Investigating Cancer Clusters in Louisiana and Interpreting Results

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Physicians are often asked questions related to cancer frequency in their communities, particularly in Louisiana because of the perception of high cancer rates in this region. When individuals perceive a higher than normal rate of cancer in their geographic area, time frame, or group of people, questions about the potential role of environmental contamination are often raised. The purpose of this article is to educate clinicians about the concept of cancer clusters so they can further disseminate this knowledge to patients concerned about increased cancer frequency in their communities. This article will accomplish this goal through the consideration of potential questions or concerns patients might present related to cancer frequency in their communities.

INTRODUCTION

Physicians are often asked questions related to cancer frequency in their communities, particularly in Louisiana because of the perception of high cancer rates in this region. An area in southeast Louisiana along the lower Mississippi River has gained notoriety as a suspected "cancer corridor" due to the high concentration of petrochemical industrial sites and concern over increased cancer rates in the area, though multiple investigations have not validated this regionally perceived cancer cluster.[1] The concern that industrial and environmental contamination may be leading to what is known as a "cancer cluster" has become more popularized in recent years.[2] Media has contributed to the public's perception of environmental contamination leading to cancer clustering through such films as *Erin Brockovich* and *A Civil Action*.[2,3] A cancer cluster is defined by the National Center for Environmental Health as seeing more cancer cases than would normally be anticipated in a particular group of people in a geographical area over a specified amount of time.[4] Apparent "cancer clusters" are often falsely identified by concerned individuals, and true cancer clusters are usually differentiated from suspected cancer clusters by the presence of an unusually high rate of rare cancer types, cancers seen in a unusual age group, or high rates of one specific type of cancer.[5] True cancer clusters may be characterized by significant differences between observed and expected cancer rates that have been stratified to the population at risk.

While there are multiple well-documented examples of environmental exposures that cause cancers in humans, only a small percentage of cancers is felt to be due to environmental or occupational exposures to carcinogens.[6] In contrast, the majority of cancers are related to smoking and the combined detrimental effects of diet, physical inactivity, and obesity.[6] Furthermore, methods used to assess cancer clustering in community settings rarely lead to confirmation of a cancer cluster or causes[2] due to multiple factors, including lack of good data regarding exposure levels and small populations being investigated.

The purpose of this article is to educate clinicians about the concept of cancer clustering so they can further disseminate this knowledge to patients concerned about increased cancer frequency in their communities. If a patient suspects a possible cancer cluster in his or her community, their physician has a responsibility to reassure the patient, or conversely, help decide when further public health investigation is necessary and educate patients about ways to reduce cancer risks and the utility of cancer screening.[2]

This article will accomplish its goal through the consideration of potential questions or concerns patients might present related to cancer frequency in their communities.

1. How do Louisiana's cancer rates compare with other states?
2. Why does my parish (city) have high cancer rates?
3. Why does my unincorporated community have high cancer rates?
4. Why does my neighborhood have high cancer rates?
5. What is the relationship between our environment and cancer?

Answers to these questions, resources for providing further information to these questions, and examples of how these questions are often addressed by public health agencies will be explored.

METHODS, RESULTS, AND DISCUSSION

The methods/results and discussion will be briefly discussed for each question addressed.

How do Louisiana's cancer rates compare with other states?

Methods/Results

A comparison of cancer rates from state and national resources can address this question. The cancer incidence rate refers to the number of new cancer diagnoses occurring in a population of interest during a specified time period and is calculated as (new cancer cases)/(size of population at risk) *100,000 a year. Records of new cancer cases are available from state and national sources and can be used in conjunction with census population data to calculate incidence rates.

In Louisiana, a government mandate requires that all new cancer cases be reported to the Louisiana Tumor Registry (LTR).[7] The LTR then collects, processes, and distributes data on cancer in Louisiana.[7] State-based cancer data is compiled at the national level by the following sources: the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI) and the National Program of Cancer Registries (NPCR), which is administered by the Centers for Disease Control and Prevention (CDC).[8] The NPCR covers about 96% of the US population through support of cancer registries in 45 states.[8] The SEER Program collects and analyzes cancer data from 18 population-based cancer registries that cover about 28% of the US population.[9] The SEER Program is considered a comprehensive cancer data source and includes detailed information regarding cancer cases, such as stage at diagnosis and survival information. The SEER Program uses both passive surveillance methods, such as linkage with large databases, and active methods, in which registry workers follow-up with patients, families, and healthcare providers.[9] Cancer information from the LTR, NPCR, and SEER are updated regularly and easily accessible by the public. Cancer data for Louisiana can be assessed using data from these resources.

According to statistics from the NCI and CDC, the incidence of cancer from 2005-2009 for all races, genders, and sites was significantly higher in Louisiana at 488.9 cases per 100,000 per year (95% CI: 485.8, 491.9) than in the United States at 465 cases per 100,000 per year (95% CI: 464.7, 465.4).[10] According to the Louisiana Tumor Registry for 2004-2008, the incidence rate for cancers of all sites for white and black men in Louisiana were significantly higher than national rates. The incidence rate for black women, however, was near the national rate for black women, and the incidence rate for white women was significantly lower.[7]

Discussion

These statistics should be interpreted carefully because differences among the racial/ethnic composition of Louisiana and differences in health behaviors in Louisiana may explain the higher rates of cancer. Some types of cancers affect different race/ethnic groups more frequently (for example, black men have higher rates of prostate cancer), and differences in Louisiana's racial/ethnic make-up could explain differences when compared to the United States as a whole.[11] Such effects can be mostly remedied by a comparison of rates stratified on gender, race, and age. Direct and indirect standardization methods may also be used to reduce the influence of population differences in characteristics such as age, race, and gender. For example, in direct standardization, characteristic-specific rates (such as age-specific rates) from each group to be compared are applied to a common reference population; this is done when characteristic-specific rates are known.[12] Indirect standardization is used when characteristic-specific rates are unknown in the groups that are being compared. In indirect standardization, a common set of characteristic-specific rates serve as the standard and are applied to the two groups being compared.[12]

Similarly, the prevalence of certain health behavior risk factors (such as smoking) varies according to state and could account for differences in a state's rate and the United States as a whole.[11] Much of the geographical differences in cancer rates are felt to be attributable to geographical differences in the distribution of health behaviors.[11] About 75-80% of cancer is attributable to non-hereditary factors, and of those, about 30% are related to smoking and 35% are related to obesity, nutrition, and inactivity.[6] Louisiana has higher proportions of adults who are overweight or obese, have poor nutrition, are physically inactive, and are smokers compared to the United States as a whole.[13] In 2010, 22.1% of Louisiana adults were smokers compared to 17.2% for the United States and 66.4% of Louisiana adults were overweight or obese compared to 63.8% for the United States.[13] In 2009, 43.5% of Louisiana adults engaged in moderate-to-vigorous physical activity compared to 50.9% for the United States, 24.6% of Louisiana adults ate fruits at least two times daily compared to 32.5% for the United States, and 21.3% of Louisiana adults ate vegetables at least three times daily compared to 26.3% for the United States.[13]

Why does my parish (city) have high cancer rates?

Methods/Results

In easily defined geographical regions, such as a parish or a city, cancer rates can be calculated and compared to state levels using data from the LTR along with population estimates from the national census. Furthermore, census data can be used to determine the age and gender structures of the population at risk in order to provide gender-specific, age-adjusted cancer rates. Age-adjustment is important because cancer is a disease that increases substantially with advancing age, so populations consisting of mostly older people would naturally have much higher cancer rates. Also, age-specific rates are usually calculated according to gender, since males have a somewhat higher cancer risk than females. Age- and gender-adjustment for cancer can be performed by examining the age-adjusted standard incidence ratios (SIR) for men and women separately.

First, age-and gender-specific cancer incidence rates are calculated for a "standard" such as the state of Louisiana as a whole. Age- and gender-specific cancer incidence rates are calculated as (new cancer cases in an age and gender group group)/(size of population at risk in the age and gender group) *100,000 a year. These age- and gender-specific rates are then applied to the city population in each age/gender group to obtain an overall estimate of how many cancer cases would be expected if the rates in the city had the same rates as the state; this is done by multiplying the age- and gender-specific cancer rates by the number of people in the corresponding age and gender group in the city of interest. Then, the actual observed cases in the city are divided by the expected number of cases to get the SIR. The SIR provides a relative measure of whether the city has higher rates than the state (SIR greater than one), about the same rates (SIR around one), or lower rates (less than one).

For example, residents in the Livonia Fordoche area were concerned about perceived high rates of cancer in their community and the possible relationship of cancer in their area to environmental exposures.[14] The Louisiana Department of Health, Office of Public Health, Section of Environmental Epidemiology & Toxicology prepared a report that assessed for higher rates in Livonia Fordoche as compared to the rest of the state, using the process described above.

For the time period 1988-2004, the total number of cancers cases expected in males was 151 (using Louisiana age- and gender- specific cancer incidence rates applied to the male population of Livonia Fordoche), whereas the total number of cancers documented in the Livonia Fordoche area in males over the same time period was 134.[14] The SIR was 0.89 (134/151), indicating that the number of cancer cases occurring in males in the Livonia Fordoche area was lower than expected if the cancer rates were the same as the state overall.[14] Similarly, for females (1988-2004), the total number of cancer cases expected using state-rate estimates was 107, whereas the total number of cancer cases documented in the Livonia Fordoche area over the same period in females was 105, giving a SIR of 0.98 (105/107), indicating that cancer incidence in females in Livonia Fordoche was very close to that of the state as a whole.[14] No unusual patterns of cancers were seen according to site in Livonia Fordoche, with most cases occurring at common sites (lung, colorectal, breast in females, and prostate in males).[14]

Discussion

The SIRs for males and females in Livonia Fordoche were very close to or slightly less than one, indicating that cancer incidence was lower than or about the same as cancer incidence in the state as a whole over the same time period. No unusual patterns of cancer types were seen.[14] This assessment effectively ruled out the possibility of a cancer cluster with straightforward calculations.

Oftentimes, a preliminary, rough assessment such as described in this example is adequate to decide that there is not enough evidence of a cancer cluster, and no further investigation is necessary. In other cases, in-depth investigations are pursued if there is evidence suggesting a true cancer cluster: detection of an elevated SIR, detection of one specific cancer type, detection of cancer cases in unexpected age groups, detection of unusual cancer types, detection of exposure to a cancer-causing substance, and biologic plausibility.[4] Political pressure may also contribute to the decision to pursue more intense investigations.[4]

Why does my unincorporated community have high cancer rates?

Background

In the previous example, it was possible to readily calculate age- and gender-specific cancer rates in the geographical region of interest because the Livonia Fordoche area was easily defined. Since city names and zip codes were available for the Livonia Fordoche area, it was relatively easy to obtain details regarding genders and ages of individuals living in Livonia Fordoche using census data and then to further identify corresponding cancer cases from Livonia Fordoce in the LTR.

However, sometimes residents of a poorly defined community have concerns about elevated cancer rates, and in these cases, different techniques must be used to obtain estimates of cancer incidence. Because these poorly delineated communities lack geographic boundaries that correspond to census tracts, zip codes, or city names, estimates of these communities' populations are more difficult to approximate. Linking corresponding cancer cases in the LTR to persons residing in the community of interest is also a challenge, since cases in the LTR cannot simply be searched according to city or zip code. Also, the LTR cannot be adequately queried or searched by years in a specific occupation, which are required for occupational standardized mortality ratio investigations.

As an example, methods of assessing cancer rates in a poorly defined community will be demonstrated. Mossville is a small, unincorporated community in southwest Louisiana near Lake Charles, and for years, residents expressed concerns about possible health problems related to potential chemical exposures originating from nearby factories and plants.[15,16] Despite multiple assessments done by federal and state agencies such as the EPA, ASTDR, and LDHH, no clear consensus had been reached regarding the health impact of potential environmental exposures so an assessment of cancer rates was performed.

Methods/Results

The Mossville community is not a city in the postal system. Therefore, the main Mossville area was defined using boundaries defined by previous EPA environmental assessments that utilized geographic information systems (GIS) technology. Geographic information corresponding to the Mossville area was used to search the Louisiana Tumor Registry.

The Louisiana Tumor Registry was searched using street, street number, city, and zip code information corresponding to the main Mossville area, as defined by prior assessments, for the years 1988-2010. Estimates for the population in Mossville were made by using a weighted estimate based on how many homes were located in the main Mossville area out of the total number of homes in the geographical region with a known population. The estimated population for each year was calculated by extrapolating between census year populations. The total population at risk was calculated by summing each year's estimated population. The yearly cumulative incidence was calculated by dividing the total cases reported by the total population at risk. The 1988-2010 cumulative cancer incidence for Louisiana was estimated by dividing the total number of cancer cases from the Louisiana Tumor Registry by the summation of the state population from 1988-2010.

From 1988-2010 in Mossville, a total of 97 cases of cancer were reported from an estimated 23,347 at-risk individuals (the cumulative population for 12 years), resulting in a cumulative incidence of cancer of 415.5 cases per 100,000 individuals. The 1988-2010 cumulative cancer incidence for Louisiana was 490 cases per 100,000 (492,791/100,782,467).

The top sites for new cancer cases were lung and bronchus (18.6%), breast (16.5%), prostate (16.5%), and colorectal (10.3%).

Discussion

GIS methods and census data were used to define boundaries of the Mossville community, produce a crude estimate of the population at risk in Mossville, and identify cancer cases in the LTR that corresponded to the defined Mossville area. The estimated cancer incidence for the Mossville area was lower than that for Louisiana as a whole. Detailed information regarding the age- and gender-structure of this community was not available so age- and gender-adjustment methods were not used. When investigating cancer rates in relatively small areas with relatively small populations, the total number of cancer cases is usually a fairly small number so much variability can occur from year-to-year. Due to the somewhat crude methodology used in assessing cancer incidence rates for poorly defined communities, such estimates provide gross assessments of cancer rates that are mainly useful in detecting rates that are substantially higher and cause for further investigation.

Also, as mentioned in the previous example, the sites at which cancers are occurring are reviewed for unusual trends. In Mossville from 1988-2010, the top four sites of cancer occurrence corresponded to the top four sites across the United States: lung, prostate, breast, and colorectal; there was no indication of "unusual" types of cancer occurring.

Why does my neighborhood have high cancer rates?

Background

Individuals sometimes perceive what they feel are inordinately high cancer rates if they encounter several cases of cancer in their neighborhood or among their relatives. Often the most reasonable explanation of apparent cancer clusters is simply chance.[2] While an overall pattern of cancer occurrence is random over a large area such as the entire United States, some random grouping of cancer cases will occur by chance[2] and may be perceived as environmentally significant cancer clusters when seen from the perspective of an inhabitant of a small community. Additionally, cancer is a common disease; about 1/2 males and 1/3 females will be diagnosed with cancer at some point in their lives,[6] and relatives often share similar high-risk cancer behaviors such as smoking, high-fat diets, and lack of exercise. To illustrate these ideas, an apparent cancer cluster of four Leukemia cases will be described, as well as an illustration of how many households would be expected to contain someone living with cancer.

Methods/Results

Residents of Coteau, Louisiana, became concerned about a possible leukemia cluster when four children were diagnosed with acute lymphocytic leukemia (ALL) in the time period from 1986 to 1996.[17] The children ranged in age from 2 to 8 years old at diagnosis; two were male and two were female.[17] A preliminary assessment determined that the incidence of childhood leukemia was higher than expected using New Orleans incidence as a reference population.[17] The rate ratio in male children was 7.7 in Coteau compared to New Orleans, meaning the incidence of ALL in Coteau was almost eight times the incidence of ALL in New Orleans.[17] The rate ratio in female children was 13.3 in Coteau compared to New Orleans, meaning the incidence of ALL in Coteau was almost 13 times the incidence of ALL in New Orleans.[17]

At the insistence of the public, an in-depth case-control study to investigate potential risk factors to explain the increased incidence of ALL was performed by the Louisiana Office of Public Health, despite health officials' knowledge that such in-depth studies of very small cancer clusters rarely provide definitive answers.[17] As anticipated, the study was costly and inconclusive in determining what exposures (if any) that led to leukemia in these children.[17]

Discussion

This example highlights the limitations of in-depth studies performed on small clusters and demonstrates that chance occurrence was the most likely explanation. Though data clearly indicated that incidence of ALL was higher in Coteau from 1986-1996, a more in-depth assessment was not helpful in determining a causative exposure. As noted previously, this was not an unanticipated result and was, therefore, a costly and unnecessary assessment. In studies dealing with small populations, it is often most appropriate to do a descriptive study, looking for prominent shared risk factors and then proceeding to a formal investigation if indicated.[17] In studies such as this one where a long questionnaire is used to explore multiple exposures of interest and look for potential associations post-hoc, false-positive associations (when a statistical relationship is found that is not truly a clinical relationship) become problematic because some statistical associations will be seen simply due to chance. In this study, more than 80 potential associations were examined, ranging from contact with monkeys to immunization history.[17] Four possible exposures reached statistical significance, which is the expected number of incidental associations that would be seen by chance.[17] Additionally, these exposures were not clinically consistent, indicating that these were likely false positives. Despite the substantial resources dedicated to this investigation, the best explanation remained that four cases of ALL occurred by chance.

An exercise that looks at the number of people in the United States living with cancer can help illustrate the high prevalence of cancer in this country. About 12,000,000 people in the United States were living with cancer in 2004 in about 100,000,000 households, which means that about one person in every eight households would have a cancer diagnosis.[14] Additionally, about 1/2 males and 1/3 females will be diagnosed with cancer at some point in their lives.[6] Many times, the public may perceive an unusually higher number of cancer cases because they are simply unaware of how common cancer actually is among their neighbors and relatives.[5] By simply educating individuals about the reality of cancer risk, they may be more likely to perceive cancer as less unusual and dispel fears of potential clustering.

What is the relationship between our environment and cancer?

Methods/Results

Pertinent associations between environmental exposures and cancer were explored in the literature. The ACS describes two classes of factors that can affect cancer risk: hereditary factors, those which are attributable to genetics and cannot be changed, and environmental factors, which are potentially modifiable.[6] Environmental factors that can increase cancer risks include things such as health behaviors (smoking, physical inactivity, obesity), as well as exposures to environmental contaminants.[6] The majority of cancer cases (75-80%) are due to behavioral environmental factors rather than hereditary factors.[6] Only a small fraction of these (about 6%) are attributable to occupational or environmental carcinogen contaminants.[6] The majority of environmental risk factors associated with increased cancer risk are secondary to health behaviors, with about 30% of cancers related to smoking and 35% related to obesity, nutrition, and inactivity.[6]

Important relationships between environmental exposure and cancer exist, and rare historical cancer cluster investigations have resulted in impactful clinical findings. Classic examples include mesothelioma in asbestos workers, scrotal cancer among chimney sweeps, and vaginal clear cell carcinoma in women exposed to diethylstilbestrol in utero.[2] Causative relationships between exposures and cancers were established in these cases because the cancer cases occurred in persons with clear histories of specific exposures, and the kinds of cancer identified were limited to specific cell types. This is a markedly different situation than that described in many suspected cancer clusters, where environmental exposures are unknown and there are multiple cancer types in question.

Discussion

These statistics demonstrate that the majority of potentially modifiable risk factors for cancers are related to lifestyle choices such as smoking or exercise, and a relatively small percentage are attributable to environmental contaminants. When investigating potential cancer clusters related to environmental contaminants, these relatively small associations can easily be dwarfed by the relatively large contributions of unhealthy lifestyle choices to increased cancer risk, making it very difficult to tease out specific contributions of particular pollutants toward cancer risk. In Louisiana, this is made particularly difficult by the high prevalence of unhealthy lifestyle factors in Louisiana residents, in addition to the small areas under investigation and the lack of adequate data to reliably describe human carcinogen exposure. When important environmental factors are determined to be causal, these relationships often demonstrated in cases of exposures, which are clearly defined or well-documented, higher magnitude exposures than the general population and/or long-term exposures as described in historical examples.[2]

Even so, environmental causes for cancer should not be discounted. While only 6% of total cancers are attributable to environmental contaminants or occupational exposures, the absolute number of cancer cases caused by them remains substantial, given cancer is a common disease. An estimate from 2011 shows that about 34, 320 cancer deaths were due to environmental contaminants or occupational exposures.[6] So, the relative contribution of environmental/occupational sources must not be ignored.

FINAL CONCLUSIONS AND RECOMMENDATIONS

Cancer is a greatly feared, yet common, disease. The general public often perceives environmental or occupational sources as likely causes for increased cancer occurrence, though unhealthy behaviors like smoking are more substantial contributors to cancer occurrence. Proving the mere existence of cancer clusters is challenging, and determining causation for probable cancer clusters is even more difficult. This article demonstrated examples of various Louisiana cancer cluster assessments, which either resulted in lack of cluster confirmation or inconclusive findings in terms of etiology. Findings from other health department investigations show compatible results; a review of 108 cancer cluster investigations occurring in 29 states and five foreign countries failed to reveal consistent etiologic relationships for clusters.[18]

Clinicians should be aware of the utility and limitations of cancer cluster assessment techniques so that they are armed with knowledge to reassure concerned patients or call for further assessment when appropriate. Furthermore, healthcare providers should remember to counsel patients regarding the importance of behavioral cancer risk factors such as diet and smoking and the risks and benefits of cancer screening measures.

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