Cancer patients who refuse treatment

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(Received 17 September 1992; accepted in revised form 12 January 1993)

The value of cancer treatment was assessed using a ‘natural experiment’ where patients who refused treatment served as no-treatment controls in a situation where withholding treatment to form a control group is unethical. Each cancer patient who refused treatment in Alberta, Canada between 1975 and 1988 was compared with five subjects who accepted treatment, matched on cancer site, age, number of cancers, and time period. Variables associated with treatment-refusal were included in Cox’s proportional hazards model of survival, with death from cancer as the endpoint and deaths from other causes as censored observations. Treatment was refused at a rate of 7.5 per 1,000. One-third of patients who refused treatment had lung cancer and most had unstaged disease. Treatment refusal was associated with a difference in median survival of approximately nine months. Site-specific analyses showed a range of effects. Case fatality among the treated patients fell by approximately 10 percent during the 14-year study period. Even in advanced disease, treatment can result in improved survival. However, the results of this study must be interpreted with caution and cannot be generalized to all cancer patients.

Key words: Canada, cancer, healthcare economics, survival, treatment, treatment refusal.

Introduction

Among seven anticipated changes affecting the North American healthcare system in the 1990s are: (i) the aging of the population resulting in increases in the absolute prevalence and incidence of cancer despite improved treatment techniques; (ii) increasing deliberations and questions about the ethics of the healthcare system and treatment decisions; and (iii) continuing debate about the need for a rationing of healthcare and the right of individual privacy versus the state’s right to preserve life. Although clinical trials continue to be the hallmark of scientific investigations of treatment efficacy, their usefulness in answering questions relating to the population impact of treatment advances is limited: “The discovery of large geographical variations in the incidence of certain services, unaccompanied by any discernible differences in outcome, has led to the suspicion that in many cases, we still have much to learn about the indications for a given course of action or the reasons for choosing one procedure over another.”

Since withholding cancer treatment to form a control group is unethical, cancer patients who refuse treatment can serve as no-treatment controls in a ‘natural experiment’ to assess the value of some cancer treatments. Because treatment refusal is a rare event, a cancer registry which captures this information is invaluable. Alberta, Canada has a cancer registry which has been population-based since 1961. All records are in machine-readable form and the quality and completeness of the data are high. By the 1980s, over 90 percent of registrations were verified histologically. Ascertainment of death is achieved by computer linkage with the provincial department of vital statistics; when patients are known to have died out of province,
death confirmation is sought from other provincial registries or vital statistics departments.

This paper presents the characteristics of patients in Alberta, Canada who refused treatment for their cancer during a 14-year period, and an analysis of their survival relative to those who accepted treatment. The main hypotheses were: first, that treatment refusal is associated with a shortened expectation of life (and hence with covariables such as site, stage, and age); second, that its effect on survival varies by site; and third, that as treatments have improved, the effect of refusing treatment has become greater.

Materials and methods

Predictors of refusing treatment

Patients diagnosed between the years 1975 and 1988 and refusing treatment were selected from the Alberta Cancer Registry. Refusal was defined as being offered a conventional cancer treatment and refusing it entirely, as opposed to partial compliance with a treatment plan. However, no determination of the competence of the patient to refuse could be made and therefore refusal of treatment may have included some instances where the decision was made by a family member on behalf of a nonautonomous patient. Also, because the cancer registry captures treatment information within six to nine months of diagnosis, patients who initially refused treatment but accepted it more than six months later could have been counted as having refused treatment. Unavailable from the registry were the reasons for treatment refusal, the type of treatment that was refused, and whether it was curative or palliative.

Urban was defined as a municipality with a population greater than 20,000 in 1981, and occupation was coded according to the Statistics Canada’s Standard Occupational Classification. Stages according to systems other than TNM (e.g., Dukes or FIGO) were converted to their TNM equivalents. Refusal rates were calculated by characteristics of the patients and the disease and tested for differences in proportions in the comparison of two large independent samples (Z statistic).

Effects of refusing treatment

To compare outcome between patients who refused with those who accepted treatment, each patient who refused treatment was matched with five control subjects who accepted. The 5:1 matching ratio was calculated to be optimal in terms of maximizing statistical power. Matching variables were: time period of diagnosis (1975-82 and 1983-88); site (broad categories of ICD-9); age (plus or minus five years); whether this was a first or subsequent primary; and whether the cancer was staged. The endpoint was death from the cancer for which treatment was refused. The effect of using this endpoint rather than death from all causes was examined by comparing the differences in the proportions who died using the two endpoints. The termination date for the study was 1 May 1990. Covariables associated with refusing treatment and not controlled by matching were identified and were incorporated into Cox’s proportional-hazards regression-model of survival. Sites with at least 50 subjects were analyzed separately. Finally, to assess the effect of treatment advances, case fatality in each of the groups was correlated with year of diagnosis.

Results

Predictors of refusing treatment

Between 1975 and 1988, cancer patients in Alberta, Canada, refused treatment for 914 of 122,095 cancers. This yielded a refusal rate of 7.5 per 1,000 cancers. Rates rose from 6.4/1,000 in 1975 to 8.4/1,000 in 1988 ($P = 0.001$). Therefore, time period (1975 to 1982 and 1983 to 1988) was included as a matching variable in the second design. Table 1 presents refusal rates by characteristics of the patient and the disease. As hypothesized, refusing treatment was associated with three variables known to predict survival, i.e.: age ($P = 0.007$); number of prior primaries ($P = 0.04$); and site ($P < 0.001$). Patients who refused treatment were older and had more cancers and cancers with known poorer prognosis. Men were overrepresented among patients who refused treatment ($P < 0.005$) as were non-healthcare workers ($P < 0.005$). More patients who refused treatment were from rural than urban areas. Although there was a tendency for refusal to occur more often in more advanced disease ($P = 0.07$), this difference did not achieve conventional statistical significance, likely because of the relatively small numbers with known stage available for analysis.

Results of refusing treatment

The outcome analysis was based on a total sample size of 798 cases (refusers) and 3,990 matched controls (acceptors). Five matches could not be found for 116 cases. Three potentially confounding variables not controlled by matching were identified. Patients who refused treatment were more likely to be rural (44.9 percent of 38.0 percent), less likely to have ever worked in healthcare (0.6 percent of 2.1 percent), and more likely to have advanced disease—Stages III and IV (6.5 percent of 4.1 percent; all $P$ values < 0.01).