The Impact of Race and Gender on the Prognosis of Breast and Pancreatic Cancer

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Abstract

Cancer is a unique but complex group of diseases that affect millions of people every year. While some cancers are more common but easily treatable, others are less common but far more detrimental. For example, while breast cancer affects over two million women worldwide every year., the five-year survival rate for localized breast cancer is around 99%, which decreases with advanced stages. However, pancreatic cancer affects a little less than half a million people worldwide annually, but it accounts for 7% of cancer deaths and has a five-year survival rate of only 11%. Despite tissue differences, these cancers still have a large gap between the number of people affected by them and their mortality rates, but the contributing factors are still not understood completely. Two factors that are known to affect various cancers are gender and race, which may play a role in the differences between breast and pancreatic cancer. Here we review the impact of gender and race on the prevalence and prognosis of breast and pancreatic cancer to understand how these factors play a cancer-specific role in the overall lives of patients.

Introduction

Cancer is a term that is heard often within the world. Not everyone really knows what cancer is, leading to the misuse of the term over the years. Cancer is a devastating disease that continuously affects people's day-to-day lives all around the world. According to the World Health Organization, in 2020 in the United States, cancer was the second leading cause of death, but worldwide it was the leading cause of death (WHO 2022). Cancer has been researched and analyzed by researchers across the world trying to find a cure for this treacherous disease. This disease affects people of all ages, genders, and races. There are many factors that can affect any type of medical prognosis including cancer prognosis, two major ones are gender and race. Breast cancer is one of the 100+ cancers that is an extremely common cancer but it is much more treatable than other cancers. On the other hand, pancreatic cancer is one that is not as common but has one of the highest death tolls of any cancer. Given their distinct natures, breast and pancreatic cancer may be affected differently by various factors. Of particular interest are race and gender, and how these two factors contribute differently to breast and pancreatic cancer will be the focus of this review.

What is Cancer?

Cancer is a genetic disease in which specific cells in the body start growing extremely fast and eventually spread to other body parts. The definition of cancer is, "Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body" (NCI 2021). It is caused by changes in genes that tell the cell what to do and how to work. It can start anywhere in the human body due to the number of dividing cells that resonate in the body. Each person's cancer has its own combination of genetic changes that are unique to it. Cells go through a process known as cell division, allowing tissues to form new cells as needed. The

other cells die off when old or damaged and are replaced by new cells. The process of cell division is not always perfect, leading to malfunctions where the damaged cells that are supposed to die off instead grow and multiply as healthy cells should. Cancer cells can be a result of these malfunctions in cell division which forms a tumor that can spread into nearby tissues and form new tumors, a process known as metastasis. Cancer cells do not listen to signals that the body sends them when instructed to grow or stop dividing to die while normal cells listen to all of these signals, therefore, keeping our body healthy. Normal cells do not move around the body but cancer cells tend to invade multiple parts of the body and grow there as well. Cancer cells tell the blood vessels to move towards the tumor so the tumor can be supplied with the oxygen and nutrients that it needs to survive in the body, known as angiogenesis. Another ability of cancer cells is to trick the immune system into helping them stay alive but they can also hide from it if it is trying to fix the damage made. One major infidelity of cancer cells is the change in chromosomes, including doubling or deleting parts of the chromosome, thus changing up how the cell carries genetic information. They can go as far as making energy from nutrients to allow them to grow much faster compared to the rate normal cells grow. According to the National Cancer Institute, "Many times, cancer cells rely so heavily on these abnormal behaviors that they can't survive without them. Researchers have taken advantage of this fact, developing therapies that target the abnormal features of cancer cells" (NCI 2021). The capabilities of cancer are being looked into more and more such cancer therapies which could eventually lead to a big discovery.

Tumors are lumps of tissues and can either be malignant, meaning they are cancerous or benign meaning they are non-cancerous. Cancerous tumors can grow back when removed while benign tumors normally don't, making them a lot more serious to deal with. According to the National Library of Medicine, "One of the fundamental features of cancer is tumor clonality, the development of tumors from single cells that begin to proliferate abnormally" (National Library of Medicine 2000). If tumors can be copied this can result in an increase of tumors, making it even harder to treat the cancer. Metastatic cancer is where cancer has spread to another part of the body from where it originally started. There is a genetic change involved in cancer, the three main types of genes that are affected by this are DNA repair genes, proto-oncogenes, and tumor suppressor genes. The role of DNA repair genes is to fix damaged DNA, therefore, cells with mutations in these types of genes are prone to additional mutations in various other genes and even changes in chromosomes. Apoptosis is a significant difference between normal and cancer cells, "Normal cells also undergo apoptosis following DNA damage, while many cancer cells fail to do so. In this case, the failure to undergo apoptosis contributes to the resistance of cancer cells to irradiation and many chemotherapeutic drugs, which act by damaging DNA. Abnormal cell survival, as well as cell proliferation, thus plays a major role in the unrelenting growth of cancer cells in an animal" (National Library of Medicine 2000). The lack of apoptosis in cancer cells is one of the biggest factors in the spread of these cells. These gene mutations can lead to cancerous cells. Proto-oncogenes are related to cell division and growth but when the genes are mutated, they can become oncogenes which are cancer-causing genes that drive cell division. Tumor suppressor genes inhibit cell division and growth but when there are mutations in these genes, it leads to cell division regulation being further disrupted. As time has gone on it has been found by scientists that certain cancers are related to certain mutations which are common and get targeted using some treatments.

There are many types of cancer, over 100 but they have been put into categories based on the type of cell that they start in. A few of the most common categories are carcinomas, sarcomas, and leukemia. The most common group is carcinomas, which occur in epithelial cells that line both the inside and outside surfaces of the body. Sarcomas are cancers that begin in bones and soft tissues which can include anything from muscles to blood vessels. Leukemia is cancer of blood-forming tissue of the bone marrow which has different characteristics compared to other categories of cancer.

There are many factors that affect cancer that are either controllable or non-controllable.These risk factors are not always directly correlated to cancer but can be proved, "Most cancer risk (and protective) factors are initially identified in epidemiology studies. In these studies, scientists look at large groups of people and compare those who develop cancer with those who don't. These studies may show that the people who develop cancer are more or less likely to behave in certain ways or to be exposed to certain substances than those who do not develop cancer" (National Cancer Institute 2017). There are numerous controllable factors such as diet, radiation exposure, tobacco, and certain substances. It has not been completely proven that diet is a direct cause of cancer but it can be associated with it. Radiation can also be a risk factor because it can cause DNA damage and that can possibly lead to cancer. It has been found that tobacco is the leading cause of cancer prognosis and death because of the chemicals in tobacco and how harmful they are to many parts of the body. Although there aren't as many non-controllable factors, the few big ones are age, race, and gender. Older people are much more prone to cancer because their body has been working for a long time which makes it more common for a possible malfunction that could damage cells. Race and gender are two factors that hold a lot of importance in the prognosis of cancer. Race and gender haven't been looked into as much compared to some other factors that could affect cancer. There have been epidemiological studies that have found that different races are more susceptible to certain cancers and subsequently have lower survival rates. According to Ozdemir and Dotto, Genetic variants are correlated with specific cancer types, and these specific variants result in a marginal increase for risk of cancer. (Dotto and Ozdemir 2017). It varies for each cancer and how specific cancers could have possibly adapted to the race. The molecular biology of different races plays a significant role in their cancer susceptibility. Gender is another significant factor in certain cancers as males and females have different body structures. There have also been epidemiological studies showing how cancer susceptibility varies between males and females relating to different exposures and their organs. "We found that exposure-related tumors in non-reproductive organs were 1.7 times more often developed in male rats compared to females (7) and we identified 68 'male-specific' and 19 'female-specific' carcinogens (carcinogens that induced cancer in one gender only). Furthermore, we found that spontaneous tumors in control animals were 1.6 times more common in male rats. The similarity in gender differences both in human and rat data suggests that these differences may depend on common endogenous biological factors leading to male sensitivity" (Ali et al. 2016). Although the study was focused on rats, there are similarities to humans, and is valid evidence for looking into the effect of gender.

Breast and pancreatic cancers are two very different cancers in terms of where they start out in the body, the global survival rate, and the way that they function. Breast cancer is a very common type of cancer that affects primarily women due to the organ that is affected but it has a

high survival rate. There are three subtypes of breast cancer: hormone receptor-positive, HER2 positive, and triple negative. Unlike breast cancer, pancreatic cancer is one of the less common cancers that affect both genders but its survival rate is much lower due to how much harder it is to treat. Race and gender have an important role in both types of cancer, studies have found that certain races and genders are more commonly diagnosed with breast cancer but other races and genders are more commonly diagnosed with pancreatic cancer.

Effects of Important Factors on Different Cancers

Due to pancreatic cancer and breast cancer differing in many important ways, they variably affect different races and genders. For pancreatic cancer, African Americans are more likely to develop it as opposed to Asians, Hispanics, and white people. This could be due to the risk factors that are more common for African Americans including smoking, diabetes, and being overweight. Smoking is one of the leading risk factors for pancreatic cancer, according to American Cancer Society, The risk of getting pancreatic cancer is double in people who smoke versus people who do not, about 25% of pancreatic cancer is correlated with smoking (American Cancer Society 2020). A few other reasons can include a higher likelihood for African Americans to have pancreatitis and diabetes mellitus which are some of the leading risk factors for pancreatic cancer. Men are also more likely to be diagnosed with pancreatic cancer, likely due to many of the same risk factors mentioned previously.

Regarding Breast cancer, white people are more likely to develop this cancer but African Americans and Asians are close behind. Hispanic and Native Americans are least likely to get breast cancer. Black people are most likely to have a more aggressive form of breast cancer and are more likely to be diagnosed at a younger age than white people. African Americans also have the highest death rate for breast cancer out of the races. Women are much more likely to get breast cancer due to the female body part but men can still get it. Breast development for a woman takes around 3-4 years and is normally completed by around the age of 14. Men do not have fully formed breasts, they normally have fat, not formed glands. Once breasts are in full formation, the breast cells become very active and can even be termed "immature." They act like this until a woman's first full-term pregnancy; therefore, there is a long period of time where they are extremely responsive to hormones such as estrogen and even hormone disruptors. The cells in men's breasts are inactive and men have low levels of estrogen, which reduces their susceptibility to breast cancer immensely. It was also found that for cancer in general men are more susceptible because of their X chromosome. According to Carey Goldberg, "If there's a tumor suppressor gene on the X chromosome, it would be equally likely to be mutated in a male or a female, because they each essentially have one that's active. The other one is supposed to be shut down" (Goldberg 2016). Women have two X chromosomes while men only have one, when this one is possibly damaged it shuts down but since women have two the other X chromosome can balance it out.

The prognosis of pancreatic cancer depends on numerous factors including the size and type of the tumor. Whether lymph nodes are involved and the degree of metastasis are also major prognostic factors. Pancreatic cancer is more likely to be found in later stages, but the earlier it is found the easier it is to treat, According to John Hopkins Medicine, a patient diagnosed with stage IV pancreatic cancer has a five-year survival rate of 1% and on average will live for about

1 year after diagnosis (John Hopkins Medicine 2021). With the diagnosis of pancreatic cancer at such a late stage, it makes it nearly impossible to do anything about it. Resectable tumors also play a big part in the survival rate of breast cancer patients because if the tumor can be even partially resected it helps to spread the cancer. Gender and race are two of the factors that are taken into account when diagnosing one with pancreatic cancer.

Breast cancer prognosis depends on the stage of cancer, whether it has spread to lymph nodes, the size, and grade of the tumor, hormone receptor status, and HER2 status. All of these aspects combined help determine the prognosis and each one has an important role. Catching any cancer earlier is always better, and in the case of breast cancer when it is caught earlier it lessens the chance of it coming back or spreading too much. The most important part of the prognosis is whether it has spread to the lymph nodes because the moment it spreads to the lymph nodes, the more lymph nodes that contain cancer. The more positive lymph nodes means there is a higher risk of cancer coming back. Breast cancer that spreads to more than 4 lymph nodes has the highest recurrence rate. Tumor size is the second most important prognosis because the bigger the tumor, the more likely it is to have spread and it also makes it harder to shrink or resect. Along with that, the lower the tumor grade the better the prognosis is going to be. Tumors that are hormone receptor-positive have a good prognosis for the most part due to them having a lower risk of spreading. The HER2 gene is the gene that controls the protein on the surface of the cells and that leads to their growth. According to the Canadian Cancer Society, "HER2-positive breast cancer is more aggressive and more likely to spread than HER2-negative breast cancer. They are also more likely to come back after treatment. This means that HER2-positive breast cancer has a less favorable prognosis than HER2-negative breast cancer" (Canadian Cancer Society). Cells positive for the HER2 gene are more likely to spread and cause recurrence, resulting in a worse prognosis.

Does Gender and Race Matter in Medicine?

Both gender and race play a significant role in breast cancer and pancreatic cancer in different ways. Gender is an aspect that is always important in any medical prognosis because the male and the female body vary regarding certain body parts and functions. Diagnosis of an individual always requires the knowledge of the patient's gender especially if gender-specific body parts are involved. Race also has its significance in medical prognosis, although it's not as prominent compared to gender. The race of a patient can be useful in scenarios with infants, for example, as it is an important predictor of birth weight, gestational age, and risk of infant mortality. As mentioned earlier, certain races are more susceptible to specific diseases and the outcomes of these diseases. This makes race a factor that must be considered in any type of medical diagnosis.

In cancer prognosis, gender is most important in cancers such as breast cancer, prostate cancer, and ovarian cancer because they deal with body parts that are gender specific. Gender is also important for any type of cancer prognosis because it is known that one gender is more susceptible to certain cancers for different reasons, including environmental issues and bodily structure. Anatomically speaking, males and females have different structures that play a part in cancer prognosis and is one of the leading causes of why one gender could be more likely to be diagnosed with a particular cancer. Race has a part in cancer prognosis as well, as some races

are more prone to a few of the cancer risk factors. Epigenetic alteration and genetic polymorphisms are two reasons genetically why there is a difference in the severity, survival rate, etc. for different types of cancers. Various environmental and genetic factors to which certain races are more prone can play a direct role in increased cancer diagnoses. Diet has also been found to be a significant reason why certain races are commonly diagnosed with certain cancers opposed to others.

Breast cancer is greatly affected by gender because the organ that breast cancer deals with is the breast. The breast is a female body part and although men have a less developed version, it is not significant enough to be affected as much. Men are still able to be diagnosed with breast cancer, it is just much more unlikely. The genes that cause breast cancer are directly affected by race as certain races are more likely to have a mutation on specific genes. Men and women also have different chromosomes which have been found to be a big factor in breast cancer diagnosis. Race has not been found to be a major factor but there have been studies as mentioned earlier that show that there is some sort of correlation.

According to the SEER database, people of the white race are extremely more likely to be diagnosed with breast cancer compared to those other races (**Table 1; SEER, 2019**). It is also shown that the presence of estrogen which is found in women is significant. There are other variables that are mentioned and do show an effect but looking at the estrogen status variable, that is one of the most significant factors. Race is also shown to be important as white people have more than 10 times the likelihood to be diagnosed with breast cancer compared to black people and those in the other category such as asians.

Variables	Levels	N (%)	Range	Mean	HR (95% PI)
Age	30-39	230 (5.7%)	30-69	53.97	
	40-49	1124 (27.9%)			
	50-59	1390 (34.5%)			
	60-69	1280 (31.8%)			
Race	White	3412 (84.5%)			1
	Black	291 (7.2%)			1.04 (0.94-1.14)
	Other	320 (7.95%)			1.09 (0.89-1.31)
Marital status	Divorced	485 (12%)			0.98 (0.94-1.04)
	Married	2643 (65.7%)			1
	Separated	45 (1.11%)			1.02 (0.95-1.09)
	Single	615 (15.3%)			1.04 (0.91-1.13)
	Widowed	235 (5.8%)			1.07 (0.87-1.31)
T stage	T1	1602 (39.74%)			0.62 (0.54-0.70)
	T2	1786 (44.4%)			1
	T3	533 (13.2%)			1.62 (1.42-1.84)
	T4	103 (2.48%)			2.64 (2.04-3.42)
N stage	N1	2732 (67.9%)			1
	N2	820 (20.4%)			1.46 (1.08-1.95)
	N3	472 (11.7%)			2.13 (1.17-3.82)
6th stage	IIA	1305 (32.4%)			1
	IIB	1130 (28%)			0.70 (0.60-0.81)
	IIIA	1050 (26%)			0.49 (0.36-0.67)
	IIIB	67 (1.67%)			0.34 (0.22-0.54)
	IIIC	472 (11.73%)			0.24 (0.13-0.41)
Grade	Well differentiated; Grade I	543 (13.5%)			0.90 (0.81-0.99)
	Moderately differentiated; Grade II	2351 (58.4%)			1
	Poorly differentiated; Grade III	1111 (27.6%)			1.11 (1.00-1.23)
	Undifferentiated; anaplastic; Grade IV	19 (0.47%)			1.23 (1-1.51)
A stage	Regional	3932 (97.7%)			1
	Distant	92 (2.28%)			0.33 (0.25-0.43)
Tumor size	<36 mm	2956 (73%)	1-140	30.47	
	36 mm - 70 mm	846 (21%)			
	71 mm - 105 mm	186 (4.6%)			
	>105 mm	36 (0.89%)			
Estrogen status	Positive	3755 (93.3%)			1
	Negative	269 (6.68%)			1.38 (1.03-1.94)
Progesterone status	Positive	3326 (82.7%)			1
	Negative	698 (17.3%)			1.11 (0.88-1.4)
Regional nodes	Total examined	4024 (100%)	1-61	14.35	
	Positive examined	4024 (100%)	1-46	4.15	
Survival months		4024 (100%)	1-107	71.3	
Status	Alive	3408 (84.7%)			
	Dead	616 (15.3%)			

Table 1. SEER data showing various variables and their effect on breast cancer. (SEER, 2019)

Pancreatic cancer, on the other hand, is affected a lot less by gender compared to breast cancer. Risk factors are a big part of this as the genders that are more susceptible are correlated closely to more than one of the risk factors for pancreatic cancer. Risk factors such as obesity, tobacco use, and pancreatitis tie into which races have been found to be more likely to be diagnosed with the disease. Pancreatitis can be due to certain other risk factors like drinking which is connected closely to certain races rather than others, being an important factor in pancreatic cancer prognosis. Race has been found to still have a significant effect on the diagnosis of a pancreatic cancer patient. Black people have been found to have a significantly larger prognosis rate compared to white people for reasons including environmental and epigenetics. White people on the other hand have a lower prognosis rate which is most likely because of their environment, it is a stereotype that those of the black race drink more. Drinking affects the pancreas which can eventually lead to pancreatic cancer, although it is not a direct correlation.

The diagnosis for pancreatic cancer for black people was much higher all of those years, some more than others (**Figure 1A**). The diagnosis rate for white people shows to be a lot lower with less variation. The death rate for black individuals with pancreatic cancer is still higher than white individuals, although it is not as significant compared to the diagnosis (**Figure 1B**). It still proves the point that race has a clear and definite effect on pancreatic cancer. The 5 year survival rate is displayed (**Figure 1C**). In this diagram there is less of a difference between black and white individuals and they do intertwine a few times. This could mean that after being

diagnosed the long term effects are different for different races and as technology and medicine has improved it has also affected the races and their prognosis. In the 1960s, both races were at a certain level but over time black people were having a higher survival rate but then around the 1990s there was a decrease in the survival rate for black people but an increase for white people. After that they both increased but overall white people now have a higher 5-year survival rate.

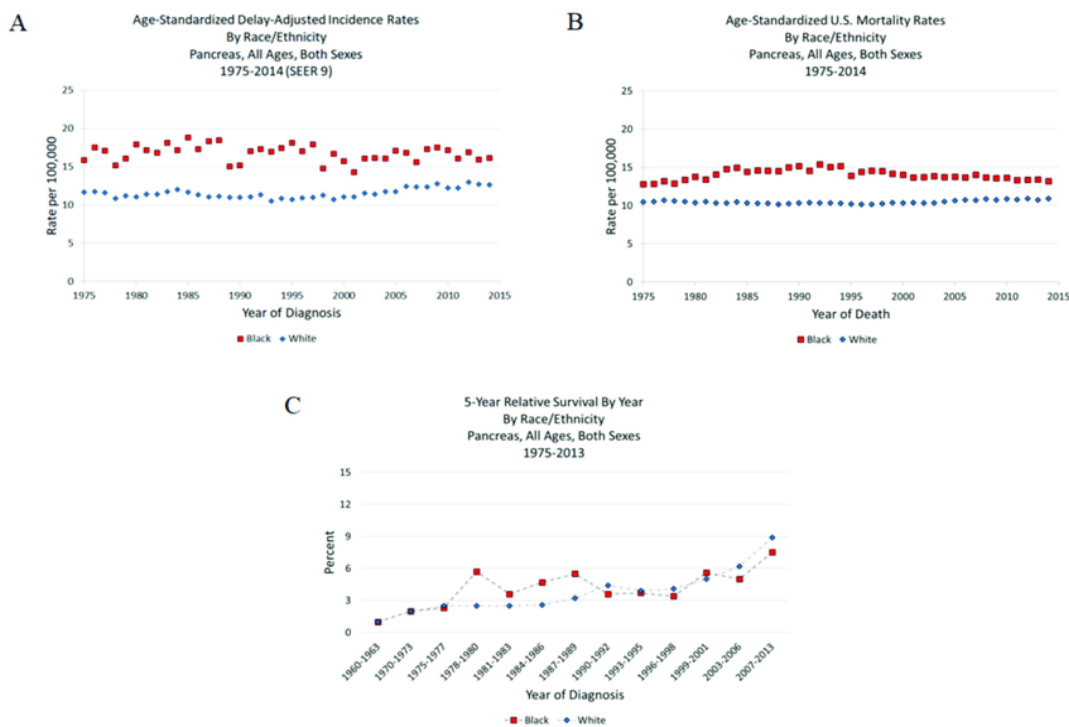Gender and race are two obvious factors that play a significant part in medical prognosis

Figure 1. Pancreatic Cancer Statistics by Race A) Pancreatic Cancer Diagnosis by Race B) Pancreatic Cancer Death Rate by Race C) Pancreatic Cancer 5 Year Survival Rate by Race (Scarton et al. 2018)

Discussion

Cancer is a disease that has been affecting millions of people around the world every single day in more ways than one. There is cancer for almost every human body part, adding up to over 100. Of the many factors that can affect cancer prognosis, gender and race are some of the most important ones. Gender is a factor that is looked at in any type of medical prognosis, serving just as much significance in any type of cancer prognosis. We know that males and females have body structures that vary from each other, in specific to our reproductive organs and other traits. Gender will always be an important factor and can vary the prognosis of cancer tremendously. Race has a vital significance because bodies of different races are also built slightly differently from each other. This unique body composition has some sort of differences even if minor which are significant to cancer prognosis of all types. Breast cancer, one of the

gender-specific cancers that affects so many women each year but has a lower mortality rate heavily on the gender of the patient when making a prognosis. It is also affected by race because of the specific gene that is normally mutated and how certain races are more susceptible in comparison to others. Pancreatic cancer, a cancer affecting the pancreas that is not as common but has a much higher mortality rate in comparison to breast cancer and a lot of other cancers. It is affected both by gender and race in different ways but mainly relates to risk factors of each and the differences in bodies of males and females as well as different races. It does not compare as much to breast cancer in how much gender and race affect the cancer. The data reviewed in this paper raise some questions for the future. Do the factors, race and gender have a stronger effect on other types of cancers, or are breast cancer and pancreatic cancer the cancers most affected? Since race did not have as much of an effect, how differently are bodies of different races built? More research is warranted in studying how these factors, both alone and in the context of others, affected cancer prognosis and treatment.

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