Epidemiology of Cancer Survivorship among Young and Emerging Adults

Katherine Perlman, MPH Candidate
Advisor: Elizabeth Hibler, PhD
Northwestern University Program in Public Health
Master of Public Heath: Culminating Experience

ABSTRACT

Background: Each year in the United States, an estimated 70,000 incident cancer cases are diagnosed among the young and emerging adult (YEA) population, and cancer is one of the top five leading causes of death in this age group. The YEA cancer population consists of those diagnosed with cancer between ages 18-39. YEA cancer patients present with unique risk factors for late effects of cancer treatment due to their transitional life status as they are undergoing social, emotional, and developmental transitions during the period of their cancer diagnosis, treatment, and survivorship. The goal of this study is to better understand the unique epidemiological factors in this population to improve care recommendations.

Methods: Data was collected using the Northwestern Enterprise Data Warehouse (EDW), which contains medical records on YEA cancer survivors treated in the Northwestern Hospital system. Participants were eligible if they were diagnosed with any cancer in the Northwestern Hospital system between ages 18-39 and were diagnosed between 1/1/2000 and 1/1/2019. The dataset contained information for 14,552 patients including the patient's study ID, gender, ethnicity, race, cancer diagnosis date, cancer type, age at diagnosis, secondary cancer, date of death, cerebrovascular disease, coronary artery disease, diabetes, heart failure, hyperlipidia, hypertension, peripheral arterial disease, and renal failure. Frequency analyses were used to determine distribution of each cancer type in the cohort and each cancer type by gender. Mann Whitney U test was used to determine mean age at diagnosis for each cancer type. Frequency distribution was used to determine racial and ethnic demographic distribution among the five most common cancers. Logistic regression was used to determine odds of developing comorbidities (heart failure, hyperlipidia, hypertension, secondary cancer). Survival analyses

were conducted using Kaplan-Meier Survival Curves and Cox Proportional Hazards Models for breast cancer and lymphoma patients and time to hypertension diagnosis.

Results: The most prevalent cancers in this population are breast, lymphoma, thyroid, melanoma, and brain and nervous system. Compared to non-breast YEA cancer survivors, breast cancer patients had a significantly higher odds of a secondary cancer diagnosis (OR= 2.4, 95% CI= 2.2-2.6). Compared to non-lymphoma YEA cancer survivors, lymphoma patients had a significantly higher odds of heart failure diagnosis (OR= 2.2, 95% CI= 1.7-3.0), hyperlipidia diagnosis (OR= 1.6, 95% CI= 1.4-1.9), and hypertension diagnosis (OR= 1.2, 95% CI= 1.1-1.4). Thyroid cancer patients had a significantly higher odds of a secondary cancer diagnosis (OR= 1.4, 95% CI= 1.2-1.5) compared to non-thyroid YEA cancer survivors. Kaplan-Meier estimates showed that race and secondary cancer status may play a role in time to hypertension diagnosis in YEA breast cancer patients. However, in Cox Proportional Hazards model, race and secondary cancer status had no impact on time to hypertension diagnosis. For lymphoma patients, Kaplan-Meier estimates showed that gender, race, and secondary cancer status may play a role in time to hypertension diagnosis. However, Cox Proportional Hazards model showed no impact of these variables on time to hypertension diagnosis.

Conclusions: This study provides important public health implications by identifying the most prevalent cancers, mean age at diagnosis, and risk of future comorbidities among YEA cancer survivors in the Northwestern Medicine health system. It also provides evidence for possible factors impacting survival in this population.

INTRODUCTION

To date, cancer epidemiology research has primarily focused on cancer in children and older adults, while cancer occurring during young and emerging adulthood (YEA) is understudied (1, 2). The YEA cancer population consists of those diagnosed with cancer between ages 18-39 (2). Each year in the United States, an estimated 70,000 incident cancer cases are diagnosed among this population (2). Further, cancer is one of the top five leading causes of death in the YEA age group, and YEA cancer survivors present with unique risk factors for late effects of cancer treatment due to their transitional life status (3, 4). Many YEA cancer survivors are undergoing social, emotional, and developmental transitions during the period of their cancer diagnosis, treatment, and survivorship (5-8). Also, a cancer diagnosis can affect one's sexuality, fertility, physical and psychosocial aspects (5). Moreover, no study has examined the impact of YEA cancer survivorship on health behaviors in this population, which may alter their risk for cancer recurrence, secondary cancers, or other chronic diseases. Consequently, understanding how the YEA cancer survivor population is affected by their diagnosis in these various aspects will allow researchers to design effective interventions to improve quality of life in this population.

The YEA cancer survivor population is an important cohort to study because of the unique challenges they face. During this period in life, YEA cancer patients may be diagnosed and treated while in school or in the beginning of their professional career (9). YEA cancer survivors have an increased risk of behavioral adjustment problems, which has been shown to affect academic and professional capabilities (9). Further, compared to older adult patients, this cohort is more likely to be uninsured due to the transition between their parents' health insurance coverage and their own health insurance coverage. Consequently, dealing with this problem can cause financial and psychological issues. The YEA cancer survivor population also has unique

problems regarding relationships and sexuality. Research has shown that, compared with their healthy peers, YEA cancer survivors are less likely to marry and procreate due to the fear of passing down their risk of cancer to their offspring (9). Similarly, YEA patients have issues regarding their fertility status. Studies have revealed that a large portion of YEA cancer survivors are unsure about their fertility status, and many report that their health care providers did not discuss fertility issues with them during their treatment (10). YEA cancer survivors have also been shown to have increased risk of distress, depression, hopelessness, despair, anxiety, and poorer self-image (9, 11, 12).

The YEA population has unique cancer trends compared to other age groups. Compared to pediatric and older adult patients, YEA cancer survivors have increasingly higher cancer incidence rates and significantly lower survival rates (13). Research suggests that these differences may be attributed to differences in disease biology, delayed cancer diagnoses, complex social factors, and decreased participation in clinical trials (14). Also, less than 10% of YEA cancer patients are entered into clinical trials, compared to 60-65% of pediatric and adolescent patients (13). Epidemiological differences are further illuminated when comparing patients treated in pediatric oncology groups versus adult oncology groups (15). YEA cancer patients treated in pediatric wards tend to have better outcomes compared to those treated in adult settings (15).

The YEA cancer survivor population presents a unique public health challenge. This population is undergoing their cancer diagnosis, treatment, and survival period during a highly transitional period in their lives. During this age range, people may be in post-secondary education, starting jobs or families, and changing health insurance status (9, 16). The YEA cancer survivor population also raises questions about how to best treat this population. Cancer

care has been divided between pediatric and medical oncology teams, even though this population contains characteristics of both of these groups (17). Care recommendations may necessitate changing to a more multidisciplinary patient care approach, in order to best treat this unique population. Another important difference in YEA cancer care is the lack of relevant clinical trials (14, 16). Clinical trials can increase scientific knowledge about the unique biological and social factors that may be necessary to optimize treatment (14). The lack of clinical trials for YEA cancer patients may be another important factor that is hindering improvements in this population.

Overall, many YEA cancer survivors are undergoing social, emotional, and developmental transitions during the period of their cancer diagnosis, treatment, and survivorship (3, 4). These factors may place them at increased risk of comorbidities or cancer recurrence. There is a recognized critical need to better understand the impact of cancer treatment across the lifespan for YEA cancer survivors on a variety of lifestyle, mental health, and biological biomarkers in order to recognize risk factors early and intervene to prevent late-effects of cancer treatment among this population. It is important to better understand how these issues change over time in order to improve clinical care and support services and identify novel risk factors for recurrence or mortality in this unique population.

The goal of this study is to 1) examine factors related to the epidemiology of specific cancer types in the YEA cancer survivor population, 2) examine longitudinal associations of the YEA cancer diagnosis with late-effects of cancer treatment including rates of comorbidities such as hypertension.

METHODS

Study population

Data was collected using the Northwestern Enterprise Data Warehouse (EDW), which contains medical records on YEA cancer survivors treated in the Northwestern Hospital system. Participants were eligible if they were diagnosed with any cancer in the Northwestern Hospital system between ages 18-39 and were diagnosed with cancer between 1/1/2000 and 1/1/2019. The EDW was searched based upon diagnosis (ICD-9/ ICD-10 codes) and procedures (CPT codes). The data was de-identified to protect patient privacy with the exception of date of diagnosis, which was necessary to examine the longitudinal associations.

The EDW dataset contained 14,552 patients and information including the patient's study ID, gender, ethnicity, race, cancer diagnosis date, cancer type, age at diagnosis, secondary cancer, and date of death. The dataset also contained information about the following comorbidities: cerebrovascular disease, coronary artery disease, diabetes, heart failure, hyperlipidia, hypertension, peripheral arterial disease, and renal failure. Subjects with any of these comorbidities contained the date of diagnosis.

Ninety people were excluded from analysis; 52 subjects did not have a specific cancer tissue type diagnosis, and 38 subjects were diagnosed before 1/1/2000. After these 90 subjects were excluded, the final dataset used contained 14,462 subjects. Each remaining subject was categorized by primary cancer type into 25 categories (abdomen, bladder and other urinary system, bone and connective/ soft tissue, brain and nervous system, breast, cervix, colorectal and anal, endocrine glands, eye, head and neck, kidney, leukemia, liver, lung, lymphoma, melanoma, multiple myeloma, ovary, pancreas, prostate and male genitals, testicles, thyroid, upper gastrointestinal, uterus, other female reproductive). The dataset was also analyzed by gender, ethnicity, race, age at diagnosis, secondary cancer, cerebrovascular disease, coronary artery

disease, diabetes, heart failure, hyperlipidia, hypertension, peripheral arterial disease, and renal failure.

Statistical Analysis

Statistical analysis was conducted using SAS software version 9. The dataset was first analyzed by examining the demographic characteristics of the cohort. Frequency distributions were conducted to examine this relationship through determining frequency distributions of each cancer type among the entire cohort, as well as frequency distributions by gender among each cancer type. Next, we examined the associations between age at diagnosis and specific cancer types. Since the data was highly skewed, a Mann Whitney U Test was used to evaluate the associations between cancer types and age. A significance level of 0.05 was used.

After determining the most common cancer types among the 25 subgroups, only the five most common subgroups were used for further analysis. This was decided due to the complexity and amount of results, as well as small sample sizes. The five most common cancer types were breast, lymphoma, thyroid, melanoma, and brain and nervous system. Frequency distributions were conducted to determine frequency distributions of each of these cancer types by categories of race and ethnicity. Race was categorized as White, Black, Asian, Native Hawaiian or Pacific Islander, and other. Ethnicity was categorized as Hispanic/Latino or not Hispanic/ Latino. Next, frequency distributions and logistic regressions were conducted for the associations between the most common cancer types and comorbidities. Chi-squared tests were used to evaluate these relationships. Logistic regression was also conducted to determine the odds ratios with corresponding 95% confidence intervals. Logistic regression compared the odds of a subject with the specific cancer having the comorbidity, compared to those without the specific cancer. In order to better understand the comorbidities in this population, separate analyses were conducted

and reported between each comorbidity and the five most common cancers among these populations. Chi-squared tests and logistic regression were similarly used to measure these relationships.

Analyses were then conducted to further examine the comorbidity relationships. For these analyses, only the two most common cancer types (breast and lymphoma) and the most common comorbidity (hypertension) was used. This was chosen due to the small sample sizes within the comorbidity groups. For breast cancer, only female breast cancer patients were used because of the very small population of male breast cancer patients. Kaplan-Meier survival curves were created for the breast cancer population and reported the survival estimates from time of breast cancer diagnosis until hypertension diagnosis. This relationship was assessed for possible confounding by race, ethnicity, and secondary cancer status. The lymphoma population was also examined using Kaplan-Meier survival curves for the survival probability between lymphoma diagnosis and hypertension diagnosis. This relationship was assessed for possible confounding by gender, race, ethnicity, and secondary cancer status. The follow-up time between cancer diagnosis and hypertension diagnosis is reported in years, due to the long follow-up period.

Cox Proportional Hazards models were then created for the breast and lymphoma relationships with hypertension diagnosis. The Cox Proportional Hazards Model for breast cancer patients was assessed with race and secondary cancer status, and the Cox Proportional Hazards Model for lymphoma patients was assessed with gender, race, and secondary cancer status.

RESULTS

Demographic Results

Overall, 14,462 subjects were included in the analyses and spread among 25 cancer subgroups. Table 1 showed the number and frequencies of each cancer type by gender. Among the 14,462 subjects, 5123 (35.4%) were male and 9335 (64.5%) were female. Four subjects (0.03%) did not have a reported gender. Table 1 also reported the total number of subjects in each cancer subtype. Breast cancer is the most common cancer subtype [N=2501 (17.3%)], followed by lymphoma [N= 2148 (14.9%)], thyroid [N= 1739 (12.0%)], melanoma [1530 (10.6%)], and brain and nervous system [N= 1065 (7.4%)]. The least common cancer subtypes were cancer in the abdomen [N=57 (0.4%)], eye [N=63 (0.4%)], prostate and male genitals [N= 63 (0.4%)], pancreas [N=93 (0.6%)], and bladder and urinary system [N=95 (0.7%)].

The age at diagnosis distribution among the entire cohort (Figure 1) showed a strong left skew. Frequency continuously increased as age at diagnosis increased. Table 2 reported the mean age of diagnosis for each cancer type and the Mann Whitney U test p-value using a 0.05 significance level. The mean age at diagnosis of the entire population was 31.5 (SD= 5.7). Most of the cancer subtypes, other than cancer in the abdomen, liver, lung, melanoma, ovary, pancreas, thyroid, and other female reproductive organs had a significantly different mean age at diagnosis compared to that of the entire cohort. Breast cancer and multiple myeloma had the highest mean age at diagnosis at 34.4 years of age. Cancer in the endocrine glands had the lowest mean age at diagnosis at 28.5 years of age. The range for age at diagnosis was 5.9 years.

Table 3 showed the number and frequencies of race and ethnicity among the five most common cancer types (breast, lymphoma, thyroid, melanoma, and brain and nervous system). There were no subjects who identified as Native Hawaiian or Other Pacific Islander in these five cancer subgroups. All of these subgroups consisted of a majority White population. Smaller proportions of each of these subgroups identified as Black, Asian, or other. Breast cancer

patients identified as 61.8% White, 11.2% Black, 4.4% Asian, and 9.5% other. Lymphoma patients identified as 59.0% White, 8.7% Black, 3.1% Asian, and 10.5% other. Thyroid patients identified as 68.1% White, 3.7% Black, 6.2% Asian, and 9.1% other. Melanoma patients identified as 80.0% White, 0.7% Black, 0.6% Asian, and 5.6% other. Brain and nervous system patients identified as 68.3% White, 5.1% Black, 2.3% Asian, and 6.9% other. Similarly, a majority of the subjects in all of these cancer subgroups identified as not Hispanic or Latino. This included 8.2% of breast cancer patients, 8.2% of lymphoma patients, 9.8% of thyroid cancer patients, 2.6% of melanoma patients, and 7.2% of brain and nervous system cancer patients.

Table 4 showed the number and frequencies of each comorbidity among the most common cancer types, as well as the odds ratios for these relationships. Using a significance level of 0.05, breast cancer patients had a significantly lower odds of a heart failure diagnosis (OR= 0.7, 95% CI= 0.4-0.98), hyperlipidia diagnosis (OR= 0.5, 95% CI= 0.4-0.6), and hypertension diagnosis (OR= 0.6, 95% CI= 0.5-0.7) compared to YEA cancer survivors without breast cancer. Breast cancer patients had a significantly higher odds of a secondary cancer diagnosis (OR= 2.4, 95% CI= 2.2-2.6). Lymphoma patients had a significantly higher odds of heart failure diagnosis (OR= 2.2, 95% CI= 1.7-3.0), hyperlipidia diagnosis (OR= 1.6, 95% CI= 1.4-1.9), and hypertension diagnosis (OR= 1.2, 95% CI= 1.1-1.4) compared to non-lymphoma YEA cancer survivors. Lymphoma patients had a significantly lower odds of secondary cancer diagnosis (OR= 0.4, 95% CI= 0.3-0.4). Thyroid cancer patients had a significantly lower odds of heart failure diagnosis (OR= 0.3, 95% CI= 0.1-0.5) and hypertension diagnosis (OR= 0.8, 95% CI= 0.7-0.9) compared to subjects without thyroid cancer. Thyroid cancer patients had a significantly higher odds of a secondary cancer diagnosis (OR= 1.4, 95% CI= 1.2-1.5). Melanoma patients had a significantly lower odds of heart failure diagnosis (OR= 0.2, 95% CI=

0.1-0.5), hyperlipidia diagnosis (OR=0.5 , 95% CI= 0.4-0.7), hypertension diagnosis (OR= 0.5, 95% CI= 0.4-0.6), and secondary cancer diagnosis (OR= 0.3, 95% CI= 0.3-0.4) compared to subjects without melanoma. Brain and nervous system cancer patients had a significantly lower odds of having a heart failure diagnosis (OR= 0.4, 95% CI= 0.2-0.8) and secondary cancer diagnosis (OR= 0.4, 95% CI=0.4-0.5) compared to subjects without brain and nervous system cancer.

Table 5 showed the logistic regression results for the most common cancer types among those with heart failure. 1.60% (N=231) of the entire cohort had heart failure. Cancer subgroups that had a significantly higher odds of a heart failure diagnosis include lymphoma (OR= 2.2, 95% CI= 1.7-3.0), leukemia (OR= 3.3, 95% CI= 2.3-4.9), and kidney (OR= 3.9, 95% CI= 2.4-6.2). As previously mentioned, breast cancer patients had a significantly lower odds of having a heart failure diagnosis (OR= 0.7, 95% CI= 0.4-0.98).

Table 6 showed the logistic regression results for the most common cancer types among those with hyperlipidia. 6.20% (N=896) of the entire cohort had hyperlipidia. Cancer subgroups that had a significantly higher odds of a hyperlipidia diagnosis include lymphoma (OR= 1.6, 95% CI= 1.4-1.9) and leukemia (OR= 1.6, 95% CI= 1.2-2.1). As previously mentioned, breast cancer patients had a significantly lower odds of having a hyperlipidia diagnosis (OR= 0.5, 95% CI= 0.4-0.6).

Table 7 showed the logistic regression results for the most common cancer types among those with hypertension. 11.17% (N=1616) of the cohort had hypertension. Cancer subgroups that had a significantly higher odds of a hypertension diagnosis include lymphoma (OR= 1.2, 95% CI= 1.1-1.4), kidney (OR= 5.6, 95% CI= 4.5-6.9), and leukemia (OR= 2.2, 95% CI= 1.8-

2.7). Both breast cancer (OR= 0.6, 95% CI= 0.5-0.7) and thyroid cancer patients (OR= 0.8, 95% CI= 0.7-0.9) had a significantly lower odds of a hypertension diagnosis.

Table 8 showed the logistic regression results for the most common cancer types among those with a secondary cancer diagnosis. 24.29% (N=3513) of the cohort had a secondary cancer diagnosis. Cancer subgroups that had a significantly higher odds of a secondary cancer diagnosis include breast (OR= 2.4, 95% CI= 2.2-2.6), thyroid (OR= 1.4, 95% CI= 1.2-1.5), colorectal and anal (OR= 3.7, 95% CI= 3.1-4.4), and bone and connective/ soft tissue (OR= 1.2, 95% CI= 1.1-1.5). As previously mentioned, lymphoma patients had a significantly lower odds of having a secondary cancer diagnosis (OR= 0.4, 95% CI= 0.3-0.4).

Survival Analysis Results

Survival analyses were conducted for female breast cancer patients and all lymphoma patients who were later diagnosed with hypertension. Survival time was the number of years between cancer diagnosis and hypertension diagnosis. Figure 2 showed the Kaplan-Meier survival curve for the time from breast cancer diagnosis until hypertension diagnosis stratified by race. As seen in Table 3, the breast cancer subgroup contained a majority White subjects (61.8%) and smaller proportions of Black (11.2%), Asian (4.4%), and other races (9.5%). No breast cancer patients identified as Native Hawaiian or other Pacific Islander race. Figure 2 showed crossing lines and provided evidence that the proportional hazard assumption is violated. The two largest race categories (White and Black) showed fairly even curves where the survival probability for Black breast cancer patients was consistently lower than that of White breast cancer patients. The median survival time for White breast cancer patients for hypertension diagnosis was 3.2 years after breast cancer diagnosis. The median survival time for Black breast cancer patients for hypertension diagnosis was 1.4 years after breast cancer diagnosis.

Figure 3 showed the Kaplan-Meier survival curve for the time from breast cancer diagnosis until hypertension diagnosis stratified by ethnicity. The lines cross, violating the proportional hazards assumption. The median survival time for non-Hispanic or Latino breast cancer patients for hypertension diagnosis was 1.8 years after breast cancer diagnosis. The median survival time for Hispanic or Latino breast cancer patients for hypertension diagnosis was 3.0 years after breast cancer diagnosis.

Figure 4 showed the Kaplan-Meier survival curve for the time from breast cancer diagnosis until hypertension diagnosis stratified by secondary cancer status. The two lines touched multiple times but did not cross, indicating that the proportional hazards assumption was upheld. The survival probability for those with a secondary cancer was consistently higher than those without a secondary cancer. The median survival time for breast cancer patients without a secondary cancer for hypertension diagnosis was 1.4 years after breast cancer diagnosis. The median survival time for breast cancer patients with a secondary cancer for hypertension diagnosis was 2.0 years after breast cancer diagnosis.

Figure 5 showed the Kaplan-Meier survival curve for the time from lymphoma diagnosis until hypertension diagnosis stratified by gender. The proportional hazards assumption was met in this association due to the lines not intersecting. Compared to males, females had a consistently higher survival probability. The median survival time for female lymphoma patients for hypertension diagnosis was 2.1 years after lymphoma diagnosis. The median survival time for male lymphoma patients for hypertension diagnosis was 1.3 years after lymphoma diagnosis.

Figure 6 showed the Kaplan-Meier survival curve for the time from lymphoma diagnosis until hypertension diagnosis stratified by race. In the lymphoma subgroup, 59.0% of subjects were White, 8.7% were Black, 3.1% were Asian, and 10%% were another race. No subjects with

lymphoma identified their race as Native Hawaiian or other Pacific Islander. The two largest race categories (White and Black) showed a consistent pattern throughout the time period. After year three, Black patients tended to have a higher survival probability compared to White patients. The median survival time for White lymphoma patients for hypertension diagnosis was 1.7 years after lymphoma diagnosis. The median survival time for Black lymphoma patients for hypertension diagnosis was 1.3 years after lymphoma diagnosis.

Figure 7 showed the Kaplan-Meier survival curve for the time from lymphoma diagnosis until hypertension diagnosis stratified by ethnicity. The two lines intersected, violating the proportional hazards assumption. Before year four, Hispanic or Latino lymphoma subjects had a higher survival probability compared to non-Hispanic or Latino lymphoma subjects. After year four, the pattern was reversed. The median survival time for non-Hispanic or Latino lymphoma patients for hypertension diagnosis was 1.4 years after lymphoma diagnosis. The median survival time for Hispanic or Latino lymphoma patients for hypertension diagnosis was 2.3 years after lymphoma diagnosis.

Figure 8 showed the Kaplan-Meier survival curve for the time from lymphoma diagnosis until hypertension diagnosis stratified by secondary cancer status. Between follow-up years 1-13, there was a fairly consistent pattern where those without a secondary cancer diagnosis had a higher survival probability compared to those with a secondary cancer. Also, the proportional hazards assumption was not violated due to the lines never crossing. The median survival time for lymphoma patients without a secondary cancer was 1.8 years after lymphoma diagnosis. The median survival time for lymphoma patients with a secondary cancer was 1.0 year after lymphoma diagnosis.

Cox Proportional Hazards models were conducted for the breast cancer and lymphoma relationships with hypertension. Table 9 showed the results of the Cox Proportional Hazards model between female breast cancer patients and hypertension diagnosis. This model used 116 patients and examined the relationship with the covariates race and secondary cancer. Using a significance level of 0.05, both race (HR= 1.0, 95% CI= 0.9-1.2) and secondary cancer status (HR= 0.8, 95% CI= 0.6-1.2) were not significant. Similarly, Table 10 showed the results of the Cox Proportional Hazards model between lymphoma patients and hypertension diagnosis. This model used 192 patients and examined the relationship with the covariates gender, race, and secondary cancer status. Using a significance level of 0.05, neither gender (HR= 1.3, 95% CI= 0.9-1.7), race (HR= 1.0, 95% CI= 0.9-1.2), nor secondary cancer status (HR= 1.4, 95% CI= 0.9-1.9) were significant.

DISCUSSION

The results of this analysis demonstrate the unique epidemiological factors related to the YEA cancer survivor population. Demographic analyses revealed the most common cancers in this cohort, the gender distribution, and the mean age at diagnosis. Analyses of comorbidities in this population suggest significant associations between the most common cancers and heart failure, hyperlipidia, hypertension, and secondary cancers. Survival analyses between breast cancer and lymphoma patients who developed hypertension illuminated the possible confounding factors that may impact these associations.

Table 1 in this study shows the most common cancer types in the YEA population: breast, lymphoma, thyroid, melanoma, brain and nervous system. This varies from the most common cancers in children (leukemia, brain and nervous system, neuroblastoma, kidney cancer,

lymphoma) and in adults (breast, lung, prostate, colorectal, melanoma) (18, 19). These results emphasize that the YEA age range is separate from both younger and older cancer patients. It is important to focus resources on these common cancers in the YEA cohort to better support the increasing YEA cancer survivor population.

The study results also provide helpful information regarding the mean age of diagnosis for each cancer subtype (Table 2). This information is especially important for YEA cancer research, as this can specify the age range to recruit for clinical trials and focus resource allocations. For example, the American Cancer Society currently recommends women to begin annual breast cancer screening with mammograms starting at age 40 (20). However, breast cancer comprised 17.3% of the entire YEA cancer survivor cohort and had a mean age at diagnosis of 34.4 years. Further, the 5-year survival rate for localized breast cancer is 99%, while the 5-year survival rate for distant breast cancer is only 27% (21). This provides support that women who may be at increased risk for breast cancer, or other cancers, should be screened regularly years before the current guidelines suggest. It is important to catch a developing cancer at the earliest stage possible in order to increase survival probability. Consequently, research should be conducted in this younger age range to better determine who should start regular screenings at earlier ages and how to best treat these people.

Another clinically significant result from this study is the comorbidities analyses. Breast cancer patients, which is the most common cancer in this population, have significantly lower odds of developing heart failure, hyperlipidia, and hypertension, but have a significantly higher odds of having a secondary cancer. The higher risk of having a secondary cancer has been seen in previous research in older breast cancer survivor populations (22, 23). This finding is important for focusing care plans in YEA breast cancer survivors. Since YEA breast cancer

patients have 2.4 times the odds of having a secondary cancer, their oncology teams must be aware of this high risk and more closely monitor YEA breast cancer survivors for secondary cancers. Moreover, YEA breast cancer patients tend to be diagnosed with higher stage cancers compared to their older counterparts, due to more aggressive phenotypes, genetic predispositions, and lack of screening (24).

The study also showed that lymphoma patients have significantly higher odds of developing heart failure, hyperlipidia, and hypertension. Past research has shown similar results where lymphoma survivors have an increased risk for cardiovascular diseases, and cardiovascular complications are the leading cause of death in lymphoma survivors (25). Consequently, it is important for YEA lymphoma survivors to be closely monitored for the development of these complications.

The comorbidity analyses provided further important information that thyroid cancer patients also have significantly greater odds of having a secondary cancer. Previous research shows similar results, and thyroid cancer survivors treated with radioactive iodine or diagnosed with the medullary type of thyroid cancer are at an even greater risk for secondary cancers (26). Further, females have three times the risk for thyroid cancer compared to men, and there are various hereditary conditions (i.e. familial adenomatous polyposis (FAP), Cowden disease, Carney Complex Type 1) and environmental factors (i.e. iodine and radiation exposure) that can increase YEA risk for developing thyroid cancer (27). Cancer support teams should be made aware of this greater risk in order to better monitor thyroid cancer survivors for secondary cancers.

The survival analyses for breast cancer and lymphoma cancer patients developing hypertension further provide important results. Black YEA breast cancer patients have

consistently lower survival rates compared to their White counterparts. It is important to monitor Black YEA breast cancer survivors more for development of hypertension, because past research has shown that hypertension is a predictor of increased mortality among Black breast cancer patients (28). The survival analyses also showed an interesting result, where breast cancer patients diagnosed with a secondary cancer have better hypertension survival rates compared to those without a secondary cancer. This may be caused by increased physician visits due to the severity of the disease, which may identify and prevent hypertension at earlier stages.

The lymphoma-hypertension survival analyses continued to illuminate the factors that may influence this association. Female YEA lymphoma survivors had consistently better hypertension diagnosis rates compared to their male counterparts. Previous research has shown that YEA males have higher hypertension rates compared to their female counterparts, and YEA males tend to see health professionals less often for cardiovascular health visits (29). This information is important to share with healthcare providers, who can better monitor male lymphoma survivors for development of hypertension and explain the importance of regular cardiovascular health appointments.

While this study produced interesting and significant results, there are important limitations with this analysis. First, the cohort was derived solely from the Northwestern Medicine system. Consequently, it may only represent this small geographic area and its population. While the study results may not be completely generalizable to the entire YEA cancer survivor population, it is still important to guide health care practices for the YEA cancer survivor population. Second, there was not an equal distribution between races and ethnicities in this population. As seen in Table 3, a majority of the population was White and not Hispanic or Latino. This may further hinder generalizability but can also still help guide care guidelines.

Third, the sample sizes for the comorbidities was small. This may explain the violations in the proportional hazards assumptions seen in the Kaplan-Meier curves.

Due to the interesting results but important limitations, future studies should be conducted to better understand the YEA cancer survivor population. Studies should be conducted using a wider range of participants across the country, a more even distribution of races and ethnicities, and a higher sample size for comorbidities. This study can provide guidance for where to focus research, such as investigating the more common comorbidities such as hypertension and hyperlipidia. Also, future research should investigate survival analyses for developing secondary cancers in these cancer subgroups.

PUBLIC HEALTH IMPLICATIONS

This study provided many statistically and clinically significant results that can be used to reform care recommendations for the YEA cancer survivor population. Overall, the results further illuminate the unique aspects of the YEA population and explains why YEA cancer patients cannot be lumped into either pediatric or adult oncology care.

First, the YEA cancer population has very different common cancers compared to their younger and older counterparts. The five most common cancers (breast, lymphoma, thyroid, melanoma, brain and nervous system) should be widely known among oncology groups. In order to diagnosis and treat patients at the earliest stage possible, oncology groups should be familiar with common cancers, mean age at diagnosis, and gender distributions for cancers in the YEA population. Although cancer is considered a disease of aging, the increasing cancer incidence rates and mortality rates in the YEA population illuminate the importance of ignoring cancer in young adults (2, 3).

Second, various cancer subtypes are at an increased risk for secondary cancers, cardiovascular disease, or other health complications. Oncology teams should discuss with YEA cancer survivors applicable environmental/ social, genetic, or treatment-related risk factors. For example, YEA breast cancer survivors have a significantly higher odds of developing a secondary cancer. This population should be counseled to understand their environmental/social risks (i.e. weight, activity levels, diet, alcohol consumption), genetic risks (i.e. BRCA genes), and treatment-related risks (i.e. history of chemotherapy or radiation) so they can try to reduce risk of secondary cancers (23). Similarly, oncology teams and primary care providers must undergo more education to increase their awareness of the late effects of cancer treatments to best help their patients. Research has shown surprisingly low awareness rates among oncologists and primary care providers of the many late effects of chemotherapy and radiation treatment (30).

Third, there must be more clinical trials that recruit YEA cancer patients. Currently, less than 10% of YEA cancer patients are entered into clinical trials, compared to 60-65% of younger patients (13). Many clinical trials focus on pediatric cancer patients or older adult cancer patients, where the diseases are more common (16, 31). Clinical trials are very important because they can provide more specific findings and support which can help tailor treatment to best help the specific cohort (31).

In conclusion, the YEA cancer survivor population is an understudied but increasingly important population. There must be increased awareness and education regarding this unique population, as well as more clinical trials for YEA cancer patients and survivors. Taking these steps may improve survival rates and reduce this growing health problem.

TABLES & FIGURES

Table 1: Number and Frequencies of Cancer Type by Gender

Cancer Type	**Total N(%)**	**Male N(%)**	**Female N(%)**
Abdomen	57 (0.4)	21 (36.8)	36 (63.2)
Bladder and other Urinary System	95 (0.7)	57 (60.0)	38 (40.0)
Bone and Connective/ Soft Tissue	801 (5.5)	419 (52.3)	382 (47.7)
Brain and Nervous System	1065 (7.4)	585 (54.9)	478 (44.8)
Breast	2501 (17.3)	19 (0.8)	2481 (99.2)
Cervix	439 (3.0)	-	439 (100)
Colorectal and Anal	488 (3.4)	266 (54.5)	222 (45.5)
Endocrine Glands	99 (0.7)	45 (45.5)	54 (54.5)
Eye	63 (0.4)	26 (41.3)	37 (58.7)
Head and Neck	245 (1.7)	134 (54.7)	111 (45.3)
Kidney	360 (2.5)	204 (56.7)	156 (43.3)
Leukemia	665 (4.6)	336 (50.5)	328 (49.3)
Liver	170 (1.3)	80 (47.1)	90 (52.9)
Lung	113 (0.8)	47 (41.6)	66 (58.4)
Lymphoma	2148 (14.9)	1110 (51.7)	1038 (48.3)
Melanoma	1530 (10.6)	490 (32.0)	1040 (68.0)
Multiple Myeloma	117 (0.8)	55 (47.0)	62 (53.0)
Ovary	378 (2.6)	2 (0.5)	376 (99.5)
Pancreas	93 (0.6)	44 (47.3)	49 (52.7)
Prostate and Male Genitals	63 (0.4)	51 (81.0)	11 (17.5)
Testicles	734 (5.1)	732 (99.7)	2 (0.3)
Thyroid	1739 (12.0)	315 (18.1)	1424 (81.9)
Upper GI	168 (1.2)	83 (49.4)	85 (50.6)
Uterus	192 (1.3)	-	192 (100)
Other Female Reproductive	139 (1.0)	2 (1.4)	138 (99.3)
Total	*14462*	*5123 (35.4)*	*9335 (64.5)*

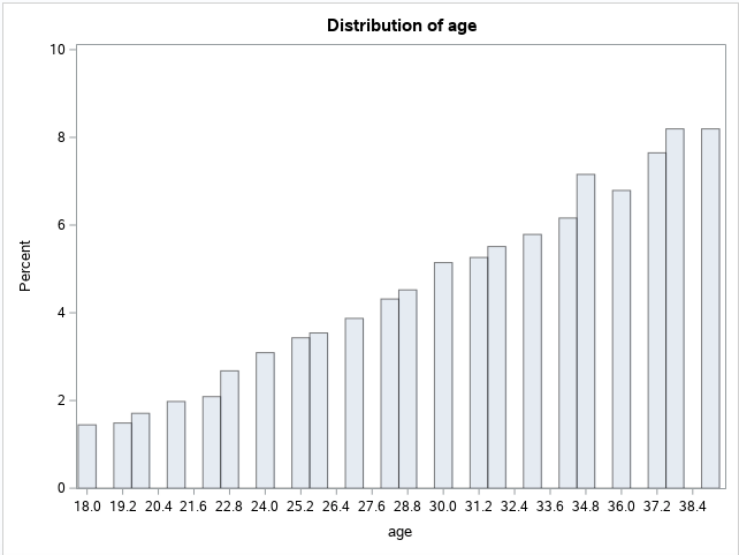

Figure 1: Distribution of age among entire cohort (N=14462)

Table 2: Cancer Type by Age at Diagnosis

Cancer Type	**Mean Age (SD)**	**P-Value[1]**
Abdomen	31.9 (5.0)	0.869
Bladder and other Urinary System	32.9 (4.8)	0.031
Bone and Connective/ Soft Tissue	29.3 (6.2)	<0.001
Brain and Nervous System	29.7 (6.0)	<0.001
Breast	34.4 (4.1)	<0.001
Cervix	32.8 (4.6)	<0.001
Colorectal and Anal	33.6 (4.7)	<0.001
Endocrine Glands	28.5 (6.8)	<0.001
Eye	29.6 (6.1)	0.012
Head and Neck	32.2 (5.6)	0.048
Kidney	32.2 (5.5)	0.016
Leukemia	29.4 (6.2)	<0.001
Liver	31.9 (5.7)	0.251
Lung	32.3 (5.3)	0.169
Lymphoma	29.6 (6.0)	<0.001
Melanoma	31.6 (5.0)	0.352
Multiple Myeloma	34.4 (4.9)	<0.001
Ovary	31.5 (5.6)	0.984
Pancreas	30.8 (6.5	0.471
Prostate and Male Genitals	33.3 (5.8)	0.004
Testicles	29.9 (5.4)	<0.001
Thyroid	31.3 (5.6)	0.100
Upper GI	32.8 (5.5)	0.002
Uterus	33.8 (4.4)	<0.001
Other Female Reproductive	32.0 (5.5)	0.297
Total	*31.5 (5.7)*	

[1]Mann Whitney U Test used

Table 3: Most Common Cancer Types by Race and Ethnicity

Characteristic	Breast N (%)	Lymphoma N (%)	Thyroid N (%)	Melanoma N (%)	Brain and Nervous System N (%)
Race					
White	1545 (61.8)	1267 (59.0)	1185 (68.1)	1224 (80.0)	727 (68.3)
Black	280 (11.2)	186 (8.7)	65 (3.7)	10 (0.7)	54 (5.1)
Asian	110 (4.4)	67 (3.1)	108 (6.2)	9 (0.6)	24 (2.3)
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Other	237 (9.5)	225 (10.5)	158 (9.1)	85 (5.6)	73 (6.9)
Ethnicity					
Hispanic or Latino	204 (8.2)	177 (8.2)	171 (9.8)	40 (2.6)	77 (7.2)
Not Hispanic or Latino	1910 (76.4)	1471 (68.5)	1308 (75.2)	1242 (81.2)	790 (74.2)

Table 4: Comorbidities among Most Common Cancer Types

Cancer Type	Heart Failure			Hyperlipidia			Hypertension			Secondary Cancer		
	N (%)	P-Value[1]	OR (95% CI)	N (%)	P-Value[1]	OR (95% CI)	N (%)	P-Value[1]	OR (95% CI)	N (%)	P-Value[1]	OR (95% CI)
Breast	28 (12.1)	0.036	0.7 (0.4-0.98)	79 (8.8)	<0.001	0.5 (0.4-0.6)	177 (11.0)	<0.001	0.6 (0.5-0.7)	980 (27.9)	<0.001	2.4 (2.2-2.6)
Lymphoma	64 (27.7)	<0.001	2.2 (1.7-3.0)	192 (21.4)	<0.001	1.6 (1.4-1.9)	279 (17.3)	0.004	1.2 (1.1-1.4)	253 (7.2)	<0.001	0.4 (0.3-0.4)
Thyroid	8 (3.5)	<0.001	0.3 (0.1-0.5)	118 (13.2)	0.277	1.1 (0.9-1.4)	159 (9.8)	0.004	0.8 (0.7-0.9)	516 (14.7)	<0.001	1.4 (1.2-1.5)
Melanoma	5 (2.2)	<0.001	0.2 (0.1-0.5)	51 (5.7)	<0.001	0.5 (0.4-0.7)	87 (5.4)	<0.001	0.5 (0.4-0.6)	150 (4.3)	<0.001	0.3 (0.3-0.4)
Brain and Nervous System	7 (3.0)	0.011	0.4 (0.2-0.8)	54 (6.0)	0.114	0.8 (0.6-1.1)	102 (6.3)	0.086	0.8 (0.7-1.0)	135 (3.8)	<0.001	0.4 (0.4-0.5)
Total	112 (48.5)			494 (55.1)			804 (49.8)			2034 (57.9)		

[1]Chi-Squared Test used

Table 5: Most Common Cancer Type among those with Heart Failure (N=231)

Cancer Type	N (%)	P-Value[1]	OR (95% CI)
Lymphoma	64 (27.7)	<0.001	2.2 (1.7-3.0)
Leukemia	31 (13.4)	<0.001	3.3 (2.3-4.9)
Breast	28 (12.1)	0.036	0.7 (0.4-0.98)
Kidney	20 (8.7)	<0.001	3.9 (2.4-6.2)
Bone, Connective and Soft Tissue	16 (6.9)	0.353	1.3 (0.8-2.1)
Total	159 (68.8)		

[1]Chi-Squared Test used

Table 6: Most Common Cancer Type among those with Hyperlipidia (N= 896)

Cancer Type	N (%)	P-Value[1]	OR (95% CI)
Lymphoma	192 (21.4)	<0.001	1.6 (1.4-1.9)
Thyroid	118 (13.2)	0.277	1.1 (0.9-1.4)
Breast	79 (8.8)	<0.001	0.5 (0.4-0.6)
Leukemia	63 (7.0)	<0.001	1.6 (1.2-2.1)
Brain and Nervous System	54 (6.0)	0.114	0.8 (0.6-1.1)

Total	506 (56.5)

[1]Chi-Squared Test used

Table 7: Most Common Cancer Type among those with Hypertension (N=1616)

Cancer Type	N (%)	P-Value[1]	OR (95% CI)
Lymphoma	279 (17.3)	0.004	1.2 (1.1-1.4)
Breast	177 (11.0)	<0.001	0.6 (0.5-0.7)
Thyroid	159 (9.8)	0.0042	0.8 (0.7- 0.9)
Kidney	142 (8.8)	<0.001	5.6 (4.5-6.9)
Leukemia	138 (8.5)	<0.001	2.2 (1.8-2.7)
Total	895 (55.4)		

[1]Chi-Squared Test used

Table 8: Most Common Cancer Type among those with Secondary Cancer (N= 3513)

Cancer Type	N (%)	P-Value[1]	OR (95% CI)
Breast	980 (27.9)	<0.001	2.4 (2.2-2.6)
Thyroid	516 (14.7)	<0.001	1.4 (1.2-1.5)
Colorectal and Anal	257 (7.3)	<0.001	3.7 (3.1-4.4)
Lymphoma	253 (7.2)	<0.001	0.4 (0.3-0.4)
Bone, Connective and Soft Tissue	227 (6.5)	0.0060	1.2 (1.1-1.5)
Total	2233 (63.6)		

[1]Chi-Squared Test used

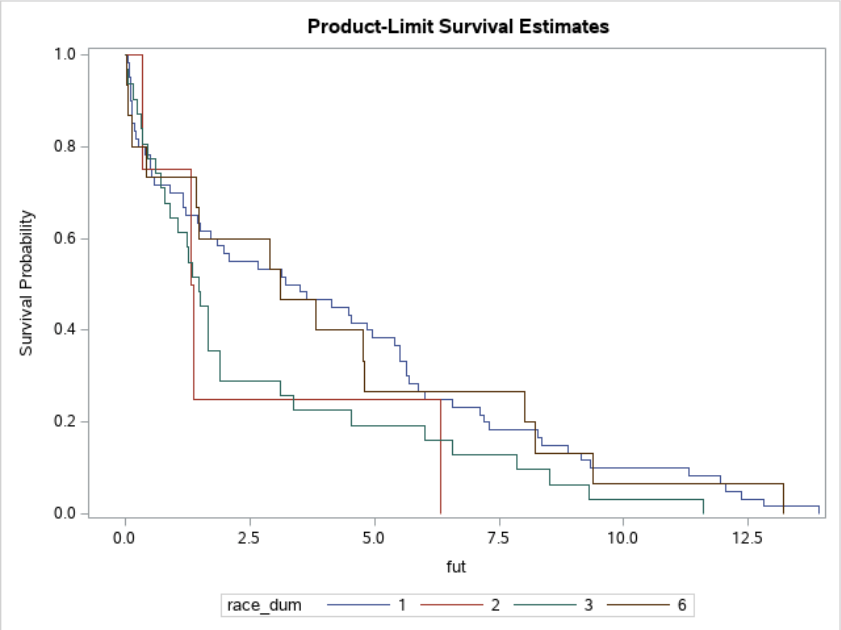

Figure 2: Kaplan-Meier Survival Curve for time from Breast Cancer Diagnosis until Hypertension Diagnosis by Race

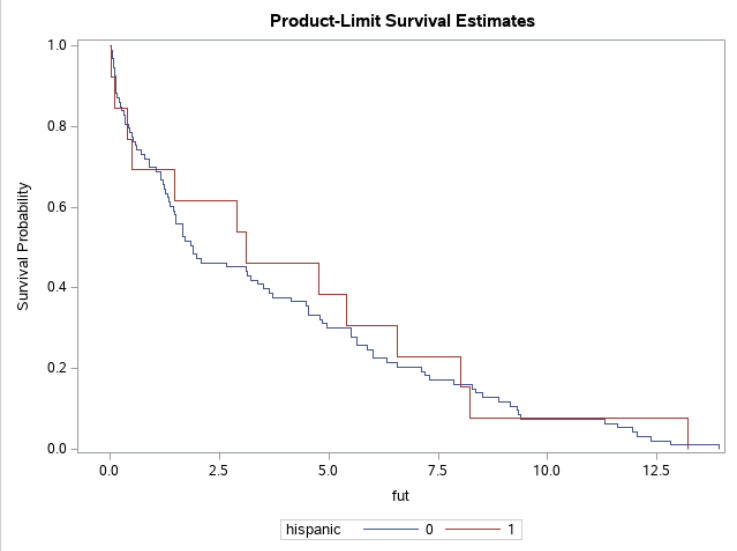

Figure 3: Kaplan-Meier Survival Curve for time from Breast Cancer Diagnosis until Hypertension Diagnosis by Ethnicity

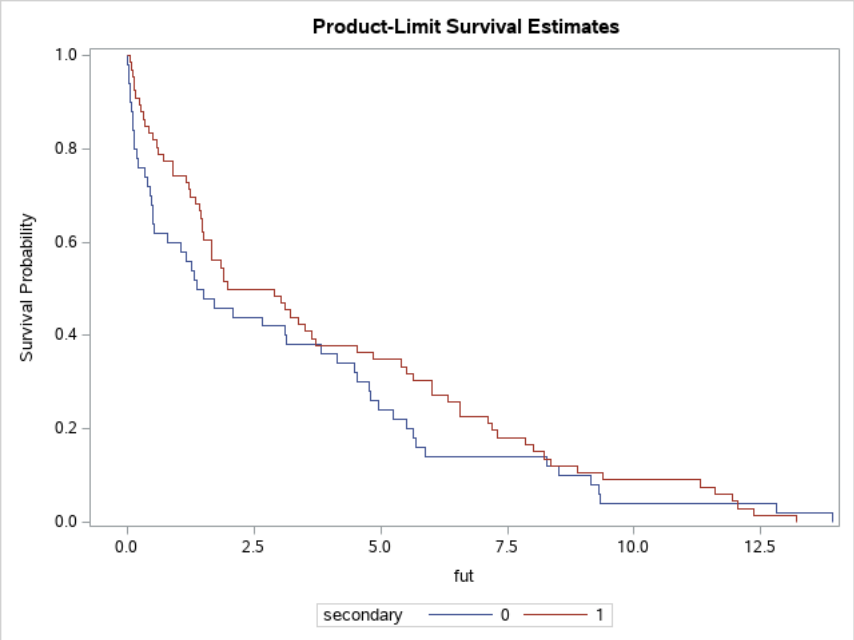

Figure 4: Kaplan-Meier Survival Curve for time from Breast Cancer Diagnosis until Hypertension Diagnosis by Secondary Cancer Status

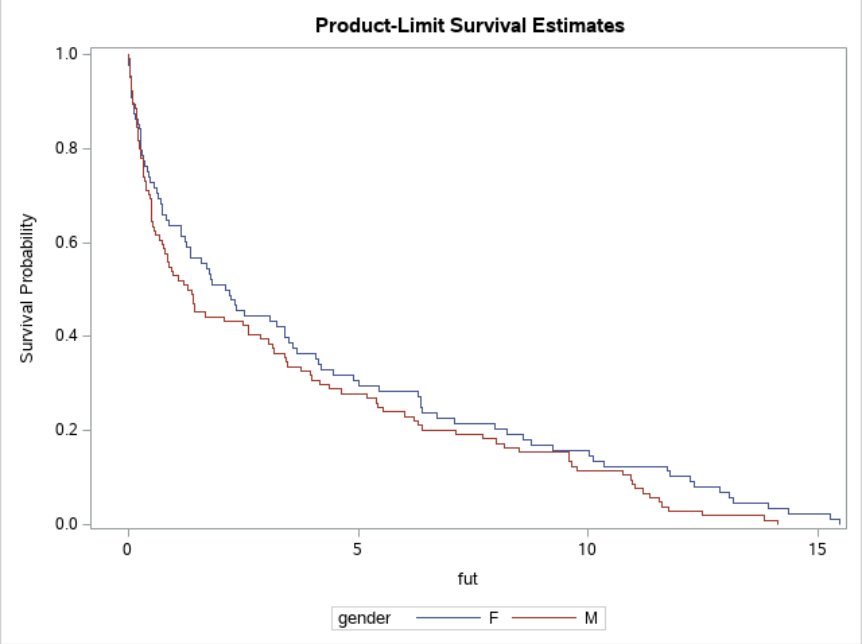

Figure 5: Kaplan-Meier Survival Curve for time from Lymphoma Diagnosis until Hypertension Diagnosis by Gender

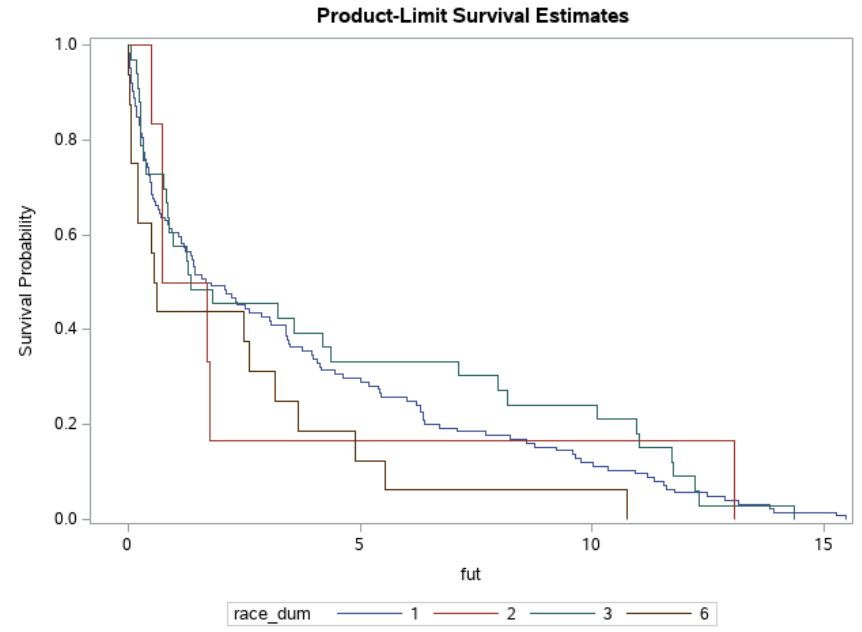

Figure 6: Kaplan-Meier Survival Curve for time from Lymphoma Diagnosis until Hypertension Diagnosis by Race

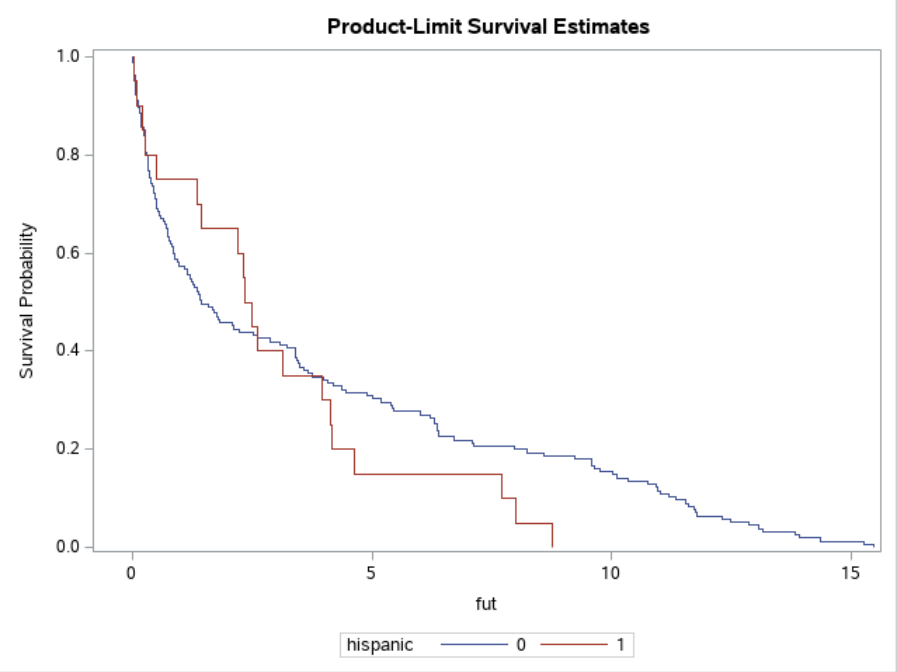

Figure 7: Kaplan-Meier Survival Curve for time from Lymphoma Diagnosis until Hypertension Diagnosis by Ethnicity

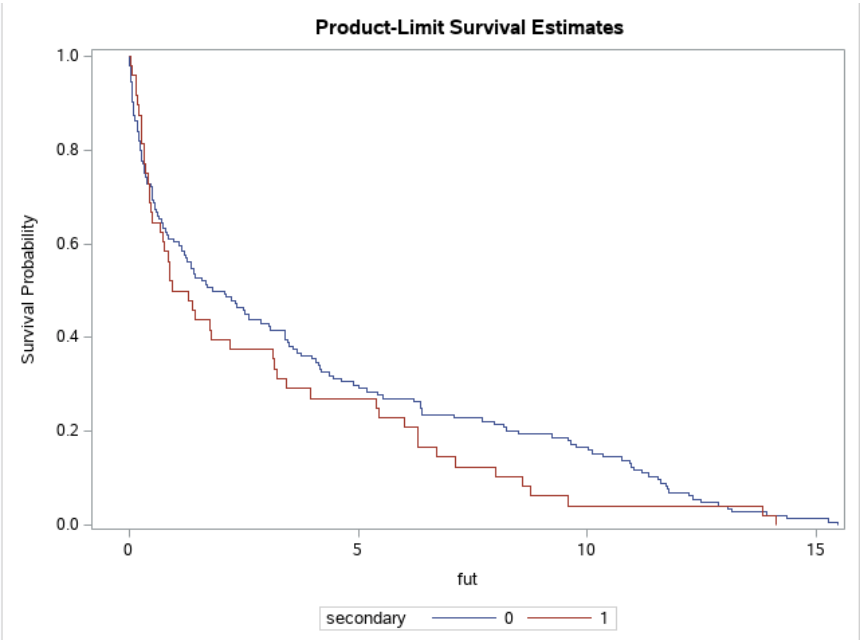

Figure 8: Kaplan-Meier Survival Curve for time from Lymphoma Diagnosis until Hypertension Diagnosis by Secondary Cancer Status

Table 9: Cox Proportional Hazards Model for Breast Cancer Patients with Hypertension (N=116)

Variable	Hazard Ratio	95% CI	P-Value
Race			
White[1]			
Asian	1.7	0.6-4.8	0.288
Black	1.5	1.0-2.4	0.063
Other	1.0	0.6-1.9	0.897

Secondary Cancer	0.8	0.6-1.2	0.351
No			
Yes			

[1]Reference Group

Table 10: Cox Proportional Hazards Model for Lymphoma Patients with Hypertension (N=192)

Variable	Hazard Ratio	95% CI	P-Value
Male	1.3	0.9-1.7	0.100
Female			
Male			
Race			
White[1]	1.1	0.5-2.5	0.820
Asian	0.9	0.6-1.3	0.625
Black	1.6	0.9-2.7	0.079
Other			
Secondary Cancer	1.4	0.9-1.9	0.094
No			
Yes			

[1]Reference Group

REFERENCES

1. Fidler MM, Gupta S, Soerjomataram I, Ferlay J, Steliarova-Foucher E, Bray F. Cancer incidence and mortality among young adults aged 20-39 years worldwide in 2012: a population-based study. Lancet Oncol. 2017;18(12):1579-89.
2. Smith AW, Seibel NL, Lewis DR, Albritton KH, Blair DF, Blanke CD, et al. Next steps for adolescent and young adult oncology workshop: An update on progress and recommendations for the future. Cancer. 2016;122(7):988-99.
3. Lewis DR, Seibel NL, Smith AW, Stedman MR. Adolescent and young adult cancer survival. Journal of the National Cancer Institute Monographs. 2014;2014(49):228-35.
4. Keegan TH, Lichtensztajn DY, Kato I, Kent EE, Wu XC, West MM, et al. Unmet adolescent and young adult cancer survivors information and service needs: a population-based cancer registry study. J Cancer Surviv. 2012;6(3):239-50.
5. Zebrack B, Hamilton R, Smith AW. Psychosocial outcomes and service use among young adults with cancer. Semin Oncol. 2009;36(5):468-77.
6. Albritton K, Bleyer WA. The management of cancer in the older adolescent. Eur J Cancer. 2003;39(18):2584-99.
7. Arnett JJ. Emerging adulthood. A theory of development from the late teens through the twenties. Am Psychol. 2000;55(5):469-80.
8. Fernandez CV, Barr RD. Adolescents and young adults with cancer: An orphaned population. Paediatr Child Health. 2006;11(2):103-6.
9. Soliman H, Agresta SV. Current issues in adolescent and young adult cancer survivorship. Cancer Control. 2008;15(1):55-62.
10. Zebrack BJ, Casillas J, Nohr L, Adams H, Zeltzer LK. Fertility issues for young adult survivors of childhood cancer. Psycho-oncology. 2004;13(10):689-99.
11. Zebrack B, Isaacson S. Psychosocial care of adolescent and young adult patients with cancer and survivors. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2012;30(11):1221-6.
12. Kazak AE, Derosa BW, Schwartz LA, Hobbie W, Carlson C, Ittenbach RF, et al. Psychological outcomes and health beliefs in adolescent and young adult survivors of childhood cancer and controls. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2010;28(12):2002-7.
13. Bleyer WA. Cancer in older adolescents and young adults: epidemiology, diagnosis, treatment, survival, and importance of clinical trials. Med Pediatr Oncol. 2002;38(1):1-10.
14. Crombie JL, LaCasce AS. Current considerations in AYA Hodgkin lymphoma. Br J Haematol. 2019;184(1):72-81.
15. Henderson TO, Parsons SK, Wroblewski KE, Chen L, Hong F, Smith SM, et al. Outcomes in adolescents and young adults with Hodgkin lymphoma treated on US cooperative group protocols: An adult intergroup (E2496) and Children's Oncology Group (COG AHOD0031) comparative analysis. Cancer. 2018;124(1):136-44.
16. Bleyer A, Budd T, Montello M. Adolescents and young adults with cancer: the scope of the problem and criticality of clinical trials. Cancer. 2006;107(7 Suppl):1645-55.
17. Kahn JM, Kelly KM. Adolescent and young adult Hodgkin lymphoma: Raising the bar through collaborative science and multidisciplinary care. Pediatr Blood Cancer. 2018;65(7):e27033.

18. Society AC. Cancers that Develop in Children https://www.cancer.org: American Cancer Society; 2016 [updated 08/22/2016. Available from: https://www.cancer.org/cancer/cancer-in-children/types-of-childhood-cancers.html.
19. Institute NC. Cancer Statistics https://www.cancer.gov: National Institutes of Health; 2018 [updated 04/27/2018. Available from: https://www.cancer.gov/about-cancer/understanding/statistics.
20. Society AC. American Cancer Society Guidelines for the Early Detection of Cancer https://www.cancer.org: American Cancer Society; 2018 [updated 05/30/2018. Available from: https://www.cancer.org/healthy/find-cancer-early/cancer-screening-guidelines/american-cancer-society-guidelines-for-the-early-detection-of-cancer.html.
21. Society AC. Survival Rates for Breast Cancer https://www.cancer.org: American Cancer Society; 2019 [updated 02/07/2019. Available from: https://www.cancer.org/cancer/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-survival-rates.html.
22. Marcu LG, Santos A, Bezak E. Risk of second primary cancer after breast cancer treatment. European journal of cancer care. 2014;23(1):51-64.
23. Society AC. Second Cancers After Breast Cancer https://www.cancer.org: American Cancer Society; 2017 [updated 08/21/2017. Available from: https://www.cancer.org/cancer/breast-cancer/living-as-a-breast-cancer-survivor/second-cancers-after-breast-cancer.html.
24. Anders CK, Johnson, R., Litton, J., Phillips, M., Bleyer, A. Breast Cancer Before Age 40 Years. Semin Oncol. 2009;36(3):237-49.
25. Ng AK. Current survivorship recommendations for patients with Hodgkin lymphoma: focus on late effects. Hematology Am Soc Hematol Educ Program. 2014;2014(1):488-94.
26. Society AC. Second Cancers After Thyroid Cancer https://www.cancer.org: American Cancer Society; 2019 [updated 03/14/2019. Available from: https://www.cancer.org/cancer/thyroid-cancer/after-treatment/second-cancers.html.
27. Society AC. Thyroid Cancer Risk Factors https://www.cancer.org: American Cancer Society; 2019 [updated 03/14/2019. Available from: https://www.cancer.org/cancer/thyroid-cancer/causes-risks-prevention/risk-factors.html.
28. Michener K. High blood pressure linked to earlier death among African-American breast cancer patients. https://www.ucsf.edu: University of California San Francisco; 2009.
29. Everett B, Zajacova A. Gender differences in hypertension and hypertension awareness among young adults. Biodemography Soc Biol. 2015;61(1):1-17.
30. Nekhlyudov L, Aziz NM, Lerro C, Virgo KS. Oncologists' and primary care physicians' awareness of late and long-term effects of chemotherapy: implications for care of the growing population of survivors. Journal of oncology practice / American Society of Clinical Oncology. 2014;10(2):e29-36.
31. Parsons HM, Harlan LC, Seibel NL, Stevens JL, Keegan TH. Clinical trial participation and time to treatment among adolescents and young adults with cancer: does age at diagnosis or insurance make a difference? Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2011;29(30):4045-53.