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The correlation between depression and anxiety levels and quality of life in essential thrombocytosis and polycythemia vera patients

Esansiyel trombositoz ve polisitemi vera hastalarında depresyon ve anksiyete düzeyleri ile yaşam kalitesi arasındaki ilişki

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Abstract

Purpose: This study was conducted to assess the correlation between depression and anxiety and quality of life (OQL) in essential thrombocytosis (ET) and polycythemia vera (PV) patients.

Material and methods: The study was conducted in the Hematology Clinic of a training and research hospital in the Aegean region of Turkey between July 2016 and May 2017. A total of 60 patients (30 ET and 30 PV) were included in the study. Eastern Cooperative Oncology Group (ECOG), Karnofsky scale, EORTC QLQ-C30, and Hospital Anxiety and Depression Scale (HADS) were used to collect the data. The data was analyzed using SPSS 20.0 packaged software. The results were assessed at the confidence interval of 95% and significance level of $p<0.05$.

Results: The average age of ET and PV patients were 60.3±11.2/years and 58.7±11.7/years, respectively. ECOG and Karnofsky performance scores were similiar in two groups. There was no significant difference between the groups in terms of EORTC QLQ-C30 overall QOL and HADS-D scores. HADS-A score mean rank was higher in PV patients ($p=0.000$) (ET:22.1 in, PV:38.9). Score mean rank of EORTC QLQ-C30 fatigue, dyspnea and financial difficulty subscales (41.5, 38.2, 38.1) in ET patients and score mean rank of EORTC QLQ-C30 cognitive functioning, pain and diarrhea subscales (43.8, 38.9, 41.1) in PV patients were higher ($p=0.000$). There was a significant correlation between HADS-A and HADS-D scores and EORTC QLQ-C30 overall QOL score ($p<0.01$) in ET patients.

Conclusion: Cognitive function, pain and diarrhea subscale scores of anxiety level and quality of life were higher in PV patients. Fatigue, dyspnea and financial difficulties subscale scores of the quality of life were higher in ET patients. As the depression and anxiety levels of both ET and PV patients increase, quality of life decreases.

Key words: Anxiety, depression, quality of life, thrombocytosis, polycythemia.

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Özet

Amaç: Bu çalışma, esansiyel trombositoz (ET) ve polisitemi vera (PV) hastalarında gözlenen depresyon ve anksiyete durumları ile yaşam kalitesi (YK) arasındaki ilişkinin değerlendirilmesi amacıyla yapıldı.

Gereç ve yöntem: Araştırma, Temmuz 2016-Mayıs 2017 tarihleri arasında Türkiye'nin Ege Bölgesi'ndeki bir eğitim araştırma hastanesinin Hematoloji Kliniği'nde yürütüldü. Toplam 60 hasta (30 ET ve 30 PV) araştırmaya dahil edildi. Veriler, Eastern Cooperative Oncology Group (ECOG), Karnofsky skalası, European Organization for Research and Treatment of Cancer Quality of Life Group (EORTC QLQ-C30) ve Hastane Anksiyete Depresyon Skalası (HADS) ile toplandı. Veriler SPSS 20.0 paket programı kullanılarak analiz edildi. Sonuçlar %95'lik güven aralığında $p<0,05$ düzeyinde değerlendirildi.

Bulgular: Araştırmaya katılan ET ve PV hastalarının yaş ortalaması sırasıyla 60,3±11,2/yıl ve 58,7±11,7/yıl idi. ECOG ve Karnofsky performans skalalarına göre ET ve PV hastalarının performans durumu benzerdi ($p>0,05$). ET ve PV hastaların EORTC QLQ-C30 genel YK ve HADS-D puanları benzerdi ($p>0,05$). PV hastalarının HADS-A puanı sıra ortalaması 38,9 olup ET hastalarına göre daha yüksekti ($p=0,000$). ET hastalarında EORTC QLQ-C30 halsizlik, nefes darlığı ve mali zorluklar alt boyut puanları sıra ortalaması (41,5, 38,2, 38,1), PV

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hastalarında ise EORTC QLQ-C30 bilişsel fonksiyon, ağrı ve diare alt boyut puanları sıra ortalaması (43,8, 38,9, 41,1) daha yüksekti (p=0,000). ET hastalarında HADS-A ve HADS-D puanları ile EORTC QLQ-C30 genel YK puanı arasında anlamlı ilişki vardı (p<0,01).
Sonuç: Anksiyete düzeyi ile yaşam kalitesinin bilişsel fonksiyon, ağrı ve ishal alt ölçek puanları PV hastalarında daha yüksekti. Yaşam kalitesinin yorgunluk, dispne ve finansal güçlükler alt ölçek puanları ise ET hastalarında daha yüksekti.

Anahtar kelimeler: Anksiyete, depresyon, yaşam kalitesi, trombositoz, polisitemia.

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Introduction

Essential thrombocytosis (ET) and polycythemia vera (PV) are diseases with an insidious onset and they are included in chronic myeloproliferative neoplasm (MPN) [1]. PV and ET are characterized by the excessive production of erythroid or megakaryocyte series and the other disease characteristics include leukocytosis, splenomegaly, thrombosis, hemorrhage, microcirculation symptoms, itching and leukemic or fibrotic transformation risk. ET and PV may transform to myelofibrosis and acute myeloid leukemia (AML) in the course of time. This transformation is the most serious complication among all MPNs [2]. In the diagnosis of both diseases, the morphological examination of bone marrow is quite important. Also, the existence of JAK2 mutation is expected in PV and JAK2, calreticulin (CALR) or myeloproliferative leukemia (MPL) mutations are observed in patients with ET [3].

Anxiety and depression are the most common psychological disorders observed in patients with both solid tumors and hematologic malignancy. It was reported in a study that the prevalence of clinical depression in malignancy patients was between 13% and 40% [4]. Due to the stress and negative effects in the daily lives of the patients caused by the microvascular and thrombotic symptom profile of ET and PV, quality of life (QoL) of the patients is significantly impaired and the patients have an increased tendency to anxiety and depression during treatment [5].

Health-related QoL has many variables ranging from physical, emotional, social and cognitive functions to disease symptoms. QoL assessments is an important method used by clinicians in recent years especially in examining the psycho-social wellbeing of the patients with malignity [6]. In the literature, there is a limited number of studies that have examined the changes observed in quality of life and depression and anxiety levels of the patients with ET and PV. The aim of this study was to assess the correlation between depression and anxiety observed in ET and PV patients and their quality of life.

Material and methods

Participants and data collection

The study was conducted in Hematology Clinic of Health Sciences University Tepecik Training and Research Hospital between July 2016 and May 2017. A total of 60 patients including 30 followed due to the diagnosis of ET and 30 followed due to the diagnosis of PV were included in the study. Patients diagnosed at least one year and at most five years ago were included in the study. Patients diagnosed with both ET and PV were using ASA. Patients using any drug groups other than ASA were not included in the study. Patients who have artery disease, heart failure, chronic obstructive pulmonary disease, asthma, iron-deficiency anemia, connective tissue disease, with chronic psychiatric disorders or physical disabilities, active infection and malignancy, smoking and/or alcohol use were excluded from the study. Patients who were not residing in the province of izmir, illiterate, did not agree to participate in the study and did not sign the written consent form were excluded from the study.

The performance of the participants was assessed with two different performance scales: Eastern Cooperative Oncology Group (ECOG) and Karnofsky. The data on quality of life was collected using European Organization for Research and Treatment of Cancer Quality of Life Group (EORTC QLQ-C30). Anxiety

and depression were assessed using Hospital Anxiety and Depression Scale (HADS).

Eastern Cooperative Oncology Group (ECOG)

It is used to measure performance. The scale, also known as WHO or Zubrod performance score, was developed in 1960. In ECOG Performance scale, 0 signifies normal health status and 5 signifies death. Low scores indicate good general condition and high scores indicate bad prognosis [7].

Karnofsky performance scale

It is used to measure performance. The scale was developed in 1948 and revised in 1949. The scale questions the symptoms of patients, performing daily activities, addiction status and medical care requirements. 100 points signify normal health status and the functions get worse by ten points of decreases and 0 point signifies death [7].

European Organization for Research and Treatment of Cancer Quality of Life Group (EORTC QLQ-C30) Quality of Life Questionnaire

The content validity and reliability study of EORTC QLQ C-30 QoL Questionnaire (Cronbach's alpha coefficient, r=0.9014) was performed by Beşer and Öz (6) and the questionnaire is a quality of life scale used commonly throughout the world [3]. EORTC-QLQ-C30 QoL Questionnaire includes 3 domains; general wellbeing, (general QoL), functional score and symptom score, and 30 questions. Functional scales include physical, role, cognitive, emotional and social functioning (5 subscales). Symptom scales includes fatigue, pain and nausea-vomiting, dyspnea, sleep disturbance, loss of appetite, constipation, diarrhea and financial difficulty (9 subscales). If functional score subscale scores and general wellbeing domain scores are high, and symptom score domain score is low, this indicates high QoL [8].

Hospital Anxiety and Depression Scale (HADS)

Turkish reliability and validity study of the scale, which was developed by Zigmond and Snaith to determine the risk in terms of anxiety and depression and to measure anxiety level, was conducted by Aydemir. This 4-point Likert type scale includes a total of 14 questions and odd numbers measure anxiety and even numbers measures depression. The scale has anxiety (HAD-A) and depression (HAD-D) subscales. The cutoff score was found to be 10/11 for anxiety subscale and 7/8 for depression subscale. Accordingly, the patients with scores higher than these points are considered to be under risk. The minimum score is 0 and the maximum score is 21 in both subscales [9].

The study was conducted in accordance with the Declaration of Helsinki. The ethics committee approval was obtained. Written permission was obtained from the clinical education supervisors and hospital management of the units, where the study would be conducted, in order to conduct the study. Verbal consents of the patients included in the study were obtained by explaining the purpose of the study and their written consents were obtained by using Informed Consent Form (ICF).

Data analysis

IBM SPSS Statistics 20.0 packaged software was used for evaluating the data of the study. Shapiro-Wilks test was used to determine whether or not the data showed normal distribution. Normally distributed variables were analyzed using parametric tests and non-normally distributed variables were analyzed using nonparametric tests. The descriptive statistics included median and interquartile range for continuous variables, and frequencies and percentages for categorical variables. The homogeneity of ET and PV groups was compared with Mann-Whitney U test and Pearson Chi square test. Logistic regression was used to evaluate the correlation levels. Spearman correlation tests in data showing no normal distribution were utilized. High scores from general QoL and functional score subscales of EORTC QLQ-C30 questionnaire and low scores from symptom score subscales of EORTC QLQ-C30 questionnaire indicate high quality of life. In ECOG performance evaluation, the performance of the patients with ECOG of 0 and 1 was considered to be good, and the performance of the patients with ECOG of ≥2 was considered to be bad. The results were evaluated at a significance level of $p<0.05$.

Results

The age average of ET and PV patients included in the study was 60.3±11.2/years and 58.7±11.7/years, respectively. Based on the age grouping change performed in 2017 by WHO, 54.1% of the adult patients were ET patients and 56.5% of the middle-aged patients were PV patients and there was no statistically significant difference between the groups in terms of age variable (p>0.05). Gender, education and income status, marital status, concomitant diseases and duration of diagnosis were similar for ET and PV patients. (p<0.05). When the performance of the patients was assessed with ECOG performance scale, it was considered that the performance of the patients with ECOG 0 and 1 was good and the performance of the patients with ECOG of ≥2 was bad. 47.4% of 19 patients with ECOG 0 performance level were ET patients, 48.8% of 41 patients with ECOG 2 performance level were PV patients and no statistically significant difference was determined between ET and PV patients in terms of ECOG performance (p=0.781). While 57.1% of 42 patients with a Karnofsky performance score of 90 and above were ET patients, 75% of 16 patients with a Karnofsky performance score of 80 and below were PV patients and no statistically significant difference was determined between ET and PV patients (p=0.781) (Table 1).

There was no statistically significant difference between HADS-D score mean ranks of ET and PV included in the study (p=0.347). HADS-A score mean rank of PV patients was 38.9, it was higher than the rank of ET patients at a statistically significant level (z=-3.756, p=0.000). GQoL score, functional and symptom scores of EORTC QLQ-C30 were similar in ET and PV patients (p>0.05). EORTC QLQ-C30 cognitive function score mean rank was 43.8 and it was higher compared to ET patients (z=-5.999, p=0.000). In ET patients, score mean ranks of pain and diarrhea subscales, which are among EORTC QLQ-C30 symptom score subscales, were 22.2 and 19.8, respectively, and they were lower compared to those of PV patients (p=0.000). In PV patients, score mean ranks of fatigue, dyspnea and financial difficulty, which are among EORTC QLQ-C30 symptom score subscales, were 19.5, 22.9 and 22.9, respectively, and they were lower compared to those of ET patients (p=0.000) (Table 2)

There was a negative correlation between HADS-A and HADS-D scores of ET patients and their EORTC QLQ-C30 GQoL, physical functioning, role functioning, emotional functioning and social functioning subscale scores (p<0.01) There was a positive correlation between HADS-A and HADS-D scores and EORTC QLQ-C30 nausea and vomiting, pain and diarrhea subscale scores of ET patients (p<0.05). In PV patients, there was a negative correlation between HADS-D score and EORTC QLQ-C30 physical functioning, role functioning and cognitive functioning subscale scores (p<0.05) In PV patients, there was a positive correlation between HADS-D score and EORTC QLQ-C30 GQoL loss of appetite and financial difficulty subscale scores (p<0.05) (Table 3).

Table 1. Sociodemographic characteristics and performance levels of ET and PV patients

Variables	ET		PV		Total		Test Statistic	
	n (30)	%	n (30)	%	n (60)	%	x^2	*p*
Gender								
Female	15	60.0	10	40.0	25	100.0	1.714	0.190
Male	15	42.9	20	57.1	35	100.0		
Age groups								
Adult “aged between 18-65 years”	20	54.1	17	45.9	37	100.0	0.635	0.426
Middle Age “ aged between 66-79 years “	10	43.5	13	56.5	23	100.0		
Education level								
Primary school	20	51.3	19	48.7	39	100.0	0.517	0.772
Secondary school	6	54.5	5	45.5	11	100.0		
High school	4	40.0	6	60.0	10	100.0		
Economical status								
income<payments	16	44.4	20	55.6	36	100.0	1.228	0.541
income=payments	8	61.5	5	35.5	13	100.0		
income>payments	6	54.5	5	45.5	11	100.0		
Marital Status								
Married	24	53.3	21	46.7	45	100.0	0.800	0.371
Single	6	40.0	9	60.0	15	100.0		
Comorbidity								
Only HT	4	36.4	7	63.6	11	100.0	2.479	0.479
Only DM	6	40.0	9	60.0	15	100.0		
HT and DM	7	58.3	5	41.7	12	100.0		
No additional diseases	13	59.1	9	40.9	22	100.0		
Duration of disease								
1-3 years	18	52.9	16	47.1	34	100.0	0.271	0.602
4-5 years	12	46.2	14	53.8	26	100.0		
ECOG								
=0-1 (Good Performance)	9	47.4	10	52.6	19	100.0	0.077	0.781
≥2 (Bad Performance)	21	51.2	20	48.8	41	100.0		
Karnofsky								
≥90	24	57.1	18	42.9	42	100.0	2.857	0.091
≤80	6	25.0	12	75.0	16	100.0		

	ET	PV	Total
	Mn±Sd (Min-Max)	**Mn±Sd (Min-Max)**	**Mn±Sd (Min-Max)**
Average age /year	60.3±11.2 (38.0-79.0)	58.7±11.7 (35.0-75.0)	59.5±11.4 (35.0-79.0)

x2:Chi-square Test, mn:mean SD:standard deviation, min:minimum, max:maximum, HT: Hypertension, DM:Diabetes Mellitus

Table 2. HADS-Depression, HADS-Anxiety and EORTC QLQ-C30 subscale scores of ET and PV patients

	Variables	ET		PV		Test Statistic	
Mean rank		Median (25%-75% quarter)	Mean rank	Median (25%-75% quarter)	z	*p*	
HADS	**HADS-Depression**	28.4	10.0 (7.5-11.3)	32.6	10.0 (9.0-12.0)	-0.940	0.347
	HADS- Anxiety	22.1	12.0 (9.8-13.0)	38.9	14.5 (12.0-15.0)	**-3.756**	**0.000**
EORTC QLQ-C30 Life Quality Scale	**General Quality of Life Score**	32.9	75.0 (58.3-83.3)	28.0	66.7 (56.3-77.1)	1.218	0.264
	FS: Functional Score	27.1	33.3 (31.1-46.1)	33.9	35.6 (33.3-53.3)	-1.541	0.123
	PF: Physical Functioning	29.6	66.7 (46.7-66.7)	32.4	66.7 (66.7-66.7)	-0.430	0.667
	RF: Role Functioning	32.7	66.7 (66.7-75.0)	28.3	66.7 (62.5-66.7)	-1.125	0.249
	EF: Emotional Functioning	33.9	66.7 (56.3-70.8)	27.1	66.7 (33.3-66.7)	-1.649	0.099
	CF: Cognitive Functioning	17.2	25.0 (16.7-33.3)	43.8	66.7 (33.3-66.7)	**-5.999**	**0.000**
	SF: Social Functioning	33.0	66.7 (50.0-66.7)	27.9	66.7 (66.7-83.3)	-1.252	0.210
	SD: Symptom Score	32.3	38.5 (25.6-51.9)	28.7	35.8 (30.8-41.0)	-0.809	0.419
	FA: Fatigue	41.5	88.9 (75.0-100.0)	19.5	44.4 (33.3-69.4)	**-4.983**	**0.000**
	NV: Nausea and Vomiting	31.8	66.7 (33.3-83.3)	28.2	66.7 (33.3-66.7)	-0.849	0.396
	PA: Pain	22.2	66.7 (50.0-66.7)	38.9	83.3 (66.7-83.3)	**-3.859**	**0.000**
	DY: Dyspnea	38.2	66.7 (66.7-100.0)	22.9	66.7 (33.3-66.7)	**-3.847**	**0.000**
	SL: sleep disturbance	32.5	66.7 (66.67-66.67)	28.5	66.7 (58.3-66.7)	-1.183	0.237
	AP: Loss of appetite	33.3	66.67 (66.7-100.0)	27.7	66.7 (58.3-66.7)	-1.395	0.163
	CO: Constipation	27.9	66.7 (58.3-66.7)	33.2	66.7 (66.7-66.7)	-1.595	0.111
	DI: Diarrhea	19.8	0.0 (0.0-33.3)	41.2	66.7 (58.3-66.7)	**-5.032**	**0.000**
	FI: Financial Difficulties	38.1	100.0 (66.7-100.0)	22.9	66.7 (66.7-66.7)	**-3.718**	**0.000**

z=Mann-Whitney U test

Table 3. Correlation of HADS scores and EORTC QLQ-C30 subscale scores of ET and PV patients

	ET		PV	
	HADS-A	**HADS-D**	**HADS-A**	**HADS-D**
GHS: General Quality of Life	-0.498**<0.01**	-0.497**<0.01**	-0.180 0.341	0.030 0.851
PF: Physical Functioning	-0.656**<0.01**	-0.613**<0.01**	-0.055 0.772	-0.438**<0.05**
RF: Role Functioning	-0.707**<0.01**	-0.575**<0.01**	-0.255 0.174	-0.490**<0.01**
EF: Emotional Functioning	-0.714**<0.01**	-0.502**<0.01**	-0.098 0.608	-0.144 0.448
CF: Cognitive Functioning	0.229 0.224	0.250 0.182	-0.149 0.432	-0.377**<0.05**
SF: Social Functioning	-0.652**<0.01**	-0.612**<0.01**	0.028 0.885	0.047 0.806
FA: Fatigue	-0.024 0.900	0.336 0.069	-0.300 0.107	-0.24 0.901
NV: Nausea and Vomiting	0.728**<0.01**	0.510**<0.01**	-0.138 0.475	-0.202 0.292
PA: Pain	0.406**<0.05**	0.406**<0.05**	-0.019 0.922	-0.084 0.801
DY: Dyspnea	-0.002 0.992	0.001 1.000	-0.173 0.361	-0.139 0.463
SL: sleep disturbance	0.008 0.968	-0.093 0.627	-0.184 0.330	-0.316 0.089
AP: Loss of appetite	-0.313 0.093	-0.005 0.979	-0.092 0.627	0.437**<0.05**
CO: Constipation	-0.083 0.662	-0.118 0.535	-0.173 0.359	-0.332 0.073
DI: Diarrhea	0.367**<0.05**	0.368**<0.05**	0.151 0.425	-0.201 0.286
FI: Financial Difficulties	-0.324 0.080	-0.048 0.800	0.089 0.641	0.442**<0.05**

r: Spearman Correlation Test. first row: r, second row: *p*

Discussion

In the patients with MPN, arterial and venous thrombotic complications as well as complications such as progression to AML shorten lifetime [10]. But some disease-based or treatment-related symptoms also impair quality of life of this patient group whose life expectancy reduces. In a study assessing the quality of life of 699 patients diagnosed with MPN, 90% of the patients had symptoms related to the disease. Even in the patients with mild symptoms, impairment was observed in quality of life. In the patients receiving treatment, the quality of life of the patients enhanced with decreasing symptoms [11].

The most frequent symptom in MPN patients is fatigue. Hydroxyurea, anagrelide and interferon given especially for cytoreductive treatment are observed due to alpha usage [12, 13]. In their study, Mesa et al. [14], examined 1179 MPN cases and determined that fatigue was the most frequent symptom determined at the time of diagnosis in 80.7% of the patients. And the other symptoms included itching (53%), night sweating (50%), bone pain (44%), fever (14%), and weight loss (13%). One point drawing attention in this study was that all the symptoms apart from bone pain were observed more frequently in PV patients compared to ET patients [14].

The studies comparing the symptoms and quality of life between MPN subgroups have also been reported. Also, in their study, Abelsson et al. [6], examined 179 cases diagnosed with MPN using EORTC-QLQC30 and determined that fatigue, inactivity, dizziness, coughing, itching and depression scores were higher in PV patients compared to ET patients. Total QoL score was determined to be lower [15]. In the present study, EORTC QLQ-C30 symptom score for fatigue was higher in ET patients compared to PV patients.

In hematological malignancies, prevalences of anxiety and depression increased. In the present study, no statistically significant difference was determined between ET and PV groups in terms of HADS-D subscale, higher scores were determined in PV group compared to ET group in HADS-A subscale. The fact that PV and ET groups have similar ECOG and Karnofsky scores show that the difference in anxiety score is independent of the patients' performance status. In the literature, there are also other studies researching the anxiety and depression prevalence in MPN patients. It was investigated in a multi-centered study

investigating the prevalence of anxiety and depression in 2029 cases with Philadelphia-negative MPN, the prevalence of anxiety was 21%, the prevalence of depression was 12% and prevalence of anxiety and depression co-occurrence was 8%. In the subgroup analyses, the prevalences of anxiety and depression were 23% and 13%, respectively, in ET and 19% and 12%, respectively, in PV [15]. The prevalence rates reported by Scherber et al. [16] in patients with MPN were 18% for anxiety and 12% for depression. There was no statistically significant difference between ET and PV subgroups [16].

HADS-D score 6.1 and HADS-A 8.3 were found in a study using the EORTC QLQ-C30 scale in patients diagnosed with chronic phase Chronic Myeloid Leukemia (CML) which another group of myeloproliferative neoplasia. These results are lower than the PV and ET groups in our study. However, to investigate the cause of this difference, results comparing CML, ET and PV patients are not reported in the literature [17].

In conclusion, the symptoms and anxiety observed in MPN patients cause a decrease in quality of life. In the present study, EORTC QLQ-C30 and HADS subscales and ET and PV patients' the general quality of life, functional and symptom scores and depression levels were similar. However, there were differences between the groups in terms of the physical scores of life quality, in the subscales related to symptom scores and anxiety levels. Anxiety level was higher in PV patients.

Conflict of interest: There is no conflict of interest among authors.

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Limitations of the study

The study was designed to evaluate the relationship between depression and anxiety levels of ET and PV patients and QOL, and healthy controls were not included in the study. In addition, due to the low number of patients, subgroup analyzes could not be performed.

Ethics committee approval: Tepecik Training and Research Hospital Local Ethics Committee (decision date: 26.08.2016, decision number: 8).

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