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Cancer survivors referred to a long-term survivorship outpatient service within academic medical oncology: descriptive study

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Abstract

Purpose Long-term cancer survivors (LTCS) are a vulnerable and continued growing population. To date, only few studies have been conducted in the Spanish population; none of them with a comprehensive analysis of the most common problems identified for cancer survivors in order to improve their care and quality of life.

Methods We conducted an observational descriptive study in 347 patients recruited between January 2015 and December 2016 from our newly created medical office for the specific care and follow-up of LTCS. Variables that describe the medical history were completed by the oncologist and measures on common problems previously reported for LTCS, related to cancer diagnosis and treatment, function, lifestyle, and emotional concerns, were collected from the patient.

Results The mean age of our patients was 65.1 years at the time of the study and a median time without any antitumor treatment of 5.7 years. At the time of cancer diagnosis, 298 patients (85.9%) had at least one related chronic disease and 184 patients (53%) were retired. In addition, in 17.9% of those who continued working, income had been reduced. The incidence of health problems showed an increase during follow-up, even after 5 years, and required evaluation in an emergency department in 157 cases (45.3%). Regardless of age or sex, 239 patients (68.9%) had a significant decrease in sexual activity and 120 (34.6%) were diagnosed with clinical depression.

Conclusions LTCS are patients with significantly high socioeconomic, labor, sexual, health, and psychological problems, 5 years after completion of cancer treatment, especially in older survivors.

Implications for Cancer Survivor Common concerns of LTCS were identified and are consistent across many countries. It is important to realize that even 5 or so years following treatment, both medical and non-medical problems can exist and may need attention by an expert.

Keywords Long-term Cancer Survivor · Follow-up · Quality of life · Care plan

Abbreviations

CI	Confidence interval
HADS	Hospital Anxiety and Depression Scale
IQR	Interquartile range
FIGO	International Federation of Gynecology and Obstetrics
LTCS	Long-term cancer survivor
REDECAN	Spanish Network of Cancer Registries

SEOM	Society of Medical Oncology
SF	Short form
OR	Odds ratio
VAS	Visual analogue scale

Introduction

In recent decades, the survival rates of cancer patients significantly increased, due to a gradual improvement in the diagnostic and therapeutic procedures [1–3]. Several studies carried out in Europe and in the United States (US) support this improvement. As of January 2019, there were an estimated 16.9 million cancer survivors in the US [4], with figures expected to reach 21.7 million by 2029. In Europe, the last EURO CARE study (European Cancer Registry based on

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survival and care of cancer patients) [1], published in 2014, describes a generalized increase in cancer survival rates between 1999 and 2007 regardless of the region, mainly for non-Hodgkin's lymphoma and prostate and rectal cancer. Specifically, in Spain, data from the Spanish Society of Medical Oncology (SEOM) [2], as well as from the Spanish Network of Cancer Registries (REDECAN) [3], verify this increased survival. The 5-year survival rate in men was comparable to the European average (49% vs 50%) and in the case of women was about the same (58%) [3]. As these studies show, long-term cancer survivors (LTCS) are increasing annually. In Spain there are around one million cases, with an expected growth of up to 50% in the year 2020 [5].

However, in many of these cases, aggressive treatments were needed to control the tumor, which implies long-term sequelae that can contribute to disability and mortality in the case of second tumors. In addition, patients can experience psychological suffering related to diagnosis with social stigma and potentially fatal consequences. Therefore, in a majority of patients, the diagnosis and treatment of cancer have marked a "before and after" demarcation and the transition from treatment to post-treatment can be an especially challenging phase that requires a careful consideration [6]. In those tumors diagnosed in children or young adults with even a greater life expectancy, more than two thirds develop late sequelae [7], and potential limitations in specific daily activities occur, mainly in survivors of central nervous system and bone tumors [8]. Moreover, LTCS have many other problems to deal with, related to their sexual life and their social, economic, and labor situations [9, 10].

In the last few years, we have learned that these issues are common worldwide [11]. However, in most countries, there still is not an organized system of survivorship care and LTCS must "seek" their own care [12]. This combination of socioeconomic, geographic, and demographic factors may cause an inequity in care among cancer survivors, even within the same region [13]. On the other hand, oncology departments are more overcrowded, focusing their care on specific cancer treatment and palliative care in most cases. In this regard, the shared cared model for LTCS, involving primary care physicians, could be a successful strategy in the future, although its effectiveness still needs to be improved [14]. There remains a widespread lack of awareness of what longer term cancer survivors need, and currently there is very little structured research for LTCS that can impact quality of care and quality of life [15, 16].

This study describes the major concerns of long-term cancer survivors, assessing the problems from patient's and doctor's point of view, after 5 years from the end of cancer treatment based on a specific medical office dedicated to LTCS care.

Methods

Study design and contextualization

We conducted an observational descriptive study carried out in 347 patients recruited from January 2015 to December 2016 in the Long-term Cancer Survivors Medical Office at La Paz University Hospital (Madrid, Spain), one of the major hospitals of the Spanish Public Health National System. This medical office was created in January 2015 within the Medical Oncology Department to ensure quality care of LTCS, including follow-up of cancer recurrence and second primary tumors, health promotion, early intervention for complications related to cancer and its treatment, evaluation of psychosocial and socioeconomic concerns, and care coordination with other health professionals involved in cancer survivorship care.

Target population

All the patients had a history of cancer, were disease-free and without any antitumor therapy for at least 2 years, including hormonal and biological treatment. Patients with tumor recurrence or with a second tumor meeting the previously specified criteria were included. All LTCS over 18 years old with ability to understand and voluntarily sign the informed consent and no neurological impairment observed during this 2-year period were asked to participate in the study. Most patients were referred between 2015 and 2016 from oncologists from the same department an average of 2–3 years following the end of cancer treatment.

Each of the patients included in the study was informed and signed an informed consent. The privacy of information was guaranteed, and the use of data provided for scientific purposes authorized, in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was granted by the Medical Ethical Committee of La Paz University Hospital.

Measures

Oncologist measures of medical history

The oncologist responsible for the medical office completed the questionnaire providing the following clinical variables: tumor characteristics, cancer treatment received, cancer treatment sequelae, comorbidities at cancer diagnosis, medical conditions after cancer therapy, second primary tumors, tumor relapse and its treatment, number of visits to the emergency department, and hospital admissions. The stage of the tumor was determined, according to the eighth edition of TNM [17] classification system, except in 7 of the cases that another classification system was used, as in the case of ovarian cancer, which was used in the classification of the International Federation of Gynecology and Obstetrics (FIGO).

Patient-reported measures

Patients completed a set of questions based on the Assessment of Survivor Concerns [18] and the Spanish versions of the SF-36 Health Survey [19, 20] and the Hospital Anxiety and Depression Scale (HADS) [21, 22]. Patient reports of education level, economic and employment status, lifestyle and sleep habits, alcohol and tobacco consumption, regular medication intake, symptoms related to cancer diagnosis, and treatment and status regarding sexual activity were obtained using a questionnaire format. In terms of the measure of anxiety and depression (HADS), a score ≥ 11 indicated depressive syndrome, between 7 and 10 was considered indeterminate, while those with ≤ 7 were categorized as asymptomatic. Pain severity was rated using a visual analogue scale (VAS) with values from 0 to 10.

Data collected and data analysis

After signing the informed consent, data related to cancer diagnosis and treatment were collected at the first visit to this office, as well as socioeconomic, physical, and mental health baseline conditions of LTCS. The socioeconomic, physical, and mental health features of patients were measured at the time of cancer diagnosis and at the time of follow-up in the long-term service. Additionally, treatment sequelae, presence of depressive syndrome, and lifestyle acquired as a result of the diagnosis were assessed.

The statistical analysis was conducted in 2018. Most of the variables studied were analyzed according to age, gender, time of follow-up, and type of cancer and, in some cases, were also based on the income and the level of education. The age was categorized into two groups, 18–70 years old and ≥ 70 years old, referenced by the mean and its standard deviation (SD). The follow-up time was divided into two follow-up periods: 2–5 years or ≥ 5 years, and was mentioned as the median and interquartile range (IQR). The incidence and cumulative incidence of different illnesses observed throughout the follow-up period were calculated. The comparison of categorical variables was performed using Pearson's chi-square, and these were considered significant when p values < 0.05 ($p < 0.05$). Variables not normally distributed were compared using the Mann-Whitney U test. The Spearman correlation coefficient was also used to calculate the cumulative incidence of the main comorbidities during the follow-up. All variables were entered in a database and graphs, and statistical analyses were performed using SPSS 18 program (IBM®, Somers, NY, USA), with cooperation of the Biostatistics Department of the La Paz University Hospital.

Results

Data obtained from the oncologist

Three hundred forty-seven patients were included in the study, 187 were women (53.9%) and 160 men (46.1%). The mean age at diagnosis of cancer was 56.8 ± 14.7 SD (range: 16–89 years). The mean age of the patients at the time of inclusion in the study was 65.1 years ± 13.5 SD (range: 24–91), with a median time from cancer diagnosis of 7.1 years (IQR: 2–37 years) and without any antitumor treatment of 5.7 years (IQR: 2–31.5 years).

The characteristics of the patients at the time of diagnosis are summarized at Table 1.

The tumors most commonly diagnosed were breast cancer in 88 patients (25.4%) and colon cancer in 85 patients (24.5%). The types of cancers included in the study are specified at Table 2. Regarding TNM [12] classification system, 35.5% were diagnosed at stage I, 31.9% at stage II, 25.6% at stage III, and 5.4% at stage IV. A surgical intervention was performed in 91.8% of patients, 32.3% were treated with radiotherapy, and 59.6% also received chemotherapy. In addition, 10.5% of patients received treatment with biologic drugs, more than half with trastuzumab, and 11.8% were treated with aromatase inhibitors or tamoxifen. The main fields of radiation were the breast/axilla and pelvic region as (neo)adjuvant treatment for breast and rectal cancer, respectively. Ninety-three patients were treated with fluoropyrimidines (26.8%) and 92 with platinum salts (26.5%). The types of treatment that patients of the study received are outlined in Fig. 1.

Two hundred fifty-five patients (73.5%) had some type of functional disorders secondary to cancer treatment: 11.5% had a mastectomy, 7.8% axillary lymphadenectomy, 4% had moderate to severe cervicofacial functional disorder, and 3.4% had a permanent colostomy or ileostomy. Furthermore, 45.3% of the patients were assessed in the emergency department during the follow-up period, 33.9% were admitted to hospital due to an infectious disease, 15.6% were checked for moderate to severe pain, and 12.4% for superficial or deep venous thromboembolic disease.

The annual cumulative incidence of hypercholesterolemia during the follow-up period was 5.8%, while in the case of type II diabetes mellitus, osteoporosis and arterial hypertension was 1.6%, 1.4%, and 0.6% per year, respectively. The increase in the incidence of hypercholesterolemia was higher in patients with an age ≥ 70 years [OR = 2.3 (95% CI: 1.31–4.05; $p = 0.004$)], as well as in the case of osteoporosis [OR = 4.81 (95% CI: 1.9–11.9; $p = 0.001$)]. These variables were analyzed according to gender, diagnosis, and follow-up time without finding statistically significant differences.

The relapse rate was 10.7% and 15.8% had second tumors, defined in Table 3. The incidence of second

Table 1 Patient characteristics at the time of diagnosis

Patient's characteristics at the time of diagnosis			Collected data
Number of patients	347		
Mean age	56.8 years		Medical questionnaire
Sex	Female	53.9%	Patient questionnaire
	Male	46.1%	
Relationship status	Married	72%	Patient questionnaire
	Widower	14.1%	
	Single	6.6%	
	Divorced	7.3%	
Academic status	Primary education	45.3%	Patient questionnaire
	High school	26.8%	
	University studies	27.9%	
Employment status	Working/studying	61.2%	Patient questionnaire
	Retires	33%	
	Unemployment	5.8%	
Harmful habits	Smoke	23%	Patient questionnaire
	Drink alcohol (regularly)	44.9%	
Comorbidity (≥ 1: 85.9%)	Hypercholesterolemia	35.4%	Medical questionnaire
	Arterial hypertension	26.3%	
	Diabetes mellitus type II	13%	
	Osteoporosis	3.7%	
	Depressive syndrome	3.2%	

tumors was significantly higher with a follow-up longer than 5 years ($p < 0.05$).

Data obtained from the long-term cancer survivors

Residual peripheral neuropathy was reported in 20.7% of patients, and statistically significant differences were noted

Table 2 Distribution by tumor type

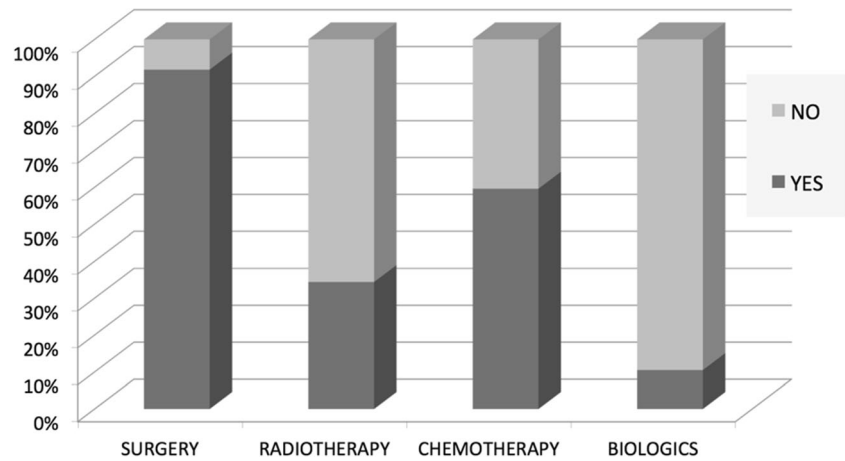
Cancer types	Frequency (Number of cases)	Percentage of patients
Breast	88	25.4 %
Colon	85	24.5 %
Melanoma	42	12.1 %
Rectal	27	7.8 %
Gastric	12	3.5 %
Sarcoma (soft tissue and bone)	12	3.5 %
Lung	10	2.9 %
Prostate	7	2.0 %
Head and neck	6	1.7 %
Ovarian	4	1.2 %
Bladder	3	0.9 %
Other (incidence = 1)	51	14.7 %
Total	347	100.0 %

between patients treated for colon and breast cancer [OR = 3.37; 95% CI: 1.58–7.2; $p = 0.001$]. In addition, 14.7% of patients required joint prosthesis replacement, 9.8% reported some type of chronic pain, 12.1% constipation, and 5.5% disabling asthenia for daily activities of living. Moreover, 29.1% of the patients reported memory loss, regardless of age, previous chemotherapy treatment (only 17.4% of patients who received this treatment), or tumor type.

According to employment status, 29.3% remained in their current employment while 19.9% were retired (6.9% age-based and 13% due to early retirement related to cancer treatment sequelae). Only 1.4% of patients changed their jobs, 3.6% reduced their working hours, and 3.6% were not renewed after cancer diagnosis. Furthermore, in 17.9% of patients who continued working reported their income was reduced, while in 4.3% salary improved over time.

In accordance with the HADS measure, 34.6% of patients scored at a level of clinical depression during the follow-up. These findings did not significantly relate to age, gender, or follow-up time. However, patients who had some experience of university study had a lower percentage of clinical depression than those with only a primary education [OR = 0.53 (95% CI: 0.3–0.8; $p = 0.015$)]. Patients with an equal or higher income level also had a lower percentage of clinical depression [OR = 0.4 (95% CI: 0.2–0.8; $p = 0.008$)]. In addition, 53.1% of patients reported sleep difficulties, with significant differences between women and men [OR = 3.36 (95% CI: 1.37–8.37; $p = 0.007$)]. Patients who reported a complete loss

Fig. 1 Treatment received for cancer.



of interest in their own physical appearance were 19.6% of and 68.8% reported a significant decrease in sexual activity. In addition, 18.8% reported sexual impotence or a complete loss of sexual interest, regardless of age or sex. Patients diagnosed and treated for colon cancer reported higher sexual activity than those with history of breast [OR = 3.36 (95% CI: 1.37–8.37, $p = 0.007$)] or rectal cancer [OR = 3.83 (95% CI: 0.99–14.7, $p = 0.007$)]. However, only 40.4% of colon cancer patients had sexual activity equal to or greater than pre-diagnosis activity, 15% in rectal cancer patients, and 16.7% in breast cancer. We did not find differences in sexual life or physical condition based on the follow-up time.

Of the patients, 24.3% reported a diet change following a cancer diagnosis, while 15.7% reported some change to a diet low in fat and rich in vegetables and fruit, 4.9% to a low-salt diet, and 3.9% to other types of diet. In addition, 8.9% of patients took herbal products. According to weight, 25.4% of patients gained at least 5 kg weight from cancer diagnosis, 23.8% of them were patients with breast cancer. A total of 62.6% of smokers were noted at diagnosis reported that they quit smoking and only 5 patients began smoking. Among heavy drinkers, 25.6% stopped drinking alcohol regularly.

Table 3 Second primary tumors

Cancer types	Frequency (Number of cases)	Percentage of patients
Breast	10	2.9 %
Colorectal	9	2.6 %
Melanoma	8	2.3 %
Prostate	7	2 %
Lung	6	1.7 %
Renal	2	0.6 %
Thyroid	2	0.6 %
Other (incidence = 1)	11	3.2 %
Total	55	15.6 %

No significant differences were found according to age, sex, diagnosis, or follow-up time.

Discussion

The results of this descriptive case series indicate that long-term cancer survivors defined as those with a median of 5.7 years following treatment for cancer experience an array of medical, functional, and emotional problems. The descriptive data from this long-term cancer survivor oncology service does indicate that complex medical, functional, and emotional problems are present even years following treatment.

While surveillance of tumor status or new tumors is a common standard of care [23, 24] for follow-up of medical needs, it is well known that once cancer treatment is finished, there is little specific follow-up for these long-term non-medical-related issues [25]. In particular, we noted a high rate of early retirement, and a decrease in income in almost one fifth of working patients, perhaps contributing to the occurrence of this depressive syndrome. A meta-analysis published by Mitchell AJ et al. in 2013 [26] reported a prevalence anxiety rate of 17.9% and depression rate of 11.6% in LTCS as compared to 13.9% and 10.2% in healthy controls, respectively. In our study, the prevalence of anxiety-depressive syndrome was higher at 34.6%. However, only 6 of these patients required hospital admission and committed suicide as reported in other series [27]. Another interesting finding was the high incidence of memory loss reported, particularly in patients without common known risk factors, such as advanced age or previous chemotherapy treatment [28].

It is interesting to note that the long-term cancer survivors in our series had greater comorbidity prior to cancer diagnosis than the Spanish population in general. The rate of hypercholesterolemia is 26.3% and 16.4% of hypertension [29] in the population as a whole, in contrast to 35.4% and 18.5%,

reported in the population of our study. Furthermore, our LTCS had a high cumulative incidence in several diseases during follow-up. For this reason, it is important to have specific preventive programs for these patients. These programs have been developed many years ago in childhood cancer survivors [30, 31]. Lifestyle behaviors including the limited perception of alcohol as a risk factor as compared to tobacco [32] and the significant increase in weight [33] are of concern because of the higher risk of relapse in some tumor types (e.g., breast cancer) [34].

As indicated previously, one of the primary problems identified in this series is the high incidence of sexual dysfunction. In some cases, this problem has multifactorial origin, without significant age differences in our study, but in other cases there is a clear relation with type of cancer treatment, such as radiotherapy in rectal cancer. In addition, the incidence of sexual dysfunction might even be underestimated in our series, because of the relative low levels of cases with gynecological tumors and prostate cancer [35, 36]. Solving this problem would require, first of all, a greater acceptance by providers and patients so as to identify the problem, as well as greater involvement of specialists in this field, who should be responsible for applying of specific treatments and follow-up plans [37].

This description of these cancer survivors approximately 6 years post treatment is based on a single practice that focuses on long-term cancer survivors. As such, the group seen in the service may be a more problematic group of patients. Large-scale studies from multiple sites of long-term survivors that vary the time from treatment will provide a more representative description of this group; nevertheless, the current description of our findings indicate that a mix of medical, functional, and emotional challenges can occur years past the medical treatment for cancer.

One of the most difficult and important objectives of comprehensive healthcare in this cancer survivorship population is the early identification of vulnerable long-term cancer survivors, those patients who require greater follow-up and support. While different models of care have been proposed for cancer survivorship care [16], the persistent care of these long-term cases remain a problem. Prospective studies that identify these individuals early on and more evidence-based intervention represent steps forward. However, we need a greater recognition that “all is not well” in a group of long-term survivors and greater efforts on the part of both healthcare providers and government policy makers need to ensue actual implementation of a long term comprehensive approach.

Compliance with ethical standards

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

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