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ORIGINAL RESEARCH

Real-life daily activity: the impact of misbeliefs on quality of life among cancer patients

E. Shachar[1,2], S. P. Hasson[1,2], L. Ferro[1,2], C. Pundak[3], A. Nikolaevski-Berlin[2], E. Waller[1,2], T. Safra[1,2], T. Rubinek[2] & I. Wolf[1,2*]

[1]Faculty of Medicine, Tel Aviv University, Tel Aviv; [2]Division of Oncology, Tel Aviv Sourasky Medical Center; [3]Division of Psychology, Tel Aviv University, Israel

Background: While side-effects and health-related quality of life (QoL) are routinely assessed in clinical trials, commonly used tools do not measure patients' ability to maintain normal daily activities. QoL can be severely affected directly by the disease, the treatment side-effects and by personal and societal misconceptions promoting avoidance from activities perceived as dangerous for cancer patients. We examined practices of actively treated patients with cancer.
Methods: A questionnaire was designed, assessing daily activities (11 items) and dietary limitations (7 items) distributed between October and December 2019 (before the coronavirus pandemic) among patients treated at the Oncology Division of Tel Aviv Sourasky Medical Center.
Results: The study population comprised 208 patients who participated in the survey. The majority reported at least one social-environmental avoidance or dietary limitation (136, 65% and 120, 57.7%, respectively), including abstaining from social contact, avoiding pets, public domains, traveling and maintaining dietary constraints. Adoption of these measures was not associated with clinical, demographic factors and treatment type. The major sources guiding restrictions came from advice of non-medical personnel (55.7%), the Internet (7.2%) and personal choice by the patients themselves (24%).
Conclusions: Most cancer patients reported compromised daily activities, which are likely attributed to misbeliefs about disease and treatment, and have a deleterious impact on QoL, in its wider sense, namely, the ability to conduct a full and meaningful life. These findings call for the development and implementation of tools examining patients' real-life activity, beyond side-effects or health-related QoL (HRQoL). We propose this assessment as an integral part in the evaluation of new drugs and technologies and as an additional endpoint in pivotal clinical trials.
Key words: cancer, behavior, restrictions, quality of life, avoidance, misbeliefs

INTRODUCTION

Health-related quality of life (HRQoL) is an independent predictor of overall survival and has become a standard endpoint of many clinical trials.[1,2] QoL is assessed by validated questionnaires, often in the form of patient-reported outcomes (PROM).[3] Numerous items of HRQoL questionnaires deal with the question of how disease and treatment interfere with normal life; however, commonly used and validated tools focus on specific health-related signs and symptoms (e.g. pain, fatigue, diarrhea) but do not fully reflect patients' maintenance of normal life, including the continuity of routine social interactions and daily activities.[4,5] Misbeliefs about disease and treatment may also

interfere with normal life, a measure that is not grasped in HRQoL questionnaires. Namely, we measure if patients suffer from neutropenia or mucositis but not if they avoid holding their children or do not participate in social events. Evaluating cancer patients' ability to conduct a full and meaningful life is, therefore, of utmost importance. The ability of actively treated cancer patients to lead a full life is a composite endpoint of three major parameters: (i) disease-related factors (e.g. pain, shortness of breath), (ii) treatment-related factors (e.g. rash, diarrhea) and (iii) personal, social and cultural factors influencing adoption of restrictive measures (misbeliefs about disease and treatment interfering with normal life, e.g. the fear of meeting others in order to avoid infections).

Evaluating the first two, more 'objective' factors is relatively easy and indeed has become a standard component of pivotal clinical trials. However, measuring the ultimate outcome—ability to conduct a full and meaningful life—is complicated mostly by the highly subjective and culture-dependent nature of the third parameter. For example,

Correspondence to: Prof. Ido Wolf, Tel Aviv Medical Center, 6 Weizmann Street, Tel Aviv 64239, Israel. Tel: +972-3625623
E-mail: idow@tlvmc.gov.il (I. Wolf).

even leading cancer associations, including the American Cancer Society,[6-8] Cancer Research UK[9,10] and the Israeli Cancer Association,[11] continue to endorse various restrictions on daily activity, often without sound scientific basis. For example, many of the leading cancer associations consider actively treated cancer patients, often not justifiably, to be at increased risk of infection,[12,13] although various studies looking at the role of environmental, social and dietary restrictions failed to show any benefit even in very-high-risk patients.[14-18] As a result of this complexity, actual real-life activity is not evaluated in most clinical trials and is completely overlooked in the pivotal registration trials, as well as by the regulators. Thus, the medical community has limited its responsibility to the evaluation and treatment of side-effects, while somewhat neglecting its ultimate mission, improving QoL in its broader sense.

We developed and implemented a questionnaire assessing real-life behavior and activity of actively treated cancer patients, referring to various social, environmental and dietary abstentions. We also aimed to evaluate sources endorsing these limitations. Our findings indicate adoption of restrictive behavioral measures by a large number of patients, which may have a detrimental impact on real-life QoL.

METHODS

Study objectives

The survey was developed and implemented to assess real-life behavior and activity of actively treated cancer patients, referring to various social, environmental and dietary abstentions, beyond the standard assessment of HRQoL. Moreover, it aimed to evaluate sources endorsing patient practices and misbeliefs guiding patients. We also aimed to explore potential factors associated with abstentions and identify a population with more and less restrictive behavior.

Study design

We conducted a cross-sectional anonymous survey at the Oncology Division of Tel Aviv Sourasky Medical Center (TASMC), a tertiary referral center, among actively treated solid tumor patients. The surveys were completed by patients treated between October 2019 and December 2019, before the coronavirus disease 2019 (COVID-19) pandemic.

Study population

Adult patients with solid tumors (>18 years old) receiving active intravenous treatment, either chemotherapy, immunotherapy or targeted therapy with an Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0-3[19] at the oncology day care center or in-patient oncology ward, were included in the study. Excluded patients were those <18 years old, tourists who did not speak proficient Hebrew, ECOG PS of 4 and patients receiving only best supportive care. The study was approved by the local research Helsinki ethics board (TASMC Helsinki Review Board

Approval number 0456-19-TLV). Respondents signed a written consent form.

Characteristics of the survey

We reviewed the standard validated QoL questionnaires[20,21] and understood that they did not address the misbeliefs associated with disease and treatments and its impact upon compromised daily activities as a measure of QoL. We searched alternative sources guiding patient behavior such as cancer association recommendations. The survey was developed by the investigators and was pilot tested before dissemination. Before initiation of the study, we conducted a pilot study of ten patients and five medical personnel to ensure that the survey addressed relevant daily activities that are reflective of QoL. Patients and health care personnel perceptions and suggestions contributed to the final development of the survey.

The items selected were based on common social, environmental and dietary abstentions endorsed by various esteemed cancer organizations, deemed to be an essential part of daily activity and adjusted to variables unique to the Israeli health care system and population. The questionnaire consisted of the following components: demographic and clinical data (6 items), adoption of social and environmental restrictions (11 items) and dietary limitations (7 items, Supplementary data, available at https://doi.org/10.1016/j.esmoop.2022.100498).

Data sources

Clinical data, including primary tumor site, presence of metastatic disease and PS, were collected from electronic medical records. Clinical data were confirmed and abstracted from the hospital charts including therapy regimen. Treatment regimen myelosuppressive potential was graded according to the National Comprehensive Cancer Network (NCCN) guidelines.[22]

Statistical analysis

Independent demographic (sex, age during questionnaire completion, education level, vaccination and hand washing compliance) and clinical [primary cancer type, treatment intent, ECOG, cycle number group, myelosuppressive potential and body mass index (BMI)] variables were characterized by appropriate descriptive measures.

A scoring system was developed for analysis, in which each question received a score of 1 for restricted, and 0 for never restricted, thus creating a summary variable restriction score for social-environmental, dietary measures, and a general restriction score based on all social-environmental and dietary measures.

The relationship between demographic and clinical characteristics of patients and the general restriction score (receive a value 1 for strict restricted patients and a value 0 for less restricted) was assessed using a χ^2 test or Fisher's exact test (in the case of an expected frequency <5).

Multivariate logistic regression model was carried out to identify factors (demographic and clinical characteristics of patients) which predict restrictive behavior.

Statistical analysis was done by the SPSS 25 software. Statistical significance was set at $P < 0.05$, using two-tailed tests.

RESULTS

The questionnaire was distributed to 320 patients; 208 (65%) respondents agreed to participate. The distribution of demographic characteristics of patients is presented in Table 1. Median age was 65 years (range 53-73 years); 117 (56.2%) were female and 91 (43.8%) were male. The majority of patients were born in Israel: 123 (59.1%). One hundred twenty-eight (61.5%) participants had a higher education including an academic degree. One hundred sixty-one participants (77.4%) had an ECOG PS of 0-1. The most common tumor types included gastrointestinal malignancies ($n = 60$, 29.4%), breast ($n = 42$, 20.6%) and lung ($n = 27$, 13.2%). The majority of the patients, 147 (71.2%), were treated for a metastatic disease with palliative intent. Chemotherapy was administered to 140 (67.3%) patients, while the other patients were treated with either immunotherapy or targeted therapy. One hundred and fourteen (55%) received previous lines of therapy. Only 23 (11.1%) of the patients were treated with a highly myelosuppressive regimen, as graded according the NCCN.[22]

The majority of participants (136, 65.4%) reported on at least one social and environmental limitation, and 43 (20.7%) maintained more than half of these constraints (Table 2). Social and environmental restrictions included avoiding contact with their children and grandchildren (67, 32%), friends (47, 23%), child day cares, nurseries and schools (79, 38%), indoor public places such as malls (67, 32%), outdoor public spaces (55, 26%), contact with pets (69, 33%), sun exposure (136, 65%), the beach (112, 54%), hair dyeing (78, 38%), domestic tourism (79, 38%) and international travel (120, 58%, Figure 1A).

One hundred and twenty (57.7%) patients reported on at least one dietary measure and 37 (17.8%) upheld more than half of the dietary limitations. These included omission of raw meat, fish, vegetables, nuts and tap water, and abstaining from restaurants and take-out food (Figure 1B).

Multiple sources were implicated by patients which guided their behavior (Table 2), with the most common being non-medical authorities (55.7%), including the Internet (7.2%) and personal choice (24%), while nurses and physicians (36.5%) guided the decision in over a third of the cases.

In an effort to identify demographic and clinical characteristics associated with stricter behavior, patients who maintained ≥50% of the environmental-social and dietary restrictions (70, 33.7%) were compared to those maintaining <50% of these restrictions (138, 66.3%). Clinical and demographic factors were not associated with patient practices (Table 3). Patients who maintained strict and less strict restrictions (social, environmental and dietary) demonstrated no significant association between age

groups ($P = 0.55$), sex ($P = 0.43$), education ($P = 0.49$), ECOG ($P = 0.45$), treatment type ($P = 0.55$), intent of care ($P = 0.16$), primary cancer ($P = 0.72$), myelosuppressive potential of therapy ($P = 0.32$), treatment cycle number ($P = 0.31$) influenza vaccination ($P = 0.34$) and BMI ($P = 0.59$). However, hand washing compliance was associated with strict restrictional behavior ($P < 0.0001$).

Table 1. Demographics and clinical characteristics of the study population

$N = 208$, n (%)	
Age, years	
Median (range)	65 (53-73)[a]
<65	102 (49)
≥65	105 (50.5)
Sex	
Female	117 (56.2)
Male	91 (43.8)
Ethnicity[b]	
Europe	54 (26)
Africa/Asia	28 (13.5)
Israel	123 (59.1)
N/A	3 (1.4)
Education level[c]	
Low	75 (36)
High	128 (61.5)
N/A	5 (2.5)
Religiosity	
Secular/agnostic	129 (62)
Traditional	49 (23.6)
Orthodox	16 (7.7)
N/A	14 (6.7)
ECOG	
0	97 (46.6)
1	64 (30.8)
2	23 (11.1)
3	7 (3.4)
N/A	17 (8.2)
Primary cancer diagnosis	
Breast	42 (20.6)
Colorectal/other GI	60 (29.4)
Lung	27 (13.2)
Gynecological	26 (12.7)
Other	49 (24)
Treatment intent	
Curative	61 (29.3)
Palliative	147 (70.2)
Treatment type	
Chemotherapy	140 (67.3)
Immunotherapy	32 (15.4)
Combination chemotherapy[b] immunotherapy	12 (5.8)
Targeted therapies[d]	24 (11.5)
Treatment myelosuppressive potential	
High (G-CSF)	23 (11.1)
Intermediate	34 (16.3)
Low	150 (72.1)
N/A	1 (0.5)
BMI	
<18.5 kg/m²	11 (5.3)
18.5-24.9 kg/m²	97 (46.6)
25-29.9 kg/m²	63 (30.3)
≥30 kg/m²	32 (15.4)

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; G-CSF, granulocyte colony-stimulating factor; GI, gastrointestinal; N/A, not applicable.
[a]Interquartile range.
[b]Ethnic origin by continent.
[c]Education level—Low: public middle school, agricultural, professional school, public high school, yeshiva. High: academic degree, post-high school non-academic degree.
[d]Targeted therapies—monoclonal antibodies, endocrine regimens.

Table 2. Limitations adopted by oncology patients

N = 208, n (%)	
Social and environmental limitations[a]	
Adopting any restriction[b]	136 (65.4)
Adopting ≥50% of restrictions	43 (20.7)
Dietary limitations[a]	
Adopting any restriction[b]	120 (57.7)
Adopting ≥50% of restrictions	37 (17.8)
Strict ≥50% environmental-social and dietary restrictional behavior[c]	70 (33.7)
Patients' perception of limitations	
Difficult	64 (30.8)
Not difficult	92 (44.2)
N/A	52 (25)
Preventative measures	
Hand washing	123 (59.1)
Influenza vaccination	74 (35.6)
Sources of information guiding behavior	
Physicians	45 (21.6)
Nurses	31 (14.9)
Other professional sources	16 (7.7)
Spouse encouragement	22 (10.6)
Psychologists/dieticians	14 (6.7)
Other patients/friends	15 (7.2)
Online information	15 (7.2)
Personal choice	50 (24)

N/A, not applicable.
[a]Option of choosing multiple answers.
[b]Avoided at least one limitation ≥1.
[c]Strict restrictional behavior—patients maintaining ≥50% of social-environmental and dietary restrictions.

Multivariate logistic regression was carried out to identify factors associated with strict restrictional behavior. Patient's strict behavior was not associated with sex [odds ratio (OR) = 0.60, 95% confidence interval (CI) 0.24-1.48, P = 0.27], education (OR = 0.58, 95% CI 0.37-1.75, P = 0.58), influenza vaccination compliance (OR = 1.19, 95% CI 0.52-2.70, P = 0.68), treatment intent (OR = 0.62, 95% CI 0.25-1.54, P = 0.3), ECOG status (OR = 1.23, 95% CI 0.436-3.46, P = 0.70), treatment cycle number (OR = 0.92, 95% CI 0.37-2.27, P = 0.72), treatment myelosuppressive potential (OR = 1.04, 95% CI 0.40-2.72, P = 0.95) and BMI (OR = 0.94, 95% CI 0.21-4.20, P = 0.97). Importantly, no differences were noted between those treated with chemotherapy-containing regimens compared with patients receiving immunotherapy or targeted therapies (OR = 0.72, 95% CI 0.206-2.54, P = 0.84). Primary cancer type had no bearing upon patient behavior (OR = 1.08, 95% CI 0.33-3.50, P = 0.19).

A significant association was noted between the elderly age group (aged ≥65 years) and adoption of strict restrictional behavior (OR = 2.36, 95% CI 1.08-5.16, P = 0.03). Additionally, stringent hand washing compliance was associated with strict restrictional behavior (OR = 3.5, 95% CI 1.6-8, P = 0.002).

As expected from previous studies,[23,24] no association was noted between restrictions and febrile neutropenia (Supplementary data, available at https://doi.org/10.1016/j.esmoop.2022.100498).
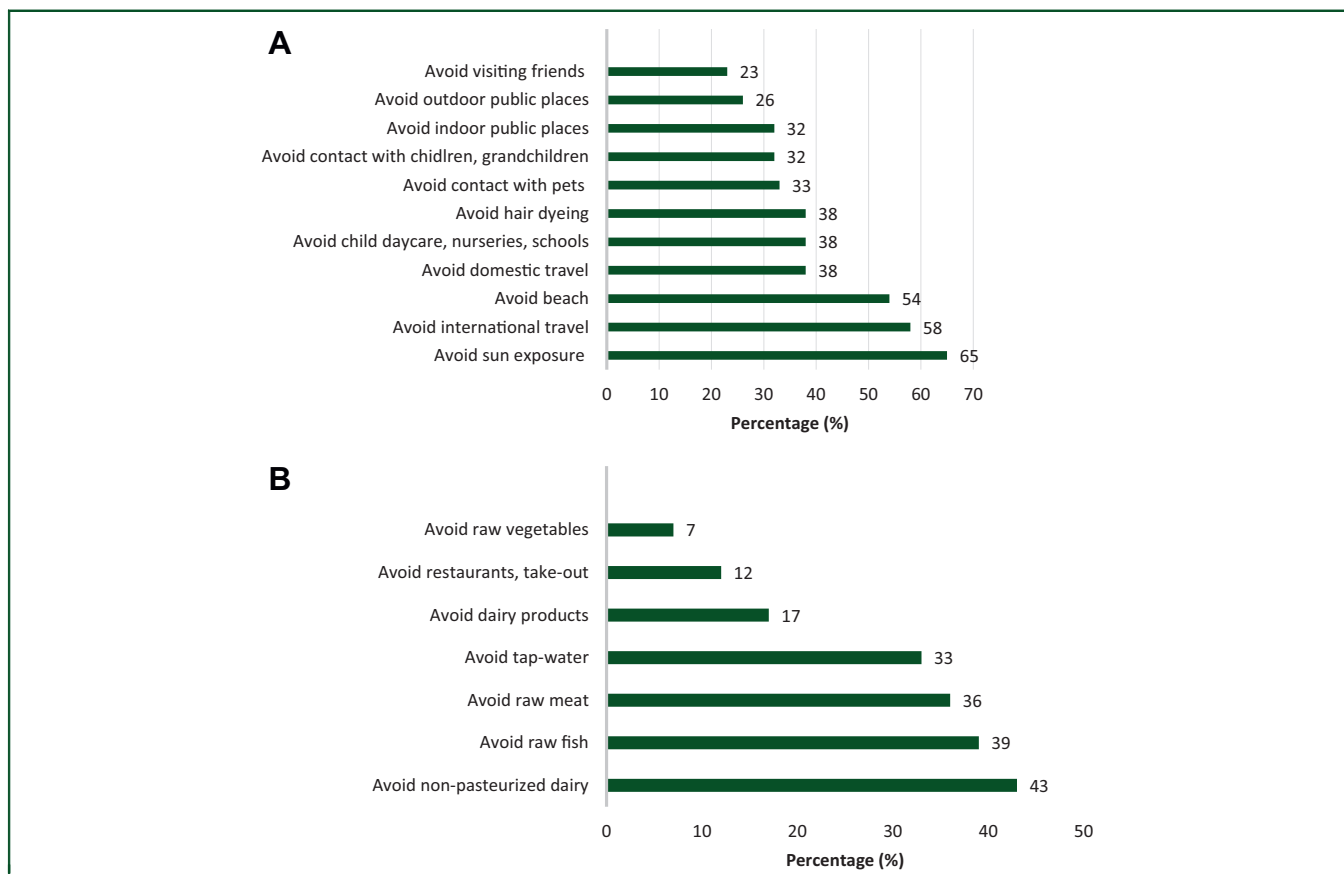

Figure 1. Daily activity of actively treated cancer patients. (A) Social and environmental avoidances. (B) Dietary limitations.

Table 3. Strict and less strict restrictional behavior of actively treated patients with solid tumors

N = 208, n (%)	Strict restrictional behavior[a] n = 70 (33.7)	Less strict restrictional behavior[b] n = 138 (66.3)	P value[c]	Statistical test: Pearson Chi-Square[d]
Age group, years				
<65	32 (31.4)	70 (68.6)	0.55	0.348
≥65	37 (35.2)	68 (64.8)		
Sex				
Female	42 (35.9)	75 (64.1)	0.437	0.603
Male	28 (30.8)	63 (69.2)		
Education				
Low	27 (36)	48 (64)	0.487	0.483
High	40 (31.3)	88 (68.8)		
ECOG				
0-1	53 (32.9)	108 (67.1)	0.452	0.565
2-3	12 (40)	18 (60)		
Treatment				
Chemotherapy/chemo + immunotherapy	53 (34.9)	99 (65.1)	0.554	1.180
Immunotherapy	8 (25)	24 (75)		
Targeted therapies	7 (31.8)	15 (68.2)		
Intent of care				
Curative	25 (41)	36 (59)	0.159	1.985
Palliative	45 (30.8)	101 (69.2)		
Cancer type				
Breast	14 (33.3)	28 (66.7)	0.722	2.076
Colorectal/other GI	23 (38.3)	37 (61.7)		
Lung	8 (29.6)	19 (70.4)		
Gynecological	6 (23.1)	20 (76.9)		
Other	16 (32.7)	33 (16)		
Myelosuppressive potential[e]				
High + intermediate	22 (38.6)	35 (61.4)	0.322	0.981
Low	47 (31.3)	103 (68.7)		
Vaccination influenza				
Vaccinated	22 (29.7)	52 (70.3)	0.335	0.930
Not vaccinated	48 (36.4)	84 (63.6)		
Hand washing				
Yes	54 (43.9)	69 (56.1)	<0.0001	12.499
No	15 (19.5)	62 (80.5)		
Cycle number				
0-3	25 (37.3)	42 (62.7)	0.308	2.357
4-6	21 (37.5)	35 (62.5)		
≥ 7	21 (26.9)	57 (73.1)		
BMI				
<18.5 kg/m^2	4 (36.4)	7 (63.6)	0.591	1.924
18.5-24.9 kg/m^2	32 (33)	65 (67)		
25-29.9 kg/m^2	19 (30.2)	44 (69.8)		
≥30 kg/m^2	14 (43.8)	18 (56.3)		

ECOG, Eastern Cooperative Oncology Group; NCCN, National Comprehensive Cancer Network.
[a]Strict restrictional behavior—patients maintaining ≥50% of social-environmental and dietary restrictions.
[b]Less strict maintenance of limitations includes patients who kept <50% of the restrictions (social-environmental and dietary behavior limitations).
[c]Statistical significance was set at $P < 0.05$, using two-tailed tests.
[d]Statistical test—the variables were assessed using a χ^2 test; in the case of an expected frequency <5, Fisher's exact test was carried out.
[e]Myelosuppressive potential—high myelosuppressive potential requiring granulocyte colony-stimulating factor according to NCCN guidelines.

DISCUSSION

Our study indicates that a large number of actively treated patients with solid tumors adhere to major social, environmental and dietary restrictions. These limitations were adopted across patients with different tumor types, treatments and clinical variables and are likely to severely affect the ability of cancer patients to pursue normal daily life.

The ultimate measure of QoL can be defined as the ability to conduct a full and meaningful life.[25] Commonly used validated tools, including the EORTC Core Quality of Life questionnaire (EORTC QLQ-C30), account for disease and treatment impact on normal life. However, current assessment of QoL relies on surrogate endpoints and focuses mostly on health-related outcomes, and the presence of specific signs and symptoms secondary to treatment adverse effects. Misbeliefs about disease and treatment may also compromise daily practices, a measure which is overlooked in HRQoL questionnaires.[4,20] Although measuring HRQoL endpoints is critical, they reflect an incomplete evaluation of daily activity of cancer patients in its wider sense. The activities addressed in the current survey are not routinely addressed in the commonly used side-effects or HRQoL tools implemented in pivotal clinical trials. Thus, the development of measures to assess real-life activity is of utmost importance, and should be integrated

in the evaluation of new drugs and biomedical technologies, serving as an additional endpoint in clinical trials. The questionnaire presented in this work provides an initial basis, which may serve as a potential tool bridging the gap between the currently available QoL measures and assessment of real-life consequences of cancer and its treatments.

A comprehensive evaluation of patients' ability to conduct daily activities is complex, not only influenced by the disease or treatment, but also requiring the integration of multiple dimensions: physical, psychological, cultural and social components. Indeed, we noted similar patterns of behavior regardless of clinical characteristics or treatment type (chemotherapy versus non-chemotherapy), reflecting adoption of non-evidence-based measures. For example, the data suggest patients' misconception regarding immunesuppressive effects of immunotherapy and targeted therapies.

In the absence of formal recommendations regarding daily activities as part of the registration materials or clinical trial data, patients rely on alternative sources of information. These include medical personnel, advocacy groups and unreliable sources such as friends and social media. Unfortunately, even reliable sources, including the American Cancer Society,[26] Cancer Research UK[9,10] and also the Israeli Cancer Association[11] sites, reinforce adoption of various, often unproven or unnecessary, restrictive measures, for example, avoiding contact with pets,[27] abstaining from eating raw fruits and vegetables and dyeing hair.[8,9] In accordance with previous reports, we observed no relationship between strict behavioral restraint and febrile neutropenia, further supporting the recommendation to maintain routine daily activities[15,18,23,24] including normal contact with children, grandchildren and friends.

Behavioral restrictions may reflect patients' need for control. Even if patients are aware that their restrictions are not useful, they might adopt restrictions as a means to gain control in a situation in which they have limited control over their disease and treatment—possibly explaining why 24% of restrictions came from personal choices, even if these personal choices probably have other sources of information. Additionally, there is most likely a link between applied restrictions and fear. Anxious people might maintain more restrictions, even in the presence of clear evidence that their behavior does not help in any way. The elderly population also maintained stricter limitations. It is also possible that some patients report some restrictions that actually serve as an excuse to justify their behavior: for example, patients reporting abstaining from travel or visiting friends and family, whereas they may actually suffer from symptoms of the treatment and disease. Danger can be a valid excuse, whereas fatigue, lack of desire and will may be more delicate to share with friends and family.

The survey was conducted before the COVID-19 pandemic. During the pandemic, actively treated cancer patients have been believed to be at higher risk of severe infection compared to patients without cancer.[28] Thus, heightened protective measures were recommended worldwide. It would be of major interest to study the long-term effects of COVID-19 on the daily behavior and activities of cancer patients.

There are several potential limitations to the current study. This is a single-institution survey. TASMC is a tertiary center, with nearly 70% of the patients residing out of Tel Aviv area, possibly explaining the relatively young age of the patients compared to the median age of cancer patients in Israel and the relatively high proportion of patients with higher education. The survey was conducted among patients with diverse cancers and treatments, thus limiting the ability to analyze the specific effect of each of these parameters on daily activity. This work surely is only the initial step and should be followed by direct analysis of each tumor and treatment type upon QoL. The adoption of such a questionnaire will require further validation and refinement. As the questionnaire evaluates the activity of the patients within the society, and not merely symptoms and signs, it may necessitate adjustments to unique cultural and societal characteristics specific to each country and its demographics. Moreover, in an effort to achieve the ultimate goal of improving QoL, we propose that registration materials of new drugs should include not only instructions regarding the management of side-effects but also clear, reliable and scientifically established information for patients regarding management of all aspects of normal daily activities.

Conclusions

The survey we conducted is, to our knowledge, the first to reflect compromised daily routines of actively treated cancer patients. Our findings indicate that cancer patients practice behavioral measures, which have a deleterious impact on real-life QoL. Our results call for the urgent development of tools allowing assessment of patients' real-life activity, beyond health-related QoL, and also for the implementation of education programs and practical instructions enabling patients to sustain normal life even during times of active cancer treatment.

DISCLOSURE

The authors have declared no conflicts of interest.

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