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Breast cancer treatment causing cardiovascular complications: how can we prevent it?

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Abstract

Breast cancer has the highest incidence rate of any cancer in the United States, and it is the second most deadly. It comprises 30% of all diagnosed cancers in women, and it is predicted that the incidence of breast cancer will continue to rise. Most common chemotherapeutic agents utilized in the treatment of breast cancer are known to be cardiotoxic, each with differing mechanisms and possible damage done to the patient. In turn, cardiovascular diseases are the number one killer of women in the United States, and their prevalence is continually growing. It is unknown exactly how many women who are treated with chemotherapeutic agents and survive breast cancer develop cardiovascular complications, and there is no predictive model to assist with discerning the patients who would be affected by this complication. The following is a review of literature that was conducted to determine the potential impact of utilizing the cardiac biomarkers C-reactive protein (CRP), homocysteine, brain natriuretic peptide (BNP), lipid profiles, and cardiac troponins as predictors of increased cardiovascular risk in women who require or have required chemotherapeutic treatment for breast cancer and to potentially establish a route to determining prevalence. This was completed by reviewing PubMed; Surveillance, Epidemiology, and End Results Program (SEER) databases; National Institutes of Health (NIH) reports; Tennessee Cancer Registry; Baroness Erlanger Hospital registry abstracting; and National Cancer Institute (NCI) reports. It was found that, with diligent monitoring, all the biomarkers studied could be used to quantify the women affected by cardiovascular disease (CVD) due to breast cancer treatment as well as to predict CVD in breast cancer patients to prevent or reduce damage.

Introduction

In the United States alone, 276,480 new cases of breast cancer will be diagnosed in 2020; it is predicted that this number will continue to rise ("How Common"). Breast cancer comprises 30% of all diagnosed cancers in women. It is the most common form of cancer and the second most deadly, behind lung cancer. Currently, the two most common forms of treatment for breast cancer are surgical removal (mastectomies) and chemotherapy, respectively ("How Common"). Some of the most common chemotherapeutic agents used to treat breast cancer are anthracyclines, trastuzumab, 5-fluorouracil, taxanes, cyclophosphamide, carboplatin, and vinorelbine. Of these, all are known to be cardiotoxic except carboplatin. Some of these agents are more damaging to the heart than others, and they each cause different problems in the cardiovascular system.

Anthracyclines result in damage to the mitochondria, disrupt ATP production, increase production of free radicals that affect cellular membranes, and induce apoptosis in healthy cells. This has led to many cardiovascular manifestations including left ventricular dysfunction (LVD), heart failure, myocarditis, and arrhythmias (Schwartz, et al. 1109; Zhou, et al. 771). Trastuzumab affects oncoprotein receptors, specifically ErbB2, expressed on the myocardium; it has been shown to cause LVD, heart failure, and arrhythmias (Crone, et al. 460; Park, et al.). 5-fluorouracil is toxic to the vascular endothelium that leads to spasms of the arteries resulting in vasoconstriction. This agent may lead to ischemia, heart failure, pericarditis, and cardiogenic shock (Lieutaud, et al. 368). Taxanes, antimicrotubular drugs, damage the myocardium through effects on subcellular organelles or by causing a histamine release. They may cause sinus bradycardia, ventricular tachycardia, atrioventricular blocks, heart failure, and ischemia (Rowinsky, et al. 1704). The mechanisms for cardiotoxicity of cyclophosphamide is not known,

but it is hypothesized that it causes oxidative stress, damage to capillaries, and breakdown of endothelial cells (Dhesi, et al. 2); it also causes heart failure (resulting in neurohumoral activation) and mitral regurgitation (Zver, et al. 413). Again, the mechanisms for toxicity for vinorelbine are unknown, but it is hypothesized that the alkaloids from the drug affect microtubules in cells, impact the metabolism of myocardial cells, or cause issues with coagulation mechanisms. It has been shown to cause myocardial infarctions, pulmonary edema, and arrhythmias (Lapeyre-Mestre, et al. 97).

Although these drugs are known to be cardiotoxic, they are preferred for the treatment of breast cancer due to their overall effectiveness. Many of these drugs are used in conjunction with one another to enhance the effects, increase the survival rate, and lower the recurrence rate. Success rates for these drugs vary by patient, stage of breast cancer, dosage, and time administered. The most popularly used drugs, like anthracyclines, have been at the forefront of chemotherapeutic treatment of breast cancer for decades (Shah and Gradishar 1153); this makes them more trusted chemotherapeutic agents. Although there are new developments in breast cancer treatment, these chemotherapy drugs are the most time-tested agents with high success rates.

Cardiovascular disease (CVD) consists of a variety of conditions such as atrial fibrillation, which results in altered electrical systems in the heart which affects rhythm and rate; coronary artery disease, in which the arteries and vessels narrow and can become blocked; congestive heart failure, in which the heart cannot pump enough blood to organs; high blood pressure, which increases pressure on the vascular system and the work required of the heart; strokes, which disrupt blood flow to the brain and can cause altered mental status and reduced limb function; and many other heart, cerebrovascular, and peripheral artery diseases (Virani, et

al. 333). The risk of CVD increases due to smoking, obesity, family history, poor diet, and lack of exercise. CVD accounts for roughly one third of all deaths worldwide; it has been the number one killer in the United States since 1920. By 2035, it is predicted that 45.1% of the population of the United States will have some form of CVD (Virani, et al. 337). A study in 2019 by Abdel-Qadir et al., found that, compared to cancer-free women in the same age categories, breast cancer patients had a significantly higher risk of hospitalization due to CVD within 10 years of treatment. The hazard ratios, the probability of a cardiovascular event occurring in the cardiotoxic treatment group compared to the age-matched control groups, show the relative increase in risk of developing cardiovascular complications from treatment. The data for heart failure was found to have a hazard ratio of 1.69; this means that women being treated with cardiotoxic drugs are 69% more likely to develop heart failure than age-matched, cancer-free women. Similarly, the data for arrhythmias showed a 93% increase in risk for women being treated with cardiotoxic drugs. Additionally, this study found that, on average, women treated with anthracyclines and/or trastuzumab were having cardiac issues much earlier, in some cases 10 years earlier, than the cancer-free women.

Although it is known that cardiotoxic drugs can lead to a variety of cardiovascular problems throughout the patient's life, it is unknown exactly how many women who survive breast cancer develop cardiovascular complications. Given the known cardiotoxicity of many common chemotherapeutic drugs for breast cancer treatment and the risk they pose for women's cardiovascular health, there is a need to quantify the total number of women affected and identify those at highest risk prior to treatment in order to allow opportunity for providers to choose the best overall treatment option. This research emphasizes the need for the addition of biomarkers in monitoring cardiac health before, during, and after treatment of patients with

chemotherapeutic drugs. Addition of this data to the SEER database abstracting would standardize the data being collected as well as compel collection of biomarker data from multiple time periods during the treatment process. This would allow for interpretation and utilization of this data for the development of predictive protocol for the determination of cardiovascular complications in breast cancer patients using biomarkers. A review of literature was conducted to determine the potential impact of utilization of the cardiac biomarkers C-reactive protein (CRP), homocysteine, brain natriuretic peptide (BNP), lipid profiles, and cardiac troponins as predictors of increased cardiovascular risk in women who require or have required treatment for breast cancer and to potentially establish a route to determining prevalence through implementation of biomarker testing.

Discussion

After a review of the literature in PubMed, SEER, NIH, Tennessee Cancer Registry, Baroness Erlanger Hospital registry abstracting, and NCI, there was no routinely followed regimen for the monitoring of cardiac biomarkers in breast cancer patients. The purpose of this research is to outline the importance of cardiac biomarkers in the prevention and treatment of cardiovascular complications in breast cancer patients. The biomarkers of interest are linked to CVD in breast cancer patients, but they are not elements on SEER registry data for the research studies currently being conducted. Additionally, the studies confirming linkages between these biomarkers and CVD, such as those by Clos, Ganguly and Alam, Harvard Health Publishing, and Sharma, et al, did not utilize them as predictive elements in preventative awareness for breast cancer patients. This lack of unified data prevents the development of further research to use as possible predictive elements or markers of damage.

The SEER database is a program through the National Cancer Institute (NCI) which collects data from cancer registries throughout the United States. This information is routinely collected and updated. The data collected is submitted using a comprehensive registry application. Making biomarkers items on the registry application for SEER would homogenize the data being collected by individual studies and allow the data to be used in larger studies. Also, forced inclusion of this data would make providers collect data before and during treatment which allows for a more informed, adaptable approach to treatment. With more data, researchers have the potential to develop more accurate protocols for the determination of cardiovascular health in breast cancer patients.

In addition, since there is an experimentally demonstrated link between the biomarkers of interest and CVD, these biomarkers, if monitored, could be used to assess cardiovascular health in breast cancer patients before, during, and after chemotherapy administration. Each biomarker should signal different events or risks in the patient. Further, each biomarker presents with varying applicability as an indicator for cardiovascular health due to the differing signals interpreted in each test; some signals are not present before an event occurs, thus making it incapable of predicting an event. The applicability of the biomarker relies on its ability to detect changes in the patient that are a sign of or a precursor to cardiovascular damage.

C-Reactive Protein (CRP) is a protein made by the liver in humans as a response to inflammatory cytokines in all areas of the body but primarily in arteries. Inflammation of cardiac tissue suggests an increased risk for a myocardial infarction (MI) or stroke. CRP acts as a surveillance molecule for changes in somatic cells as well as foreign molecules and is important in signaling and activating the immune responses. It binds to damaged tissue or pathogens and activates complements (Clos 275). The complement system is a response of the innate immune

system in which complement proteins help improve the effectiveness of antibodies and phagocytes. This process helps the immune cells attack and remove pathogens, as well as increase inflammation in the area ("The Complement System" 60). When injured, blood vessels create an inflammatory response which seals molecules with a collagen cap to prevent further damage to the blood vessel. Eventually, the deposit bursts open because of degradation by the immune response, releasing plaque and creating clots; this leads to blocked arteries or MIs. CRP is a highly sensitive indicator of the inflammatory response created by the body; there are multiple studies correlating high CRP levels with an increased chance of an MI. These studies are outlined in articles by Shomanova et al., Clos, and Harvard Health Publishing. The high sensitivity-CRP (hs-CRP) test, as opposed to a non-specific CRP test, is commonly used to evaluate the risk of a patient developing coronary artery disease because it indicates a narrowing of arteries, instead of just a general inflammatory response detected in non-specific CRP tests. However, the CRP test alone may be less accurate in predicting a cardiac event in some patients because of inflammation caused by arthritis, trauma, or other health issues elsewhere in the body (Harvard Health). Lee, et al. found in a study of 80,781 hospital patients that hs-CRP levels were consistently higher in cancer patients as opposed to patients without cancer, with the average hs-CRP level being 1.5 mg/L higher. In patients with inflammatory disorders, including cancer patients, CRP levels can be chronically high, so baseline numbers of CRP should be used to detect differences from the patient's normal levels. Overall, CRP is an effective biomarker in predicting a cardiovascular event because it suggests inflammation which could result in an MI; the high sensitivity CRP test shows greater promise in more accurately predicting only cardiac inflammation.

Homocysteine is an amino acid found in blood plasma that is formed as an intermediate during the metabolism of methionine to cysteine. All organs of the body have homocysteine, but it is primarily found in the kidneys and liver where it is used in protein synthesis. The presence of an abnormally high level of homocysteine is known as hyperhomocysteinemia. This condition can develop from genetic abnormalities in the metabolism of homocysteine, nutritional deficiencies, lack of vitamin B, and exposures to disease, drugs, alcohol usage, and tobacco usage. A strong correlation between this condition and cardiovascular disease has been shown through many studies, and elevated homocysteine levels have been shown to increase the risk of CVD (Ganguly and Alam 4; Shenoy et al., 339). The methods by which high homocysteine is thought to increase the risk of CVD include an increase in the synthesis of vascular smooth muscle cells, endothelial dysfunction, oxidative damage, increased production of collagen, and the breakdown of arterial walls. Homocysteine has also been linked with arteriosclerosis that leads to an increased amount of work required by the heart to pump blood throughout the body; this overworking can eventually lead to heart failure (Ganguly and Alam 5). A study by Shenoy et. al. showed homocysteine as an atherosclerotic promoter, that is, a link between homocysteine and the development of atherosclerosis was observed. In this study, fasting homocysteine levels were significantly higher in patients with coronary artery disease than those without (Shenoy, et al. 342). Therefore, homocysteine can be used as a predictor of cardiovascular disease because it is shown to be elevated in patients with conditions proven to lead to CVD. This is an important biomarker for monitoring cardiovascular health and preventative care for patients at risk of developing CVD due to chemotherapy.

Brain Natriuretic Peptide (BNP) is a peptide hormone synthesized in the atria and ventricles. It is released upon stretching or expansion of the walls of the atria and ventricles

which is often due to increased blood volume. BNP promotes diuresis, natriuresis, and vasodilation. In multiple studies, it has shown to be produced during heart failure, MI, or in the presence of cardiomyopathies (Morita, et al. 88; Shomanova, et al. 3). Skovgaard, et al. found a moderate increase in BNP during chemotherapy treatment with this increase being irreversible in some patients. In the study of 333 observed patients, 21 were admitted for congestive heart failure (CHF). 79% of the patients admitted for CHF had high (>30 pg/mL) BNP levels. The authors concluded that BNP in conjunction with left ventricular ejection fraction (LVEF) are accurate predictors of cardiac impairment (Skovgaard, et al. 9). Shomanova, et al. suggest that it can be used in detection of cardiac impairment. Maisel, et al. establishes BNP as a useful predictor of short-term outcomes and the diagnosis of HF. If monitoring data is made more uniform, the amount of BNP that signals cardiac danger could be identified, and the accuracy of BNP as a predictor or as an aid in the diagnosis of heart failure and cardiomyopathies could be confirmed.

Lipid profiles analyze the levels of total cholesterol in the blood. Cholesterol is made of high-density lipoproteins (HDL), triglycerides, and low-density lipoproteins (LDL). Cholesterol is necessary fat, as it stabilizes outer membranes of cells; however, high cholesterol levels are known to lead to CVD. LDL is known as “bad” cholesterol because it can stick to vessel walls, forming plaque that can ultimately clog the vessels; this build-up is called atherosclerosis. LDL can cause blood clots which ultimately could lead to MIs or strokes (Harvard Health). There is a known correlation between LDL and CVD, as patients with hyperlipidemia have approximately twice the risk of developing CVD compared to those with normal levels (Ibrahim and Jialal). This suggests that LDL is an indicating factor for CVD or other cardiovascular events. However, only about 50% of people who have an MI have high LDL levels (Harvard Health). This

suggests that the accuracy of LDL testing as a predictive tool for cardiac events could be successful, but in a limited capacity. According to the CDC, 26.2% of women used prescription medication to lower LDL levels, and the trend shows that this number is increasing. From 2013-2016, on average, 12.9% of women in the United States over 20 years old had high cholesterol levels; this percentage increases to 18.6% when only considering the age category of 45-64 years (National Center). Also, more than 70% of adults with diagnosed CVD take these medications to lower LDL levels to improve their CVD ("Products – Data Briefs"). On average, certain medications reduce LDL levels up to 60% depending on the form taken, however it is important to note that risk factors such as diet, age, smoking, or family history impact effectiveness (Nelson 197). It is not clear exactly how many of these patients continue to have CVD related issues such as an MI. An article by the Cleveland Clinic discusses that studies have shown that these drugs can positively affect atherosclerosis in patients with CVD. Additionally, the Jupiter Trial project on patients with high risk of CVD found that, when compared to a placebo, patients on medication to lower LDL levels had an approximately 54% lower chance of an MI and a 46% lower chance of needing a coronary artery bypass (CABG) or an angioplasty, two surgeries to treat blockages in the heart or blood vessels (Ridker, P. et al. 2201). Given this information, LDL could be valuable as a CVD predictor due to its indication of vessel damage and clotting which can ultimately lead to MI. This biomarker, with more uniform data, could be more accurately analyzed to determine the success rates of its predictive capabilities.

Cardiac troponins are proteins found in the muscle fibers of cardiac tissue that regulate muscular contraction and the calcium mediated interactions between actin and myosin. They have not been identified outside of the heart, which allows for an accurate depiction of what is occurring in the heart and increases the specificity of the marker. Tests for cardiac troponins can

detect injury to the heart because they are released into the blood when damage to the heart occurs. Cardiac troponins are most commonly used to detect when an MI has occurred in a patient. However, they can also be used to identify patients at high risk for a cardiac event or CVD (Sharma, et al. 1025). Since troponin levels are very sensitive, they have been shown to slightly increase when a patient has cancer and increase more when treatment begins. They have been shown to increase significantly with escalating or prolonged treatment. This is due to the increased stress on the heart because of weakened heart muscles, cardiovascular apoptosis, and blood vessels due to oxidative stress developed by the production of free radicals while undergoing chemotherapy. Free radicals result in an influx and build-up of calcium, degradation of myocytes, and mitochondrial dysfunction. This damage is a side effect of most chemotherapeutic drugs, but it is most commonly reported in anthracyclines (Quryshi, et al. 11). There is also experimental indication confirmed by echocardiography that increasingly abnormal troponin levels directly reflect diminishing LVF. Timing of administration of cardiac troponin testing may be key in determining damage done to the heart; Cardinale, et al. found that in the 63 patients with consistently increasing cardiac troponin levels within the month after treatment had an 84% incidence rate of a cardiovascular event within three years of completing treatment. The 145 patients that had high troponin levels within the first three days after each chemotherapy treatment but reduced values a month after treatment had a cardiovascular incidence rate of 37%. Highly sensitive cardiac troponin tests can detect minute amounts of troponins and monitoring the changes in these small amounts was shown to be useful in the prediction of cardiovascular complications (Sawaya, et al.). A study by Ky, et al. in 2014 showed the predictive power of troponins by monitoring cardiac troponin levels in patients every three months for a total of fifteen months. These patients were being treated with doxorubicin and trastuzumab. A

significant average increase of 13.9 ng/L was found between the baseline troponin levels and the levels at the patient's second visit three months after the baseline was taken. The researchers found that a statistically significant increase in the number of cardiac troponins from the baseline levels to levels after treatment was an accurate predictor of cardiac dysfunction. The hazard ratio predicting the cardiotoxicity for patients with increasing troponins was found to be 1.38, indicating a 38% increased risk. Cardiac troponins are some of the most tested and effective biomarkers directly related to the risk of CVD. Cardiac troponin testing could be used in decision-making for enhanced preventative measures for CVD if correctly timed because of its ability to detect not just damage but myocardial stress without damage. This testing timeline would have to be experimentally developed by determining the timing of the most accurate test results. Routine testing of patients at different points throughout their treatment would allow for more accurate predictive data. The updated registry submitted data in a SEER database could decrease the time needed to determine an accurate timeline for predictive monitoring of patients due to the amount of data reported simultaneously by multiple ongoing research projects.

All the biomarkers of interest can be tested through common blood tests. Some of these biomarker levels are not tested before a cardiovascular event for preventative measure; rather, they are often taken during or after a suspected cardiovascular event to confirm it or to diagnose patients with cardiac disorders. These tests are seldom run on breast cancer patients. However, lipid profiles are commonly tested in many patients, and homocysteine testing is being used more often on patients with risk factors. The usage of a SEER database to increase and homogenize the data from these biomarkers in breast cancer patients could result in the development of predictive protocol to prevent CVD in breast cancer patients.

The cost of the biomarker tests is significantly less than the cost of CVD or cardiovascular events. Biomarker testing often costs less than $100. For example, according to Harvard Health Publishing, the CRP test costs between $12 and $16, but there are always discrepancies with the cost of medical procedures due to hospital, governmental, and insurance fees (figure 1). Medical costs for CVD are the highest medical costs for any disease, accounting for 14% of the United States' total medical expenditures from 2014-2015. The total cost of CVD in the United States is projected to increase from the 2015 direct medical cost of $318 billion to $749 billion by 2035 (Virani, et al. 337; figure 2). For example, in a study performed by Kilgore, et al. in 2017, the mean per-patient cost of a cardiovascular related hospitalization without a procedure involved was $16,000 with 40.2% of patients being readmitted within 90 days. Data from Giacomino, et al. gives the average value for a CABG procedure in the United States in 2016 as $151,271. This cost is high because of the extended hospital stay required with this difficult procedure; additionally, this procedure occasionally results in complications and follow up-costs. On average, an angioplasty and placement of a stent to clear a clogged artery, is $49,245 (Sen, et al. 210). The cost-benefit analysis of preventative testing measures versus common treatments for CVD shows the financial importance of biomarker screening.

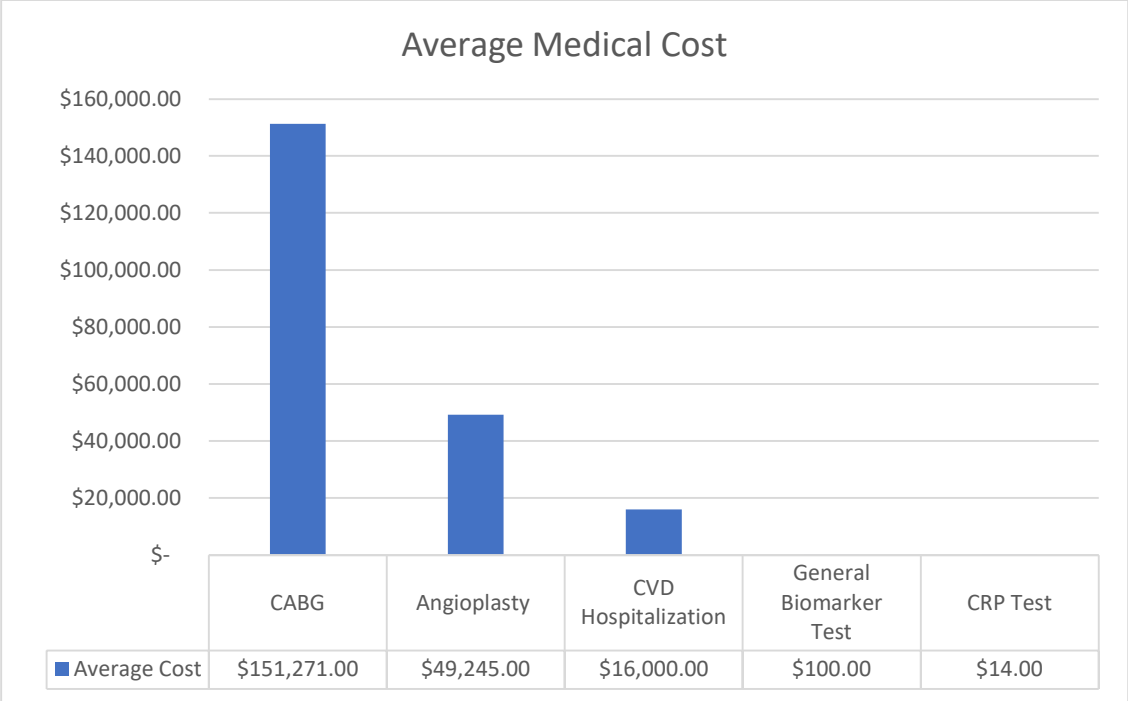

Figure 1: This figure outlines the medical costs of CVD related procedures, non-procedure related CVD hospitalization, and biomarker test prices (Giacomino, et al. 1103; Harvard Health Publishing; Kilgore, et al. 63; Sen, et al. 210). The investment of time, resources, and money into biomarker testing lessens the risk of more serious, expensive, life-threatening procedures through early detection and prevention.

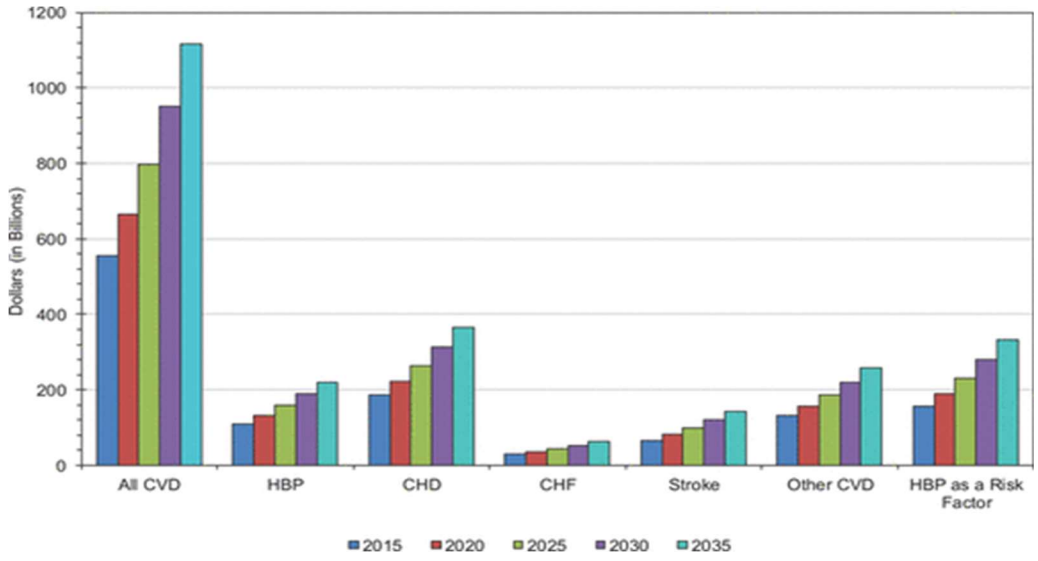

Figure 2: This figure outlines a cost breakdown for CVDs showing an increase in cost through 2035 (Virani, et. al. 337). CVD indicates cardiovascular disease; HBP, high blood pressure; CHD, coronary heart disease; and CHF, congestive heart failure. This data shows how significant the increase in cost is for CVD in the United States. This increase in cost will continue to increase as the relevance of CVD increases.

The field of cardio-oncology is new, and the growth of practice and research in this field provides a promising future for cancer patients experiencing the cardiotoxic effects of cancer treatment. Using preventative measures such as monitoring biomarkers has promise in changing the outlook of treatment for female breast cancer patients, as it offers a way to individualize and adapt treatment to minimize cardiovascular damage in every patient. Monitoring of biomarkers that signal cardiovascular damage will allow medical professionals to understand how their patient is being affected by the treatment, and it gives them time to alter the treatment plan to safely reduce the damage being done while still successfully treating the cancer. There are many strategies and pharmacological approaches to the reduction of cardiovascular damage in patients

receiving chemotherapy. Cardioprotective drugs, adjustments in chemotherapy administration timelines, changes in chemotherapy agents used, and many other techniques have shown promise in managing cardiovascular damage if administered early in the treatment process. Studies such as the Cardiac CARE trial are attempting to determine the effectiveness of different treatment options to reduce cardiovascular damage (MacLean).

Clinical application of biomarkers as possible predictive tools for CVD in breast cancer patients has yet to be established on a large scale. Exact timelines for biomarker testing administration can be developed upon further experimentation and normalization of protocol outside of controlled trials through collaborative usage of SEER databases and the determination of the most accurate results. The methodology of experiments reviewing biomarker levels in cancer patients already completed or in progress have similar timelines for testing their patients. First, a baseline is taken before beginning the administration of treatment; then, readings are taken soon after the first administration to obtain a baseline of treatment levels. Next, the biomarker levels are retaken every 3-5 months throughout treatment. Depending on the study, patients were monitored up to three years after termination of treatment to track biomarker levels (Sawaya, et al.; Ky, et al. 811; Garrone, et al. 136). Patients with increased risk of CVD should have more frequent testing to more closely monitor their cardiac health. An example of an experimental timeline tracking biomarker levels and cardiac impairment throughout breast cancer treatment in a patient who is not at increased risk of CVD is shown in figure 3.

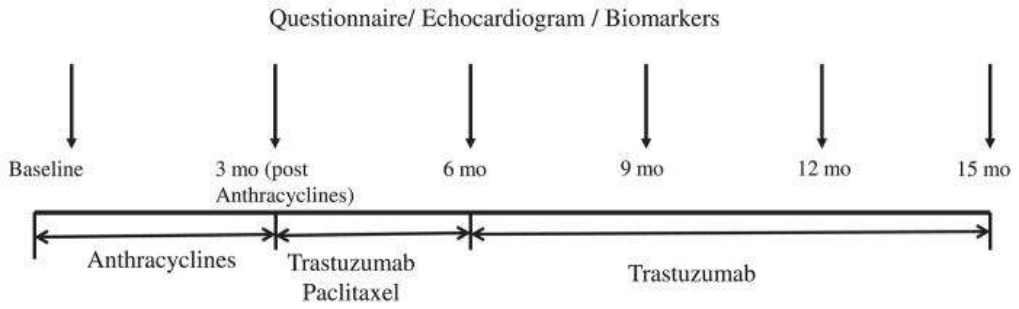

Figure 3: Outlines suggested course of study for administration of questionnaire of cardiac health, an echocardiogram, and blood biomarker testing at various points during treatment (Sawaya, et al.).

Based on the results of this review, high sensitivity cardiac troponins show the most promise as a predictive tool for the detection and prevention of CVD in breast cancer patients. However, CRP, homocysteine, BNP, and lipid profiles could potentially serve as predictive biomarkers as well. These biomarkers could be less accurate as a result of interference from other bodily functions, such as inflammation due to chemotherapy. However, with more extensive research and the development of an accurate timeline of testing, these biomarkers could be useful as predictors of CVD.

Limitations

This study was limited by access to databases that are private or non-disclosed to the public. These databases could possibly contain relevant information to this study, but they were unable to be analyzed for this purpose. Only information that is publicly available was used. There was no funding for this project, so the development of patient testing models was not

possible. Therefore, this study could not conduct trials on patients. Additionally, this study was limited to the biomarkers with known linkage to cardiotoxicity. There may be other biomarkers better suited for this study that have yet to be discovered or published.

Conclusion

Biomarkers present exciting potential for monitoring chemotherapeutic agent related cardiotoxicity and would allow for quantification of the number of women affected by the cardiotoxicity of the drugs used. They would also offer the opportunity to provide prevention or cessation of any potential or actual cardiac damage. Since these biomarkers are not being routinely monitored, the addition of cardiac biomarkers in the registry application for a database such as SEER would increase the amount of data, quality of predictive mechanisms, and relevance of preventative treatment. All the biomarkers outlined in this review can be used to identify the women treated for breast cancer who develop cardiovascular complications such as CVD. The biomarkers CRP, homocysteine, lipid profiles, and cardiac troponins show the most promise of being used as markers to guide preventative care for women if they are correctly monitored. However, each biomarker has varying levels of accuracy. Changes in these biomarkers are indicative of worsening cardiac health and can be used to predict future cardiovascular events. This would create an opportunity for an adjusted plan of treatment to reduce cardiovascular damage.

Future Research

Further research and implementation of these predictive measures is important. A machine learning algorithm could be used to offer a more individualized breast cancer treatment plan after training it with known patient data and outcomes. Other possible predictors or indicators such as genomic information, ventricular function, or wall thickness should be explored.

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