (67-74)	72	77 (75-78)	78	78 (74-82)	78	80 (76-83)	79
9-year	70 (66-74)	72	76 (74-77)	77	76 (72-80)	76	79 (75-82)	78
10-year	69 (65-73)	73	75 (73-76)	77	75 (71-79)	75	78 (74-81)	77

* With period and hybrid approaches, only the most recently diagnosed survivors are included (the included incidence years are specified in Figure 1).

The observed survival curve resulting from Kaplan-Meier analysis of the complete data set is added to Figure 2, showing that the ten-year survival of breast cancer patients is higher by 10 to 20 percentage points (or relatively from 15% to 30%) if non-cancer causes of death are analysed properly. Comparing the effect of such elimination of non-cancer causes of death already after five years after diagnosis, relative survival is higher by 2 to 10 percentage points.

The four compared relative survival approaches give similar results only for the first year after diagnosis (Table 1). The gap among the curves widens with time, proving to be the largest after ten years of a follow-up: the difference in ten-year survival between the approach giving the highest results (the hybrid analysis) and the approach giving the lowest results (the cohort analysis) is 9 percentage points (11%). Complete and period approaches' results are between cohorts an hybrid approach, but the gap between them narrows with time after a diagnosis. In the first six years after a diagnosis, there is practically no difference between the results of period and hybrid approaches, as only after several years the difference inpatients' selection results in better hybrid survival estimates. The estimates are expectably the most precise in complete
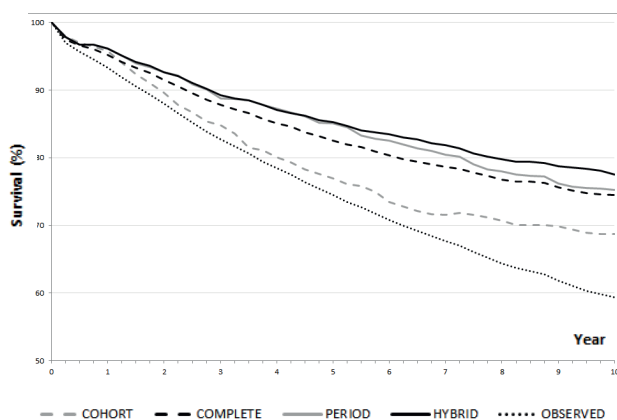
Figure 2. The relative survival curves derived by cohort, complete, period and hybrid approaches, and Kaplan-Meier observed survival for Slovenian female breast cancer patients diagnosed between 2000 and 2009.

approach, where all available patients are included in the calculation, but with all other approaches the precision of the estimates is similar.

Within the pool of the same patients, the highest survival is reported with the hybrid approach. The results slightly differ only with period and complete approaches, but they are significantly lower with cohort approach.

3.2 The Selection of the Relative Survival Approach in Practice

Currently, comparable population-based survival statistics are provided by three prominent research groups: CONCORD, EUROCARE and OECD Health Care Quality Indicators (HCQI) Project (3-8). They all report relative survival for selected countries in successive time periods. Table 2 gives an overview of the included data and relative survival calculation approach. The final findings are published in the most prominent science journals, and they have a major impact on the understanding of the inequalities in cancer control between countries, meanwhile also influencing regional health policies and health systems.

Table 2. The differences in the relative survival calculation approaches between and within major population-based cancer survival studies, aiming to compare cancer care in several countries.

Population-based relative survival comparison study	Diagnosis year of included patients	End of follow-up year	Relative survival approach
CONCORD-1 (3)	1990-1994	1999	cohort
CONCORD-2 (4)	1995-2004	2009	cohort
CONCORD-2 (4)	2005-2009	2009	period
EUROCARE-4 (5)	1995-1999	2003	cohort
EUROCARE-4 (5)	1996-2002	2003	period
EUROCARE-5 (6)	2000-2007	2008	complete
EUROCARE-5 (6)	1999-2007	2008	period
OECD HCQI 2011 (7)	1995-2004	2009	not specified
OECD HCQI 2013 (8)	1995-2009	2012	period or cohort

The data for these studiesare gathered from population-based cancer registries; in many cases, the same registries provide data for all three studies. The CONCORD and EUROCARE studies collect individual data and perform all data quality checks and calculations, while the OECD HCQI Project collects only the end results on relative survival. What causes certain confusion in the evaluation of all these results is that the relative survival calculation approach is inconsistent between and within studies.

In the studies designed before the empirical evaluation of the period relative survival approach in 2002 (23), the method of choice was always the cohort approach. Currently, it appears that the researchers tend to choose, if the data are sufficient, the period approach for more recently diagnosed patients. The cohort approach remains the method of choice only for the relative survival calculations when patients are followed-up for longer periods. In EUROCARE-5, the classical cohort approach is replaced by the complete approach (6).

Considering the choice of relative survival approach, the OECD results are rather unclear. In their report in 2011, the choice of the approach was completely left to the cancer registries, and for the 2014 report, the OECD recommends using the period approach as a priority. Alternatively, the cohort analysis can also be used. Bearing in mind that different approaches give different results with the same data, such comparisons of relative survival would not be very efficient.

From the relative survival data, which are available through online systems, the SEER system offers the most flexibility in choosing different approaches with respect to the year of diagnosis and follow-up time. The SEERStat software (27) allows the user to select from the cohort, complete and period analyses, but the pre-prepared tables for Cancer Statistics Review (9) provide only the conditional survival probabilities for a specific diagnosis year and survival time, and thus the reader is left with the choice of selecting the research study design. In the NORDCAN project, the cohort survival approach is generally used, but for the later periods, the hybrid approach is applied (10). SLORA provides its users only with the relative survival calculated by the cohort approach (11).

4 DISCUSSION

In our research, we point out the discrepancy in the end results when the relative survival is estimated by four different study designs: cohort approach, complete approach, period approach and hybrid approach. The approaches differ according to the selection of patients that contribute to the calculation of survival and by the definition of the follow-up date. The extent of difference in the end results depends on the type of cancer and patients' age, but generally, when used on the same population, the relative survival is the highest with the hybrid approach and the lowest with the cohort one. As a rule, the final measure calculated by means of any of the presented approaches is entitled only as "relative survival" and it is compared and interpreted

in the common perspective. The biostatisticians and epidemiologists might be aware of differences and incomparability of the different approaches, however, when the results are disseminated, the journalists, public officials and general public can neither understand their complexity nor correctly interpret the results.

A tendency to use the approach which yields numerically better survival of cancer patients was noticed in most reports reviewed in this paper, and can be observed also in survival studies performed directly on cancer registry data (28). The period approach to relative survival calculation was developed in order to enable the use of information from the most recently diagnosed patients contributing to survival calculation. Namely, the continuous advances in medicine are associated with a better prognosis in patients diagnosed in recent years. However, the period approach has been often criticised, as, by definition, it selectively includes the most recently diagnosed patients and hence predicts the survival of patients whose follow-up was too short. On the other hand, the cohort and complete approaches consider only the existing data, and the results represent the real situation. The results of period relative survival should be presented and interpreted with a certain degree of caution. As evident from the procedure described in Figure 1, by means of the period relative survival approach we are including only the best (i.e. the most recent) available conditional survival probabilities. By performing such selection we are ignoring the fact that the patients contributing to the calculation of the one- to four-year conditional survival probability might not even survive five years. Thus we can only predict what their five-year survival would be like.

There are also other methodological issues that, besides the selection of a study design, distort the end results of survival analysis. Among the most important are: age-adjustment procedures, the expected survival calculation method, and the quality assurance of the input data. Data quality is carefully monitored by the CONCORD (3, 4) and EUROCARE (5, 6) studies, but the OECD studies relies only on the internal quality controls performed by individual cancer registries. The scientific discussion on the appropriate life-table method for the calculation of the expected survival has been long-lasting and is not finished yet. The Ederer II method (24), recognised as the least biased, was chosen by the recent EUROCARE studies (5, 6), while in the OECD Project, the Hakulinen method (29) is accepted as well. Age adjustment should be performed in all international comparisons, as this appears to be the best procedure to avoid the variation in survival due to differences in the age profile of cancer patients between the populations (30). The International Cancer Survival Standard weights (31) have become a golden standard for age standardisation of relative survival in the CONCORD, EUROCARE and OECD HCQI. Identical weights promise

the comparability of end results of different studies. However, the procedure of age standardisation itself irregularly affects the relative survival results; the study of Slovenian cancer patients' survival empirically showed that the downward deviation of survival results after age-standardisation is greater in cancer sites with a small number of cancer patients in particular age groups (2).

Recently, Pohar-Perme et al. (25) showed mathematically that all classical methods of relative survival calculation provide biased estimates of net survival, since the results are not independent of the national general population mortality. Therefore, they are particularly unsuitable for comparison between countries. Pohar-Perme et al. proposed a new estimator (the Pohar-Perme estimator – PPE) that enables the desired unbiased comparability. Roche et al. compared the PPE with the classical estimators commonly used in population-based survival studies on the actual data from FRANCIM cancer registries network. They concluded that, in estimating net survival, cancer registries should abandon all classical (relative and cause-specific) methods for calculating population based survival, and adopt the new PPE (13). Despite the fact that Roche's assessment has been criticised (22), it seems that PPE is currently recognised as the most appropriate estimator of net survival. Moreover, it has been applied in the CONCORD-2 study (4). However, even if not biased theoretically, the researcher must decide on one of the patient selection approaches (cohort, complete, period or hybrid) also in the PPE calculation. The values of one- to ten-year relative survival estimated by the PPE using the cohort, complete, period and hybrid approaches were calculated for our empirical example and added to Table 1. The results are only slightly different from our basic calculation performed using the Ederer II method, but the difference between the four approaches is again evident.

5 CONCLUSIONS

In conclusion, population-based cancer relative survival, which is continually reported by recognised research groups, could not be compared directly. Even though the studies are performed with the same statistical methods, on the matching patients' pool and identical time periods, the sample of patients included in the calculation and, consequently, the final scores of countries differ. As relative survival is the basic cancer care indicator, the results of the survival analysis should not be misleading. Conclusions based on biased comparisons could lead to unnecessary public health interventions as well as unfavourable clinical decisions. The epidemiological and biostatistical scientific communities should standardise the relative survival methodology, providing the policy-makers and the clinicians with a uniform survival measure. In any case, results should always be properly commented

and the approach used in the analysis should be clearly described.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

FOUNDING

We have not gained any special founds to perform this study.

ETHICAL APPROVAL

The data for this study was derived from the national population-based Cancer Registry of Republic of Slovenia (prescribed by laws: Official Gazette of SRS, No 10/50, 29/50, 14/65, 1/80,45/82 and 42/85; Official Gazette of RS, No 9/92 and 65/00). All the analyses were performed on the aggregated data and did not include personal information.

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THE ROLE OF THE PSYCHOSOCIAL DIMENSION IN THE IMPROVEMENT OF QUALITY OF CARE: A SYSTEMATIC REVIEW

VLOGA PSIHOSOCIALNE DIMENZIJE V IZBOLJŠEVANJU KAKOVOSTI OBRAVNAVE BOLNIKA: SISTEMATIČNI PREGLED LITERATURE

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ABSTRACT

Keywords:
general practice,
social problems,
psychosocial care,
quality of health care,
reviews

The aim of our systematic review was to analyse the published literature on the psychosocial dimension of care in family medicine and its relationship with quality of care. We wanted to find out whether there is any evidence on the psychosocial approach in (family) medicine. The recommended bio-psycho-social approach, besides the biomedical model of illness, takes into account several co-influencing psychological, sociological and existential factors. An online search of nine different databases used Boolean operators and the following selection criteria: the paper contained information on the holistic approach, quality indicators, family medicine, patient-centred care and/or the bio-psycho-social model of treatment. We retrieved 743 papers, of which 36 fulfilled our inclusion criteria. Including the psychosocial dimension in patient management has been found to be useful in the prevention and treatment of physical and psychiatric illness, resulting in improved social functioning and patient satisfaction, reduced health care disparities, and reduced annual medical care charges. The themes of patient-centred, behavioural or psychosocial medicine were quite well presented in several papers. We could not find any conclusive evidence of the impact of a holistic bio-psycho-social-approach. Weak and variable definitions of psychosocial dimensions, a low number of well-designed intervention studies, and low numbers of included patients limited our conclusions.

IZVLEČEK

Ključne besede:
*splošna medicina,
socialne težave,
psihosocialna obravnava,
kakovost zdravstvene
oskrbe, pregled
literature*

Priporočen biopsihosocialni pristop poleg biomedicinskega modela bolezni upošteva številne psihološke, socialne in eksistenčne dejavnike. Želeli smo izvedeti, ali v družinski medicini obstajajo dokazi o psihosocialnem pristopu. Cilj našega sistematičnega pregleda je bil analizirati objavljeno literaturo s področja psihosocialne dimenzije dela zdravnika družinske medicine in njegovo povezavo s kakovostjo obravnave bolnikov. Spletno iskanje je potekalo v devetih bazah s pomočjo Boolovih operatorjev in vključenimi kriteriji iskanja, kot so, da članek vsebuje nekaj o celostni medicini, kazalnikih kakovosti, družinski medicini, modelu, usmerjenem na pacienta, ali/in biopsihosocialnem modelu obravnave. Vključeni so bili tudi članki, povezani z družinsko medicino, ki so poročali o meritvah kazalnikov kakovosti. Iskanje je ponudilo 743 zadetkov, od teh je 36 člankov izpolnilo kriterije za vključitev v analizo. Psihosocialna obravnava se je izkazala za uporabno pri preventivi ter pri obravnavi telesnih in psihiatričnih bolezni. Rezultati takšne obravnave so izboljšano socialno funkcioniranje, večje zadovoljstvo pacientov, zmanjšane razlike pri zdravstveni oskrbi in nižji letni stroški zdravljenja. Teme, kot sta osredotočenost na pacienta in psihosocialna medicina, so v člankih kar dobro zastopane. Ni pa bilo možno najti nobenih virov o vplivu celostnega biopsihosocialnega pristopa. Nepopolna in različna definicija psihosocialne dimenzije, majhno število dobro osnovanih intervencijskih raziskav na tem področju in majhno število vključenih pacientov so omejitve, ki so vplivale na sklepe te raziskave.

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1 INTRODUCTION

The majority of modern healthcare is based on a biomedical model of illness, which allows the identification and treatment of a very large number of diseases, fails to recognise the multi-factorial and complex nature of many (including non-organic) illnesses (1). A biomedical approach considers only the easily measurable biological aspects of the patient's body during the illness episode – the patient's feelings and ability to function are outside the responsibility of the health care (2). From a biomedical perspective, the patient is just a passive recipient of the doctor's instructions, and treatment is focused on the repair of malfunctions in the patient's body. For many diseases, this approach is not sufficient (3). The psychosocial dimension takes into account various different factors which influence health, health care, and health care outcomes (4). This results in differences in disease prevalence, health outcomes, and access to health care based on the characteristics of the population (5). Keeping psychosocial problems hidden in the consulting room can lead to the medicalization of normal life events and trigger unwarranted illness behaviour in patients (6). A combination of bio-psycho-social approachesaddresses the complexity of the presentation of illness in modern family practice(7). A view of the human body that goes beyond the reductionist tendencies of naturalistic and social constructionist perspectives sees the body as an unfinished, biological and social phenomenon (8).

Quality of care encompasses patients (the adequate identification of vulnerable/eligible patients), doctors, and resources (9). There have been different definitions of quality, but the most recent one (from 2001) defines six criteria: patient-centred, safe, effective, timely, efficient and equitable (10). The use of evidence-based measures (indicators) has been suggested as a part of the process of quality improvement (11). Quality of health care may be reflected in (health-related) quality of life. Illness, disease and their treatments can have significant impact on mobility, mood, life satisfaction and social roles. Health-related quality of life also encompasses the patient's general well-being and satisfaction with treatment, as well as education, housing, income and the context of cultural and value systems (12). According to a definition by the World Health Organisation, health as a social phenomenon is a state of physical, mental and social well-being, and not merely the absence of disease or infirmity (13).

Diseases can have somatic and psychological causes on the one hand, and physical and social/environmental influences on the other. Such a framework is required in order to capture diverse disease and health conditions and their intricate relationships (14). Health and happiness go together and both result in more productive and viable communities (15). The community, i.e. the social environment we live in, and its capacity for both harm and good, are integral to personal health (16). People's health may also depend on the size and quality of their social network. Further associations arise between education, work and social class, resulting in different healthcare outcome rates or even mortality rates (17). Social characteristics (gender, class, ethnicity, etc.) lead to different positions in working life (18). Changes in social and environmental conditions could do much to improve living conditions and the health status of the population (17).

Primary care is the entry point into the health care system for all patient's health problems and needs. The approach to the patient is personal, lasts for an appropriate length of time, is comprehensive, and includes the possible coordination or integration of other options or levels of health care (19). One of family medicine's definitions is that it sees health in a broader way, dealing with health problems from a psychological, social, cultural and existential perspective (20), as well as a medical one. The family physician is aware of a patient's social environment, which leads to more effective and humane care. This does not mean that comprehensive care means using a less scientific approach; on the contrary, it means being even more scientific and individually-oriented (21). Understanding and trust between the doctor and the patient must be achieved for quality health care (22). Primary care is oriented towards people and populations and not just towards pre-defined diseases or interventions (23). A comprehensive approach to family medicine is also defined by Wonca Europe as one of the six essential characteristics (knowledge and skills) of a family physician (24). A family physician's ability should be in using a bio-psycho-social approach while taking into account cultural and social dimensions (20). First contact with the health care system, i.e. with primary care, is extremely important. It has been shown that countries with a superior primary care infrastructure have better health outcomes (22). Strong and effective primary care leads to better health of the whole population (23, 25).

It is difficult to measure the quality of psychosocial health care, because the model does not lend itself to easy definition or measurement. The aim of our systematic review was to analyse the published literature on the psychosocial dimension of care in family medicine and its relationship with quality of care. We wanted to find out whether there is any evidence on the psychosocial approach in (family) medicine and its outcomes. This was the first time that the relationship between well-known quality indicators and the less clearly defined psychosocial model of health care was investigated.

2 METHODS

Online databases were used to search several key-words in October 2011. Different combinations of Boolean operators were included, such as: social medicine, psychosocial model, comprehensive health care, holistic health, holistic nursing, patient-centred care, health care, well-being, quality indicators, general practice/family practice/family medicine, and comparative effectiveness research. We also applied different search parameters: the paper was published in the last five years, concerned human beings, was written in English and had the search expressions in the title or abstract.

We carried out searches on: Pubmed, Google Scholar, EBSCOHost, JSTORE, the Cochrane Library, OVID MEDLINE, Embase, All EBM Reviews and PSYCInfo. While searching online with Boolean operators, the selection criteria were that the paper contained something on: holistic medicine, quality indicators, family medicine, patient-centred care or the bio-psycho-social model of treatment. We did not include papers which were not related to family medicine or did not measure quality indicators. We excluded articles about education, educational programs, palliative nursing or alternative medicine. The final selection criteria included papers concerning prevention methods, communication between doctor and patient, the holistic approach and holistic healing, chronic disease management and evidence-based medicine. From a total of 743 hits, 63 papers matched all the inclusion criteria. A detailed reading of these papers resulted in 36 final hits for the purpose of this review (see Figure 1).
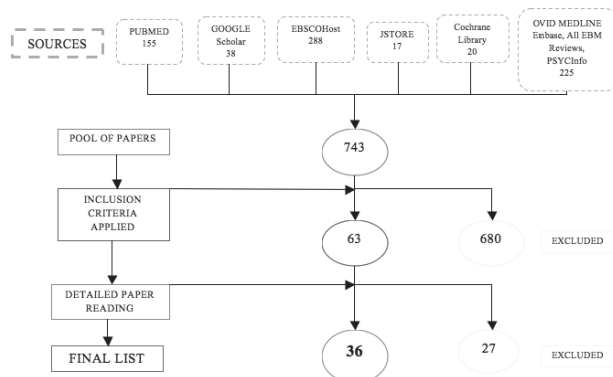

Figure 1. Flow diagram.

Those 36 hits were first classified according to study type, and then the findings were summarized according to the topic of the study, size of the sample, methods and main results (see Table 1). For the second evaluation, two independent researchers evaluated all the listed papers on a rating scale from 1 to 3, where 1 means that this study did not measure quality (directly or at all), 2 means that the measurement of quality was a secondary outcome, and 3 means that measure of quality was the primary aim of the study.

On PUBMED, there were 155 papers from various searches: social medicine AND quality indicators (6); quality indicators AND general practice AND comprehensive health care (27); social medicine AND family practice (47); comparative effectiveness research AND holistic nursing OR holistic health AND family medicine (15); patient centred care AND quality indicators, health care (56). We applied four search limits: the paper was published in the last five years, concerned human beings, was written in English and had the search expressions in the title or abstract.

On GOOGLE SCHOLAR (search expressions: holistic nursing OR holistic health OR quality indicators OR health care) we found 38 papers written from 2007 onwards with the key words in the title.

EBSCOHost gave us 288 papers (holistic nursing OR holistic health AND quality indicators AND Health care (147); patient centred care AND family medicine (141)) limited to publications in the last five years.

JSTORE gave us 17 papers (holistic nursing OR holistic health AND Quality indicators AND Health care (1); psychosocial model (16)) limited to the last five years and written in English.

In the Cochrane Library we found 20 systematic review papers (psychosocial model (17); quality of care AND family medicine (3)) with the search words in the abstract and written between 2007 and 2011.

From OVID MEDLINE, Embase, All EBM Reviews and PSYCInfo we got 225 papers with different search terms (patient-centred AND family medicine AND quality indicators (95); well-being AND family medicine AND quality indicators (69); psychosocial-model (61)) with the limits of publication in the last five years, written in English and about human beings.

3 RESULTS

There were ten randomised controlled and uncontrolled trials or cohorts (26-35), one meta-analysis (32), twelve cross-sectional studies (36-47), three case control studies (48-50), and ten qualitative study designs (focus groups (19, 51-53) and interviews (54-60)).

Thirty-six of the included papers were written from different perspectives. Some papers measured quality of health (care) (58), outcomes (38) or quality of life (59); others measured patient-centred care (35), or a holistic (19) or (bio)psychosocial approach (28); and some papers focused on preventive approaches in primary care: health promotion (30, 50), avoiding hospitalization (48, 33), prevention (34), or physical activity (26).

The main results, including sample size, applied methods and our rating of how much the paper measures the impact of the psychosocial dimensions on quality of care, and what exactly is measured, are presented in Table 1. For the purpose of the evaluation, the following scale was used – 1: the study measured only the psychosocial approach; 2: the study measured quality of care as a secondary outcome; 3: the study measured quality of care as the primary outcome. Here quality meant not just the quality of health care, but also quality of life and health as a whole (we included indirect measures, such as satisfaction, lower costs, etc. to show the quality of care). Altogether, there were 16 papers measuring both the psychosocial approach (or one aspect of it) and quality (health care or health outcomes, quality of life and outcomes that could affect quality – for instance, (higher) satisfaction could result in (higher) quality if we measured it afterwards). There were 19 papers that measured only the psychosocial field, without quality indicators. One paper measured only quality according to primary care or family medicine, but without a special field covering the psychosocial dimension. Only one paper really directly measured the quality of the psychosocial approach, and unfortunately this paper had too small a sample to draw firm conclusions.

Table 1. Findings.

Paper	Topic, study question	Sample size	Methods	Main results	Rating of the results[1]
(26)	Measuring the quality of motivation for physical activity from the health worker and whole professional team (pilot study)	N=424 (both sexes, over age 18, with a low level physical activity)	Systematic random sampling; intervention (professional health worker and team support physical activity) or control group	Motivational intervention by a physician and primary care team increased physical activity and improved social support	2
(27)	Differences in health care costs, doctor's visits, quality of well-being according to wellness intervention	N=33, N= 28 (23 finished the first and 15 the last study)	Intervention (1: relaxation and problem-solving practice; 2: psycho-educational and skill oriented: nutrition, relaxation, exercise, etc.) or control group; pre- and post- test values	Short wellness program in family medicine improved quality of life	3
(49)	Testing what influences adherence to medication	N=236 (mean 41 years, male majority, mostly African-Americans)	To test a model of medication adherence among individuals taking anti-retroviral medication	Taking of medication was affected by different psychosocial variables (self-efficacy, depression, and social support) and provided directions for adherence intervention	1
(28)	Measuring depression outcomes, satisfaction and functioning in women	N=123 (women with depression)	2 interventions (social intervention and anti-depressants) and control group (only antidepressants); tested after 3 and 9 months	Social treatment improved social functioning and satisfaction	3
(50)	Measuring the quality of promotion of physical activity	N= 38 patients (out of 55) over 65 years visiting a medical practice by appointment N=12 physicians for 2 focus groups	Activity counselling in primary care: written assessment and personal counselling evaluated by focus group with primary care physicians, second mailing to inactive patients, evaluated by questionnaire	Physical activity promotion must be included in multidimensional health promotion; promotion through primary care has high potential (healthy aging)	3

Paper	Topic, study question	Sample size	Methods	Main results	Rating of the results[1]
(29)	Measuring the association between health beliefs and negative health outcomes	Sample 1 N=202, Sample 2 N= 209	Prospective 2-panel design; psychosocial model of behaviours: social cognitive theory and theory of planned behaviour	Perceptions of the efficacy of treatment predicted outcomes of treatment and prevention	2
(30)	Measuring the influence of physical activity on drug prescribing in PC on physical activity levels, stages of change and quality of life	N=481 (both sexes, 12 to 81 years)	Uncontrolled clinical study; individualized physical activity on prescription (follow up at 6 months)	Increased self-reported physical activity level, stages of action and maintenance of physical activity; quality of life increased	3
(36)	Measuring satisfaction which can influence health care outcomes	N=702 patients (from 38 resident doctors)	Expectations before visit, measures after visit, telephone interview about fulfilled expectations	The fulfilment of patient expectations influenced satisfaction and consultation outcomes	2
(35)	Measuring how practice style influences outcomes	N=509 (adult patients)	Care by family physicians or general internist	More frequent patient-centred care offered by a family physician reduced annual medical care charges	1
(31)	Measuring clinical effectiveness of primary care model for diabetic patients	N=335 (experimental group N=185, control N=145)	Model of diabetes care provided by primary care service in comparison to care provided at specialist diabetes clinic	Model of diabetes care provided by primary care service combined patient focus and holistic care well	2
(32)	Effects of psychosocial intervention on substance reduction in people with mental illness	N=25 RCTs	Meta-analysis	No compelling evidence that supports any one psychosocial treatment over another was found	1
(37)	Impact of physical limitations on perceived quality of care	N=674 (adult family medicine patients)	Telephone survey of family patients	People with physical limitations experienced a disparity in perceived quality of care	3
(38)	Model with accessibility of services and professional-patient relationship, coordination within health care team and scientific-technical quality of the service	N=213 (primary health care teams)	Descriptive study	Identified model with three dimensions: inter-personal relationships (physician's information, attention to user's needs, time dedicated to the user, etc.), team organisation (support from colleagues, work feedback, etc.) and scientific-technical quality (quality of prescription standard, % anti-depressant medications, etc.)	2

Paper	Topic, study question	Sample size	Methods	Main results	Rating of the results[1]
(39)	Association between social factors and depression	N=122 (residents in family medicine and psychiatry)	Survey at intervals	Parenting was found to be a protective factor from burnout; women not as vulnerable as previously reported	1
(40)	Assessing patient-centred decision making, interpersonal style and communication	N=1664 (adult general medicine patients)	Telephone interview	Better interpersonal process of care may predict more favourable patient outcomes and present one of the efforts to reduce health care disparities in our patients	1
(41)	Influence of work and living conditions on health	N=5666	Cross-sectional study	The greater the financial distress and shame, the greater risk of psychosocial ill health	1
(42)	Nine quality indicators in 4 countries	N=4 (countries)	Data from health statistics agencies	Socioeconomic disparities in health care quality and health status were found	3
(43)	Patient-centred medical home and preventive services	N=24 (primary care settings)	Cross-sectional analysis	Patient-centred medical home highly correlated with preventive services delivery	2
(48)	Lowering hospitalizations in association with check-ups	N=660 (hospitalized patients)	Random sample	Regular health check-ups outside of the Family Health Strategy doubled the likelihood of hospitalization	1
(44)	Quality of life (health, independence, psychological and emotional well-being) affected by frailty status (reduced energy levels, depressive status, etc.)	N=239 (community dwelling outpatients aged 65+)	Cross-sectional survey	Quality of life was negatively affected by frailty status	3
(45)	Diabetes management and quality of life	N=400 (primary care patients with diabetes)	Cross-sectional survey	Diabetes-related complications, worse subjective health and dissatisfaction with medical care influenced worsening of QoL	3
(46)	Bio-psycho-social view associated with medical prescription	N=8430 (all general practices in England)	Ecological study	Socio-economic status, ethnic density, chronic disease explained 44% of the variance in the volume of antidepressants prescribed	1
(47)	Status of behavioural medicine in psychiatric and medical illness	N=9 (family medicine residency programs)	Survey	Behavioural medicine was found to be useful in the prevention and treatment of physical and psychiatric illness	1

Paper	Topic, study question	Sample size	Methods	Main results	Rating of the results[1]
(33)	Intervention (quality improvement program; patient-oriented medical model) led to reduction in hospitalization and more optimal allocation of healthcare resources	N=808 (elderly 65+ in single clinic)	Evaluation of intervention program for reduction in the hospitalization of elderly people	Allocation of resources in primary care brought about a decrease in hospitalization figures	1
(34)	Prevention and chronic disease management as main points in primary health care	N=30 (primary care practices)	Before and after study; intervention first 12 months; preventive care, and after this another 3-9 months, chronic illness management	Intervention (preventive manoeuvres according to Canadian Task Force on Preventive Health Care recommendations) was effective in producing improvements in preventive care performance also beyond the intervention period	1
(54)	Therapeutic model that has influence on quality of life	N=15 (gastroenterological patients)	Semi-structured interviews	The sample was too small for conclusions about the psychosocial treatment on quality of life of patients	3
(19)	Holistic work (stated as) especially important in preventive work and palliative care	N=7 (focus groups with 22 GPs and 30 DNs)	Focus groups	The possibility to use (w) holistic model in their work gave family physicians and district nurses a strong motivation; organisation of primary care was shown to be a barrier or facilitator	1
(51)	Quality of consultation composed of: family physicians' competence and their empathy/caring	N=11 (72 patients)	Focus groups with local community groups (n=8) and other local residents (n=3)	Patients from deprived areas expected a holistic family physician	3
(52)	Impact of evidence -based and patient- centred care on quality of care	N=5 (45 members)	Focus groups	Evidence-based and patient-centred care may influence the quality of care	1
(53)	Patients' perceptions of development of quality indicators for chronic disease	N=6 (focus groups for adults with epilepsy); N=15 (experts)	Focus groups; Delphi study; 10 patient-generated quality indicators; 5 rated by experts	Patients' perceptions of quality may be incorporated into future development of quality indicators for chronic disease	3
(55)	Model with influence on health outcomes	N=35 (married or previously married women with depressive disorder)	Qualitative investigation - interviews	Recommendation of using the psychosocial model for public health interventions and mental health promotion (in Indian context)	1

Paper	Topic, study question	Sample size	Methods	Main results	Rating of the results[1]
(56)	Bio-psychosocial model in chronic pain management strategy	N=25 (members of pain management teams)	Semi-structured interviews	Little impact of social factors in managing chronic pain, so the model may not achieve its full potential	1
(57)	Meeting patient needs to improve quality of care	N=13 (senior citizens, 65-91 years)	Semi-structured interviews	For older people with growing health problems, continuity of care, trust, free choice of family physician and an open attitude are highly valued	3
(58)	Effect of interpersonal process quality of medical consultations	N=21 (adult patients from 3 primary care clinics)	Semi-structured interviews	Patients with lower socio-economic status are least likely to expect holistic care or empowerment, judging the quality of the treatment outcomes according to human skills and attitudes (empathic and engaged family physicians) and perceived outcomes of treatment	2
(59)	Importance of holistic approach to treatment and support in methadone maintenance treatment	N=159 (opiate-dependent individuals 5 years after start of methadone treatment)	Interviews	QoL defined by psychological well-being and other psychosocial variables	3
(60)	How the patient's and physician's sociocultural influences shape health and health care	N=22 (family physicians)	Semi-structured in-depth interviews	Medicine and physicians should be socially and culturally neutral; by seeking to avoid bias, physicians might be denying the role of sociocultural influences in patients' health (access, treatment, outcomes)	1

[1]Rating scale 1-3;

(1): the study measured only the psychosocial approach

(2): the study measured quality of care as a secondary outcome

(3): the study measured quality of care as the primary outcome.

4 DISCUSSION

The themes of patient-centred behavioural medicine or psychosocial medicine are quite well presented in several papers, but there is little evidence of how effective these approaches are in the management of family practice patients.

Some studies addressed the impact of socioeconomic status and psycho-social variables on health care outcomes. Socioeconomic status (finance, shame, physical limitations, ethnic density, parenting, etc.) has an impact on quality of care (29, 37, 42, 46), especially when measured through quality of life (44). Quality of life is also associated with psychosocial variables, such as depression, social support, self-efficacy, chronic disease, etc. (29, 49, 59). A better interpersonal process predicts a more favourable outcome for the patient (28, 40, 46), as well as a strong motivation for family physicians and

nurses in their work (19). Not only does such a (w) holistic psychosocial approach result in higher quality outcomes (26, 27, 30, 50) but it is also very useful for prevention and treatment of not merely physical but also psychiatric illnesses (26, 47, 50). Well-developed primary care services are very important for the health of the population as well as for health care systems (33-35, 43, 48). According to the articles, the psychosocial factor or approach is very important in raising quality of life and therefore quality of medical treatment. It is therefore important that family physicians use it frequently in their medical encounters. Teachers should also highlight this part of being a family doctor in family medicine specialty training.

The strength of our study is that we can see that there is a paucity of literature concerning the effectiveness of the psychosocial approach in medicine. The fact that we found 36 papers concerning this topic, but nothing particular on the psychosocial aspects, calls for further research. We did not find any articles about the association between a broader, holistic bio-psycho-social approach and quality of care. We included quality of life, quality of care, quality of consultation, quality of well-being, perceived quality, satisfaction, good steps in prevention, lower health care costs, medication adherence, social functioning, health care disparities, lower levels of hospitalization and medical prescriptions. A further problem is the poor definition of the psychosocial approach; in our review, interventions covering patient-centred care, holistic care, prevention, socio-economic status, psychosocial well-being, and health beliefs, expectations, etc. were included.

The limitations of our study are that it was done in 2011, covering the years from 2007; there are other articles before and especially after October 2011. There are also some articles that are not available online (e.g. master's or doctoral theses), and others in languages other than English which were excluded. The main challenge in performing and presenting a review of this type is asking and answering a clear question. The predictor variable (the application of a psychosocial approach) and the outcome variable (improvements in quality of care) are not clearly defined in any of those papers. As a result, we are left with a description of many papers that seem irrelevant to the question.

5 CONCLUSIONS

The evidence of effectiveness of the psychosocial approach available in the literature is scarce and inconclusive, so further studies are needed. Studies in the field of doctors' holistic approach or doctors' psychosocial orientation which influences the relationship between the doctor and the patient, and

the quality outcomes of the treatment and the healing process, should be carried out.

Although the bio-psycho-social model is well proclaimed, it has little support in the available literature, mainly due to the lack of sound research which studies differences in quality of care between traditional biomedical and bio-psycho-social approaches in patient management. As there is some evidence that some aspects of the bio-psycho-social approach correlate with better quality of care, this opens a whole new field of research.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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ETHICAL APPROVAL

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KATEGORIJA PRISPEVKA

Kategorijo prispevka predlaga z vnosov v ustrezno polje avtor sam, končno odločitev pa sprejme urednik na osnovi predlogov recenzentov. Objavljamo izvirne znanstvene članke, metodološke članke, pregledne znanstvene članke, uvodnike, pisma uredništvu in recenzije knjig.

REFERENCE

Vsako navajanje trditev ali dognanj drugih morate podpreti z referenco. Reference naj bodo v besedilu navedene po vrstnem redu, tako kot se pojavljajo. Referenca naj bo navedena na koncu citirane trditve. Reference v besedilu, slikah in tabelah navedite v oklepaju z arabskimi številkami ((1), (2, 3), (4-7)). Reference, ki se pojavljajo samo v tabelah ali slikah, naj bodo oštevilčene tako, kot se bodo pojavile v besedilu. Kot referenc ne navajajte izvlečkov in osebnih dogovorov (slednje je lahko navedeno v besedilu). Seznam citirane literature dodajte na koncu prispevka. Literaturo citirajte po priloženih navodilih, ki so v skladu s tistimi, ki jih uporablja ameriška National Library of Medicine v Index Medicus. Uporabljajte numerično citiranje. Imena revij krajšajte tako, kot določa Index Medicus (popoln seznam na naslovu URL: http://www.nlm.nih.gov).

Navedite imena vseh avtorjev, v primeru, da je avtorjev šest ali več, navedite prvih šest avtorjev in dodajte et al.

Primeri za citiranje literature:

primer za knjigo:

1. Premik M. Uvod v epidemiologijo. Ljubljana: Medicinska fakulteta, 1998.
2. Mahy BWJ. A dictionary of virology. 2nd ed. San Diego: Academic Press, 1997.

primer za poglavje iz knjige:

3. Urlep F. Razvoj osnovnega zdravstva v Sloveniji zadnjih 130 let. In: Švab I, Rotar-Pavlič D, editors. Družinska medicina. Ljubljana: Združenje zdravnikov družinske medicine, 2002: 18-27.
4. Goldberg BW. Population-based health care. In: Taylor RB, editor. Family medicine. 5th ed. New York: Springer, 1999: 32-6.

primer za članek iz revije:

5. Barry HC, Hickner J, Ebell MH, Ettenhofer T. A randomized controlled trial of telephone management of suspected urinary tract infections in women. J Fam Pract 2001; 50: 589-94.

primer za članek iz revije, kjer avtor ni znan:

6. Anon. Early drinking said to increase alcoholism risk. Globe 1998; 2: 8-10.

primer za članek iz revije, kjer je avtor organizacija:

7. Women's Concerns Study Group. Raising concerns about family history of breast cancer in primary care consultations: prospective, population based study. Br Med J 2001; 322: 27-8.

primer za članek iz suplementa revije z volumnom in s številko:

8. Shen HM, Zhang QF. Risk assessment of nickel carcinogenicity and occupational lung cancer. Environ Health Perspect 1994; 102(Suppl 2): 275-82.
9. Payne DK, Sullivan MD, Massie MJ. Women's psychological reactions to breast cancer. Semin Oncol 1996; 23(Suppl 2): 89-97.

primer za članek iz zbornika referatov:

10. Sugden K, Kirk R, Barry HC, Hickner J, Ebell MH, Ettenhofer T. et al. Suicides and non-suicidal deaths in Slovenia: molecular genetic investigation. In: 9th European Symposium on Suicide and Suicidal Behaviour. Warwick: University of Oxford, 2002: 76.

primer za magistrske naloge, doktorske disertacije in Prešernove nagrade:

11. Bartol T. Vrednotenje biotehniških informacij o rastlinskih drogah v dostopnih virih v Sloveniji: doktorska disertacija. Ljubljana: Biotehniška fakulteta, 1998.

primer za elektronske vire:

12. Mendels P. Textbook publishers extend lessons online. Available Sept 23, 1999 from: http://www.nytimes.com/library/tech/99/09.

TABELE

Tabele v angleškem jeziku naj bodo v besedilu prispevka na mestu, kamor sodijo. Tabele naj sestavljajo vrstice in stolpci, ki se sekajo v poljih. Tabele oštevilčite po vrstnem redu, vsaka tabela mora biti citirana v besedilu. Tabela naj bo opremljena s kratkim angleškim naslovom. V legendi naj bodo pojasnjene vse kratice, okrajšave in nestandardne enote, ki se pojavljajo v tabeli.

SLIKE

Slike morajo biti profesionalno izdelane. Pri pripravi slik upoštevajte, da gre za črno-beli tisk. Slikovno gradivo naj bo pripravljeno:

- črno-belo (ne v barvah!);
- brez polnih površin, namesto tega je treba izbrati šrafure (če gre za stolpce, t. i. tortice ali zemljevide);
- v linijskih grafih naj se posamezne linije prav tako ločijo med samo z različnim črtkanjem ali različnim označevanjem (s trikotniki, z zvezdicami…), ne pa z barvo;
- v grafih naj bo ozadje belo (tj. brez ozadja).

Črke, številke ali simboli na sliki morajo biti jasni, enotni in dovolj veliki, da so berljivi tudi na pomanjšani sliki. Ročno ali na pisalni stroj izpisano besedilo v sliki je nedopustno.

Vsaka slika mora biti navedena v besedilu. Besedilo k sliki naj vsebuje naslov slike in potrebno razlago vsebine. Slika naj bo razumljiva tudi brez branja ostalega besedila. Pojasniti morate vse okrajšave v sliki. Uporaba okrajšav v besedilu k sliki je nedopustna. Besedila k slikam naj bodo napisana na mestu pojavljanja v besedilu.

Fotografijam, na katerih se lahko prepozna identiteta bolnika, priložite pisno dovoljenje bolnika.

MERSKE ENOTE

Naj bodo v skladu z mednarodnim sistemom enot (SI).

KRATICE IN OKRAJŠAVE

Kraticam in okrajšavam se izogibajte, izjema so mednarodno veljavne oznake merskih enot. V naslovih in izvlečku naj ne bo kratic. Na mestu, kjer se kratica prvič pojavi v besedilu, naj bo izraz, ki ga nadomešča, polno izpisan, v nadaljnjem besedilu uporabljano kratico navajajte v oklepaju.

UREDNIŠKO DELO

Prispelo gradivo z javnozdravstveno tematiko posreduje uredništvo po tehnični brezhibnosti v strokovno recenzijo trem mednarodno priznanim strokovnjakom. Recenzijski postopek je dvojno slep. Po končanem uredniškem delu vrnemo prispevek korespondenčnemu avtorju, da popravke odobri in upošteva. Popravljen čistopis vrne v uredništvo po spletni aplikaciji Editorial Manager. Sledi jezikovna lektura, katere stroške krije založnik. Med redakcijskim postopkom je zagotovljena tajnost vsebine prispevka. Avtor dobi v pogled tudi prve, t. i. krtačne odtise, vendar na tej stopnji upoštevamo samo še popravke tiskarskih napak. Krtačne odtise je treba vrniti v treh dneh, sicer menimo, da avtor nima pripomb.

V uredništvu se trudimo za čim hitrejši uredniški postopek. Avtorji se morajo držati rokov, ki jih dobijo v dopisih, sicer se lahko zgodi, da bo članek odstranjen iz postopka.

Morebitne pritožbe avtorjev obravnava uredniški odbor revije.

Za objavo članka prenese avtor avtorske pravice na Nacionalni inštitut za javno zdravje kot založnika revije (podpiše Izjavo o avtorstvu in avtorskih pravicah). Kršenje avtorskih in drugih sorodnih pravic je kaznivo.

Prispevkov ne honoriramo in tudi ne zaračunavamo stroškov uredniškega postopka.

Avtor dobi izvod tiskane revije, v kateri je objavljen njegov članek.