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RESEARCH ARTICLE

ANXIETY AND DEPRESSION AS REACTION TO DISTRESS AND PTSD AMONG CANCER PATIENTS

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ABSTRACT

Purpose To explore relationship between untreated psycho- social distress and return to work among cancer patients in the first year after diagnosis. **Methods** This longitudinal study was conducted in family practice among 174 cancer (out) patients in the first year after diagnosis from 2011 to 2016. Psycho- social distress screen of each individual case with questionnaire HADS, and the total sample was divided into 3 groups during the evaluation. A key factor in the creation of the groups was the time elapsed from the moment of confirmation of the diagnosis: T1, 1-14 days, n = 56 patients, the first group; T2, 15 days- 6 months, n = 79 patients; the second group; and T3, 7-12 months n = 39 patients, the third group. **Results** The prevalence rate of distress was very high: 70% in the first 14 days, 66% from 15 days to 6 months and 100% from 7 to 12 months after diagnosis. **Conclusion** Untreated anxiety and depression symptoms are common problems in cancer patients from the first day since cancer diagnosis and programs that routinely screen anxiety and depression among cancer patients are feasible.

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INTRODUCTION

Because cancer patients during treatment use long-term sick leave, they perceived poorer physical health, poorer mental health, greater usage of medical services, poorer social integration, loss of worth and self-confidence, less monetary resources and trans-generational effects. Returning to work can reverse these negative changes. Across all diagnosis, cancer patients are at significantly increased risk for psychological symptoms and mental health disorders (Mitchel et al., 2011: Bultz, 2006; Wells, 2013). About, one- third of cancer patients experience symptoms of psychological distress (Mitchel et al., 2011; Bultz, 2006). Distress of cancer patients is defined as a multifactorial unpleasant emotional experience of a psychological, social and spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment. Distress is expressed with different emotional experiences, symptoms of anxiety and depression (Wells, 2013). On other site, or cancer survivors, the ability to work is important to maintaining social relationships, self esteem and psychological well-being.

The return to workplace is strongly influenced by the degree to which cancer affected four key factors: self-identity, meaning and significance of work, family and financial context and work environment (Wells, 2013). For possibility to returning to work needs to be healthy enough to work and to have safe health workplaces, physically and emotionally. Many researchers have come to the conclusion that the oncology patients have common difficulty expressing emotions, inability to open expression of aggression and suppression of depressive moods (Mitchel et al., 2011; Bultz, 2006; Wells, 2013; Aaronson, 2014; Bultz, 2011; Carlson, 2004; Gregurek, 2010). In short, these people are well adapted to others, and alienated from themselves (Aaronson, 2014; Bultz, 2011). Diagnosing mental disorders is difficult because the clinical picture superimposed psychic and somatic symptoms, particularly in relation to pain (Aaronson, 2014). Patients are most often anxious at the time a doctor suspected malignant disease and they submit to treatment (Gregurek, 2010; Holland, 2010). Cancer can be observed as a direct threat to life, it represents the exposure to catastrophic traumatic event that results in acute stress reaction or powerful stress exposure (Shimizu, 2005; Schmitt, 2003; Holland, 2013; Tope, 1993; Carlson, 2003). Early detection and management of unhealthy behaviors and mental health issues in primary care has the potential to prevent or ameliorate many chronic diseases and increase patients' well- being (Pranjić, 2012). The aim of the research is evaluating anxiety and depression in relation to the time elapsed from the moment of acknowledgment and confirmation of the carcinoma diagnosis among patients.

METHODS

This longitudinal study for evaluating anxiety and depression was conducted from January 2011 to December 2016 in compliance with Declaration of Helsinki, 2011 (Dunn, 2012).

Study subjects: The participants of the study were 174 cancer patients who are control and treat in Family Medicine clinics in Tuzla Canton, Bosnia and Herzegovina. Patients were recruited using face-to-face methods via 6 family medicine physicians and based on pre-defined inclusion criteria where physicians invited each patient with cancer diagnosis confirmed before ≤ 12 months to participate in screening for anxiety and depression. The inclusion criteria for patients were diagnosis of cancer from the first day to 12 months. Cancer patients were conducted screen for anxiety and depression during control examination in the family clinic.

Screening tool: The survey contained clinical screening examination and interviewing with Hospital anxiety and depression scale (HADS), as screening instrument. The subjects were divided into three groups. A key factor in creation of the group was the time elapsed from the moment of acknowledgment and confirmation of the diagnosis of disease: T1 < 14 days; T2 from15 days to 6 months; T3 >7 months (at the most 12 months) according to the stress theoretical approach (13-16). Questions on the clinical characteristics of malignant disease with demographic and individual characteristics of patients were set and recorded responses of patients during clinical examination.

The Hospital Anxiety and Depression Scale (HADS) were developed by Zigmond and Snaith, 1983 (19-21). HADS is a validated screening instrument for anxiety and depression in somatically ill patients and excludes symptoms that may arise from somatic aspects of illness (e.g. insomnia, weight loss and fatigue). (20). The measure consists of 14- items on a 4-point Likert scale (range 0-3) comprising an anxiety and depression subscale. For both subscales a total score is calculated (ranging from 0- 21). According to the German Manual of the HADS (20-21), a score (aHADS) of 11 or above indicates anxiety and a score (bHADS) of 11 or above indicates depressive disorder.

Statistical analysis: The data were managed and analyzed by SPSS software version 18.0 (SPSS, Inc., Chicago, IL, USA). All continuous variables were shown as the mean and standard deviation (SD). Demographic, clinical data of disease of patients, anxiety and depression symptoms per groups were compared using the chi- square carried out analysis of variance for continuous variables and the chi- square test for categorical variable. Nonparametric Spearman correlation test and logistic regression analysis ANOVA were used to test the predictive potential demographic (individual) characteristics and medical characteristics of the disease, the values of dichotomized HADS. All statistical tests were carried out with a level of statistical probability of 95% (p < 0.05).

Ethical approval: The participation in the survey was voluntary. The study protocol was approved by the Ethics Committee of Medical Sciences, University Family Centre Tuzla.

RESULTS

The mean age of our 174 patients was 54.63 ± 11.46 years (94.5% in active working age, <65 years) and the mean age of the respondents at which their cancer diagnosis was confirmed 54.34 ± 26.11 years. The mean score of anxiety as distress reaction aHADS 19.24±4.804 (>11) and mean score of depression as distress reaction bHADS 12.48±3.927 (>11), were revealed potential distress in all patients (Figure 1). Table 1 shows that were more women 91(52%) in relationship to men (48%). The first group consists of 56 subjects; the second group includes 79 respondents and third group 39 patients. There were significant gender differences between groups (male: women in three groups- 23:33(I):35:44 (II):25:14 (III) vs. 41%:59% (I): 44%:56% (II):64%:36% (III), χ^2 test= 5.558, P=0.041). The breast cancer was the most common diagnosis, followed by abdominal and lung cancer. Fifty one percent of carcinoma patients had a primary tumor. No significant were found regarding education levels, differences employment conditions, family environment characteristics, carcinoma location and treatment of cancer. Metastases was not developed in 53 (30%) of cases. The majority patients had undergone radiotherapy 89 (51%). Palliative care was treatment in 13 (8%) respondents. Metastasis was most frequent in the first group (P=0.007), and has revealed that the most often cancer was diagnosed late which led to development of metastases.

Table 2 indicates that the prevalence rate of respondents who have scored high on the anxiety is generally high in oncological patients in each groups. In a total sample 130/174 (75%) respondents suffered anxiety. Anxiety was most frequent 39 (100%) in third group. From depression according to bHAD score suffered 88 (51%) patients. Prevalence rate of anxiety (39:52:39 vs. 70%:66%:100%, x2-test= 105.190, P< 0.000) and depression (21:36:31 vs. 38%:46%:79%, χ 2-test= 83.226, P< 0.000) significantly increased in relation to increased time passed from diagnosis of malignant disease. Table 3 shows that patients of the first group most often felt tense (P=0.009), were excessively worrying (P=0.001) and had unexpected panic attacks (P=0.001) than patients in the other 2 groups. The highest prevalence of constant worries (P=0.028) and anticipating the worst (P=0.001) was in second group. The third group was expressed with inability to relax and stomach upset significantly more than the other two groups. The most common symptoms of distress in oncological patients was perception of restless in each three groups. Patients in the first group most often felt stopped and slowed down than patients in the other 2 groups (P = 0.003). Be cheerful was significantly very rare perception (P=0.003) among patients in second group in relationship to the other 2 groups. The inability to still enjoy the things they used to enjoy (P=0.004), inability to laugh and see the funny side of things (P=0.007), inability look forward with enjoyment to things (P=0.005) and inability to enjoy a good TV or radio programme or book (P=0.005) were most often depresive symptoms among patients of third group than in the other 2 groups. Table 4 shows multivariate association of demographic and clinical characteristics of malignant disease (independent variables) and the anxiety and

Participant characteristics	No (%)			Differences
(No=174)	L group <14	II group 14 days 6 months	III > 6 months	between groups
	days n=56	n=79	n=39	χ^2 test, P
Sex				
Mele	23 (41)	35 (44)	25 (64)	5.558,
Female	33 (59)	44 (56)	14 (36)	0.041
Education level				5.000
Elementary school	22 (39)	18 (23)	14 (36)	0.287
High school	29 (52)	50 (63)	20 (51)	
Higher education	5 (9)	11 (14)	5 (13)	
Employment condition				5.064
working	9 (16)	16 (20)	8 (21)	0.536
on sick leave	9 (16)	17 (22)	11 (28)	
out of work	28 (50)	35 (44)	18 (46)	
retired	10 (18)	11 (14)	2 (5)	
Family environment				3.511
with husband/wife	31 (56)	35 (44)	22 (56)	0.476
aloun	8 (14)	14 (18)	3 (8)	
family with children	17 (30)	30 (38)	14 (36)	
Carcinoma localisation				6.473
breast	20 (36)	32 (41)	13 (34)	0.594
abdominal	13 (23)	11 (14)	6 (15)	
head and neck	10 (18)	21 (27)	6 (15)	
genitourinary system	2 (3)	2 (2)	2 (5)	
lung	11 (20)	13 (16)	12 (31)	
Metastasis				14.210
no	18 (32)	17 (22)	18 (46)	0.007
yes	34 (61)	43 (54)	18 (46)	
unclear	4(7)	19 (24)	3 (8)	
Treatment				15.123
Surgery	14 (25)	21(27)	8 (21)	0.057
Chemotherapy	10 (18)	9 (11)	2 (5)	
Radiotherapy	29 (52)	41 (52)	19 (49)	
Surgery and chemotherapy	3 (5)	2(2)	3 (8)	
Palliative treatment	0	6(8)	7 (17)	
Status of disease				318.584
primary tumor	31 (55)	35 (44)	22 (56)	< 0.001
metastatic tumor	8 (15)	14 (18)	3 (8)	
repeated tumor	17 (30)	30 (38)	14 (36)	

Table 1. Comparing demographic and clinical characteristics for oncological patients per groups (n=174)

 Table 2. Comparing anxiety and depression prevalence rate as reaction to distress expressed by aHAD and bHAD questionnaire per groups in oncological patients (n=174)

Anxiety and Depression	No (%)			Differences
× 1	I group <14 days n=56	II group	III > 6 months $n=39$	between groups
		14 days-6 months n=79		χ^2 test, P
Anxiety (aHAD)				
Anxiety	39 (70)	52 (66)	39 (100)	105.190.
No anxiety	17 (30)	27 (34)	0	P<0.000
Depression (bHAD)				
Depression	21 (38)	36 (46)	31 (79)	83.226,
No depression	35 (62)	43 (54)	8 (21)	P<0.000

depression as reaction to distress among oncological patients (n=174). Development of anxiety in oncological patients was statistically significant associated with to be woman (β =0.200; 95%CI, 0.388- 0.383; P=0.014), lower education level of patients (β= -0.257; 95%CI, -3.170- 0.697; P=0.002), live alone without family support (β = -0.265; 95%CI, -2.158- -0.593; P=0.001), and bad state of diseases (β=0.323; 95%CI, 1.129- 8.080; P<0.000). Predictors of depression in oncological patients were lower education level of patients (β = -0.256; 95%CI, -2.513- -0.647; P=0.001), live alone without family support (β = -0.239; 95%CI, -1.609- -0.428; P=0.001), and bad state of disease (β=0.337; 95%CI, 1.069- 2.541; P<0.000) with discovered metastasis (β = -0.216; 95%CI, -2.134- -0.420; P=0.004) as very important clinical determinants of cancer. PTSD predicted lower education level of patients (β= -0.204; 95%CI, -1.443- -0.170; P=0.013), live

alone without family support (β = -0.244; 95%CI, -1.066- -0.260; P=0.001) and clinical bad state of disease (β =0.263; 95%CI, 0.398- 1.402; P=0.001).

DISCUSSION

Key findings

- Anxiety and depression mood are common problems in cancer patients from the first day in the first year since cancer diagnosis;
- Fear and a large amount of helplessness that arises from the initial knowledge about the cancer diagnosis with varying intensity retained during disease because the constant fear of the uncertain outcome of the disease and the fear of death, in particular;

Table 3. Comparison prevalence of symptoms of anxiety (by aHAD) and depression (by bHAD) per groups as reaction to distress expressed in oncological patients (n=174)

Anxiety, the items of aHAD	No (%)			Differences
	I group <14 days	II group	III > 6 months	between groups
	n=56	14 days-6 months n=79	n=39	χ^2 test, P
Felt tense or wound up				
Most of the time	5 (9)	9 (12)	0	17.005
A lot of the time	34 (61)	41 (52)	16 (41)	17.085,
lime to time, occasionally	15 (27)	16 (20)	18 (46)	P= 0.009
Not at all Folt frightened as if excluding about to hermon	2 (3)	13 (16)	5 (13)	
Very definitely and quite hadly	1 (2)	5(6)	0	
Not quite so much	1(2) 18(32)	29 (37)	0	22.068
Only a little	26 (46)	33 (42)	1(3) 29(74)	P=0.001
Hardly at all	11 (20)	12 (15)	9(23)	1 0.001
Worrying thoughts go through mind	11 (20)	12 (13)) (23)	
A great deal of the time	4(7)	12 (15)	0	
A lot of the time	24 (43)	29 (37)	11 (28)	14.143,
From the time to time, but not to often	22 (39)	32 (41)	19	P=0.028
Only occasionally	6(11)	6(7)	9	1
Be able to sit at easy and felt relaxed				
Usually	34 (61)	40 (51)	8 (21)	18.133,
Rarely	17 (30)	32 (40)	21 (54)	P= 0.001
Not at all	5 (9)	7 (9)	10 (25)	
Felt like butterflies in the stomach				
Never	7 (13)	14 (18)	3 (8)	
Sometimes	36 (64)	36 (46)	14 (36)	16.319,
Often	7 (12)	24 (30)	15 (39)	P = 0.012
Very often	6 (11)	5 (6)	7 (17)	
Felt restless as if had to be on the move				
Very definitely and quite badly	6(11)	9(11)	0	10.000
Not quite so much	32 (57)	36 (46)	19 (50)	10.000,
Unly a little	13 (23)	24 (30)	10 (25)	P= 0.099
Hardly at all	5 (9)	10 (13)	10 (25)	
Very often	10 (19)	26 (33)	4 (11)	
Quite often	26 (47)	20 (33)	$\frac{4(11)}{12(31)}$	26.603
Not very offen	17 (30)	22 (28)	12 (31)	P = 0.001
Not at all	3(5)	5(6)	10 (25)	1 0.001
Depression the items of bHAD	5(5)	3 (0)	10 (25)	
Still enjoy the things which used to enjoy				
Definitely as much	14 (25)	10(13)	0	
Not quite so much	16 (29)	34 (43)	13 (33)	18.958,
Only a little	24 (43)	27 (34)	19 (50)	P= 0.004
Hardly at all	2 (3)	8 (10)	7 (17)	
Be able to laugh and see the funny side of things				
As much as always	21 (38)	28 (35)	3 (8)	
Not quite so much now	19 (33)	25 (32)	20 (51)	17.754,
Definitely not so much now	16 (29)	20 (25)	11 (28)	P=0.007
Not at all	0	6 (8)	5 (13)	
Felt cheerful				
Not at all	13 (23)	26 (33)	3 (8)	
Not often most of time	24 (43)	38 (48)	22 (56)	19.853, D= 0.002
Sometimes	16 (29)	6(8)	7 (18)	P= 0.003
Most of the time	3 (5)	9(11)	/ (18)	
Almost all the time	0	7(0)	2(6)	
Almost all the time	0	7 (9)	2 (6)	20.100
Sometimes	40 (71)	37 (47)	15 (38)	P = 0.003
Not at all	10 (29)	9 (11)	7 (18)	1 0.005
Have lost interest in appearance	0) (11)	/ (10)	
Completely	21 (38)	34 (43)	6(15)	
Not worried enough	15 (27)	18 (23)	12 (31)	18.786.
Not worried so much	17 (30)	24 (30)	12 (31)	P = 0.005
Worried as always	3 (5)	3 (4)	9 (23)	1
Be able look forward with enjoyment to things	- \ - /	- \ /		1
As much as always	18 (32)	25 (32)	3 (8)	1
Not quite so much now	21 (38)	33 (42)	18 (46)	23.141,
Definitely not so much now	16 (28)	20 (25)	11 (28)	P= 0.001
Not at all	1 (2)	1(1)	7 (18)	
Be able enjoy a good TV or radio or book				
Often	33 (59)	34 (43)	10 (26)	
Sometimes	15 (27)	27 (34)	12 (31)	18.388,
Rarely	6 (11)	14 (18)	9 (23)	P= 0.005
Almost never	2 (3)	4 (5)	8 (20)	

Table 4 Multivariate associations of demographic and clinical characteristics of malignant disease (independent variables); and the anxiety and depression (dependent variables) among oncological patients

Predictors of anxiety as reaction to distress (a HAD dependent variable)*	β and 95% confidence interval(95% CI)		
	β	P	95%CI
Sex	0.200	0.014	0.388-0.383
Age	-0.002	0.995	-0.219-2.218
Education level	-0.257	0.002	-3.170-0.697
Family environment	-0.265	0.001	-2.1580.593
State of employment	0.065	0.416	-0.461-1.109
Tumour localisation	-0.027	0.728	-0.451-0.316
State of disease	0.323	0.000	1.129-8.080
Metastasis	-0.064	0.422	-1.598-0.673
Type of treatment	-0.069	0.404	-0.985-0.398
Passed time since diagnosis of carcinoma (groups)	-0.154	0.558	-0.284-0.154
Predictors of depression as reaction to distress (b HAD dependent variable)	β	Р	95%CI
Sex	-0.040	0.591	-1.438-0.822
Age	0.126	0.610	-0.122-0.208
Education level	-0.256	0.001	-2.5130.647
Family environment	-0.239	0.001	-1.6090.428
State of employment	0.049	0.505	-0.392- 0.793
Tumour localisation	-0.070	0.322	-0.435-0.144
State of disease	0.337	0.000	1.069-2.541
Metastasis	-0.216	0.004	-2.1340.420
Type of treatment	0.012	0.875	-0.480-0.563
Passed time since diagnosis of carcinoma (groups)	-0.060	0.804	-0.186-0.144
Predictors of PTSD (dependent variable	β	Р	95%CI
Sex	-0.005	0.952	-0.747-0.795
Age	0.145	0.582	-0.144-0.081
Education level	-0.204	0.013	-1.4430.170
Family environment	-0.244	0.001	-1.0660.260
State of employment	0.046	0.556	-0.525- 0.283
Tumour localisation	-0.004	0.958	-0.203-0.192
State of disease	0.263	0.001	0.398-1.402
Metastasis	-0.010	0.902	-0.621-0.548
Type of treatment	0.141	0.084	-0.043-0.669
Passed time since diagnosis of carcinoma (groups)	0.154	0.550	-0.079-0.147
*ANOVA			

- anxiety is dominant mental disorder in all cancer patients the seven month after confirmed diagnosis;
- depression accompanies anxiety leads the patient to depersonalization and decrease self-esteem and destroys him secure social connections;
- the mental support of cancer patients should begin with the diagnosis of cancer.

Depression is highly prevalent in cancer patients. In clinical practice there is concer about both insufficient and excessive diagnosis and treatment of depression (Jacobson, 2007). Fever studies have examinated the 4-week-, 12 month and lifetime prevalence rates prevalence of mental disorders in cancer patients (Dunn, 2012; World Medical Association Declaration of Helsinki, 2006). Because the psychological adaptation of patients with malignant disease passes through three stages we conducted screening and evaluation of anxiety and depression in relation to the time after the confirmed cancer diagnosis: from 1-14 days (T1), from 15 days -6 months (T2), and 7-12 months (T3). Acute phase occurs during the diagnosis, followed by prolonged stress reaction during treatment and the third chronic phase occurs after treatment (Carlson, 2004; Gregurek, 2010). Our results showed that is often the hardest the third chronic phase occurs after treatment. The prevalence of anxiety among all of 39 respondents who knew that they had cancer more than 6 months is extremely high, 100%. On the other hand, cancer patients belittle their psychological problems and oncologists often dont think about mental disorders of their cancer patients (Mitchel, 2011; Bultz, 2006). Therefore, patients are usually left without timely and adequate treatment of anxiety that usually turns into chronic suffering burn-out syndrome, post-traumatic stress disorder or severe episodes of depression or anxiety (Wells, 2013).

Symptoms of anxiety and depression may also occur independently and progress quite differently after cancer diagnosis. Anxiety symptoms vary between 10%-30% [Stark, 2008; Zabora, 2001]. Anxiety is common in cancer patients and most often was not recognized [Zabora, 2001].

Anxiety symptoms are common at the initial stage of cancer diagnosis during treatment decisions, as well as with concerns about return of the disease or disease progression but rate of fully developed anxiety disorders is not significantly higher from the one in general population. The prevalence rate of depressive symptoms varies between 10%-25%, relatively Anxiety is common in cancer patients and most often was not recognized. (Pranjić, 2016; Reich, 2008; Connor, 2011; Mehnert, 2007; Stark, 2000; Zabora, 2001). Results of our study were not in accordance with results of previous cited studies. Our cancer patients had higher prevalence rate of depression in the first year after diagnosis, 51% (at least two times more). The significant level of vulnerability to anxiety was found in women, patients with low level of education, patients who live alone without family support and patients who have bad clinical state of disease. Anxiety was associated with bad state of cancer.

Strengths and weaknesses: Groups of sample of cancer patients in the first year after confirmed diagnosis was selected to ensure that the results will be representative. Anxiety and depression mood have analysed in relatioship to the time elapsed from diagnosis in three group in accordance with theoretical model of stress. Samples of cancer patients in the first year after confirmed diagnosis was selected to ensure that the results will be representative of the population studied.

Anxiety and depression mood have analysed in relatioship to the time elapsed from diagnosis in three group in accordance with theoretical model of stress. Fever studies have examinated the 4-week-, 12 month and lifetime prevalence rates prevalence of mental disorders in cancer patients (18-19). Because the psychological adaptation of patients with malignant disease passes through three stages we conducted screening and evaluation of anxiety and depression in relation to the time after the confirmed cancer diagnosis: from 1-14 days (T1), from 15 days -6 months (T2), and 7-12 months (T3). The present study is compromised by some limitations, for example, the sample. The sample consisted of cancer patients with a good performance status, although more than half of them were in a methastatic disease phase. But, regarding that traditional criteria for a screening tool (e.g. high specificity, high sensitivity, "do not harm" to patients, ease for use, and effectiveness, to improve communication between physician and patient) is reason why we used HADS screening tool. We followed the existing literature in using HADS as psychometric questionnaire as reference criterion choice, more information is needed regarding the accuracy of the HADS with respect to a standard psychiatric screening tool. Early case- screening and evaluation of anxiety and depression is an important factor to improve the health of cancer patients (Jacobson 2007; Warmenhoven, 2012).

Conclusion

Early intervention and psychological support for anxiety and depression disorders is benefit to cancer patients, but early screen and early diagnosis of cancer and good treatment is imperativ in my country too. In summary our research data provide an important advice for a implementation of initial screening and assessment for anxiety and depression in cancer patients. The found increasing trend of anxiety and depression during the first year after diagnosis early diagnosis needs allow early, in the first day (week) and adequate psychosocial support. Timely, professional mental support will preserve not only mental health of cancer patients, but also all the life goals and motivation for work and other social values. Future research could have purpose to measure positive effects of early screening of anxiety and depression, too.

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