Common cancers in centenarians

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Background:
A Centenarian is a person who attains and lives beyond the age of 100. Four percent of centenarians die from cancer. It is therefore important to understand which cancers affect them in order to devise better methods to prevent and treat them. The aim of this study was to investigate the top cancers that affect centenarians.

Material/Method:
We identified 1385 cases with the Surveillance Epidemiology and End Result (SEER) database. Our study included centenarians age 100–115 years diagnosed with the 5 most common cancers between 1973 and 2007 in the United States. Observed survival (OS) was calculated for each cancer type. The Kaplan-Meier (KM) method was used to calculate OS at 1-month intervals for the first 40 months after diagnosis using SEER*Stat version 7.04. A log rank test was performed on KM survival output and a Cox proportional hazard model was used to calculate hazard ratios. All statistical analyses were performed with 95% confidence intervals with significance determined at $P<0.05$. Cox proportional hazard analysis was done using GraphPad Prism version 5.04.

Results:
There were 879 (63.47%) females and 506 (36.53%) males. There were 1118 (80.72%) whites, 159 (11.48%) blacks, and 108 (7.80%) other. The top cancers were 405 (29.24%) breast, 267 (19.28%) colorectal, 254 (18.34%) prostate, 247 (17.83%) lung and bronchus, and 212 (15.31%) urinary and kidney cancer cases.

Conclusions:
As the prevalence of centenarians increases, it is becoming increasingly important to become aware of the cancers that affect them in order to better manage them.

MeSH Keywords:
centenarians • elderly (>70 years) • cancer epidemiology

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Background

A Centenarian is a person who attains and lives beyond the age of 100. Centenarians were once believed to be rare, but nowadays they are becoming increasingly common [1]. In the United States, there are approximately 10–20 centenarians per 100 000 population, averaging approximately 80 000 [2]. In Okinawa Japan, there are approximately 50 centenarians per 100 000 population [2]. The general consensus suggests that for a person to live to extreme old age, there has to be a series of molecular *aging events* working harmoniously with cellular events over time to maintain health [3–5]. Otherwise, the end result of accumulated cellular errors due to aging can lead to acute or chronic co-morbid conditions and even cancer [6]. Up to 13% of centenarians reach the age of 100 without any age-related illness [5]. It has also been observed that centenarians may be predisposed to a prolonged survival because there has been significant delay in the manifestation of associated disabling symptoms and/or morbidity [7], even in those centenarians who have reached this milestone with age-related diseases. Although the factors that increase longevity are not well described, it has been suggested that new developments in medicine; better quality and increased availability of health care; worldwide access to healthy food; and access to housing and genetics may contribute to increasing the life span of a population [2].

Although cancers are the second leading cause of death in the United States, only 4% of centenarians die of cancer, compared to almost 40% mortality in the middle-age group [8]. Additionally, studies have reported that centenarians have the lowest rate of cancer metastasis [9,10], which is very surprising as it is universally known that increasing age is a major risk factor for cancer development [11–14]. According to Perls et al, centenarians may possess some genetic advantage that prevents or delays the development of cancer [15].

While the genetic studies and survivability of centenarians is well-documented, the literature on cancer incidence and mortality in this group is sporadic and sometimes confusing. The latter has partly been caused by patients falsifying their ages [16], or study designs including patients <100 years old [4,5]. What is known from reports over the last 2 decades is that most cancers have the lowest incidence in this age group. The trend seems to be that most malignancies increase and peak in the mid-80s before declining and beginning to plateau as age increases [8,17].

A previous study attained the mean age of diagnosis of centenarians for the New England Centenarian Study, and then compared that data to the mean age of diagnosis in the Surveillance Epidemiology and End Result (SEER) database [4].The study showed that the mean age of diagnosis for centenarians with all types of cancer was 80.5 years, which is 14 years older than the mean for the entire population. Surprisingly, the mean age at diagnosis for each cancer was relatively low, except pancreatic cancer, which was 104 years [4]. This shows that the majority of centenarians do not develop cancer after age 100.

To the best of our knowledge, there is no single statistical study that has exclusively looked at the cancers of centenarians. Our aim in this study was therefore to determine the most common cancers in this age group and how they affect these patients' overall survival after diagnosis.

Material and Methods

The National Cancer Institute records 26% of cancer incidence and survival data from 17 geographical regions reporting in the Surveillance Epidemiology and End Result (SEER) database. The SEER database was used to collect data from 1973 to 2008. Patients included in this study were centenarians (100–115 years old) diagnosed with lung, prostate, breast, urinary (including kidney), and colon/rectal cancers between 1973 and 2007 in the United States. These cancer types were identified as the 5 most common cancers in centenarians. Using these criteria, 1385 cases were identified in the research database. Exclusions were made for patients alive with no survival time. Demographics based on age, race, and sex were tabulated for all 5 types collectively, as well as by each individual cancer type.

Observed survival (OS) was calculated for each cancer type based on sex. The Kaplan-Meier (KM) method was used to calculate OS at 1-month intervals for the first 40 months after diagnosis using SEER*Stat version 7.04. A log rank test was performed on KM survival output and a Cox proportional hazard model was used to calculate hazard ratios (HR). All statistical analyses were performed with 95% confidence intervals (CI) with significance determined at $P < 0.05$. Cox proportional hazard analysis was done using GraphPad Prism version 5.04 (GraphPad Software Inc, 2012, La Jolla, CA, *www.graphpad.com/prism*).

Results

A total of 1385 centenarians met our inclusion criteria, with 3.39%, 7.29%, 10.25%, 19.21%, 25.13%, and 34.73% diagnosed in 1973–1978, 1979–1984, 1985–1990, 1991–1996, 1997–2002, and 2003–2008, respectively (Table 1). There were 879 (63.47%) females and 506 (36.53%) males. Among races, there were 1118 (80.72%) whites, 159 (11.48%) blacks, and 108 (7.80%) other. There were 64 Hispanics (4.62%). Among cancer sites there were 405 (29.24%) breast, 267 (19.28%) colon and rectum, 254 (18.34%) prostate, 247 (17.83%) lung and

Table 1. Showing the number of centenarians diagnosed with cancer within the given time periods.

Year of diagnosis		
1973–1978	47	(3.39%)
1979–1984	101	(7.29%)
1985–1990	142	(10.25%)
1991–1996	266	(19.21%)
1997–2002	348	(25.13%)
2003–2008	481	(34.73%)

bronchus, and 212 (15.31%) urinary and kidney cancer cases (Table 2).White females were proportionally the most common demographic with breast, lung and bronchus, colon and rectal, and urinary/kidney cancers. White males were proportionally the most common demographic with prostate cancer.

Among white centenarians, the most common types of cancers were breast (351 cases, 31.40%), colorectal (216 cases, 19.32%), lung (186 cases, 16.64%), urinary system (183 cases, 16.37%), and prostate (182 cases, 16.28%). Among the black population, the most common cancers were breast (43 cases, 27.04%), prostate (40 cases, 25.16%), lung (37 cases,

23.27%), colorectal (25 cases, 15.72%), and urinary (14 cases, 8.81%) (Table 2).

Among all male centenarians, 382 (75.49%), 61 (12.45%), and 63 (12.45%) were white, black, and other, respectively. In female centenarians, 736 (83.73%), 98 (10.13%), and 45 (5.12%) were white, black, and other, respectively (Table 3).

Among supercentenarians, defined as ages 110+, 3 were white, 2 were black, and 1 was in the "other" group (Tables 3 and 4). Notably, no cases of breast or colorectal cancer were found beyond 108 years of age (Table 4).

Hazard proportional models showed males with colorectal cancer were associated with the greatest hazard (HR=1.85, P<0.0001), followed by lung cancer (HR=1.65, P<0.0001), and urinary system cancer (HR=1.18, P=0.0099), with prostate cancer as the baseline. In females with breast cancer as the baseline, lung cancer (HR=1.52, P<0.0001) had the worst prognosis, followed by urinary system cancer (HR=1.05, P=0.194), and colorectal cancer (HR=0.92, P=0.0076). When comparing male and female cases (with female as the baseline) of lung colorectal, and urinary system cancers, HRs were 1.09 (P=0.1485), 2 (P<0.0001), and 1.12 (P=0.0073), respectively, showing that females have a significantly lower hazard ratio than males who have colorectal and urinary system cancer (Table 5).

Table 2. Showing the common cancers seen in centenarians.

Site	No.		Male		Female		White		Black		Other	
Breast	405	(29.24%)	2	(0.49%)	403	(99.51%)	351	(86.67%)	43	(10.62%)	11	(2.72%)
Prostate	254	(18.34%)	254	(100.00%)	0	(0.00%)	182	(71.65%)	40	(15.75%)	32	(12.60%)
Lung and bronchus	247	(17.83%)	78	(31.58%)	169	(68.42%)	186	(75.30%)	37	(14.98%)	24	(9.72%)
Colon and rectum	267	(19.28%)	73	(27.34%)	194	(72.66%)	216	(80.90%)	25	(9.36%)	26	(9.74%)
Urinary and kidney	212	(15.31%)	99	(46.70%)	113	(53.30%)	183	(86.32%)	14	(6.6%)	15	(7.08%)

Table 3. Showing the distribution of cancers in centenarians with respect to age, gender and race.

Race	Sex	100	101	102	103	104	105	106	107	108	109	110–115	Total
White	M	142	91	75	28	22	15	5	2	1	–	1	382
	F	283	183	118	77	28	13	14	13	5	–	2	736
Black	M	19	14	6	9	4	4	1	1	1	–	2	61
	F	42	23	8	5	5	5	7	2	–	1	–	98
Other*	M	21	17	8	5	6	1	3	–	–	1	1	63
	F	15	10	5	3	6	2	1	1	2	–	–	45
Total		522	338	220	127	71	40	31	19	9	2	6	1385

Table 4. Showing the distribution of the top 5 cancers with age and gender.

Cancer	Sex	100	101	102	103	104	105	106	107	108	109	110 −115	Total	All cases*
Lung	M	36	16	13	6	5	1	1	–	–	–	–	78	467,797
	F	67	40	20	19	10	3	6	2	1	–	1	169	337,669
Colorectal	M	22	19	18	3	5	3	2	1	–	–	–	73	343,983
	F	77	52	30	23	7	3	1	–	1	–	–	194	338,214
Urinary system	M	38	25	20	6	5	2	2	–	–	–	1	99	296,352
	F	39	33	21	5	4	3	1	3	2	1	1	113	128,506
Breast	M	–	–	–	1	1	–	–	–	–	–	–	2	6,157
	F	157	91	60	38	18	11	14	11	3	–	–	403	871,728
Prostate	M	86	62	38	26	16	14	4	2	2	1	3	254	843,896
	F	–	–	–	–	–	–	–	–	–	–	–	–	–
Total		522	338	220	127	71	40	31	19	9	2	6	1385	3,634,302

Table 5. Showing the hazard ratios of the common cancers seen in centenarians.

		HR	95% CI low/high		P Value
Males	Lung	1.65	1.52	1.77	<.0001
	Colorectal	1.85	1.83	1.87	<.0001
	Urinary system	1.18	1.18	1.18	0.0099
Female	Lung	1.52	1.40	1.63	<.0001
	Colorectal	0.92	0.90	0.95	0.0076
	Urinary system	1.05	1.01	1.08	0.194
M *vs.* F	Lung	1.09	1.08	1.09	0.1485
M *vs.* F	Colorectal	2.00	1.96	2.05	<.0001
M *vs.* F	Urinary system	1.12	1.09	1.17	0.0073

Discussion

As seen from the SEER database, the number of centenarians diagnosed with cancer has increased since 1973. This may reflect an increase in cancer incidence, such as that experienced in the general population, or it may simply reflect an increase in diagnosis of cancer secondary to improved methods of cancer detection since that time.

Contrary to the general population, it is surprising that in the centenarian population, the number of cancers detected decreased with increasing age (Tables 3 and 4). This finding may be due to a genetic predisposition to evade or hinder the development of cancer in some people. According to Anderson et al, centenarians may have variations that shield them from developing cancer or they might be deficient in certain genetic variations that would normally increase their chances of cancer development [4]. Another possible reason for the decrease could be that in the elderly population, less invasive tests such as biopsies are performed to confirm the presence of cancer.

The most common cancers found in the centenarian population were breast, prostate, lung, colorectal, and cancers of the urinary system. There was significant variation of these cancers with race, gender, and increasing age.

We found that white centenarians had a greater incidence of cancer compared to the other races. This finding may not necessarily reflect the statistics of the general population, as our study had a disproportion in the number of participants from

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the respective races. However, there was a trend with the ratio of females to males among the blacks and whites. In the white centenarian population, 66% were female and 34% were male. Similarly, in the black population, 62% were female and 38% were male. However, in the remainder of cases, there were 42% females and 58% males. The most common cancers among the white population (in descending order) were breast cancer, followed by colorectal cancer, lung cancer, urinary system cancer, and prostate cancer. In the black population, the most common was breast followed by prostate, lung, colorectal and then cancers of the urinary system. There is a clear difference with incidence of prostate cancer between the races. This finding is also supported in the 10-year survey on prostate cancer incidence that was conducted by the CDC. In that study, prostate cancer had a higher incidence among the black population compared to whites and other races [18].

In females, the most common cancer was breast cancer, followed by colorectal cancer, lung cancer, then cancers of the urinary system. A similar trend was observed in a study conducted by Anderson et al. [4]. In males, the most common cancer was prostate cancer followed by cancers of the urinary system, lung, colorectal, and breast cancer. The incidence of these cancers may be related to the delayed developmental course of some cancers. For instance, the high incidence of prostate cancer in centenarians may be related to the slow development of prostate cancer, resulting in a large number going undetected in the general population, but detected in the centenarian population because there are many more years in which cancer can surface [19].

The mortality of the centenarian population varied with gender, race, and cancer type. In males, colorectal cancer had the highest mortality rate, followed by lung cancer and cancers of the urinary system. However, in females, mortality was higher with lung cancer, followed by urinary system cancer, then colorectal cancer. When comparing males to females, colorectal cancer in males had a significantly higher mortality rate (Table 5). Worldwide, in more developed countries, the ratio of mortality in colorectal cancer in males to females is 1.6 to 1, while in less developed countries this ratio is 1.9 to 1. This

demonstrates that worldwide, men have a lower survival rate than women [14]. Another study also showed that long-term survival in females is greater for colorectal cancer [20]. Urinary system and lung cancer showed very similar survival rates when comparing males and females.

The mortality in the centenarian population may be influenced by the fact that most cancers progress to advanced stages, making them difficult to treat. This may occur as a result of fewer options available to treat the elderly population. Surgery is generally not an option for elderly patients. In fact, surgeons frequently choose less aggressive treatment options for elderly patients, which usually leads to a worse prognosis [21–24]. These patients usually have multiple co-morbidities, which may increase the incidence of post-operative complications and make surgical procedures more difficult to perform [21,22]. As a result, there may be very little that could be done to improve survivability in centenarians.

Conclusions

Cancer in centenarians is a growing problem in healthcare. The 5 most common cancers seen in centenarians are breast, prostate, lung, colorectal, and urinary system cancers. There is a significant disparity in the prevalence of the different types of cancers with gender and race. The incidence of these cancers may be influenced by the slow progression of some cancers or a protective genetic advantage of some of these patients to resist or delay cancer development.

Mortality varies with cancer type and gender, and is influenced by the limited management options available for centenarians. Invasive procedures and surgeries are more dangerous in the elderly population, as these patients usually have multiple co-morbidities.

As the prevalence of centenarians increases, it is becoming increasingly important to become aware of the cancers that affect them in order to devise better prevention and treatment methods.

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