Does chemotherapy reduce stress?

FRANCISCO GIL, Ph.d., 1 G. COSTA, B.Sc., 2 AND F.J. PÉREZ, B.Sc. 3

(RECEIVED February 14, 2010; ACCEPTED April 15, 2010)

ABSTRACT

Objective: The purpose of this study was to assess the psychological care needs of cancer patients throughout the healthcare process: after diagnosis, after medical treatment (surgery, chemotherapy, radiotherapy) and during follow-up.

Method: A total of 703 ambulatory cancer patients were assessed in this study. The inclusion period was from April 1, 2005 to April 30, 2007. The first psychological scales used were the 14-item Hospital Anxiety and Depression Scales (HADS), which has two sub-scales for anxiety (7 items) and for depression (7 items). All patients with a score \geq 14 were assessed through the Structured Clinical Interview for Psychiatric Disorder (SCID-I) of the DSM-IV. All data were compared with sociodemographic and medical characteristics.

Results: Of the 703 cancer patients in the study, 349 were men and 354 women, with a mean age of 53 years. The median time between the cancer diagnosis and our clinical interview was 6 months (range, 12 days to 190 months). Overall, the screening tools indicated that one in four patients needed psychological care. The most common psychiatric diagnosis was adjustment disorder (129 cases), whereas 10 patients were diagnosed with major depression. Using a HADS cut-off score of >7 for anxiety and depression, 28% and 17% of patients, respectively, were classified as "possible clinical cases." Risk factors for distress included age <65 years, asthenia, constipation, and a low performance status. However, chemotherapy treatment was found to be a protector against distress in cancer patients.

Significance of Results: Chemotherapy treatment is interpreted by the patients as a protector against cancer, thereby reducing distress levels.

KEYWORDS: Cancer, Chemotherpy, Stress

INTRODUCTION

Many cancer patients show psychological morbidity and problems in the psychological adjustment to a diagnosis of cancer and during treatment (Razavi & Delvaux, 1995; Gil et al., 2008). In the landmark study by Derogatis et al. (1983), 47% (101/215 cases) of cancer patients presented with some type of mental disorder, with the most common being psychological adjustment disorders (anxiety and/or depressive mood) (68%), and clinical depression

Address correspondence and reprint requests to: Francisco Gil, Psychooncology Unit, Hospital Duran I Reynals. Institut Català d'Oncologia, 08907- L'Hospitalet de Llobregat, Barcelona, Spain. E-mail: fgil@iconcologia.net

(13%) (Derogatis et al., 1983). A study of 277 cancer patients in Italy, Portugal, and Spain reported that 28.5% of these patients were defined as clinical cases requiring psychological care (Grassi et al., 2004). Cancer patients have a higher risk of suicide than the general population. Akechi et al. (2002) found 62 of 1713 cancer patients (4%) referred for psychiatric treatment exhibited some form of suicidal behavior, generally associated with depression and low performance status.

The purpose of this study was to assess the prevalence of psychiatric diagnoses and the need for psychological care in cancer patients. In particular, we sought to identify predictors of distress and mental disorders.

¹Psychooncology Unit, Hospital Duran I Reynals, Institut Català d'Oncologia, L'Hospitalet de Llobregat, Barcelona, Spain

²Psychiatry Service, Hospital de Mataró, Mataró, Barcelona, Spain

³Clinical Research Unit, Medical Oncology Service, Hospital Duran I Reynals, Institut Català d'Oncologia. L'Hospitalet de Llobregat, Barcelona, Spain

456 Gil et al.

METHOD

The study sample consisted of ambulatory cancer patients ≥ 18 years of age who were receiving medical treatment at the Hospital Duran I Reynals, Catalan Institute of Cancer, L'Hospitalet, Barcelona, Spain. Patients with a performance status (Karnofsky & Burchenal, 1949) < 50 or with cognitive impairment (≥ 3 errors in the Pfeiffer questionnaire) (Martinez de la Iglesia et al., 2001) were excluded from the study.

Procedure

All patients who agreed to participate in the study were assessed by a clinical psychologist. Once the informed consent form was signed, several different psychological measures were used for assessment. The first psychological instrument administered was the Hospital Anxiety and Depression Scale (HADS) (Ibbotson et al., 1994; Tejero et al., 1986), a 14-item questionnaire with two subscales (7 items each) for anxiety and depression symptoms, respectively. The HADS was used as a screening instrument, with a cut-off score > 14 indicating the patient was a candidate for clinical evaluation. All patients with a score of < 14 were excluded from the study, whereas the remaining patients (HADS > 14) underwent a Structured Psychiatry Interview and were classified according to the criteria given in the Diagnosis and Statistical Handbook for Mental Disorders, 4th edition (SCID-I-DSM-IV) (SCID I y II, 1999).

This interview was used to make the definitive diagnosis using the diagnostic criteria described in the DSM-IV. In regular clinical practice, the HADS also has two cut-off scores of >7 for the aforementioned anxiety and depression subscales. Patients who surpass the minimum cut-off for either of these subscales are candidates for referral to psychological care.

In addition to the HADS and DSM-IV, other measures were also used:

- Pfeiffer Questionnaire: used to detect cognitive deficit. The cut-of score is ≥3 errors (Martinez de la Iglesia et al., 2001).
- Karnofsky Performance Status. This scale assesses functional capacity. It has a range from 100 (intact functional capacity) to 0 (death) (Karnofsky & Burchenal, 1949).
- Medical and sociodemographic characteristics of patients were assessed in the study.

Data Analysis

The Statistical Package of Social Sciences (SPSS) was used for statistical analyses. When dichoto-

mous/nominal variables between two groups were compared, the exact Fisher test/χ^2 was used. The t-test was used to compare continuous variables. The Spearman correlation coefficient was used to analyze the associations between two continuous variables. Logistic regression analysis was used to assess each of the variables separately as potential predictors of psychiatric disorder or "possible clinical case" (HADS ≥ 14), requiring referral for psychological care. Likewise, we performed multiple logistic regression analyses of all variables found in the bivariate analyses to be predictive of psychiatric disorder or "possible clinical case."

RESULTS

A total of 703 cancer patients were included in the study, 25 of whom refused to participate due to emotional difficulties in talking about the illness, physical symptoms, or for lack of time for the interview. The number of men and women was similar (349 and 354, respectively). The mean age was 53 and most (76%) of the patients were married, 85% had at least one child, and only 46% had completed high school or more. The most common cancer diagnosis was breast cancer (141 cases, 20%), followed by lung (127, 18%) and colorectal cancer (126, 18%). Of the 703 patients, 152 (22%) had metastatic disease, 417 (60%) had a family history of cancer, 321 (77%) had relatives who had died of cancer, and 618 (88%) were receiving chemotherapy. The Karnofsky performance status (Karnofsky & Burchenal, 1949) was ≥ 80 in 80% of patients, and 100% had an intact cognitive capacity. The median time between diagnosis and the clinical interview was 6 months (range, 12) days to 190 months) (Table 1).

Prevalence of Mental Disorders

Approximately 1 in 4 patients (184 cases) in our study were diagnosed with a psychiatric disorder, for a prevalence of 26% of mental disorders in our sample (Table 2). The most common psychiatric diagnosis was adjustment disorder (129 cases, 70%), followed by major depression (10 cases, 5%). At the time of diagnosis, 34% (236 patients) were receiving antidepressant or sedative treatments. Overall, 156 patients (22%) had a past history of psychiatric disorders, and 222 (32%) had a family psychiatric history. In the univariate and multivariate analysis, having children, age (<65 years), personal and family psychiatric antecedents, physical symptoms (pain, anorexia, constipation, insomnia, asthenia), previous radiotherapy treatment, hormonal treatment, use of antidepressant and sedative treatment,

Table 1. Baseline characteristics

Variable	Frequency $(N = 703)$	%
Sex		
Male	349	50%
Female	354	50%
Age (years)		
<65	571	81%
>65	132	19%
Educational degree		
University	41	6%
High school	72	10%
Middle school	203	29%
Elementary school	382	54%
Uneducated	3	0.5%
Unknown	2	0.5%
Marital Status		
Single	71	10%
Married	535	76%
Widowed	44	6%
Divorced	53	8%
Children		
0	110	16%
1	97	14%
2	332	48%
3	111	16%
>3	53	6%
Diagnosis		
Breast	144	20%
Lung	131	19%
Colorectal	126	18%
Gynecological and	104	15%
genitourinary		
Head and neck	31	5%
Leukemia	24	3%
Lymphoma	17	2%
Stomach	8	1%
Hepatocellular	7	1%
Others	111	16%
Disease status		
Local	212	30%
Loco-regional	230	33%
Metastatic	152	22%
Hemotological Malignancies	109	15%
Performance Status		- /-
(Karnofsky)		
<70	44	6%
>70	659	94%
		2 = 70

and low performance status were all predictors of mental disorder (Table 3).

Possible Clinical Cases

One-hundred and thirty-six patients (25% of the sample) had an overall HADS score \geq 14. Of these, 106 (58%) were subsequently diagnosed with a psychiatric disorder (DSM-IV). On the HADS anxiety and depression subscales, 154 patients (28%) were classified as "possible clinical cases" on the anxiety

Table 2. Prevalence of mental disorders

Number of psychiatric cases	184 (26%)
Mental disorder (DSM-IV)	
Adaptive Disorder	129 (71%)
Dysthmia	13 (7%)
Major Depression	10 (5%)
Phobia	8 (4%)
Posttraumatic stress disorder	6 (3%)
Anguish disorder with/without agoraphobia	3 (2%)
Generalized anxiety disorder	2(1%)
Bereavement	2(1%)
Others	9 (5%)

subscale (score >7) and 96 (17%) on the depression subscale (score >7). Of these, 110 of 154 cases (60%) (anxiety subscale) and 73 (40%) (depression subscale), respectively, had a psychiatric diagnosis (DSM-IV).

Risk Factors for Distress

Of the univariate analysis, the following sociodemographic and medical factors were found to be predictors of emotional distress (HADS ≥14) in cancer patients: female sex, age (<65 years), unmarried, having children, previous personal and family psychiatric antecedents, use of antidepressant or sedative treatment, previous radiotherapy treatment, current hormonal treatment, low performance status (Karnofsky, 1949) and physical symptoms (pain, anorexia, constipation, insomnia) (Table 4). Chemotherapy treatment, on the contrary, was found to protect patients from emotional distress. In the multivariate analysis, the risk factors for distress were age (<65 years), asthenia, constipation, and low performance status (Karnofsky, 1949). The multivariate analysis also showed that chemotherapy treatment was a protector of distress.

DISCUSSION

Slightly more than one in four cancer patients (26%) in our study had a psychiatric diagnosis. The main psychiatric diagnosis was adaptation disorder (70%), while only 5% of patients had clinical depression. The prevalence of mental disorders in our study was lower than that reported by Derogatis et al. (1983) (47%). The number of possible clinical cases (based on the HADS cut-off scores) in our sample was similar to the figures reported by Grassi et al (28%) (Grassi et al., 2004). However, in patients with advanced cancer, the number of psychiatric diagnoses in other studies was higher (major depressive disorder 6.8 vs 5%, generalized anxiety disorder

458 Gil et al.

Table 3. Univariate and multivariate analysis of risk factors of mental disorder (DSMIV SCID-I)

Factors		No. of Patients	Odd ratio univariate	Multivariate model
Age	<65 years	440	1.72 (1.07-2.77)	
_	≥65 years	111		
Children	No Children	83	0.46(0.24 - 0.87)	0.20(0.08 - 0.49)
	1–2 Children	336	0.59(0.37 - 0.96)	0.41(0.22-0.76)
	>2 Children	89		
Psychiatric history	Yes	130	2.76(1.84 - 4.14)	
	No	421		
Psychiatric family history	Yes	184	1.46(1-01-2.11)	
	No	367		
Psychopharmacologic treatment	Yes	201	2.89(2-4.14)	1.79(1.10-2.93)
, ,	No	348		
Previous radiotherapy treatment	Yes	108	1.80(1.17-2.77)	
10	No	443		
Current hormonal treatment	Yes	38	2.65(1.36-5.16)	2.83(1.11-7.16)
	No	513		
Karnofsky performance status	50-70%	162	1.89(1.29-2.76)	
<i>v</i> 1	80-100%	387		
Pain	Continuous from 1 to 10		1.18(1.11-1.25)	1.08(1-1.17)
Constipation	Continuous from 1 to 10		1.07 (1-1.14)	
Insomnia	Continuous from 1 to 10		1.20 (1.13-1.28)	
Fatigue	Continuous from 1 to 10		1.15(1.08-1.22)	
Dry mouth	Continuous from 1 to 10		1.08(1.02-1.14)	
Anorexia	Continuous from 1 to 10		1.13(1.06-1.20)	
			, , , , , , , , , , , , , , , , , , , ,	

3.2% vs. 1%) than what we found, likely due to the presence of physical symptoms (Kadan-Lottick et al., 2005). The presence of pain, constipation, and fatigue were associated with higher levels of dis-

tress and a greater probability of mental disorder. Our sample of patients had a good performance status (94% had a Karnofsky index \geq 70) (Karnofsky & Burchenal, 1949), and 80% (618 patients) were

Table 4. Univariate and multivariate analysis of risk factor of distress (HADS \geq 14)

Factors		No. of Patients	Odd ratio univariate	Multivariate model
Sex	Men	349	0.53 (0.37-0.77)	
	Women	354		
Age	<65 years	571	1.27(0.79-2.05)	$0.40 \ (0.18 - 0.87)$
	≥65 years	132		
Psychiatric history	Yes	156	3.05(2.06-4.51)	
· ·	No	547		
Family psychiatric history	Yes	222	$1.53 \ (1.06 - 2.23)$	
	No	481		
Psychopharmacologic treatment	Yes	236	2.94(2.04-4.25)	
	No	463		
Previous radiotherapy treatment	Yes	140	1.68(1.11-2.55)	
	No	563		
Chemotherapy treatment	Yes (20.4%)	618	0.56 (0.34 - 0.93)	0.22 (0.1 - 0.49)
	No (31.8%)	85		
Hormonal treatment	YES	40	1.97(1-3.88)	
	NO	663		
Karnofsky performace status	50-70%	184	2.81 (1.92 - 4.11)	2.09(1.16 - 3.76)
• •	80-100%	515		
Pain	Continuous from 1 to 10		1.18(1.11-1.24)	
Anorexia	Continuous from 1 to 10		1.16(1.09-1.23)	
Constipation	Continuous from 1 to 10		1.14 (1.07 - 1.21)	1.13(1.03-1.24)
Insomnia	Continuous from 1 to 10		1.26 (1.18 - 1.33)	
Fatigue	Continuous from 1 to 10		1.29(1.20-1.38)	1.22(1.10-1.34)
Dry mouth	Continuous from 1 to 10		1.15(1.08-1.21)	

receiving chemotherapy, explaining the lower prevalence of psychiatric cases compared with the Derogatis study (Derogatis et al., 1983).

Young age, personal and family psychiatric history, and physical symptoms were predictors of emotional distress in cancer patients. The only variable that was shown to be a protector against emotional distress on the both the univariate and multivariate analyses was chemotherapy. Kim et al. (2008) reported that the heavily-treated cancer patients had more positive perceptions of the benefits of chemotherapy and more willingness to participate in clinical trials. Patient perceptions of cancer treatment and the meanings they assign to these treatments play an important role in levels of emotional distress. Patients generally perceive adjuvant chemotherapy as a necessary step in minimizing future recurrence (Charles et al., 1998). Overall, all patients were positive about the clinical (life prolongation, contribution to cure) and psychological benefits (contribute to cure, less perceived likelihood of the disease recurring) of adjuvant chemotherapy and their ability to cope with this treatment, regardless of whether or not they reported having the freedom of treatment choice. In fact, many patients do not want to be involved in treatment decision-making (Jansen et al., 2006), and encouraging patients to do so may lead to undue anxiety and distress (Hack et al., 1994).

Chemotherapy is the only variable that has shown to protect patients from distress. It is the meanings the cancer patients assign to chemotherapy that reduce distress level. In contrast, both radiotherapy and hormonal treatment are predictors of distress and mental disorder, perhaps because these treatments are less well understood or rejected more often by patients. For this reason, it is important to explain the benefits of these treatments to patients when they are used as adjuvant therapy after surgery and chemotherapy, extending the notion that all these treatments are beneficial. If patients are convinced, this will reduce emotional distress.

An idea commonly expressed in both individual consultations and support groups is that if the chemotherapy hurts and causes side effects, then this must be evidence of its increased efficacy. We might call this idea "no pain, no gain." Bell (2009) found a cultural model of chemotherapy that emphasizes the value of suffering as a means of tracking treatment effectiveness and the possibility of cure. One of the patients interviewed in that study was quoted as saying "...but the chemo, now that I have it I'm much happier, being on the chemo...." Also, the way chemotherapy is administered has an important role. Some patients point out the diluted potency of oral chemotherapy versus intravenous chemother-

apy. It is clear that oncologists need to pay attention to the meaning patients assign to cancer treatments.

Even in cancer patients whose state of health is poor or only tolerable, a large percentage of patients still insist on receiving chemotherapy (Sahm & Hommel, 2005). Slevin et al. (2005) found a higher willingness among cancer patients to undergo debilitating treatments even if the chances of success were slight. In palliative care, both patients and family often demand more chemotherapy, and when the doctor refuses they tend to interpret this decision as accepting death. At this moment, which we call a "crisis of awareness" when patients and family are coping with the final step, it is important not to give false hope, but at the same time, it is important to maintain hope in the continuing care.

Although we believe the results presented here are both novel and useful, it is important to be aware of the limitations of this study. First, it may not be possible to generalize our specific results to cancer patients treated at other institutions. Our sample consisted of outpatients whose performance status (Karnofsky) was good and who were undergoing chemotherapy treatment. Second, there may be other variables, not considered in our study, which could be predictors of distress or mental disorder in cancer patients.

The role of the oncologist in clarifying the myths about chemotherapy — specifically, that suffering does not necessarily signify greater benefits — is essential. Based on our experience with breast cancer support groups, we have found that such groups provide an opportunity to address the misconceptions that our patients have about chemotherapy, including toxicity and the form of treatments (intravenous or oral)

In summary, the perceived benefits of chemotherapy help patients to better cope with the illness, thereby reducing emotional distress.

This novel finding presented here regarding patients' positive perception of chemotherapy and its positive impact on emotional distress, has implications for improving patient care, especially the emotional aspects. Our data have shown that chemotherapy is a protector against emotional distress. If physicians are aware of this, and the fact that neither to consider the importance of fully discussing the benefits of other treatments (such as radiotherapy and hormonal therapy) in order to further reduce emotional distress associated with having cancer.

ACKNOWLEDGMENT

This study was supported by a grant from the Agency of Technology Evaluation and Medical Research (AATRM 102/19/2004).

460 Gil et al.

REFERENCES

Akechi, T., Nakano, T., Akizuki, N., et al. (2002). Clinical factors associated with suicidality in cancer patients. Japanese Journal of Clinical Oncology, 32, 506–511.

- Bell, K. (2009). "If it almost kills you that means it's working." Cultural models of chemotherapy expressed in a cancer support group. Social Science and Medicine, 68, 169–176.
- Charles, C., Redko, C., Whelan, T., et al. (1998). Doing nothing is no choice: Lay constructions of treatment decision-making among women with early-stage breast cancer. Sociology of Health and Illness, 20, 71–95.
- Derogatis, L.R., Morrow, G.R., Fetting, J. et al. (1983). The prevalence of psychiatric disorders among cancer patients. *Journal of the American Medical Association*, 249, 751–757.
- Gil, F., Costa, G., Pérez, F.J., et al. (2008). Adaptación psicológica y prevalencia de trastornos mentales en pacientes con cáncer (Psychological adaptation and prevalence of mental disorders in cancer patients). *Medicina Clínica*, 130, 90–92.
- Grassi, L., Travado, L., Gil, F., et al. (2004). Psychosocial morbidity and its correlates in cancer patients of the Mediterranean area: Findings from the Southern European Psycho-Oncology Study. *Journal of Affective Disorders*, 83, 243–248.
- Hack, T.F., Degner, L.F. & Dyck, D.G. (1994). Relationship between preferences for decisional control and illness information among women with breast cancer: A quantitative and qualitative analysis. Social Science Medicine, 39, 279–289.
- Ibbotson, T., Maguire, P., Selby, P., et al. (1994). Screening for anxiety and depression in cancer patients: The effects of disease and treatment. *European Journal of Cancer*, 30, 37–40.
- Jansen, S.J.T., Otten, W. & Stiggelbout, A.M. (2006). Factors affecting patients perceptions of choice regarding adjuvant chemotherapy for breast cancer. Breast Cancer Research and Treatment, 99, 35–45.
- Kadan-Lottick, N.S., Vanderwerker, L.C., Block, S.D., et al. (2005). Psychiatric disorders and mental health service use in patients with advanced cancer. *Cancer*, 104, 2872–2881.

- Karnofsky, D.A. & Burchenal, J.H. (1949). The clinical evaluation of chemotherapeutic agents in cancer. In Evaluation of Chemotherapeutic Agents, MacLeod, C.M. (ed.). pp 191–205. New York: Columbia University Press.
- Kim, J.W., Kim, S.-J., Kwon, J.-H., et al. (2008). Cancer patient\u00ed awareness of clinical trials, perceptions on the benefit and willingness to participate: Korean perspectives. *British Journal of Cancer*, 99, 1593-1599.
- Martinez de la Iglesia, J., Dueñas, R., Onis, M.C., et al. (2001). Adaptación y validación al castellano del cuestionario de Pfeiffer (SPMSQ) para detectar la existencia de deterioro cognitivo en personas mayores de 65 años (Adaptation and validation to Spanish of the Pfeiffer questionnaire (SPMSQ) for detecting cognitive deficit in adults older than 65 years). *Medicina Clínica 1*, 17, 129–134.
- Razavi, D. & Delvaux, N. (1995). The psychiatrist's perspective on quality of life and quality of care in oncology: Concepts, symptom management, and communication issues. *European Journal of Cancer*, 31A (Supp. 6), S25–S29.
- Sahm, S., Will, R. & Hommel, G. (2005). What are cancer patients preferences about treatment at the end of life and who should start talking about it?. A comparison with healthy people and medical staff. Support Care Cancer, 13, 206–214.
- SCID I y II. (1999). Guía de Entrevista Clínica Estructurada para los Trastornos del eje I y II del DSM-IV [Structured Clinical Interview for the Psychiatric Disorders Axis I and II of the DSM-IV]. Editorial Masson.
- Slevin, M.L., Stubbs, L., Plant, H.J., et al. (1990). Attitudes to chemotherapy: Comparing views of patients with cancer with those of doctors, nurses, and general public. *British Medical Journal*, 300, 1458–1460.
- Tejero, A., Guimerá, E.M., Farré, J.M., et al. (1986). Uso clínico del HAD (Hospital Anxiety and Depression Scale) en población psiquiátrica: un estudio de su sensibilidad, fiabilidad y validez (Clinical use of HAD (Hospital Anxiety and Depresión Scale) in psychiatric population: an study of sensitivity, reliability and validation). Revista del Departamento de Psiquiatría de la Facultad de Medicine de Barcelona, 13, 233–238.