

Characteristics and Survival of Malignant Cardiac Tumors: A 40-Year Analysis of Over 500 Patients

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Abstract

Background—To investigate the incidence, histopathology, demographics and survival associated with primary malignant cardiac tumors (PMCTs).

Methods and Results—We queried the Surveillance, Epidemiology and End-Results (SEER) 18-registry from National Cancer Institute for all PMCTs diagnosed from 1973 to 2011. We describe PMCT histopathology and incidence, comparing characteristics and survival of these patients, to those with extra-cardiac malignancies of similar histopathology. From a total of 7,384,580 cases of cancer registered in SEER, we identified 551 (0.008%) PMCTs. The incidence of PMCT diagnosis is 34 cases per 100 million persons and has increased over time: 25.1 (1973-1989), 30.2 (1990-1999) and 46.6 (2000-2011). Most patients are female (54.1%), white (78.6%), with median age at diagnosis of 50 years. The most common PMCTs are sarcomas (n=357, 64.8%), followed by lymphomas (n=150, 27%), and mesotheliomas (n=44, 8%). Most patients are diagnosed with tissue sample (96.8%). Although use of chemotherapy is not documented in SEER, 19% of patients received radiation and 44% had surgery. After a median follow-up of 80 months, 413 patients had died. The 1, 3, and 5- year survival was 46%, 22%, and 17% and has improved over the eras with (1-, 3-, 5-year) of 32%, 17%, 14% (1973-1989) to 50%, 24%, 19% (2000-2011) ($p=0.009$). Cardiac sarcomas and mesotheliomas are the most lethal PMCTs, with 1-, 3-, 5- year survival of 47%, 16%, and 11%, and 51%, 26%, and 23%, respectively, compared with lymphoma 59%, 41%, and 34%, respectively (log rank test $p<0.001$). Patients with cardiac lymphomas and sarcomas are younger and have worse survival than patients with extra-cardiac disease of similar histopathology ($p<0.001$).

Conclusions—PMCTs are extremely rare and continue to be associated with poor prognosis. Over the past five decades, the incidence and survival of patients diagnosed with PMCT appears to have increased. Compared to those with extra-cardiac cancers of similar histopathology, patients with PMCTs are often younger and have worse survival.

Key words: tumor; neoplasia; epidemiology

Introduction

Primary malignant cardiac tumors (PMCTs) are extremely rare neoplasms of varying histopathology that originate within cardiac structures and display biologically aggressive behavior¹⁻³. Because most practitioners may only see a handful of such cases in their lifetime, the accumulated experience on this subject has been collated and summarized in multiple extensive literature reviews^{1, 4}. Nevertheless, the core knowledge of PMCTs has continued to come from single center studies, consisting of surgical case series and autopsy reports^{2, 4-7}. Because of the relatively small numbers and significant referral bias of these reports, the incidence of PMCTs remains unclear, their histology incompletely defined, treatment ineffectual and prognosis thought to be universally poor.

We therefore sought to better understand PMCTs by utilizing the largest cancer registry in the United States.

Methods

We conducted a retrospective analysis of all PMCTs in the Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) from 1973-2011. We used the 18-Registry Research Data with Hurricane Katrina Impacted Louisiana Cases, Nov 2013 Submission (1973-2011 varying) from the National Cancer Institute, Division of Cancer Control and Population Sciences (DCCPS), Surveillance Research Program, Surveillance Systems Branch, released April 2013, based on the November 2013 submission. SEER 18 captures cancer data from 18 cancer registries in the US: Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, Utah, Los Angeles and San Jose-Monterey, Rural Georgia, the Alaska Native, Greater California, Kentucky, Louisiana, New Jersey, and Greater

Georgia. The data collection and reporting for the SEER are described elsewhere⁸.

All data were extracted from the registry using SEER*STAT v8.2.1 from the surveillance research program of the division of cancer control and population sciences, National Cancer Institute (Calverton, MD) on March 1, 2014. We used the following selection criteria: Case selection (Site and Morphology. Primary Site – labeled) = 'C38.0-Heart'. We only included patients with known age, who were actively followed, and had tumors with malignant behavior. Our search was limited to cases within the research database. We excluded patients with either death certificate only or autopsy report only (however, no patients were excluded based on these criteria). The study cut-off date is defaulted to December 2010.

We used Code II, IX, XII (a.5) for lymphomas, sarcomas and mesotheliomas, respectively. We performed subgroup analyses based on age groups (pediatrics: ≤ 18 years vs. adults: > 18 years), histologic type (viz. angiosarcoma, selected with ICCC code IX (d.8)), and by era of diagnosis year (1973-1989, 1990-1999, 2000-2011). Data from SEER*STAT were imported into IBM SPSS v19 (2010) for statistical analyses. All categorical variables were presented as frequencies and percentages. Where appropriate, mean (standard deviation, SD) and median (25th, 75th percentiles) were presented for continuous data variables. Survival curves were formulated using Kaplan-Meier methods. All tumors were selected using the ICCC site recode (ICD-0-3/WHO 2008). Per SEER guidelines, histopathologic data are entered based on the most recent available diagnosis, and the registry does not contain information on the method used for histologic sampling- whether biopsy, excision, or autopsy.

Incidence data was calculated using rate sessions within SEER*STAT program. For the incidence calculations, we used the SEER 9 (1973-2011) based on November 2013 submission. This registry pulls data from following cancer registries: Atlanta, Connecticut, Detroit, Hawaii,

Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah. Age-adjusted incidence was standardized to the U.S.2000 standard-million population (19 age groups). Age-adjusted rates for incidence were calculated by summing the products of the age-specific rate (for each 5-year age group [0–4, 5–9, etc]), multiplied by the fraction of the 2000 U.S. population in each age range. We calculated the incidence by era of diagnosis and by histology⁹.

Chi-square was used to compare categorical data. Independent t-test was used to compare means when normally distributed and non-parametric test (Mann-Whitney) were used if data were not normally distributed. Kaplan-Meier method was used to present survival, and log-rank test was used for all survival differences throughout the manuscript. Median survival (25th, 75th percentile) is presented taking into account censoring. We compared characteristics and survival of cardiac tumors with non-cardiac tumors of similar histopathologic type (based on ICCC classifications). In all tests, $p < 0.05$ was considered statistically significant.

Results

Epidemiology

Of 7,384,580 cases of cancer with known age registered in SEER, we identified 551 (0.008%) PMCTs. The majority were females (298, 54.1%), with median age (25th, 75th percentiles) at diagnosis of 50 (35, 67) years. Most patients were white (433, 78.6%) followed by blacks (57, 10.3%), see **table 1**. A histogram of age at diagnosis is shown in **figure 1**. The majority of tumors were sarcomas (n=357, 64.8%), followed by lymphomas (150, 27.0%), and mesotheliomas (44, 8.0%), **table 2**. There were 27 (4.9%) pediatric patients: 19 with sarcoma, 7 with lymphoma, and 1 with mesothelioma.

The calculated age-adjusted incidence was 34 cases per 100 million persons. Since 1973,

the incidence has increased over 3 eras (per 100 million persons): 25.1 (1973-1989), 30.2 (1990-1999), 46.6 (2000-2011) and was higher in males than in females (38.2 vs. 30.0 per 100 million persons). Cause-specific analysis shows that the incidence of both lymphomas (2.8, 10.3, 15.8) and sarcomas (16.8, 17.1, 29.2) has increased while that of mesothelioma has decreased (5.5, 2.8, 1.5), **figure 2**.

Most patients were diagnosed by tissue samples (96.8%). Although chemotherapy data is not available in SEER, 19.1% of patients received radiation, and 43.6% of patients had surgery. Overall, 10.2% underwent both surgery and radiation as a part of their treatment.

Overall Survival

Survival data were available for 516 (93.6%) patients. At a median follow-up of 80 months (33, 119), 413 patients had died. Median survival (25th, 75th percentiles) was 10 months (1, 29) with 1-, 3- and 5- year survival of 46%, 22%, and 17% (**Figure 3**). Survival has improved over the study period from (1-, 3-, 5-year) of 32%, 17%, 14% (1973-1989) to 50%, 24%, 19% (2000-2011), $p=0.009$ (**figure 4**). Pediatric patients had better survival than adults with 1, 3, 5- year survival rate of 71%, 47%, 47% vs. 44%, 21%, 16% ($p<0.001$), **Supplemental Figure 1**.

Cardiac sarcomas have worse survival with 1-, 3-, 5- year survival of 47%, 16%, and 11% compared with lymphoma survival of 59%, 41%, and 34%, respectively (log rank test $p<0.001$).

Survival analysis reveals that more than 80% of the patients die within 20 months of diagnosis.

Specific Histologic Types

Sarcomas

Cardiac sarcomas represented 0.3% of all sarcomas with median age (25th, 75th percentiles) at diagnosis of 45 (32, 59) years. The most common histopathologic type was angiosarcoma (43.4%), followed by leiomyosarcoma (6.4%) and rhabdomyosarcoma (4.5%). Cardiac

angiosarcomas had slightly worse survival than other types of cardiac sarcomas with 1-, 3- and 5-year survival of 39%, 9% and 8% vs. 47%, 21% and 14% ($p=0.045$). There were no statistically significant differences in cardiac sarcoma survival over the 3 eras with 1-, 3-, and 5-year survival of 9%, 11%, 6% (1973-1989); 24%, 10%, 6% (1990-1999) and 31%, 11%, 8% (2000-2011), $p=0.173$.

Compared with those with extra-cardiac sarcomas, patients with cardiac sarcomas were younger (46.1 vs. 52.8 years, $p=0.001$), more likely to be female (47.1% vs. 40.8%, $p=0.02$), less likely to have previous history of malignancy (7.6% vs. 12.7%, $p=0.005$), more likely to have surgical resection (60.4% vs. 26.2%, $p<0.001$), **table 3**. Median survival (25th, 75th percentiles) was 9.0 months (1.2, 21). Patients with cardiac sarcomas had worse survival than those with extra-cardiac sarcomas (log rank $p<0.001$), **figure 5A**.

Lymphomas

Cardiac lymphomas accounted for 0.03% of all lymphomas with median age (25th, 75th percentiles) at diagnosis of 67 (50, 79) years. The most common histopathologic type was diffuse B-cell lymphoma (60.6%). There was a trend towards improved survival for cardiac lymphomas over the 3 eras with 1-, 3-, and 5- year survival of 63%, 38%, 38% (1973-1989); 38%, 23%, 19% (1990-1999) and 62%, 46%, 38% (2000-2011), $p=0.087$.

Compared with extra-cardiac lymphomas, those with cardiac disease were less likely to be black (5.0% vs. 9.6%, $p=0.002$), but had no difference in age, gender, or history of previous malignancy. There was a non-significant trend towards fewer surgeries in patients with cardiac lymphomas (16.5% vs. 24.9%, $p=0.06$); but no difference in utilization of radiation therapy, **table 3**. Median survival (25th, 75th percentiles) for cardiac lymphomas was 23 months (5, 120). Compared with extra-cardiac lymphomas, cardiac lymphomas had worse survival (log rank

$p < 0.001$), **figure 5B**.

Mesotheliomas

Pericardial mesotheliomas represented 0.3% of all mesotheliomas with median age (25th, 75th percentiles) at diagnosis of 53 (40, 70) years. Median survival (25th, 75th percentiles) of patients diagnosed with pericardial mesothelioma was 2 months (0, 12), with 1-, 3- and 5- year survival of 26%, 14%, and 9%. There was no statistically significant difference in survival for cardiac sarcoma over the 3 eras with 1- year survival of 25% (1973-1989), 20% (1990-1999) and 7% (2000-2011), log rank $p = 0.338$.

Compared with extra-cardiac mesotheliomas, patients with pericardial mesotheliomas were younger (mean 54.1 years vs. 70.2 years, $p < 0.001$), less likely to be males (45.5% vs. 77.6%, $p < 0.001$), more likely to be blacks and other minorities (15.9% vs. 4.9% and 6.8% vs. 3.3%, respectively; $p = 0.001$). Patients with cardiac mesotheliomas were more likely to have surgery (31.8% vs. 24.0%, $p < 0.001$), but had similar use of radiation therapy, **table 3**. Cardiac or extra-cardiac location of mesothelioma did not appear to impact prognosis ($p = 0.06$), **figure 5C**.

Discussion

This study reports the characteristics of PMCTs utilizing data amassed over five decades from a large-scale national registry. In it we confirm the rarity and lethality of PMCTs, and also offer insight into their epidemiology, histopathology, demographics, and outcomes. Because we have studied numbers twenty-fold larger than existing reports, we have debunked previous misconceptions and shed light on unknown aspects of PMCTs.

The pre-mortem diagnosis of PMCTs is much more uncommon than previously reported. In unselected autopsy reports, benign and malignant tumors are found in 0.021% of deaths¹⁰. Of

these, malignant cardiac tumors were even less common, representing 5.1% to 28.7% of all heart tumors in small series². Our study shows that clinically apparent PMCTs have an estimated prevalence of 34 cases per 100 million persons; over 100 times lower than previous estimates. This discrepancy may be partially explained by the possibility that many of the autopsy-discovered tumors may have been incidentalomas rather than clinically significant tumors. Indeed, in a Spanish series, one quarter of all cardiac tumors were incidental findings¹¹. In addition, SEER only includes patients diagnosed with cancer prior to death and not post-mortem findings. Although PMCTs commonly present with dyspnea, chest pain, palpitations, and edema¹¹⁻¹³, they can also remain clinically silent until causing ventricular arrhythmias¹³ and sudden cardiac death¹⁴, thus escaping inclusion in SEER. Nevertheless, more in line with our findings, a recent study in Grosseto's county in Italy (1998-2011) estimated the incidence of PMCTs at around 130 per 100 million persons¹⁵.

Over the study period, the incidence of PMCTs appears to have increased, driven by higher frequency of lymphomas and sarcomas. This increment may reflect better pre-mortem diagnostic capabilities brought about by developments in cardiac imaging, such as echocardiography, computed tomography and magnetic resonance imaging, not widely available in the first decades of the study period. The incidence of cardiac lymphomas mirrors that of non-Hodgkin lymphoma in the general population which peaked in the 1980's and 1990's but has remained stable since 2000¹⁶ because of improvements in human immunodeficiency virus management. Conversely, there has been a steady decrease in the incidence of pericardial mesotheliomas as a result of less common asbestos exposure¹⁷.

We confirm that PMCTs can present at any age, with a peak incidence in the fifth decade of life, affects predominantly whites and have slight female predilection, consistent with

previous reports^{11, 12, 18-21}. The reasons for age distribution, racial preference and slight female preponderance cannot be gleaned from this study. We can speculate, however, that women receive more chest radiation for breast cancer^{22, 23} and that blacks have less access to medical care than whites²⁴, however there may also be genetic and environmental factors that cannot be inferred from this study.

We also report and shed light on histopathologic sub-types of PMCTs and their frequencies. For example, whereas we confirm that sarcomas are indeed the most common PMCT, we demonstrate that lymphomas affect the heart ten times more frequently than previously thought. For example, a previous single-center surgical series reported only 10 (6.9%) lymphomas of 143 malignant cardiac tumors², likely a result of referral bias, since lymphomas typically are chemo-responsive and not treated surgically. Therefore, whereas lymphomas were previously believed to represent 1.3%-2% of all cardiac tumors^{2, 4}, in our series they accounted for 27% of all PMCTs. Also, although a systematic literature analysis of 197 cardiac lymphomas in 2010²⁵ reported a male: female ratio of 1.94, we show more balanced gender distribution, not different than what is seen in extra-cardiac lymphomas. While non-Hodgkin lymphoma has a strong tendency to involve the myocardium, with up to 20% of patients with NHL having evidence of myocardial involvement at autopsy²⁶, immunosuppressed patients (transplant recipients, HIV, etc) typically present with primary cardiac lymphoma without extracardiac involvement². In fact, 41% of all patients with primary cardiac lymphomas are immunocompromised, and have universally poor survival²⁵. Previous reports show that diffuse large B-cell lymphomas (DLBCL) have a predilection for the right side of the heart (92% had involvement of right atrium or right ventricle), and usually presents with dyspnea, constitutional symptoms, pain and arrhythmias^{25, 27-29}. About 90% of those patients receive anthracycline-based

regimen, with high treatment-related mortality²⁵. Historically, about 28% of patients are treated with surgery and 20% with radiation, slightly higher than what we found, at 16.5% and 15.1%, respectively²⁵.

We also investigated incidence of different subtypes of sarcomas. In the largest previous series of 143 cases of malignant cardiac tumors, angiosarcomas were most common at 23.1%, followed by leiomyosarcoma 20.3% and rhabdomyosarcoma 4.2%². Our data shows similar angiosarcoma (25.8%) and rhabdomyosarcoma (2.6%) distribution, but much lower prevalence of leiomyosarcoma (3.7%). The predominance of angiosarcoma was also reported previously by researchers in Italy (28.6%)¹⁸, Mayo Clinic (41%)¹⁹ and the British Columbia Registry²⁰. In contradistinction, a single study from Germany reported the predominance of undifferentiated sarcoma²⁰, which may suggest either regional variances in histological distribution, or differences in histological classifications across the eras. Whereas we found no gender predilection for cardiac sarcomas, we note low utilization of surgery (43.6%), and radiation (19.1%). This may suggest that these patients have advanced disease at presentation and may not be surgical or radiation candidates, or alternatively, are predominantly treated with chemotherapy, not captured in the SEER database. Also, sarcomas have been reported to present at later stages of life and are difficult to diagnose⁴. In contrast, here we show that patients with cardiac sarcomas present at a younger age than those with extracardiac disease.

For the first time we investigated demographic differences between patients with cardiac and extra-cardiac disease of similar histopathology. We found that patients with cardiac sarcomas and pericardial mesotheliomas are significantly younger than those with extracardiac disease of similar histology. Whereas the reason for this is unclear, it may be related to lead-time bias with earlier clinical presentation because of cardiac-related symptoms, or pre-existing risk

factors for early development of these cardiac malignancies. For example, because radiation has been implicated in some cases of sarcomas³⁰ and other cancers³¹, it is possible that survivors of childhood cancers who received radiation to the chest are at higher risk of developing cardiac sarcomas. Another possibility is that cardiac sarcomas are associated with gene mutations^{32, 33} that predispose patients to develop these cancers at an earlier age. Interestingly, we also found ethnic differences between cardiac and extracardiac diseases across all histopathology groups. Cardiac lymphomas and sarcomas are more prevalent in minority groups, while mesotheliomas more common in blacks. The reasons for this observation remain speculative and could be related to genetic predisposition³⁴, risk factors³⁵ or environmental exposures³⁶.

Lastly, we performed extensive survival analyses among multiple subtypes of PMCTs as well as among those with cardiac versus extra-cardiac disease. We found that, despite overall poor prognosis of PMCTs across all histopathology types, survival appears to have slightly improved over the past five decades. Because during this period, lymphoma treatment and rates of cure have improved dramatically³⁷, the overall increased survival of PMCTs may be attributable to that alone. However, it may also be possible that survival has improved because of earlier diagnosis of PMCTs due to more common utilization of cardiac imaging. Incidental detection of these tumors when echocardiography is performed for other reasons, might lead to earlier treatment with better outcomes than in the past when diagnosis relied predominantly on the presence of symptoms. . In contrast, the paucity of advances in the treatment of sarcomas and mesotheliomas as well as the low utilization of surgery and radiation, likely explain their worse survival. Because most of these patients are treated at large academic centers where radiation and surgical expertise is adequate^{19, 21}, the underutilization of these options probably reflects poor patient candidacy.

Overall, less than 50% of patients with PMCTs are alive by the end of the first year, with a sharp decrease in survival for sarcoma and mesothelioma patients. As can be expected we found that overall survival from a “real world” registry is slightly worse than at high volume tertiary centers. For example, the median overall survival was 12 months in 32 patients with PMCTs at Mayo Clinic (1975-2007)¹⁹, compared to 10 months in our series. Yet, our reported survival of sarcomas is much better than previously published reports (1 year survival of 47% vs. 20%¹¹). Most probably, the modest improvement in observed overall survival of patients with PMCTs is driven by better treatment outcomes of lymphoma and sarcoma patients.

Another unique aspect of this study is that we provide survival comparisons between cardiac and extra-cardiac malignancies stratified by histopathology. We show that cardiac sarcomas and lymphomas have significantly worse survival compared with similar cancers of extra-cardiac origin, suggesting that any cardiac involvement, whether primary or metastatic carries worse prognosis. It further implies that patients with extra-cardiac malignancies of histopathology types that affect the heart more commonly, such as angiosarcomas and diffuse large B-cell lymphoma, may need to be screened for cardiac involvement with echocardiography³⁸, cardiac MRI³⁹, or cardiac PET⁴⁰ at diagnosis. This likely does not apply to mesotheliomas, since they have similarly poor survival regardless of location.

In summary, we confirm that PMCTs are rare and currently have limited treatment options leading to poor patient survival. There may be opportunities to better understand these tumors and their survival differences in the context of cancer genomics. Minimally invasive diagnostic techniques or circulating tumor assays may be necessary for early diagnosis and eventually inform treatment decisions. Diagnostic and therapeutic clinical trials as well as locally directed approaches should be incorporated into future treatment considerations.

Limitations

Despite being the largest of its kind, this study has multiple important limitations. It is based on a national registry, which, though extensive, lacks fundamental information that severely limits our results and conclusions. Also, although SEER is frequently used as a research tool, the quality and accuracy of its data collection cannot be ascertained and is prone to human error and inaccuracy. Further, because the data in this study was collected over 5 decades and analyzed retrospectively, there are confounding factors that cannot be avoided despite adjustments. For example, histopathologic classifications, as well as diagnostic and treatment modalities most likely do not reflect modern practices³ and can therefore confound estimates of survival and incidence of PMCT types. Specifically, determination of histopathologic type is confounded by the many reclassifications of PMCTs that have occurred since the 1970's, making inferences about PMCT sub-type incidence less reliable. Therefore, it is possible that the increase in PMCTs and different subtypes that we report, more accurately reflects an increased incidence in the diagnosis of PMCTs than that of the actual disease. Unfortunately, because the SEER registry does not include data on chemotherapy and other treatment modalities, we have no information on the role of chemotherapy on specific histopathologic types. Similarly, granular clinical information cannot be gleaned by this study, such as method of diagnosis, clinical presentation, location of cardiac tumors, most common method of histologic sampling (whether biopsy, excision or autopsy) etc. In addition, we can also offer no insight on details of surgery or radiation therapy. Lastly, the lack of information on mode of death also limits our understanding of the natural history of PMCTs and potentially confounds survival analyses. Whereas no other data source will likely be able to provide such high numbers of PMCT patients, small case series will remain the only source of more granular information on this subject.

Conclusions

Cardiac sarcomas, lymphomas and mesotheliomas are the most common PMCTs but remain extremely rare and associated with dismal prognosis. Over the past five decades, the incidence and survival of patients diagnosed with PMCT appears to have increased. Compared with those with extra-cardiac cancers of similar histopathology, patients with PMCTs are often younger and have worse survival.

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Conflict of Interest Disclosures: None.

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Circulation

Clinical Perspective

Primary malignant cardiac tumors (PMCTs) are extremely rare and lethal neoplasms which most practitioners may only encounter a handful of times in their lifetime. Until now, knowledge about these tumors has remained incomplete as it has been compiled from case reports, small surgical and autopsy series and summarized in multiple reviews. In this article we attempt to shed light into unknown aspects of PMCTs by utilizing the National Cancer Institute's Surveillance, Epidemiology and End Results Program database (SEER), the largest cancer registry in the United States. We show that the incidence of diagnosed PMCTs in the United States is about 34 cases per 100 million people and has doubled over the past 5 decades. The most common histopathologic types are sarcomas, lymphomas and mesotheliomas and the average age at diagnosis is around 50, with a slight predilection for women. Overall, more than half of patients die within one year of diagnosis, although survival has slowly and modestly increased since the 1970's. Finally, we found that mortality is highest among patients with mesotheliomas and sarcomas, lowest among those with lymphomas; and compared to those with extra cardiac disease of the same histopathologic type, patients with PMCTs have worse survival.

Table 1. Characteristics of study patients.

Variable	N (%) or median (25th, 75th percentiles)
Age, years	50 (35, 67)
Era of diagnosis	
1973-1989	91 (16.5%)
1990-1999	93 (16.9%)
2000-2011	367 (66.6%)
Race	
White	433 (78.6%)
Black	57 (10.3%)
Other	59 (10.7%)
Unknown	2 (0.4%)
Gender	
Female	298 (54.1%)
Male	253 (45.9%)
History of malignancy	68 (12.3)
Diagnostic confirmation	
Histology	497 (90.2)
Cytology	36 (6.5)
Clinical	5 (0.9)
Direct visualization	2 (0.4)
Microscopy, NOS	1 (0.2)
Radiography only	9 (1.6)
Unknown	1 (0.2)
Radiation	
Yes	105 (19.1)
No	429 (77.9)
Unknown	11 (2.0)
Surgery	
Surgery	240 (43.6)
No surgery	242 (43.9)
Unknown	75 (13.6)
Surgery and Radiation	56 (10.2)



Table 2. Histopathology of PMCTs by groups.

Histopathology (WHO 2008 groups)	n	%
Sarcoma	357	64.8
IX(d.8) Blood vessel tumors	161	29.2
IX(e) Unspecified soft tissue sarcomas	77	14
IX(d.6) Leiomyosarcomas	31	5.6
IX(b.1) Fibroblastic and myofibroblastic tumors	30	5.4
IX(a) Rhabdomyosarcomas	23	4.2
IX(d.7) Synovial sarcomas	12	2.2
IX(d.5) Fibrohistiocytic tumors	10	1.8
IX(d.11) Miscellaneous soft tissue sarcomas	9	1.6
IX(d.4) Liposarcomas	3	0.5
IX(b.2) Nerve sheath tumors	1	0.2
Lymphoma	150	27.2
II(b.2) Mature B-cell lymphomas except Burkitt lymphoma	109	19.8
II(b.4) Non-Hodgkin lymphomas, NOS	15	2.7
II(e) Unspecified lymphomas	12	2.2
II(a) Hodgkin lymphomas	6	1.1
II(b.3) Mature T-cell and NK-cell lymphomas	3	0.5
II(c) Burkitt lymphoma	2	0.4
II(b.1) Precursor cell lymphomas	2	0.4
II(d) Miscellaneous lymphoreticular neoplasms	1	0.2
Mesothelioma	44	8

Table 3. Comparison between cardiac and non-cardiac tumors stratified by histopathology.

	<i>Sarcomas</i>			<i>Lymphomas</i>			<i>Mesotheliomas</i>		
	C	NC	p	C	NC	p	C	NC	p
N	357	105597		150	439341		44	15873	
Mean Age at diagnosis (+/- SD)	46.1± 18.9	52.8 ± 20.7	0.001	62.8±20.2	61.8 ± 18.5	0.11	54.1 ± 17.9	70.2 ± 12.3	<0.001
Male sex	52.9	59.2	0.02	57.6	54.3	0.45	45.5	77.6	<0.001
Race			0.001			0.002			0.001
White	77.5	81.7		82.0	84.0		77.3	91.8	
Black	11.7	12.2		5.0	9.6		15.9	4.9	
Other minorities	10.8	6.1		12.9	6.6		6.8	3.3	
History of malignancy	7.6	12.7	0.005	18.0	13.7	0.14	22.7	17.7	0.43
Treatment									
Surgery	59.4	67.5	<0.001	16.5	24.9	0.06	31.8	24.0	<0.001
Radiation	23.1	26.5	0.064	15.1	22.1	0.77	9.1	12.1	0.98

Abbreviations: C: cardiac primary; NC: non-cardiac primary

Figure Legends:

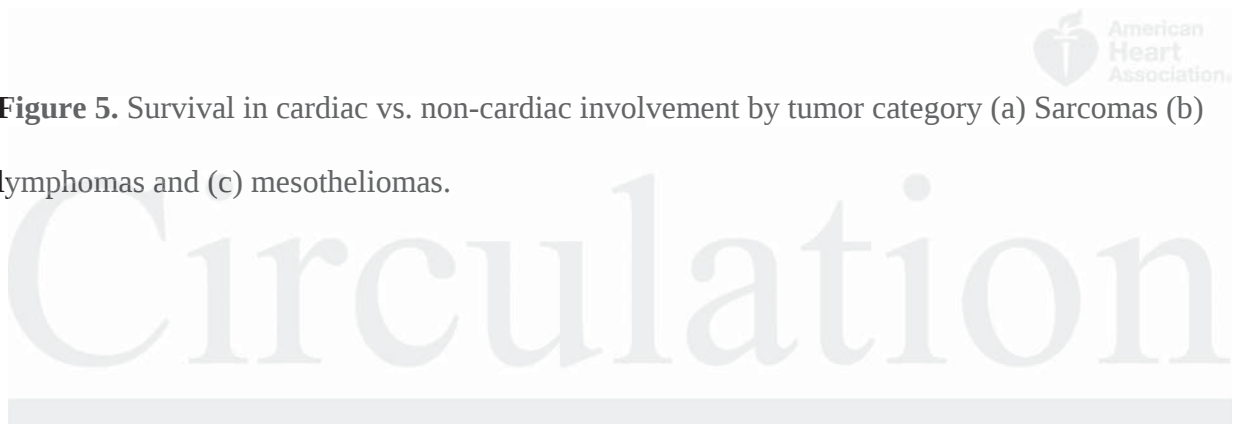
Figure 1. Histogram of age at diagnosis by cancer type.

Figure 2. Age-adjusted incidence by era and type.

Figure 3. comparative survival of cardiac tumors by type.

Figure 4. Survival of all PMCTs by era (1973-2011).

Figure 5. Survival in cardiac vs. non-cardiac involvement by tumor category (a) Sarcomas (b) lymphomas and (c) mesotheliomas.



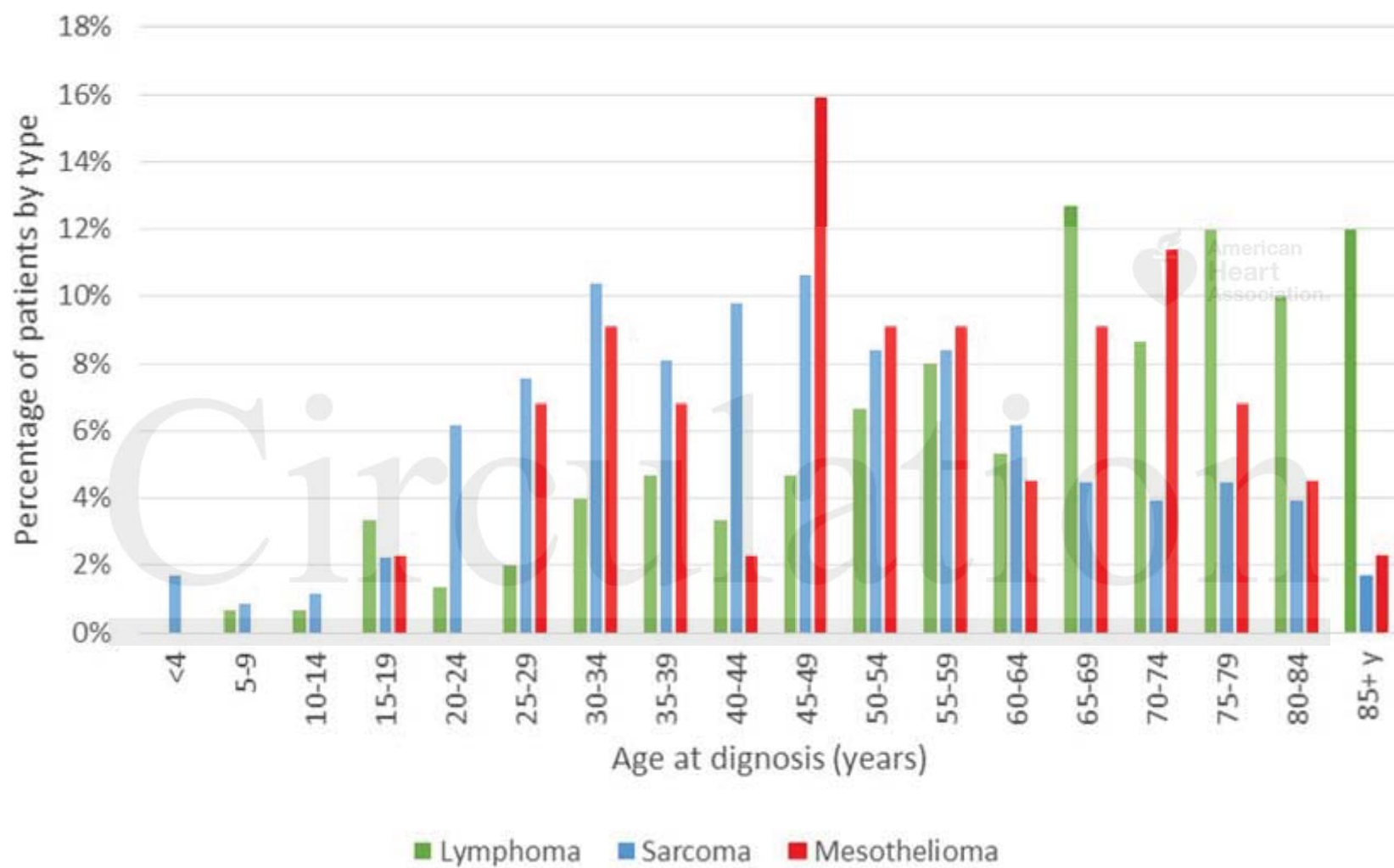


Figure 1

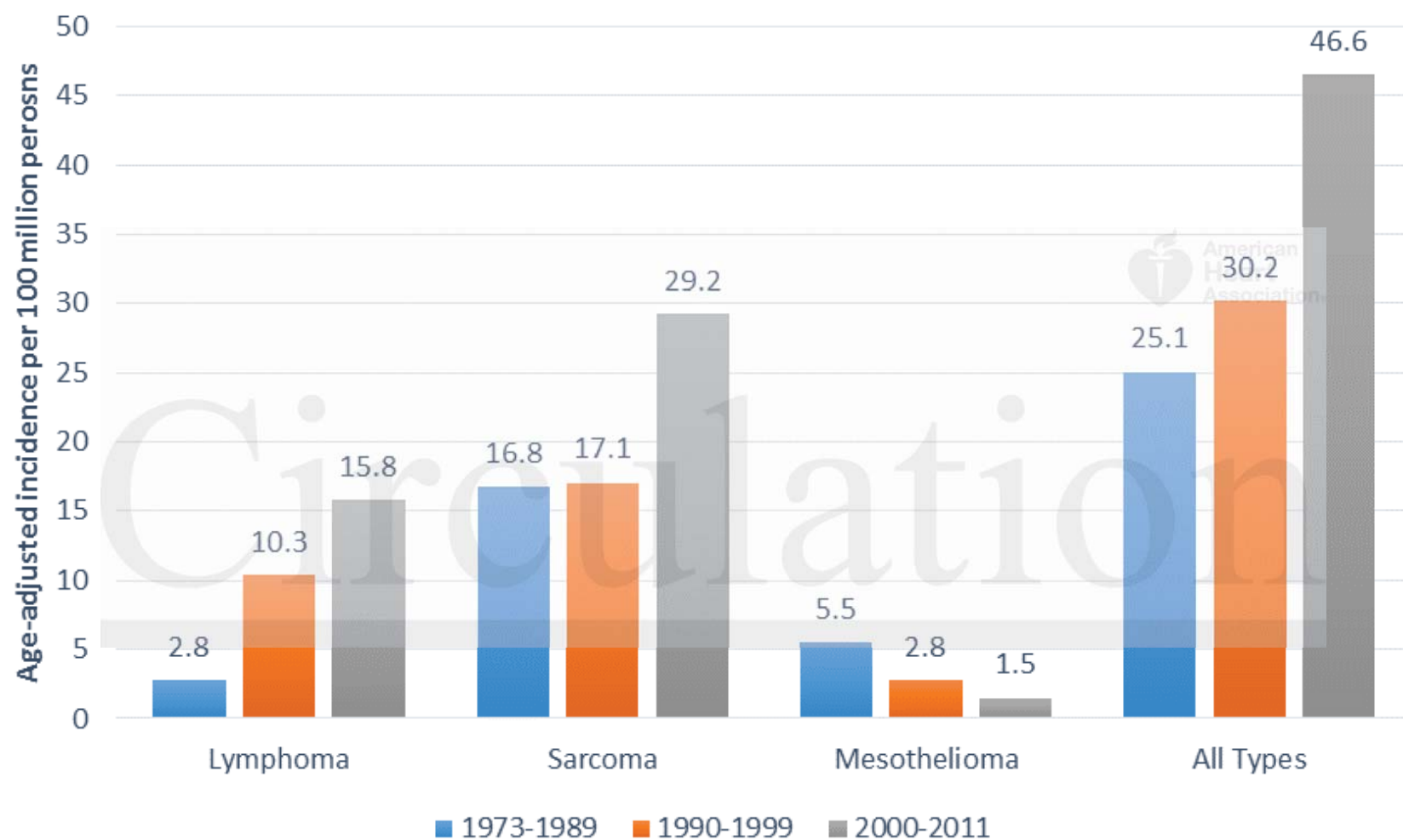
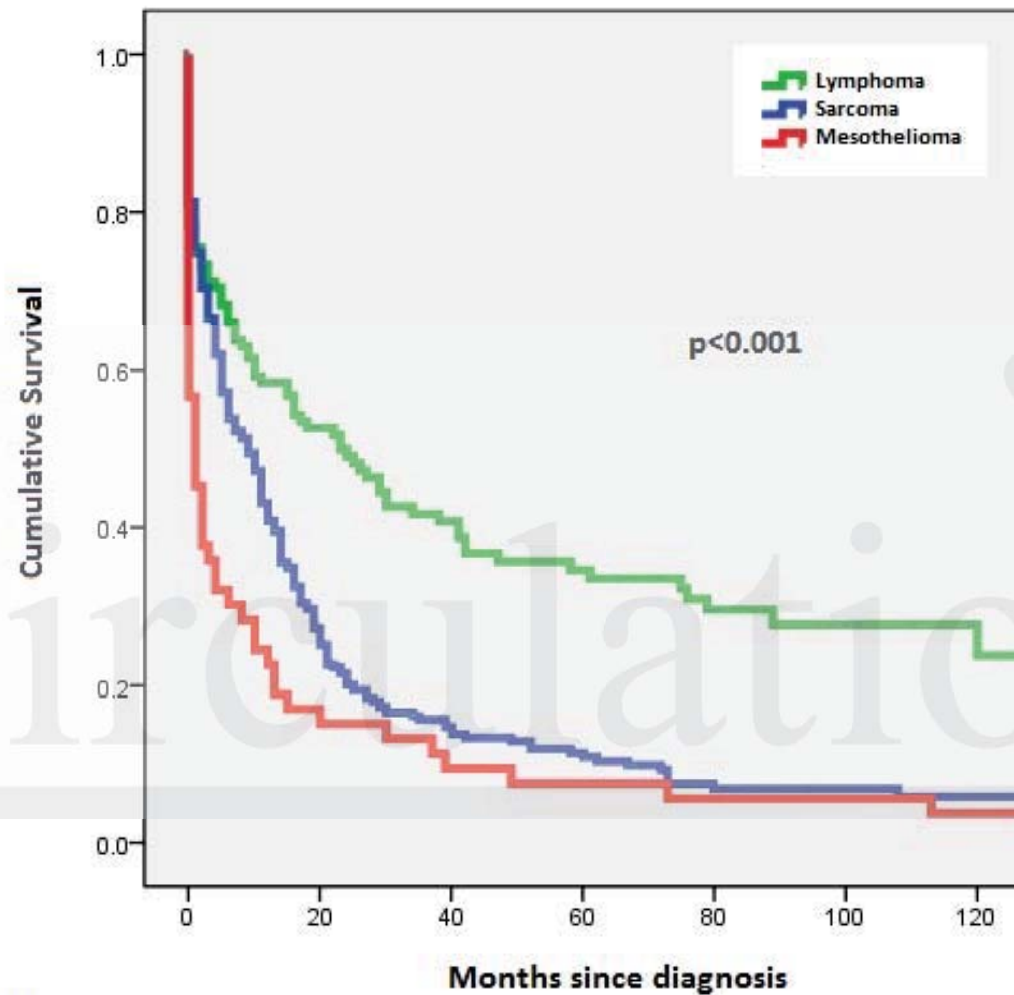


Figure 2



No. at risk

Lymphoma	139	60	42	32	21	13	7
Sarcoma	342	77	32	22	12	7	6
Mesothelioma	35	6	4	3	2	2	1

Figure 3

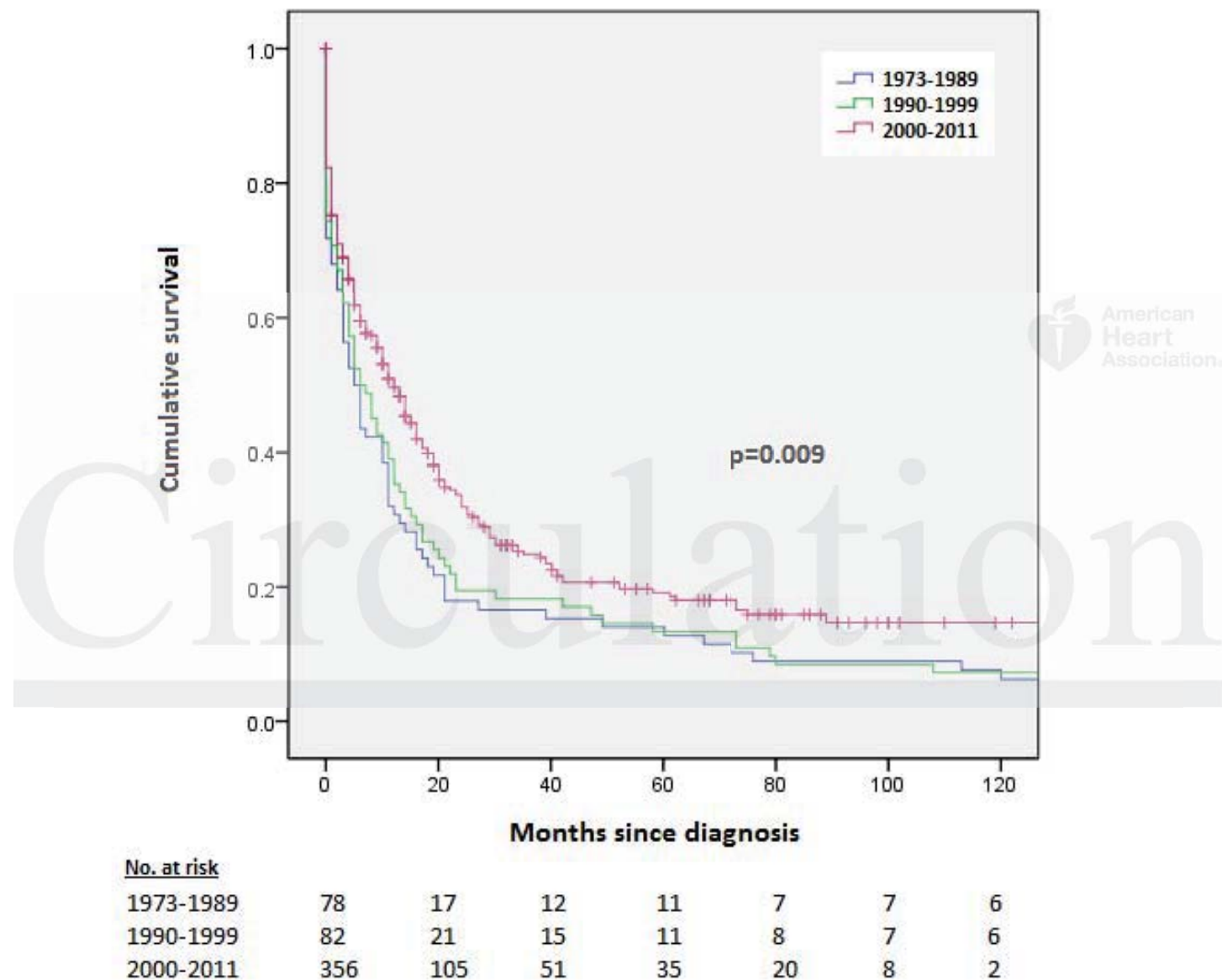


Figure 4

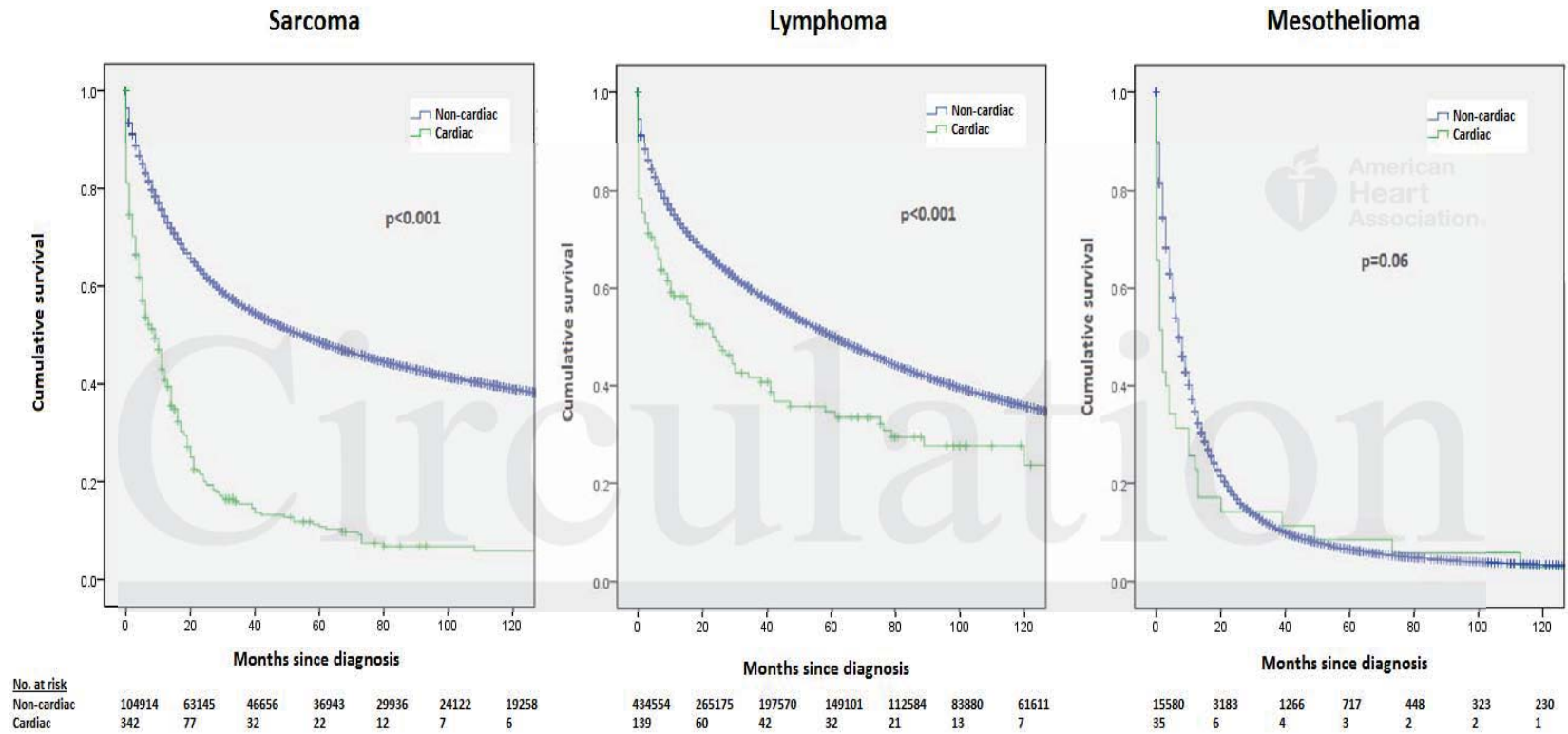


Figure 5

SUPPLEMENTAL MATERIAL

Supplemental Figure 1. Survival by age group

