

ORIGINAL ARTICLE

Frequency of comorbid illnesses in cancer patients in Turkey

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Summary

Purpose: Comorbidities in cancer patients can adversely affect the management and outcome of their primary illnesses at all levels from diagnosis to therapy. We sought to examine comorbid conditions of cancer patients, treated at 4 university hospitals, each representing a different geographic location in Turkey.

Methods: A total of 769 consecutive cancer patients presenting to outpatient clinics were recruited between November 2007 and May 2008. The patients filled in a questionnaire on comorbidities. Based on the questionnaire, Charlson Comorbidity Index (CCI) was calculated.

Results: The patient median age was 55 years (range 21-87) and 456 (59.3%) were female. Breast (36.5%), colo-

rectal (21.4%) and lung cancers (13.9%) were the 3 most frequent malignancies. Of the patients, 59.3% had at least one comorbid disease and 46.3% were using at least one medication daily. The most frequent comorbidities were hypertension (25.3%), diabetes mellitus (13.1%) and peptic ulcer (7.7%). Increasing age positively correlated with the extent of comorbidities ($r=0.30$, $p<0.001$), number of medications ($r=0.32$, $p<0.001$) and the CCI ($r=0.20$, $p<0.001$).

Conclusion: It is crucial to remember that comorbid illnesses are not rare and many patients are treated for conditions unrelated to their cancer, which potentially may affect various stages of their clinical management.

Key words: cancer, Charlson comorbidity index, comorbidity, Turkey

Introduction

Societies are aging due to improved health services provided in many countries. As a consequence, not only cancer incidence, but also comorbidities, which adversely affect cancer care at all stages from screening to therapy, are constantly increasing [1]. While a comorbid disease is present in approximately 10% of cancer patients younger than 50 years, the frequency steeply climbs to 55% in patients older than 80 [2]. Comorbidities can adversely interfere with many parameters like diagnosis, treatment, drug metabolism, follow up, quality of life and prognosis. Several publications report that patients with comorbidities have worse prognosis than those without [3-6].

Unfortunately, most of the clinical evidence that

guide our practice have derived from clinical trials which do not recruit patients with significant comorbidities, or those older than 70. Therefore, the literature is biased against comorbid patients, who may sometimes make up the majority of cases in daily practice.

There are several scoring systems to classify comorbidities; CCI is more frequently used than others [7]. Its first application was in patients with breast cancer, and it was shown that the cumulative mortality correlated with increasing CCI score. Derived from data on 559 patients at a single center, it utilizes 19 clinical conditions which increase death rate by 1.2% in 1 year. CCI and its modifications [8] have proved to be valuable tools which correlate well with the mortality and the quality of life in patients with cancer [1-4].

Epidemiological differences including incidence of

disease, neoplastic or not, may occur from nation to nation owing to genetical, environmental and socio-economical factors. For instance, the incidence of gastric cancer varies greatly across the globe [10]. In medical oncologist's view, knowing your patient in a detailed aspect, especially comorbidities, is crucial. To the best of our knowledge, the comorbidities of Turkish cancer patients to such extent have not been studied before. Our aim was to study comorbidities of oncology patients in our country.

Methods

From October 1st, 2007 to May 31st, 2008, 769 patients from 4 university hospitals located in 4 different geographical regions in Turkey were included. The centers were Mersin University Hospital in Mersin, Marmara University Hospital in Istanbul, Hacettepe University Hospital in Ankara, and Akdeniz University Hospital in Antalya.

A questionnaire which systematically asks for the 19 comorbidities included in the CCI was developed. Total scores were then calculated and patients were classified to have comorbidities as mild (0), moderate (1-2) and severe (3+). It also included the primary cancer diagnosis, age, gender and the medication(s) unrelated to cancer. Non-cancer medications were classified according to their indications for comorbid illnesses. All consecutive patients were included, regardless of the type of cancer and the line of chemotherapy. After obtaining verbal consent, a nurse or the doctor filled in the form by interviewing the patients.

Statistical analysis

The data were analysed with SPSS, version 13.0. Dichotomous variables were expressed as percentages. Spearman's rho was used for non-linear correlations. For continuous variables, mean and 95% confidence interval (95% CI), for ordinary variables or those without normal distribution median and interquartile range were given. A p-value below or equal to 0.05 was considered statistically significant. All p-values were 2-sided.

Results

A total of 769 patients were recruited. Their median age was 55 years (range 21-87) and 456 out of 750 (59.3%) were female. Breast (36.5%), colorectal (16.9%) and lung cancers (13.9%) were the 3 most frequent primary malignancies. Table 1 summarizes the demographic and clinical features of patients.

Table 1. Patient and cancer characteristics (n=769)

Characteristics	Patients, n	%
Age, years (range)	55 (21-87)	–
Gender (n=750)		
Female	456	60.8
Male	294	39.2
Primary diagnosis (n=756)		
Breast cancer	276	36.5
Colorectal cancer	162	21.4
Lung cancer	105	13.9
Gastric cancer	39	5.2
Other	174	23.0
Centers		
Akdeniz University (Antalya)	219	28.3
Mersin University (Mersin)	205	26.7
Marmara University (Istanbul)	199	25.9
Hacettepe University (Ankara)	147	19.1

Hypertension was the most frequent comorbidity (25.3%), followed by diabetes mellitus (13.1%) and peptic ulcer (7.7%). Comorbidities are listed in Table 2. Of the patients, 369 (59.3.0%) reported to have at least

Table 2. Comorbidities in participating patients*

Comorbidity	Patients, n	%
Cardiovascular		
Coronary artery disease	35	4.6
Dysrhythmias	17	2.2
Congestive heart failure	17	2.2
Hypertension	195	25.3
Pulmonary		
Bronchial asthma	17	2.2
Chronic obstructive pulmonary disease	30	3.9
Central nervous system		
Cerebrovascular event	5	0.7
Endocrine		
Diabetes mellitus	101	13.1
Dyslipidemia	42	5.5
Thyroid diseases		
Hyperthyroidism	7	0.9
Hypothyroidism	26	3.4
Multinodular thyroid disease	47	6.1
Genitourinary and Renal		
Chronic renal failure	3	0.4
Nephrolithiasis	33	4.3
Urinary tract infections	9	1.2
Gastrointestinal		
Gastric		
Peptic ulcer	59	7.7
Gastroesophageal reflux disease	29	3.8
Hepatobiliary		
Viral hepatitis	12	1.6
Cholelithiasis	30	3.9
Other	49	6.4

*Some patients reported more than one comorbid illness

one comorbid illness. Figure 1 illustrates the number of comorbid illnesses in patients.

Information on the medications was available in 738 patients: 53.7% were not on any medication at all, and 33.3% were on 1, 8.0% on 2 and 4.9% on 3 prescription medications. Of the 246 patients who took only one medication (the remaining were receiving more than 1 medication), 28 (11.2%) were on angiotensin receptor blockers, 27 (10.8%) on antiulcer drugs and 25 (10.0%) on levothyroxine. When taken as a group, antihypertensives were the most frequent medication (86 patients, 34.9%), followed by antiulcer (40 patients, 16.1%) and antidiabetic medications and insulin (34 patients, 13.7%).

CCI could be calculated in 736 patients. Only 2 patients (0.3%) had a CCI score of 0, none had a score of 1, 479 (65.1%) scored 2, 175 (23.8%) scored 3, 48 scored 4 (6.5%) and the remaining 32 (4.3%) scored between 5 and 8.

Age was significantly correlated with the number of comorbidities ($r=0.30$, $p<0.001$), number of medications taken ($r=0.32$, $p<0.001$) and CCI score ($r=0.20$, $p<0.001$). As the number of comorbidities increased, so did the number of medications ($r=0.71$, $p<0.001$). Figure 2 illustrates these correlations. In the 60-69 years age group, 108/158 (68.3%) had at least one comorbidity and 94 out of 151 (62.2%) were taking at least one medication, which is also illustrated in Figure 2.

Gender did not affect the comorbidity status ($p=0.504$) or CCI category ($p=0.360$). Comorbidity scores were similar in the participating hospitals.

Discussion

Although there have been several publications elsewhere, this is the first study to provide epidemiological information on comorbidity of cancer patients in

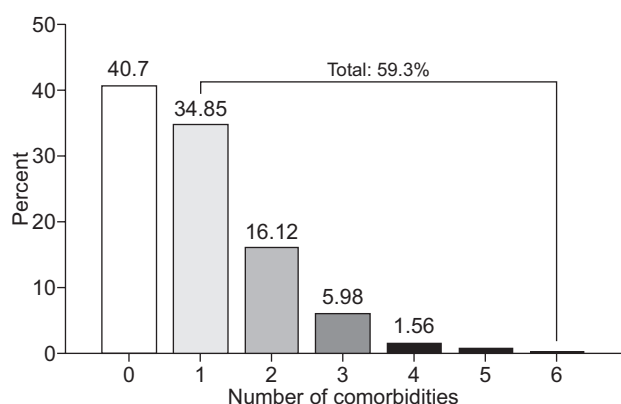


Figure 1. Number of comorbidities.

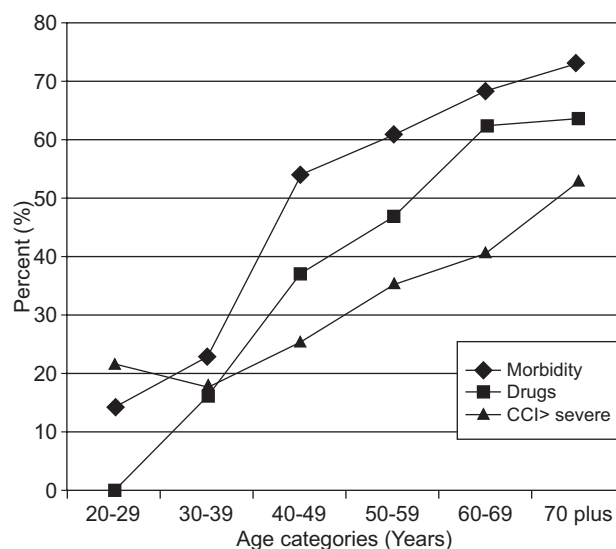


Figure 2. Comorbidity, being on medication and being in Charlson comorbidity index category severe (CCI severe). All 3 lines had p -values <0.001 on Spearman rho.

Turkey [11-13]. Of the patients, almost 60.0% at medical oncology clinics had at least one comorbidity and 46.0% were on at least one medication. The most frequently associated illnesses were hypertension (25.1%), diabetes mellitus (13.1%) and peptic ulcer (7.7%). The number of comorbidities, CCI and number of medications increased with increasing patient age.

We included all patients presenting to the medical oncology clinics regardless of the reasons that brought them in, i.e. being a new or follow-up patient, on chemotherapy or not. We think that this approach gives a better idea of comorbidities, which could potentially affect the practice of the oncologist with respect to the daily routine. One out of 3 patients had cardiovascular disease (most commonly hypertension), and 1 out of 8 patients had diabetes mellitus, which are in line with a study from the Netherlands [14]. However, in the latter study, a high prevalence of chronic obstructive lung disease was also reported.

The impact of common comorbidities, like cardiovascular disease, and diabetes, on oncology practice are important. These patients are at higher risk for contrast media nephropathy [15,16], cardiac or cerebrovascular events during interventions such as bronchoscopy or gastrointestinal endoscopies [17]. In fact, cardiopulmonary conditions, like serious congestive heart failure or recent myocardial infarction, are among the major contraindications to some of these invasive procedures. Hence, these diseases may be obstacles to optimal care in patients with cancer.

One out of 10 patients reported peptic ulcer or gastroesophageal reflux disease in our study. Such patients are at increased risk of hemorrhage or perforation sec-

secondary to thrombocytopenia and delayed-healing secondary to chemotherapy. Bevacizumab increases the risk of gastric perforation [18].

Needless to say, comorbidities may affect the oncologist's treatment decisions [2]. For example, in patients with a higher risk of impaired renal function, such as diabetic nephropathy, one avoids nephrotoxic agents, unless it is crucial. The well-established 5-fluorouracil-induced coronary vasospasm in patients with coronary artery disease is just another example. However, it is beyond the scope of this paper to list all associations.

Drug interactions are of utmost importance, especially in cancer patients with metastatic disease and those on active cancer treatment [19]. Cancer patients may be receiving pain killers, antineoplastics, steroids, 5-HT₃ receptor antagonists, antihistamines and neurokinin 1 receptor antagonists. The number of concomitant medications increases with age [20].

Prognosis is adversely affected by comorbidities in a number of ways. Since clinicians are concerned with increased risk of serious toxicities, treatment choices may involve suboptimal regimens or doses, which compromise success rates [2]. In this scenario, the most probable cause of death is cancer itself. Comorbidities are overwhelmingly the major cause of mortality in patients with early-stage cancer [20]. In this study, as age increased, the likelihood of dying from comorbidities increased too.

Our study has several limitations. As it is a relatively small study it may not reflect perfectly cancer patients in Turkey. The number of female patients, and therefore those with breast cancer, was higher than would be expected. However, gender did not affect the distribution of comorbidities to a great extent. Despite its limitations, our study gives a strong idea on comorbidities in cancer patients in Turkey. The fact that we studied patients in 4 different regions of the country is the strength of this study.

In conclusion, patients coming into the outpatient clinic are not solely cancer patients. They may have significant comorbidities, which may affect their manipulation from diagnosis to therapy. The impact of comorbidities increases with increasing patient age. Effective management of coexisting illnesses as well as the cancer itself is of paramount importance in the successful treatment of the cancer patient.

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