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ORIGINAL ARTICLE

One-minute time interval estimation as a novel ultrashort tool for distress screening

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Abstract

Purpose Our study explores the potential relationship between time estimation and level of distress in cancer patients prior to starting chemotherapy.

Methods Time estimation was assessed in 262 chemonaïve patients with solid tumors by evaluating each subject's prospective estimation of how fast 1 min passed compared to the actual time. The median value (40 s) of time estimation was used to stratify the patients into two categories of fast and slow time estimation. The National Comprehensive Cancer Network Distress Thermometer was used at the beginning of treatment to evaluate levels of distress. Patients scoring 4 or above (51.9%) were regarded as having high levels of distress.

Results The pattern of the time estimation distributions significantly changed according to the level of distress. Patients with a fast time estimation had significantly higher levels of distress (4.55 ± 3.1) than patients with a slow time estimation (3.3 ± 2.9) ($p = 0.001$). ROC analysis revealed that at the optimal cutoff value of time estimation, patients with low and high distress levels can be discriminated with an AUC = 0.60 (95% CI: 0.53–0.67, $p = 0.005$) and with a sensitivity of 62.5% and specificity of 53.2%. Moreover, in a multivariate logistic regression model, fast time estimation was an independent predictor of high levels of distress.

Conclusion Time estimation is a novel potent indicator of high levels of distress in cancer patients. This test is an easily performed, time-saving, and nonintrusive ultrashort screening tool that is even suitable for patients who are not willing to reveal their level of distress via direct questionnaires.

Keywords Time estimation · Distress · Cancer · Oncology · Screening

Introduction

Cancer patients are battling a life-threatening disease and experience severe treatment side effects that ultimately lead to high levels of distress as well as symptoms of depression and anxiety. Distress is a continuum that ranges from normal feelings of fear, sadness, and vulnerability to disabling problems, such as panic, anxiety, depression, social isolation, and existential and spiritual crises. Distress is not a transient mood change but a serious disturbance that affects patient quality of life. The National Comprehensive Cancer Network (NCCN) defines distress as "a multifactorial, unpleasant, emotional experience of a psychological, social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment" [1]. Distress can negatively impact treatment outcomes, including the course of the disease, if left unaddressed [2, 3]. These detrimental effects stem from nonadherence to the prescribed treatment [4], poor satisfaction with the provided care [5], and poor overall quality of life [6] in distressed patients. Current guidelines suggest that all patients should be screened for distress at their initial visit and as clinically indicated if there are changes in disease status (remission, recurrence, or progression) [1]. Not recognizing distress prevents treating physicians from applying appropriate therapeutic interventions (both pharmacologic and nonpharmacologic) that are known to effectively

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relieve distress [7, 8]. Distress can be measured by the distress thermometer (DT), which is usually completed together with a problem list. Clinical application of the DT has been studied in patients with various types of cancer, and this measure has demonstrated good accuracy in detecting distress [9–12].

People subjectively perceive the passage of time at different speeds—an hour may pass extremely quickly, whereas a few minutes may seem to drag. A strong connection exists between one's current emotional state and one's experience of time: distraction by entertaining activities seems to speed up time, whereas boredom during uneventful situations is associated with a subjective slowing down of time [13–15]. When time is perceived as moving quickly, one feels that less time has passed than what is actually indicated by the clock. In contrast, when time is perceived as moving slowly, one feels that more time has elapsed than what is indicated by the clock. Cognitive models of prospective time estimation suggest that an individual's perception of time depends on an internal clock, with a pacemaker that produces subjective time units [14, 16]. In these cognitive models, subjective time units are registered only at moments when attention is drawn to time [15]. Several reports, but no systematically collected information, exist on the relationship between the experience of time and distress in cancer patients.

Our study focused on the potential relationship between perception of time and level of distress in cancer patients prior to starting chemotherapy. Patients' minds are preoccupied with thoughts about their illness and its associated symptoms, cancer treatment and its side effects, and fear of death and other worrisome emotions. According to the pacemaker model, we speculated that stressful thoughts draw attention away from time and that fewer subjective time units are registered. We hypothesized that patients who have a fast time estimation have higher levels of distress.

Materials and methods

Patient selection

Our report includes 262 inpatients who were treated at the Clinic of Medical Oncology at UMHAT "St. Marina" in Varna, Bulgaria, from August 2016 to December 2017. The inclusion criteria were as follows: histologically verified cancer, age greater than 18 years, understanding of the Bulgarian language, absence of psychiatric disorders, and absence of clinical conditions that could limit the patient's understanding of the provided materials and tasks. Basic sociodemographic and clinicopathological data were collected, along with an assessment of distress and time estimation. The procedure was approved by the Scientific Research Ethics Committee of "Prof. Dr. Paraskev Stoyanov" Medical University in Varna, Bulgaria.

Assessment of distress

According to the NCCN guidelines, we chose the DT as a tool for distress screening. The DT is a validated self-reported tool that allows rapid screening. The patient is asked to indicate a number on a visual-analog scale that represents his or her psychological condition during the past week. The scale ranges from 0 (no distress) to 10 (extreme distress) [17]. A meta-analysis of 42 cancer studies found that the pooled sensitivity of DT is 81% and that the pooled specificity is 72% at a cutoff score of 4 [9]. Based on the DT score, the subjects were assigned to two groups: "low distress" (score of 0–3) or "high distress" (score of 4–10).

Measurement of time estimation

Time estimation was assessed by the subjects' individual prospective estimation of how fast 1 min passed compared to the actual time. The patient received instructions to estimate a duration of 1 min after a start signal. When the subject gave a stop signal, the interpreter stopped the chronometer, and the estimated time was recorded. For our patients, the estimation of 1 min ranged from 9 to 92 s. The median value of time estimation (40 s) was used to stratify the patients into two categories: fast ($\leq$ median) and slow ($>$ median) time estimation.

Statistical design and analysis

Data were managed and analyzed using IBM SPSS Statistics software ver. 23. The Mann-Whitney U test, χ^2 test, and Spearman correlation were used to compare and evaluate the correlations between the level of distress and clinicopathological characteristics of the patients, such as age, gender, performance status (PS) (Eastern Cooperative Oncology Group (ECOG)), primary tumor location and experience of time. For the interpretation of correlation test results, rho values were interpreted as follows, $<$ 0.19, very weak; 0.19–0.39, weak; 0.40–0.59, moderate; 0.60–0.79, strong; and $\geq$ 0.80, very strong. The diagnostic accuracy of subjective time estimation was also determined by obtaining the largest possible area under the curve (AUC) in receiver operating characteristic curve (ROC) analysis. AUC values $\geq$ 0.9 are considered "excellent," $\geq$ 0.80 "good," $\geq$ 0.70 "fair," and $<$ 0.70 "poor." Trends in the changes in time estimation relative to the level of distress were assessed using the Jonckheere-Terpstra test. The minimum sample size for regression analysis was determined to be 200 to provide 80% power at a 5% significance level. The calculation was based on the eight covariates used and a 40% proportion of positive cases [18]. Odds ratios (ORs) with confidence intervals (CIs) for categorical outcomes were

calculated using a binary logistic regression model. The Nagelkerke R-squared is reported for the logistic regression analysis. A p value < 0.05 (two-tailed) was considered significant.

Results

Patient characteristics

A total of 262 patients with malignant solid tumors participated in the study; 116 (44.3%) patients were men, and 146 (55.7%) patients were women. The median age was 62 years, and the mean age of the group was 59.8 ± 11.23 years, with an age range of 29 to 81 years. The sample included subjects with a variety of cancer types: 65 (24.8%) lung cancer patients, 67 (25.6%) breast cancer patients, 66 (25.2%) colorectal cancer patients, and 64 (24.4%, representing more than 14 different histology types) patients with other cancers. Detailed descriptions of the patient characteristics can be found in Table 1.

Table 1 Sociodemographic and clinicopathological patient characteristics

Patient characteristics	*n* (%)
Sex	
Male	116 (44.3%)
Female	146 (55.7%)
Ethnicity	
Bulgarian	244 (93.1%)
Turkish	18 (6.9%)
Religion	
Christian	180 (68.7%)
Muslim	16 (6.1%)
Atheist	40 (15.3%)
Unspecified	26 (9.9%)
Marital status	
Single	18 (6.9%)
Married	181 (69.3%)
Widowed	35 (13.4%)
Divorced	28 (10.3%)
Performance status (ECOG)	
0	118 (45%)
1	144 (55%)
Cancer type	
Lung cancer	65 (24.8%)
Breast cancer	67 (25.6%)
Colorectal cancer	66 (25.2%)
Other	64 (24.4%)
Stage	
II and III	121 (46.2%)
IV	141 (53.8%)

Correlations among time estimation, level of distress, and patient characteristics

The mean distress score was 3.94 ± 3.07. A total of 136 (51.9%) patients had high distress, and their mean distress score was 6.45 ± 1.9. A fast time estimation, PS 1, and lung or breast cancer were correlated with high levels of distress (Table 2). The distress levels of patients with lung cancer (5.05 ± 3.12) and breast cancer (4.36 ± 3.01) did not differ significantly ($p = 0.19$). Both groups had significantly higher levels of distress than patients with colorectal cancer (3.2 ± 2.8) or patients with other types of cancer (3.13 ± 2.8). Patients with PS 1 (4.15 ± 2.9) did not have significantly higher levels of distress than patients with PS 0 (3.68 ± 3.2) ($p = 0.15$). Women (4.36 ± 3.2) had significantly higher levels of distress than men (3.41 ± 2.8) ($p = 0.02$). Patients younger than 62 years (4.31 ± 2.9) had also significantly higher levels of distress than patients older than 62 years (3.52 ± 3.1) ($p = 0.024$). No significant differences in the levels of distress were observed with respect to ethnicity, religion, marital status, or stage of the disease.

A fast time estimation correlated only with patients' level of distress ($p = 0.010$) and gender ($p = 0.038$). No significant differences in time estimation were observed with respect to ethnicity, religion, marital status, stage of the disease, or age. Women exhibited a trend towards a faster time estimation (39.6 ± 16.2 s) than men (43.3 ± 16.6 s) ($p = 0.07$). Patients with a fast time estimation had significantly higher levels of distress (4.55 ± 3.1) than patients with a slow time estimation (3.3 ± 2.9) ($p = 0.001$) (Fig. 1). The pattern of time estimation distributions significantly changed with the level of distress ($p = 0.001$). ROC analysis revealed that at the optimal cutoff value of time estimation, patients with low and high distress levels can be discriminated with an AUC = 0.60 (95% CI: 0.53–0.67, $p = 0.005$) and with a sensitivity of 62.5% and specificity of 53.2% (Fig. 2). There was a weak, but significant, negative correlation (Spearman rho = − 0.191, $p = 0.002$) between time estimation and level of distress.

Predictors of a high level of distress

In univariate logistic regression analysis, patients with a fast time estimation, lung or breast cancer, or PS 1 were associated with high levels of distress. In a stepwise backward multivariate logistic regression model, fast time estimation, lung cancer, breast cancer, PS 1, and age < 62 years were independent predictors of high levels of distress (Table 3). In addition, the model accounted for 15.4% (Nagelkerke) of the variance in distress status.

Table 2 Correlations between level of distress and patient characteristics

	Low distress, *n* (%)	High distress, *n* (%)	*p*
Gender			0.294
Male	60 (47.6%)	56 (41.2%)	
Female	66 (52.4%)	80 (58.8%)	
Age			0.051
≤ 62 y	58 (46%)	79 (58.1%)	
> 62 y	68 (54%)	57 (41.9%)	
Ethnicity			0.19
Bulgarian	120 (95.2%)	124 (91.2%)	
Turkish	6 (4.8%)	12 (8.8%)	
Religion			0.10
Atheist	23 (18.3%)	17 (12.5%)	
Christian	80 (63.5%)	100 (73.5%)	
Muslim	6 (4.8%)	10 (7.4%)	
Unspecified	17 (13.5%)	9 (6.6%)	
Marital status			0.15
Single	4 (3.2%)	14 (10.4%)	
Married	90 (71.4%)	91 (67.4%)	
Widowed	18 (14.3%)	17 (12.6%)	
Divorced	14 (11.1%)	13 (9.6%)	
Performance status			0.021
0	66 (52.4%)	52 (38.2%)	
1	60 (47.6%)	84 (61.8%)	
Cancer type			0.002
Lung cancer	20 (15.9%)	45 (33.1%)	
Breast cancer	30 (23.8%)	37 (27.2%)	
Colorectal cancer	36 (28.6%)	30 (22.1%)	
Other (more than 14 types of cancer)	40 (31.7%)	24 (17.6%)	
Stage			0.486
II and III	61 (48.4%)	60 (44.1%)	
IV	65 (51.6%)	76 (55.9%)	
Time estimation			0.010
Fast time estimation	54 (42.9%)	80 (58.8%)	
Slow time estimation	72 (57.1%)	56 (41.2%)	

Discussion

In this study, we investigated the association between time estimation and level of distress among patients with malignant solid tumors. Time estimation was faster in patients with distress scores ≥ 4, as measured by NCCN's DT. The prospective time estimation test revealed that patients with a time estimation shorter than or equal to 40 s were associated with an increased risk of high levels of distress.

A cancer diagnosis can lead to detrimental effects on physical and mental health. Such a diagnosis can negatively affect social functioning and inevitably cause distress over the course of the disease. A meta-analysis showed that a combination of mood disorders can occur in 30–40% of patients admitted to the hospital [19]. Several surveys found that up to 52% of patients showed moderate/severe levels of distress [20, 21]. Evidence from research showed that the most important risk factors for distress were gender, age, marital status, stage of the disease, social status, and type of cancer [22–24]. Consistent with these findings, we discovered that patients with younger age, higher PS scores, or lung or breast cancer were more likely to have higher levels of distress. Surprisingly, our results showed that patients who anticipate chemotherapy treatment did not discriminate between metastatic and nonmetastatic disease stages and were equally distressed. Therefore, these findings suggest that the oncologist must provide more information and clarifications about the patients' stage and associated outcomes to decrease their levels of distress.

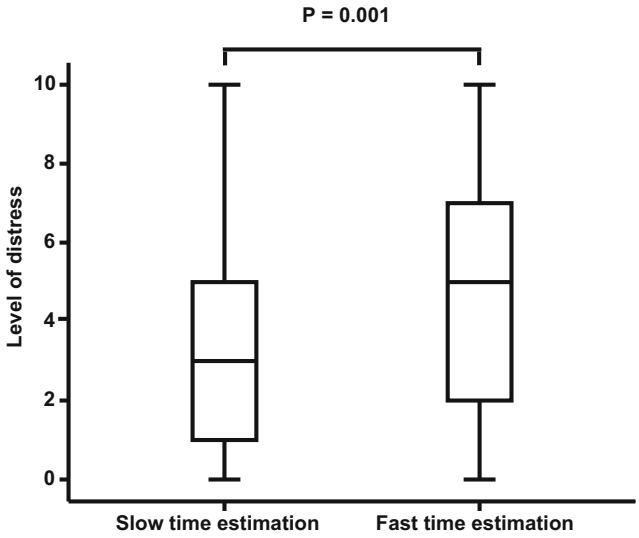

Fig. 1 A bar graph depicting the level of distress in patients with slow and fast time estimations. The Mann-Whitney U test was used to detect significant differences in the level of distress between the groups, and $p < 0.05$ (two-tailed) was considered to indicate significance

A study showed that estimation and focusing on the past is not beneficial for cancer patients; these patients frequently overestimated this period of time, which was associated with high levels of distress [25]. Other papers showed that life reviews may be beneficial in terminally ill cancer patients [26]. In contrast, if patients had future perspectives, their life review was correlated with less distress. A study reported that the speed of time was experienced differently in patients with advanced cancer

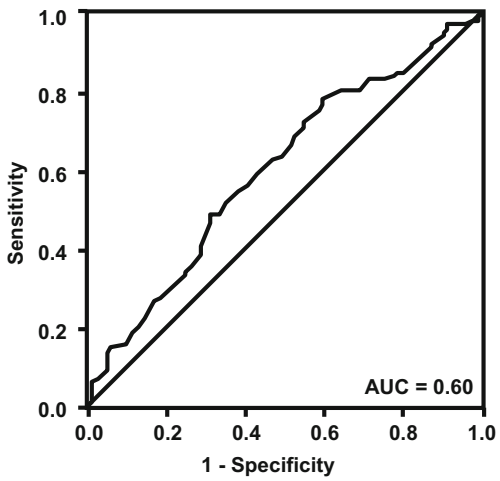

Fig. 2 Receiver operating characteristic curve (ROC) analysis in which time estimation was used to differentiate between patients with low and high levels of distress. The diagnostic accuracy of time estimation was determined by obtaining the largest possible area under the curve (AUC) in ROC analysis

than in patients without evidence of disease; the past week seemed significantly longer to advanced cancer patients [25]. Time perception is influenced by many factors, such as physiological state, personality, and activity during the test period, and therefore, estimations of longer time intervals are widely variable and imprecise [27]. Generally, people tend to overestimate brief intervals of time, such as seconds, and underestimate longer intervals, such as hours [28]. Time estimation is improved in experimental situations, such as our experimental setup in which participants were expected to make time judgements [29]. Psychological studies on time estimation incorporate different methods, and unfortunately, the results are not comparable or homogeneous across these methodologies. The collected results and their corresponding explanations are often contradictory [30]. Our method for assessing time perception by the prospective estimation of a 1-min interval is relatively simple and fast to perform. This method ensures higher compliance of both the patient and the physician and avoids emotions that are inevitably linked to one's past or future.

Several studies considered distress to be the sixth vital sign in cancer care (after pulse, blood pressure, respiratory rate, temperature and pain) [31]. The advent of distress screening led to demand for an appropriate tool or instrument to serve this purpose. The instrument must be reliable, inexpensive, and easily administered. The tool must be brief and must facilitate the rapid identification of individuals who might benefit from further or deeper assessment for use in daily practice. Our study proposes the prospective estimation of a 1-min time interval as a novel potential predictor of distress among cancer patients. Our proposed method has the practical appeal of quickly screening for distress in cancer patients. The response rate of completing various questionnaires varies between 49 and 97.5% [32, 33]. Many patients do not report their true level of distress because of embarrassment and fear of being stigmatized for having a psychological problem [34]. Furthermore, oncologists are not always trained or skilled in discussing emotional problems. For these reasons, many distressed patients are not recognized by oncologists [35]. Recent systematic reviews of screening tools for distress emphasized the issues of variation in the concepts being measured, definitions of terms, timing of measurement, and tool length and format [36]. Thus, a simple screening tool that can be used in the busy setting of everyday clinical practice is needed. In this situation, assessing the time estimation via our proposed method can help physicians easily identify patients at risk for high levels of distress.

Table 3 Univariate and multivariate regression analyses for predicting high distress levels

Variable	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	*p*	Odds ratio	95% CI	*p*
Age						
≤ 62 y vs > 62 y	1.62	0.097–2.64	0.051	1.82	1.062–3.120	0.026
Gender						
Men vs Women	0.77	0.47–1.25	0.29			
Cancer type						
Lung cancer	3.75	1.80–7.78	< 0.001	3.503	1.631–7.52	0.001
Breast cancer	2.05	1.02–4.13	0.043	2.24	1.05–4.78	0.036
Performance status						
1 vs 0	1.77	1.08–2.96	0.022	1.97	1.12–3.46	0.017
Religion						
Believers vs nonbelievers	0.64	0.32–1.26	0.19			
Marital status						
Married vs nonmarried	1.2	0.71–2.05	0.48			
Ethnicity						
Bulgarian vs Turkish	1.93	0.70–5.32	0.20			
Time estimation fast vs slow estimation	1.905	1.166–3.11	0.010	1.97	1.06–2.98	0.029

In regression analysis, the patients were stratified into groups of believers (Christians, Muslims, and Unspecified) and nonbelievers (Atheists) or married and nonmarried (not living with a partner, including single, widowed and divorced)

The main limitation of our study is that the AUC in ROC analysis was less than 0.7, which suggests poor discrimination between patients with high and low distress levels. In clinical practice, many of the currently available psychological test tools and inventories produce AUCs in the 0.7–0.8 range [37, 38]. However, when questionnaires deliver AUCs greater than 0.90, the outcome is presumed to be due to design flaws rather than remarkable test validity [39].

Another limitation of our study is that we did not include healthy subjects as a control group. It is believed that perception of time speeds up with age in healthy people [40]. Our results did not show a significant difference in time estimation according to patient age. Because of the lack of a control group, we could not determine if the normal tendency of the change in time perception with age is disrupted by underlying disease, such as cancer.

Our study revealed for the first time that an association between time estimation (assessed by the prospective estimation of a 1-min interval) and level of distress exists among patients with solid tumors prior to starting chemotherapy. Distress is a risk factor for nonadherence to treatment and may even negatively impact survival [31]. Thus, early identification of significant distress is crucial to developing a management plan. Although our proposed method for detecting distress has low sensitivity and specificity, it is an easily performed, time-saving, and nonintrusive ultrashort screening tool that is even suitable for patients who are not willing to reveal their level of distress via direct questionnaires.

Compliance with ethical standards

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

Informed consent For this type of study, formal consent is not required.

Conflict of interest The authors declare that they have no conflicts of interest.

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