Cancer and Comorbidity

Redefining Chronic Diseases

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BACKGROUND. A narrow subspecialty model of cancer care has led to cancer treatment often being given outside the full medical context of the patient. The full range of comorbid illness must be considered in all aspects of diagnosis and treatment. This study was conducted to describe the prevalence of comorbidity in cancer patients and examine its relation with multiple demographic and clinical variables.

METHODS. A case comparison study of 15,626 population-based incident cases of cancer was conducted between 1984–1992 in 3 metropolitan Detroit counties (a National Cancer Institute Surveillance, Epidemiology, and End Results program). Chronic disease status and demographics were collected by self-report; cancer diagnoses and staging were obtained by medical record review. Univariate and multiple logistic regression analyses were performed.

RESULTS. Comorbidity was present in 68.7% of cancer patients, and 32.6% of these individuals had ≥2 comorbid conditions. Frequency was increased in the elderly, African-American patients (particularly African-American women), smokers, and those with lower socioeconomic status. Rates also appeared to vary by specific tumor site.

CONCLUSIONS. Comorbid chronic diseases are common in persons with cancer. The prevalence of comorbidities has important clinical, health service, and research implications. The disease specific model of oncology may limit appropriate care for these patients, and enhanced integration of primary care into the ongoing management of cancer may offer better outcomes. ***Cancer* 2000;88:653–63.**

KEYWORDS: comorbidity, cancer, chronic disease, diagnosis, treatment.

Cancer holds a special status among the diseases that humans suffer and physicians treat. It is a dread disease whose name is spoken only in hushed tones; an implacable specter that, prior to the identification of acquired immunodeficiency syndrome, appeared unique in its ability to provoke a sense of fear and hopelessness. As the writer Susan Sontag has observed in *Illness as Metaphor,*[1] those whom cancer strikes, along with those who treat it, have been bound up in the metaphors of death against life. Just as our Western culture has viewed cancer as a disease apart, so has Western medical science. We have organized ourselves uniquely in the struggle against cancer; oncology is the only disease specific specialty. By adhering to the single-disease model, cancer treatment has been provided outside of the full context of the person with the disease.

However, the model has not been entirely static. Along with shifting scientific paradigms in the way we understand disease, new insights into human psychology and human society have prompted changes in the approach to treatment. Over the last three decades, a

biopsychosocial model advanced by Engel[2] has supplemented a purely scientific biomedical model of disease. Engel's model incorporates multiple dimensions of the illness in the context of a unique individual experiencing it. Oncology largely has integrated this broader understanding of the personal and social experience of the person with cancer into clinical practice, most notably through the introduction of interdisciplinary team care.

However, a broader view of the medical picture of the cancer patient has lagged behind. There has been a striking failure to address and integrate into our dominant clinical model the concurrent medical needs of those with cancer. In our imagination and in our practice, cancer stands alone, casting such a dark shadow that the concurrent illnesses experienced by an individual fade into a homogeneous background. The subspecialty care model that focuses on a single disease operates in that shadow, and tacitly accepts the notion that the shadow is all there is. We have paid far too little attention to the fact that cancer patients frequently do not only have cancer, but other medical problems as well. A more comprehensive approach to cancer care would begin by recognizing it as a chronic disease, often linked in incidence rate to aging. Chronic diseases, the "epidemic of the future," have long since replaced infectious diseases as the leading causes of mortality and morbidity. The demographics of aging point to two further important trends: the number of individuals with chronic diseases will continue to grow, as will the number with more than one chronic disease. The natural history of cancer may affect both the severity and outcomes of other chronic illnesses, and it can be expected to coexist commonly with other chronic illnesses.

In other clinical arenas, we have readily identified the importance of examining the interactions among chronic diseases, both for clinical and research purposes. Consider, as one example, our understanding of the interrelation between coronary artery disease and diabetes. Research trials regularly examine patients with both diseases and clinicians apply results from such work in choosing optimal strategies for the prevention, diagnosis, and treatment of either disease. Our track record with cancer has been much less satisfactory. The cancer literature largely has tended to ignore comorbid conditions.[3] Indeed, when they are mentioned at all, it is likely to be as a purely negative factor (e.g., exclusion criteria to eliminate patients from clinical trials). The understandable desire to reduce confounding variables in evaluating the effects of treatment has the significant downside of limiting the generalizability of such studies. Fewer and fewer patients with cancer resemble those on whom the clinical trials have been conducted.

In terms of the clinical implications of comorbidity, some studies have shown that comorbidity, when compared with functional status, has an independent effect on survival and that the measurement of comorbidities has a profound effect on their correlation with prognosis.[4] Furthermore, brief lists of comorbid conditions are most suitable for large-scale epidemiologic studies.[4,5] Comorbidity is measured in this study using a brief list of conditions, consistent with the results of prior methodologic assessments.[4,5]

Comorbidities are critically important in the clinical care of patients with cancer because they can have a profound impact on so many aspects of that care: from prevention, screening, and diagnosis to prognosis, cancer treatment, and health service needs. Of particular importance is the implication that primary care providers play an essential role in the care of cancer patients. We believe that further research into the effects of comorbidities on cancer will contribute powerfully to improved patient care by further development of the database from which good clinical and policy decisions are made on such issues as screening, treatment, cost containment, and service needs. We believe the current study provides a starting point for such inquiries by describing the prevalence of 6 major comorbid conditions among nearly 16,000 cancer patients in a population-based sample and examining their relation to multiple demographic variables, the other comorbidities, and cancer site, along with a multiple regression analysis for each risk factor.

MATERIALS AND METHODS

Population-Based Incident Cancer Cases

Cancer patients were identified through the population-based Metropolitan Detroit Cancer Surveillance System (MDCSS), a participant in the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program. Cases were enrolled utilizing a rapid reporting system, enabling investigators to identify and interview patients within 2–8 weeks after diagnosis. Cases are population-based for the three counties of the Detroit metropolitan area: Wayne, Macomb, and Oakland. All incident male and female cancer cases between the ages of 40–84 years who were African-American or white and were diagnosed with one of the following cancers were enrolled into the study: lung, urinary bladder, colon, rectum, esophagus, liver, mesothelioma, eye, salivary gland, stomach, and melanoma of the skin. The years of diagnosis for the total subject group were 1984–1992, but varied by site, with patients with rare tumors enrolled for the entire study period whereas those with more com-

monly occurring cancers were enrolled for 2–3 years. This report includes 15,626 cancer cases. Informed consent was obtained from all subjects by signature on a consent form describing the objectives of the study.

Cancer diagnoses and information describing the patient, the anatomic site of the incident cancer, and its histology were collected from hospital and other medical records utilizing SEER program guidelines. Data were abstracted by staff trained and supervised by the MDCSS. Completeness and accuracy of reporting population-based incident cancer cases is assessed annually by both internal and external quality assurance reviews, with MDCSS having >98% of cases accurately reported each year.

Interview

Cancer patients or their surrogates (spouse or other first-degree relative) were interviewed by telephone. These interviews collected demographic information regarding the patients (birth date, gender, ethnicity, marital status at time of cancer diagnosis, education, and birthplace), as well as an adult medical history, complete work history, tobacco use history, and adult residential history. Data describing previous chronic diseases were obtained by asking patients whether they had ever been diagnosed by a physician with the specific condition and the year of diagnosis of that condition. The response rate for these interviews was 94.3%. Other details regarding the study were presented in a previous report.[6]

Six chronic diseases were included in the comorbidity study: cardiovascular diseases, diabetes, cerebrovascular diseases, hypertension, respiratory diseases, and arthritis. Although the respondents reported other preexisting conditions, there were too few cases in those categories for analysis. In this report, the terms "preexisting chronic diseases" or "comorbid chronic diseases" refer to these six conditions. Because the focus of this report is the prevalence of these chronic diseases among cancer patients and the implications of these comorbidities for cancer care and prevention, all the demographic data describe the patient's status at the time of diagnosis of the cancer for which they were enrolled in the study.

Analysis

The current study focused on evaluating which factors are associated with the prevalence of each chronic disease for subjects diagnosed with cancer. Separate multiple logistic regression analysis was used to analyze how the covariates influence the binary response variables (being diagnosed as having a specific chronic condition or not).[7]

Before building the logistic regression models, we performed a careful univariate analysis by constructing contingency tables of the response variable versus the nominal or ordinal explanatory variable. From the univariate analysis, we determined potential risk factors and several potential confounding variables. The variables included in the logistic models were age, race, gender, education, smoking history, occupation history, and the remaining comorbid conditions.

Age was categorized by decades with "40–49" years as the referent category. Education was categorized into 4 groups with high school education (12 years) as the referent group. To measure the smoking history, the variable pack-year was created as the product of "number of packs of cigarettes usually smoked" times "the number of years smoked." The variable pack-year then was categorized into 6 levels by increments of 20 pack-years. The nonsmokers were the referent group. The cigarette smoking history is summarized into pack-years for those who have ever smoked cigarettes.

For this analysis, the detailed work histories were summarized into eight general categories for the usual occupation. The general categories are the standard summary groups of the census bureau, which were utilized because the occupations and industries were coded using the 1980 Census Bureau categories.[8] Usual occupation is the job held for the longest number of years by the subject.

Using regression techniques for model selection, we tested for stability of different models. The residual chi-square test was evaluated for each model and the Wald statistic was evaluated for each variable and compared with the coefficient from the univariate analysis for similarity of sign and magnitude.[9] Estimated odds ratios (ORs) and 95% confidence intervals were calculated that compared the odds of having a chronic health condition for two levels of a covariate.

RESULTS

This study includes 15,626 incident cancer cases diagnosed among residents of the tri-county Detroit area between 1984 and 1992 (Table 1). Overall, 37.7% of the study population were women and 20.7% were African-American. Of the 15,626 participants in the study, 59.2% (9244) of interviews were conducted with the subject and 40.8% (6382) were conducted with next-of-kin proxy respondents (26% [4062] for those who were deceased and 5% [2320] for those who were too ill to participate in an interview).

The overall prevalence of chronic disease comorbidity among these cancer patients was 68.7% of persons diagnosed with at least 1 other chronic illness (67.8% prevalence reported by subject respondents

TABLE 1
Cancer and Chronic Disease Comorbidity: Distribution of Cancer Cases by Anatomic Site, Gender, and Race

		Women		Men	
	No.	African-American	White	African-American	White
Lung	5844	6.7	27.4	16.3	49.5
Colon	2986	10.4	41.3	10.0	38.2
Urinary bladder	2255	3.9	23.7	7.3	65.1
Rectum	1318	7.4	38.4	7.1	47.2
Esophagus	1031	11.9	16.1	30.7	41.3
Stomach	759	10.3	27.8	16.1	44.0
Skin/melanoma	544	0.5	39.6	0.7	59.1
Liver	474	9.3	22.2	23.3	45.1
Salivary gland	165	6.7	41.8	4.8	46.7
Mesothelioma	129	3.1	18.9	9.4	68.5
Eye	121	0.0	50.8	2.5	46.7
Total	15,626	7.4	30.3	13.3	49.0

TABLE 2
Cancer and Chronic Disease Comorbidity: Overall Prevalence of Preexisting Chronic Diseases

	No.	% with no chronic disease	% with 1 chronic disease	% with 2 chronic diseases	% with ≥3 chronic diseases
African-American females	1149	23.5	35.3	25.7	15.5
White females	4736	32.6	35.2	21.9	10.3
African-American males	2086	29.4	35.1	22.8	12.7
White males	7655	32.1	37.1	21.4	9.3
All cases combined	15,626	31.3	36.1	22.1	10.5

and 70.9% reported by proxy respondents). Of these, 36.1% had comorbid chronic disease and 32.6% had ≥2 comorbid chronic conditions. African-American women had the highest prevalence of chronic disease comorbidity, with 76% having been diagnosed with at least 1 other chronic disease, followed by African-American men, among whom 70.6% were diagnosed with at least 1 other chronic illness (Table 2). White women and men were found to have approximately the same overall prevalence of chronic disease comorbidity (67.4% and 67.8%, respectively). White men had the highest prevalence of just one other chronic disease and the lowest rate of three or more additional conditions. African-American women had the highest prevalence of either two additional diagnoses of chronic diseases or three or more such diagnoses, followed by African-American males.

Age patterns in the prevalence of each chronic disease were found to differ by race and gender (Table 3). Among African-American women and African-American and white men, the prevalence of hypertension was greatest among cancer patients diagnosed between the ages of 60–69 years, whereas among white women, prevalence was found to increase in each advancing age group. Diabetes prevalence was highest among both African-American and white men and women when the cancer diagnosis occurred at ages 60–69 years, but among women the prevalence was similar in the 2 older age groups. The prevalence of both cardiovascular and cerebrovascular diseases increased with advancing age at diagnosis of cancer for all four race/gender groups. Respiratory diseases increased with advancing age at cancer diagnosis for African-American and white men, but had the highest prevalence among African-American and white women among those with cancer diagnoses occurring between the ages of 60–69 years. Arthritis increased with advancing age at cancer diagnosis for all but African-American men, among whom prevalence was slightly higher among those with cancers diagnoses between the ages of 60–69 years. The median number of years that each chronic disease was diagnosed prior to the cancer diagnosis differed by chronic condition, race, and gender. Previous diagnoses of diabetes occurred from 8.9 years before the cancer diagnosis for African-American men to 11.9 years for white women. Cardiovascular diseases were diagnosed an average of 8.3 years before the cancer diagnosis for African-

TABLE 3
Cancer and Chronic Disease Comorbidity: Prevalence of Preexisting Chronic Conditions By Race, Gender, and Age

	Female					
	African-American			White		
	Age groups (yrs)					
Comorbid chronic disease	40–59	60–69	70+	40–59	60–69	70+
Hypertension	49.5	60.8	58.1	27.8	43.1	47.6
Diabetes	8.6	10.7	10.2	3.4	6.1	6.4
Cardiovascular diseases	19.3	35.2	38.3	16.8	26.7	36.3
Respiratory diseases	19.3	27.2	18.6	22.7	24.8	23.0
Cerebrovascular diseases	7.9	8.7	13.3	1.8	5.3	10.4
Arthritis	5.8	6.5	9.5	2.7	6.2	8.5
None	31.2	19.7	21.2	47.9	30.7	25.8
Total no.	327	401	420	1096	1593	2045
	Male					
	African-American			White		
	Age groups (yrs)					
Comorbid chronic disease	40–59	60–69	70+	40–59	60–69	70+
Hypertension	44.2	50.1	45.4	30.6	40.8	37.7
Diabetes	4.4	9.2	6.8	3.4	6.9	5.9
Cardiovascular diseases	19.9	25.7	32.1	19.1	29.1	36.5
Respiratory diseases	25.2	26.2	27.6	21.9	26.7	28.6
Cerebrovascular diseases	7.5	9.7	14.8	3.4	7.2	11.0
Arthritis	2.2	6.0	5.8	3.5	3.9	4.5
None	31.5	25.6	20.6	47.3	30.1	26.0
Total no.	638	785	660	1862	2870	2915

American men to 10.5 years for African-American women. The prior diagnosis of arthritis ranged from an average of 10.3 years for African-American men to 16.3 years for white women. For the diagnosis of hypertension, the average number of years prior to the cancer diagnosis ranged from 9.9 for African-American men to 12.3 for African-American women. Cerebrovascular diseases were diagnosed an average of 6.0 years prior to the cancer diagnosis for white women compared with 8.2 years for African-American women. Respiratory diseases were diagnosed on average 11.2 years earlier among African-American men compared with 12.8 years among African-American women.

The prevalence of these six chronic diseases also varied by cancer site (Table 4). Cancer patients diagnosed with tumors of the lung, urinary bladder, and stomach had the highest prevalence of cardiovascular diseases. Arthritis was previously diagnosed most often among patients with tumors of the salivary gland and eye or those with mesothelioma. The prevalence of diabetes was greatest among patients diagnosed with tumors of the liver or eye. The prevalence of hypertension was $\geq$40% among all cancer patients, except those diagnosed with lung carcinoma, who had a slightly lower prevalence. Preexisting diagnoses of respiratory diseases were most prevalent among lung carcinoma patients, followed by patients diagnosed with mesothelioma. Cerebrovascular diseases were most often prevalent among patients with carcinomas of the stomach and lung.

Table 5 presents the results of the multiple regression analysis for each risk factor. Advancing age at cancer diagnosis significantly increased the risk of having a prior diagnosis of each chronic disease, with the highest ORs observed for cerebrovascular diseases, cardiovascular diseases, and arthritis. African-Americans were found to have higher risk of having previous diagnoses of hypertension, diabetes, and cerebrovascular diseases. Women were found to have a significantly higher risk of having been previously diagnosed with arthritis, hypertension, cardiovascular diseases, and respiratory diseases. Cancer patients with $<$8 years of formal education were found to have a signif-

TABLE 4
Cancer and Chronic Disease Comorbidity: Prevalence of Preexisting Chronic Diseases among Cancer Patients by Cancer Site

Cancer site	No.	Cardiovascular %	Arthritis %	Diabetes %	Hypertension %	Respiratory %	Cerebrovascular %
Lung	5844	30.1	4.7	5.2	36.7	37.1	9.1
Colon	2986	28.4	4.8	6.4	46.8	14.6	7.0
Urinary bladder	2255	31.2	5.9	6.2	43.3	20.5	8.1
Rectum	1318	28.5	3.6	5.9	43.3	15.1	6.9
Esophagus	1031	26.0	5.7	6.5	41.2	25.1	8.5
Stomach	759	30.3	4.5	8.0	43.5	19.6	10.0
Skin/melanoma	544	19.1	6.1	4.6	40.8	13.0	2.9
Liver	474	25.8	2.6	12.7	39.9	20.1	6.8
Salivary gland	165	22.5	7.9	4.3	40.8	14.6	6.7
Mesothelioma	129	28.7	8.5	8.5	40.3	31.8	6.2
Eye	121	21.0	9.2	10.1	44.5	10.9	4.2
Total	15,626	28.9	5.1	6.1	41.2	25.1	7.9

icantly increased risk of having been diagnosed with arthritis, cardiovascular diseases, and respiratory diseases. Persons with a history of smoking were found to have a significantly increased risk of each of the six other chronic diseases. Smokers had an increasing risk with increasing numbers of pack-years of smoking for cardiovascular diseases, respiratory diseases, and cerebrovascular diseases. Patients with a prior diagnosis of cardiovascular diseases had a significantly higher prevalence of each of the other five chronic diseases. Although the specific patterns of comorbidities differed, there were significant elevations of at least two other chronic conditions among those patients diagnosed with each of the six comorbidities.

The distribution of preexisting chronic diseases varied by usual occupation (Table 5). For both men and women, those in executive, managerial, and professional occupations were most likely to have none of the six comorbid chronic diseases included in this study. Women who were farmers, housewives, or in service occupations had the greatest prevalence of other comorbid chronic illnesses, as did men in farming or machine operation (Table 5). The ORs were found to be highest for both respiratory diseases and cerebrovascular diseases for other unskilled workers and service workers, followed by machine operators, craftsmen, and skilled workers. Housewives and technical workers also were found to have significantly elevated ORs for cerebrovascular diseases.

Table 6 is a matrix of the prevalence of the six comorbid chronic conditions. The highest prevalence of arthritis, hypertension, and cerebrovascular diseases was found to occur among cancer patients with a previous diagnosis of diabetes. The greatest prevalence of diabetes and cardiovascular diseases was found to occur among those patients with a previous diagnosis of cerebrovascular diseases, whereas the largest prevalence of respiratory diseases was found to occur among those with a prior diagnosis of cardiovascular diseases.

DISCUSSION

To our knowledge our study is the first American work documenting the prevalence of major medical comorbidities in a community-based population sample of patients with a wide range of cancers across adulthood. A search of the entire MEDLINE database was performed using "comorbidity", "chronic disease", and "cancer" as key words from 1996 to July 1998. It is remarkable to note that $>67\%$ of this population had at least 1 significant comorbidity, nearly 33% had ≥ 2, and $>10\%$ had ≥ 3. Furthermore, the comorbid conditions were not random. The older patient groups had higher rates of comorbidities. African-American patients had higher rates than whites, and African-American women were the highest of all. Smoking was found to increase the risk of chronic disease comorbidity for all cancer sites and each of the chronic conditions included in this study; smoking also was a risk factor for many cancer sites. Cancer patients with ≤ 8 years of education had the greatest risk of comorbidity due to arthritis, cardiovascular diseases, and respiratory diseases. There were minor variations in specific comorbidities across the various cancer sites, but comorbidity was common in all cancer sites.

The strengths of this study include the 94.3% response rate in a population-based sample of nearly 16,000 patients from a founding participant in the National Cancer Institute's SEER program. Our research employed a self-report method of ascertaining comorbidity limited to six major conditions. Self-reported disease status has the disadvantages of potential inaccuracies in labeling, recall biases, and a lack of precision in rigorous definitions. However, medical record review methods of identifying comorbidities may seriously underestimate prevalence because the

TABLE 5
Cancer and Chronic Disease Comorbidity: Characteristics of Cancer Patients Associated with a History of Chronic Diseases

	Arthritis		Hypertension		Diabetes		Cardiovascular diseases		Respiratory diseases		Cerebrovascular diseases	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Age at cancer diagnosis (yrs)												
40–49	1.00		1.00		1.00		1.00		1.00		1.00	
50–59	1.56	(0.95–2.58)	1.40	(1.17–1.68)	1.52	(0.96–2.40)	1.38	(1.10–1.74)	1.23	(0.99–1.53)	1.78	(1.06–2.99)
60–69	2.00	(1.24–3.22)	1.91	(1.61–2.28)	2.19	(1.42–3.38)	1.91	(1.54–2.37)	1.17	(0.95–1.43)	2.50	(1.52–4.12)
70–84	2.61	(1.62–4.20)	1.99	(1.67–2.37)	1.94	(1.25–3.00)	2.95	(2.37–3.66)	1.29	(1.05–1.59)	4.58	(2.79–7.52)
Race												
White	1.00						1.00					
African-American	1.10	(0.91–1.34)	1.61	(1.46–1.77)	1.39	(1.17–1.65)	0.89	(0.80–0.99)	0.96	(0.85–1.07)	1.44	(1.23–1.68)
Gender												
Male	1.00						1.00					
Female	2.06	(1.63–2.61)	1.53	(1.36–1.73)	0.84	(0.66–1.08)	1.20	(1.05–1.37)	1.33	(1.16–1.54)	1.01	(0.81–1.23)
Education:												
High school grad 12 yrs	1.00		1.00		1.00		1.00		1.00		1.00	
≤8 yrs	1.53	(1.23–1.92)	1.05	(0.94–1.17)	0.98	(0.79–1.21)	1.44	(1.28–1.61)	1.26	(1.11–1.43)	1.14	(0.95–1.37)
9–11 yrs	1.23	(0.98–1.53)	1.03	(0.93–1.15)	1.19	(0.98–1.45)	1.08	(0.97–1.21)	1.10	(0.98–1.24)	0.97	(0.80–1.17)
13–14 yrs	1.38	(1.05–1.80)	1.07	(0.94–1.22)	1.10	(0.85–1.43)	1.10	(0.96–1.27)	0.99	(0.85–1.16)	0.91	(0.70–1.17)
15+ yrs	1.02	(0.78–1.34)	0.92	(0.81–1.04)	1.06	(0.84–1.34)	1.02	(0.90–1.17)	0.92	(0.79–1.06)	1.24	(1.00–1.53)
Occupation												
Manager/Professional	1.00		1.00		1.00		1.00		1.00		1.00	
Technical worker	0.95	(0.68–1.33)	0.94	(0.81–1.10)	0.78	(0.58–1.07)	0.83	(0.70–0.98)	1.06	(0.88–1.28)	1.38	(1.03–1.85)
Service worker	0.74	(0.49–1.13)	0.84	(0.69–1.01)	1.16	(0.82–1.65)	0.87	(0.71–1.07)	1.34	(1.06–1.69)	1.61	(1.14–2.26)
Farmer/Farm worker	1.40	(0.74–2.67)	0.87	(0.61–1.24)	0.53	(0.24–1.20)	1.06	(0.74–1.53)	0.99	(0.64–1.53)	1.64	(0.94–2.87)
Craftsmen/Skilled worker	1.02	(0.73–1.44)	0.86	(0.74–1.01)	0.75	(0.55–1.02)	0.87	(0.74–1.02)	1.21	(1.01–1.47)	1.42	(1.07–1.89)
Machine operator	0.86	(0.61–1.20)	0.90	(0.77–1.05)	0.87	(0.65–1.16)	0.69	(0.59–0.81)	1.33	(1.11–1.59)	1.38	(1.04–1.82)
Housewife	0.79	(0.56–1.11)	1.03	(0.87–1.22)	1.30	(0.93–1.82)	0.89	(0.74–1.07)	1.23	(1.00–1.52)	1.40	(1.02–1.93)
Other unskilled worker	0.97	(0.56–1.68)	0.82	(0.63–1.05)	1.03	(0.64–1.66)	0.62	(0.46–0.82)	1.73	(1.30–2.31)	1.86	(1.22–2.85)
Smoking (pack-years)												
Nonsmoker	1.00		1.00		1.00		1.00		1.00		1.00	
<20	1.87	(1.41–2.48)	6.63	(5.70–7.72)	2.03	(1.59–2.59)	2.99	(2.57–3.48)	4.44	(3.72–5.28)	1.76	(1.36–2.27)
20–39	1.87	(1.46–2.39)	5.61	(4.97–6.34)	1.27	(1.00–1.61)	3.62	(3.19–4.11)	6.83	(5.94–7.85)	2.00	(1.62–2.48)
40–59	1.76	(1.39–2.23)	4.75	(4.24–5.33)	1.51	(1.22–1.88)	3.54	(3.14–3.99)	9.53	(8.36–10.85)	2.74	(2.26–3.31)
60–79	2.00	(1.49–2.67)	4.93	(4.25–5.72)	1.41	(1.06–1.87)	3.57	(3.07–4.16)	11.48	(9.80–13.44)	2.74	(2.15–3.48)
80+	1.14	(1.04–2.00)	3.93	(3.38–4.58)	2.18	(1.68–2.28)	3.84	(3.29–4.49)	17.07	(14.52–20.07)	3.62	(2.88–4.55)
History of												
None	1.00		1.00		1.00		1.00		1.00		1.00	
Arthritis	—		1.10	(0.93–1.30)	1.45	(1.12–1.90)	1.19	(1.01–1.41)	1.06	(0.89–1.28)	0.94	(0.72–1.24)
Hypertension	1.15	(0.98–1.35)	—		1.69	(1.45–1.96)	1.36	(1.25–1.47)	0.50	(0.46–0.55)	1.52	(1.33–1.74)
Diabetes	1.45	(1.11–1.89)	1.64	(141–1.91)	—		1.73	(1.49–2.01)	0.80	(0.67–0.96)	1.43	(1.15–1.78)
Diseases												
Cardiovascular	1.18	(1.00–1.39)	1.29	(1.18–1.40)	1.72	(1.49–2.00)	—		1.06	(0.97–1.17)	1.89	(1.66–2.16)
Respiratory	1.13	(0.95–1.36)	0.50	(0.45–0.55)	0.83	(0.70–0.99)	1.17	(1.06–1.28)	—		0.84	(0.72–0.98)
Cerebrovascular	0.92	(0.70–1.20)	1.41	(1.23–1.62)	1.39	(1.12–1.73)	1.86	(1.63–2.13)	0.79	(0.68–0.92	—	

OR: odds ratio; 95% CI: 95% confidence interval; grad: graduate.

TABLE 6
Cancer and Chronic Disease Comorbidity: Patterns of Multiple Chronic Diseases

Percent of patients diagnosed with	No.	Who also have: Arthritis %	Hypertension %	Diabetes %	Cardiovascular disease %	Respiratory disease %	Cerebrovascular disease %
Arthritis	796	—	48.7	9.5	37.2	31.5	10.3
Hypertension	6435	6.0	—	8.8	36.9	24.5	11.2
Diabetes	957	7.9	59.4	—	44.1	25.6	13.8
Cardiovascular disease	4516	6.6	52.7	9.4	—	33.3	13.7
Respiratory disease	3924	6.4	40.1	6.2	38.3	—	9.5
Cerebrovascular disease	1247	6.5	57.8	10.6	49.5	36.0	—

existence of a condition may go unrecognized or unrecorded. It does offer more precision in diagnostic labeling.[10–14] The major limitation of this study was the depth of information available regarding the comorbidities. Our data represent only the presence or absence of a patient-recognized diagnosis by a physician without any assessment of the severity of the condition, its effects on functional status, medical interventions for the condition, or the timing of and potential relations between the diagnoses. Previous studies have shown limitations in both the medical record and self-report as accurate measures of comorbid conditions.[14–19] One review of studies comparing interview data with the medical record found that the concordance between the two sources for the same chronic diseases that are included in our study varied, with the highest agreement observed for diabetes, asthma, and other respiratory conditions, as well as hypertension but lower rates of agreement for cardiovascular disease, arthritis, and cerebrovascular disease.[14] One study found a significant correlation between self-report and the medical record and concluded that particularly for elderly individuals (age ≥60 years), self-report of medical conditions compared favorably with the medical record.[14] Agreement between self-report and the medical record for four of the conditions included in our study was high, ranging from 86% for hypertension, 94% for myocardial infarction, and 98% for stroke and for diabetes.[15] Another study found reasonable agreement between interview and medical record data for history of chronic disease in a study of cancer patients.[16] The medical record has been found to have errors and omissions in reporting as well.[14,17,18] A study comparing the medical record with a transcript of patient-physician encounters found that only 29% of the medical records contained information regarding the patient's medical history.[17] These studies suggest that neither measure provides an ideal assessment of chronic disease comorbidity. Nonetheless, because the majority of studies use interview data, it is reassuring to note that others have found self-report to be a reasonable measure of chronic disease comorbidity. Furthermore, our data provide a foundation from which more complete studies can be developed.

Another potential limitation of the study is the inclusion of data obtained from proxy respondents for subjects who were too ill to be interviewed or who had died. This limitation had a minimal effect on the rates of chronic disease comorbidity because the overall difference in chronic diseases reported by subjects and by proxies was small. The widespread prevalence of comorbid conditions in cancer patients documented in our study is important in multiple aspects of clinical care and related research: prevention and screening, diagnosis and prognosis, cancer treatment, and health service needs.

Prevention and Screening

Even before cancer or any of the comorbidities develop, there are prevention implications. Four major risk factors are common to these six chronic diseases and many of the cancers included in this study: smoking, dietary habits, lack of physical activity, and alcohol abuse.[20,21] Therefore, primary prevention that begins at an early age and continues throughout life is critical to the ultimate reduction of the rate of incidence of these illnesses. In addition, preventive measures that are taken during the course of care of any of these illnesses achieve two objectives: reduction of the morbidity burden of the diagnosed chronic disease and prevention of further disease occurrence. Thus an essential component of health care for anyone diagnosed with cancer or with any of the other chronic diseases would be the design of preventive measures focused on the risk factors relevant to the individual patient's chronic disease risk profile. It has been shown that preventive measures are effective for populations at all ages.[3]

The implications for basic research also must be

considered. There are underlying pathologic processes that are common to cancer and some of these chronic diseases. For example, cytokines and some growth factors, as well as certain oncogenes and protooncogenes (such as p53, c-*fos* and c-*myc,* and c-*jun*) are components of the carcinogenic process for many forms of cancer and are associated with diabetes, hypertension, cardiovascular diseases, and arthritis.[22–26] Our analyses show that occurrences of chronic conditions among cancer patients are not random. This may be due to shared pathophysiology among diseases, as well as to common life-style risk factors.

The pathways that link such habits as tobacco use and obesity/high fat diets to biologic disease processes may be the same for several of these illnesses. Persons with less education or lower income, who are likely to experience a greater prevalence of chronic disease comorbidity, also are more likely to share these habits. In addition, certain comorbidities may predispose to certain cancers etiologically (chronic liver disease and hepatomas). And cancers and comorbidities also may share specific risk factors (e.g., small cell carcinoma of the lung and chronic obstructive pulmonary disease).

Comorbidities also may play a crucial role in screening. They may define the appropriateness of screening and negatively impact the willingness of both patient and clinician to screen.[5] Conversely, the presence of certain comorbidities may predispose to regular medical care and enhance routine screening.[27]

Diagnosis and Prognosis

The presence and the complexity of comorbidities may affect clinical diagnosis and prognosis. Comorbidities have been shown to lead to earlier stage of cancer at the time of diagnosis in some studies,[27] most likely due to the factors discussed previously, although not in all studies.[3,28] However, survival, both from the cancer itself and all-cause mortality, has been shown in many studies to be worse for patients with comorbidities.[5,11,29–32] Comorbidities also may affect the presentation of the illness and recognition of clinical syndromes,[31] not only at the time of diagnosis but also with subsequent changes of status or with progression of cancer. Finally, in addition to prognosis affected by diagnosis at an earlier stage, clinical prognosis at any stage may be worsened substantially by coexisting medical conditions.[30,31,33]

Cancer Treatment

The presence of comorbidities may affect the treatment of cancer substantially. This effect may take a number of forms. There is strong evidence that patients with more comorbid conditions receive less aggressive treatment options.[5,29,33–37] However, other authors[28,29] found few differences in treatment in those patients with or without other chronic conditions. Functional status influenced treatment choices for older women with breast carcinoma in one study.[38] Indeed, functional consequences of cancer treatment may significantly influence treatment choices, and these consequences may be weighted by comorbid conditions.

In addition, the majority of cancer therapies, from chemotherapy to radiation to surgery, have the potential to complicate various comorbid conditions. For example, chemotherapy-induced neutropenia may carry increased risk for a patient with diabetes, and patients with cardiac or pulmonary disease may be more prone to complications from anesthesia for surgery.[3] Finally, comorbid medical conditions may complicate the course of cancers.

To our knowledge the research literature regarding cancer treatment has tended to ignore the effects of comorbidities. And when attention has been paid to their effects, it mainly has been negative attention; comorbidity is used as a specific exclusion criterion in the majority of clinical trials.[11,12,39] Using such restrictive criteria does enhance the validity of observations of treatment effect by reducing confounding variables. However, it also limits the generalizability of the trials and restricts the applicability of their results to a relatively small proportion of people with cancer. Clinical trials that excluded patients with comorbidities cannot be extrapolated to the clinical care of those patients without risk of significant error. These severe deficits in the database on which clinical decision-making must be predicated leave us with an appalling lack of data on which to base recommendations for the majority of our patients. There is a particular risk of underestimating the symptomatic costs of therapy as well as the rate of adverse events secondary to complications of therapy. Thus benefits are likely to be overestimated and costs underestimated for patients with comorbidities in the dominant model of oncology care.

Health Service Needs

Comorbidity influences the care needs of patients with cancer in ways that have implications for family caregivers as well as formal health care systems. Evidence from recent research suggests that health service needs of patients with cancer and their families vary as a function of the health status.[38] McCorkle and Wilkerson[40] found at least 40% of cancer patients receiving home care had $\geq$1 concurrent major health problems. Moreover, their symptoms, functional ability, and emotional status all were related to family

caregiving needs and economic hardship. Depression has been linked to a variety of chronic illnesses and is more likely to be prevalent among cancer patients with multiple illnesses. Managing symptoms represents a major challenge to family caregivers for cancer patients. Indeed, cancer patients' symptoms predict the physical health of their caregivers, and levels of cancer patient dependency are related to higher perceived impact on the caregiver's health.[41]

Although continuing research is needed, it is highly likely that the care trajectory and care demands for cancer patients are influenced by comorbid conditions, particularly those that are associated with troublesome symptoms, complex medication regimens, and that produce need for assistance with activities of daily living. Members of cancer patients' families report that, as the patient's need for physical assistance and assistance with care increased, the care burden on the family increased. This burden is accentuated by many comorbid conditions. Family members of people with cancer report increasing care burden as the physical needs of the family member and their need for assistance with their care increased.[40]

Clinical care paths (models designated to guide the delivery of services for patients with specified conditions) also may need to be modified to account for patients with cancer along with other comorbid chronic conditions. For example, a care path for breast carcinoma surgery may require modification to accommodate an older woman who also has a mobility limitation from osteoarthritis that would interfere with her self-care of her surgical wound at home.

To our knowledge implications for the effects of comorbidities on the costs of cancer care have not been well defined. In 1 study performed >30 years ago, Rice estimated that chronic conditions accounted for 59% of all costs of illness, both direct and indirect.[42] More recently, Hoffman et al. reviewed the prevalence and costs of chronic conditions in U.S. populations, finding that the direct health care costs for those individuals with ≥1 chronic conditions accounts for approximately 75% of all U.S. health care expenditures.[13] Taplin et al. reviewed the costs of treating three cancer patients in a health maintenance organization, and examined the effects of comorbidity as well as other variables on the costs of initial, continuing, and terminal care. Total costs of continuing care increased significantly with higher comorbidity. They noted that, as we experience increased pressure for cost containment and cost accounting, the effects of comorbidity must be delineated more clearly in cost accounting and projection models.[43]

Conclusions

Comorbidity is common in the cancer population studied in the current report, particularly among older and nonwhite patients. Taking a broader view of the medical condition of patients with cancer has major implications for the organization of their care. The high prevalence of comorbidity clearly signals the necessity of ongoing primary care for patients with cancer. Sequential provision of services (primary care interrupted by oncology care on an episodic basis) does not offer optimal care for either comorbid conditions or for cancer. Care of comorbid conditions must be integrated throughout cancer care to provide ongoing monitoring and management of the comorbid conditions and to insure that their clinical effects are factored into cancer treatment decision-making. In addition, there are broader implications for health service delivery organizations, including recognition of the needs of the families who care for those with cancer.

Finally, we need to apply a new paradigm to the complex of chronic diseases. For research and prevention, the interplay between shared risk factors and shared pathophysiology should be viewed through a new lens. For the majority of patients with cancer who have significant coexisting chronic illnesses, such a paradigm needs to view these illnesses as a constellation rather than separate little boxes, acknowledging the lack of randomness in the groupings.

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