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THE INTERRELATIONSHIP BETWEEN TREATMENT, ETHNICITY, AND STRUCTURED EXERCISE IN CLINICAL POPULATIONS

Amanda M. F. Lopez
University of the Pacific

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By

Amanda Marie Figueroa Lopez

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Amanda Marie Figueroa Lopez

APPROVED BY:

Dissertation Advisor: Courtney Jensen, Ph.D.

Committee Member: Mark Van Ness, Ph.D.

Committee Member: Paul Vosti, M.A.

Department Chair: Mark Van Ness, Ph.D.

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DEDICATION

This thesis is dedicated to my husband, Roy Zapata. It has been an experience! Thank you for always being my biggest fan, impelling me to be selfish and pursue my education, and never allowing me to give up on my aspiration of earning my Ph.D. You've been the light and balance I needed in the toughest moments throughout this master's program. Without your constant support and love, I wouldn't have confidently accomplished as much as I have. I can't wait for our next adventure together with our boys whether it's here in California or another state. From the bottom of my heart, thank you.

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Dr. Jensen, thank you for your guidance and patience with me while I struggled to get through these years while balancing school with work and home life. As I reflect on my first undergraduate year as a transfer student I was hopeless and wanted desperately to get out of the biochemistry program. I am a completely different student because of your encouragement and teaching! HESP 129 was the start of loving research and human physiology. You pushed me out of my comfort zone, gave me confidence in my capabilities, and expanded my potential. Thank you for bringing joy to challenges and literature. I hope to be as impactful as you’ve been.

THE INTERRELATIONSHIP BETWEEN TREATMENT, ETHNICITY, AND STRUCTURED EXERCISE IN CLINICAL POPULATIONS

Abstract

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Cancer is the second leading cause of death, with about approximately 1.9 million Americans being diagnosed each year. Yet, it has high survival rates with the help of advancing treatments like radiation therapy. Cancer patients and survivors are contingent on experiencing a decline in physical functioning, quality of life, and physiological parameters. Treatment is effective and can prolong life expectancy but can be deleterious to a patient's health. Parallel with cancer's impact on Americans is cardiovascular disease. Cardiovascular disease is responsible for 1 in 4 deaths. The development of cardiovascular disease is not spread accordantly among all ethnicities. Hispanics are more likely to have a type of cardiovascular disease. Structured exercise has consistently been established to be an effective countermeasure for diminishing cardiovascular risk factors, adverse side effects, and symptoms of cancer and cancer treatment. The purpose of this thesis is to evaluate the effect of structured exercise to address 3 questions with limited data. The evaluation included the incidence of cardiovascular disease in at-risk Hispanics, physiological adaptions to a structured exercise program, and the effect of radiation therapy on exercise outcomes. Subjects for each study were enrolled in a 10-week structured exercise program consisting of aerobic, resistance, and flexibility exercises.

Conclusions were no difference in exercise benefits in ethnicity but exercise did improve cancer survivors' physical functioning in all domains.

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CHAPTER 1: INTRODUCTION

It is predicted that in 2022 approximately 1.9 billion people will be diagnosed with cancer worldwide (Siegel et al., 2021). Cancer is a "multigenic and multicellular disease that can arise from all cell types and organs with a multi-factorial etiology," (Baskar et al., 2012). In the United States, approximately 1.9 million Americans are diagnosed with cancer each year, that's about 5,000 new cases each day. An estimated 600,000 people in the United States will die from cancer, securing it the second leading cause of death (CDC, 2022). In spite of that, there are over 12 million cancer survivors and with advancements in treatment and diagnosis, the number is expected to grow to over 20 million by 2026 (Miller et al., 2016).

A few cancer treatment approaches consist of radiation therapy, chemotherapy, surgery, immunotherapy, and hormonal therapy (Wang et al., 2018). Radiation therapy (RT), also known as radiotherapy, treats approximately 50% of cancer patients and has become an essential and effective modality implemented in worldwide cancer care (Baskar et al., 2012). Its continuous advancements since it was first attempted in 1896 by Emil Grubee administer the potential for it to improve the rates of cure of 3.5 million people each year (Jaffray and Gospodarowicz, 2015). The benefits of RT encompass cost-efficiency, prolonged life expectancy, organ preservation, and control of tumor growth (Thariat et al., 2013).

Cancer is not a universal disease that is characterized to be equivalent among all survivors. Cancer is characterized by the dissimilarity of the individual cancer survivor (age, gender, race, comorbidities, etc.) and disease presentation (tissue, location, stage, etc.), of the nature that corresponds with the diversity of psychological and physical consequences patients face (Brown et al., 2012). There are psychological and physical symptoms and side effects that nearly all cancer survivors are subject to experience (Schmitz et al., 2010). Physical effects include elevated cardiovascular risks, fatigue, pulmonary dysfunction, sexual dysfunction, lymphedema, neuropathy, cognitive dysfunction, deterioration in body composition, musculoskeletal issues, and diminished physical function (Gegechkori et al., 2017). Due to compromised physical function compounding many of the other symptoms, it positions cancer survivors in a vulnerable place to obtain additional health concerns, including early death (Brown et al., 2012).

Ahead of cancer leading the cause of death is heart disease, which is one of the conditions of cardiovascular disease (CVD) which affects the heart and blood vessels (World Health Organization, 2022). In 2020, deaths attributed to CVD increased by 18.7% from 2010 to a total of approximately 19 million (Virani et al., 2022). There are known predictors (e.g., obesity, hypertension, and dyslipidemia) that increase the odds of developing CVD but it is dependent on the level of progression. However, the risk is not proportionate among all ethnicities (Ferdinand et al., 2017). Despite increases in diabetes and obesity in lower socioeconomic groups, Hispanic Americans often display markers of elevated risk. Current research subsumes persistent evidence that illustrates Hispanics being affected by excessive rates of cardiovascular risk factors even after adjusting for age, body mass index, and socioeconomic status (Shaw et al., 2018). While Hispanic Americans often display markers of elevated risk, they have longer life expectancies than their non-Hispanic counterparts (Swenson et al., 2002). An understanding of the distribution and contribution of risk factors among different ethnic groups may help in specifying treatment interventions more appropriately.

An antidote to the ramifications of cancer and CVD is exercise. Exercise is low cost and accessible for all. Consistent data demonstrates exercise programs improve cancer-related symptoms and cancer treatment-related side effects, and health-related quality of life (Silver et al., 2015). Exercise during and after adjuvant cancer therapy, such as RT, serves as an effective method to subdue negative psychological and physical side effects and symptoms from cancer and treatment, limit disease progression, and directly benefit cancer treatment (Schmitz et al., 2010; Brown et al., 2012). In regards to CVD, increasing levels of exercise improve cardiorespiratory fitness levels for all ages, races, ethnicity, and both sexes which is effective in the prevention of CVD (Lavie et al., 2019). Cardiorespiratory fitness is significant to enhance the strength of the physiological benefits including reduced blood pressure, improved heart rate variability, improved insulin sensitivity, reduction in hypertension, and reduction in depression that goes well beyond the obviation of the progression of CVD (Nauman et al., 2017).

Cancer and CVD, are the two utmost impactful diseases people encounter worldwide. The problem we confront is established that cancer and cancer treatment effects and symptoms have consequences detrimental to one's health. The other problem is the disproportionate differences in CVD risk factors among at-risk Hispanic and non-Hispanic adults.

This thesis will address three questions with limited data. The three questions I seek to bring additional findings to are; is structured exercise effective in improving cardiovascular and functional capabilities in cancer survivors, are Hispanics more vulnerable to CVD risk factors, and the incidence of adverse cardiovascular events, and lastly how does RT affect structured exercise outcomes in cancer survivors.

Above I mention three areas with limited research on clinical populations and I found structured exercise to improve physical functioning in nearly every domain and to benefit Hispanic and non-Hispanic subjects similarly. In the population of cancer survivors, we found exercise to improve strength, aerobic capacity, and flexibility. Also, we observed that structured exercise may be an effective way to mitigate some of the health consequences associated with radiation therapy.

CHAPTER 2: EXERCISE AND THE CANCER PATIENT: FUNCTION IMPROVES INDEPENDENT OF CARDIOVASCULAR AND ANTHROPOMETRIC CHANGES

Abstract

Background

Each year, approximately 1.9 million Americans are diagnosed with cancer, that's about 5,000 new cases each day. The consequences of cancer and its associated treatment include elevations in cardiovascular risk, deteriorating body composition, and diminishing physical function. Exercise is an effective countermeasure; however, limitations in adherence may compromise the magnitude of improvement experienced.

Purpose. To evaluate cardiovascular, anthropometric, and functional adaptations to an exercise program in cancer survivors.

Methods. We conducted a 10-week exercise intervention on 157 cancer survivors; 58 were retained through follow-up. At baseline, we recorded demographic, anthropometric, cardiovascular, and functional data. Anthropometric measurements were weight, body mass index (BMI), and body fat percent (BF%). Cardiovascular measurements were blood pressure and heart rate. Functional tests were VO2 max, six-minute walk, timed up-and-go, chair stand, sit-to-stand, arm curl, grip strength, Universal Machine (UM) push and pull, epic lift, sit-and-reach, functional reach, and back scratch. Paired-samples t-tests measured changes from baseline to follow-up.

Results. Anthropometric variables did not change: body weight ($p=0.585$), BMI ($p=0.477$), and BF% ($p=0.367$). Cardiovascular variables did not change: systolic blood pressure ($p=0.560$), diastolic pressure ($p=0.292$), and heart rate ($p=1.000$). Improvement was detected in 11 of 13 functional tests: VO2 max ($p=0.005$), six-minute walk ($p<0.001$), timed up-and-go ($p<0.001$), chair stand ($p<0.001$), sit-to-stand ($p=0.005$), arm curl ($p<0.001$), grip strength ($p<0.001$), UM push ($p<0.001$), UM pull ($p<0.001$), epic lift ($p=0.005$), and functional reach ($p=0.001$). Mean values improved in sit-and-reach ($p=0.321$) and back-scratch ($p=0.099$), but pre-post comparisons were not significant.

Conclusion. Exercise did not affect anthropometric or cardiovascular profiles, but physical functioning improved in nearly every domain. In this population, maintenance of functional capacity can help preserve the ability to perform tasks of daily living, and it is associated with survival. Although we found exercise to improve strength, aerobic capacity, and flexibility, the high rate of attrition is a potential limitation; further research is necessary to confirm our findings.

Introduction

It is predicted that in 2022 approximately 1.9 billion people will be diagnosed with cancer and an estimated 600,000 people in the United States will die from cancer (Siegal et al., 2022). Cancer is the second leading cause of death behind heart disease in the United States (CDC, 2022). Despite being ranked second there are over 12 million cancer survivors and with advancements in treatment and diagnosis, the number is expected to grow to over 20 million by 2026 (Miller et al., 2016). Nearly all cancer survivors are subject to experience psychological and physical symptoms and side effects (Schmitz et al., 2010). The diversity of the individual cancer survivor (age, gender, race, comorbidities, etc.) and disease presentation (tissue, location, stage, etc.) corresponds with the diversity of psychological and physical consequences patients face (Brown et al., 2012). Physical effects include elevated cardiovascular risks, fatigue, pulmonary dysfunction, sexual dysfunction, lymphedema, neuropathy, cognitive dysfunction, deterioration in body composition, musculoskeletal issues, and diminished physical function (Gegechkori et al., 2017). Compromised physical function can compound many of the other symptoms, leaving cancer survivors vulnerable to additional health concerns, including early death (Brown et al., 2012).

Exercise interventions for cancer patients and survivors have been established as safe and beneficial (Schmitz et al., 2010). Recommending the appropriate exercise plan faces a set of challenges and as a result, the prescription is often overlooked by oncology care providers (Stout et al., 2005-2017). Smaradottir et al. (2017) presented that patients consistently reported no recollection of physician-initiated conversations about exercise during treatment. The American

College of Sports Medicine (ACSM) provided guidelines on exercise for cancer survivors and it included the risk-benefit equation and addressed questions of safety and benefits (Wolin et al., 2012). The exercise guidelines by the US Department of Health and Human Services 2008 Physical Activity Guidelines for Americans (PAGA) that provide the type and duration of exercise are the same recommendations for cancer survivors (Table 1) (Wolin et al., 2012).

Table 1.
Summary of PAGA exercise guidelines for Americans. (Wolin et al., 2012)

	Aerobic	Resistance	Flexibility
US Physical Activity Guidelines for Americans (PAGA)	150 min/week of moderate-intensity or 75 min/week of vigorous-intensity activity, or an equivalent combination.	Muscle-strengthening activities of at least moderate intensity at least 2 days/week for each major muscle group	Stretch major muscle groups and tendons on days other activities are performed.

Exercise programs have been used to improve cancer-related symptoms and cancer treatment-related side effects, and health-related quality of life (Silver et al., 2015). Cancer patients' exercise interventions have demonstrated efficacy in improving quality of life domains (QOL), physical functioning, cancer-related fatigue, cardiovascular fitness, sleep quality, psychological and social well-being, and self-esteem (Knobf et al., 2007). In this context, QOL domains include physical, social, psychological, and spiritual areas of one's life. Evidence of the physical benefits of exercise also include improved recovery, decreased adverse side effects before and after treatment, prolonged survival, and reduced risk of cancer recurrence (Rajarajeswaran et al., 2009). Although exercise appears to be an effective countermeasure, limitations in adherence may diminish the magnitude of improvement experienced (Schmitz et al., 2010). In a sample of 57 prostate cancer survivors, participation in a thrice-weekly aerobic, resistance, and flexibility exercise program elicited an increase in physical functioning and lower body muscle strength (Galvão et al., 2018). McGovern et al.'s (2022) meta-analysis summarized during adjuvant chemotherapy and/or radiation therapy 1,910 cancer patients from 20 articles, participated in more than 6 weeks of resistance training which prompted improvements in muscle strength and lean mass. By proper evaluation of cancer patients, post-treatment, and assistance from ACSM cancer survivor exercise guidelines clinicians can prescribe exercise interventions to address complex negative stressors across the cancer control continuum (Schmitz et al., 2010).

The purpose of this paper is to evaluate changes in cardiovascular, anthropometric, and functional adaptations in cancer patients from an exercise program by comparing baseline and follow-up assessments.

Research Hypothesis

There will be a significant augmentation of cardiovascular, anthropometric, and functional adaptations of cancer survivors in an exercise program.

Purpose

The purpose of this paper is to evaluate cardiovascular, anthropometric, and functional adaptations to an exercise program in cancer survivors.

Null Hypothesis

There will be no significant augmentation of cardiovascular, anthropometric, and functional adaptations of cancer survivors in an exercise program.

Delimitations

Noncancer survivors and cancer survivors are not recommended safe to participate by their physicians.

Limitations

This study is not a randomized control trial. Exercise programs were individualized and created by the head clinician. Data collection and assessments were conducted by a single clinician. The low rate of adherence is a potential limitation.

Methodology

Participants/Consent

157 cancer survivors were screened and evaluated by the physician involved in the treatment of the patient to determine that no medical condition would preclude their eligibility for participation at the time of consent. The protocol and signed informed consent were approved by the Institutional Review Boards of the hospital delivering care and the University of

the Pacific. Signed consent was obtained from each participant. Participants' anthropometric, cardiometabolic, and functional changes were measured pre-and post-training.

Data Collection

At baseline and follow-up, a single clinician conducted all assessments. The sample consisted of 157 cancer patients and 58 completed the study. Anthropometric measurements were weight, body mass index (BMI), and body fat percent (BF%). Cardiovascular measurements were blood pressure (systolic and diastolic blood pressure) and resting heart rate. Physical functional tests were VO2 max, six-minute walk, timed up-and-go, timed sit-to-stand, chair stand, arm curl, grip strength, Universal Machine (UM) push and pull, epic lift, sit-and-reach, functional reach, and back scratch.

Exercise Intervention

Subjects participated in supervised biweekly group exercise classes that included aerobic, flexibility, and resistance training components for 10 weeks. Exercise programs were created by the head clinician and specific to each individual. Four aerobic exercises were performed in six-minute intervals, for a total of 24 aerobic minutes. Aerobic exercises included; treadmill, Nu-Step, UBE, and recumbent bike. Patients were asked to exert themselves between 60-75% of maximum heart rate. If the patient was on heart medication, they were asked to exert themselves at a score between 12–14 via the Borg Rating of Perceived Exertion. Various resistance exercises were performed; chest press, latissimus dorsi pulldowns, triceps extensions, standing rows with therabands, bicep curls, wall squats, and step-ups. At the end of the exercise program, all patients were reevaluated by the same clinician that conducted their baseline assessments. No major adverse events were reported.

Statistical Analysis

All statistical tests were conducted using SPSS version 24 (IBM SPSS Statistics, IBM Corporation, Chicago, IL, USA). Descriptive statistics calculated sample characteristics at baseline. Baseline data were compared to follow-up data using paired-samples t-tests on all individuals who completed the study. Significance was set at $p<0.05$. Predictors that did not meet significance were not included and were removed from the model.

Results

We conducted the intervention with 157 cancer patients at baseline and 99 subjects did not complete the study. Changes are among subjects who completed the study (n=58).

Anthropometric Variables

There were no significant differences between pre-and post-training of anthropometric measurements (Figure 1). At follow-up subjects BMI (p=0.585) and body fat percentage (p= 0.477) did not change.

Cardiovascular Variables

There were no significant differences between pre-and post-training of cardiovascular measurements (Figure 1). At follow-up subjects resting heart rate (p= 1.000), systolic blood pressure (p= 0.560), and diastolic blood pressure (p= 0.292) did not change.

Functional Tests

All physical function assessments are displayed in Figure 2. All measures of physical function were significantly increased in the post-assessment in comparison to the pre-assessment. Improvements in VO2 max (p=0.005), timed up-and-go ($p<0.001$), chair stand ($p<0.001$), arm curl ($p<0.001$), grip strength ($p<0.001$), UM push ($p<0.001$), UM pull ($p<0.001$), epic lift (p=0.005), sit-to-stand (p=0.005), and functional reach (p=0.001) (see Table 2 and Table 3 for all improvements). Figure 3 illustrates patients' improvement in a six-minute walk (p<0.001). Table 2 displays mean values improved in sit-and-reach (p=0.321) and back-scratch (p=0.099), but pre-post comparisons were not significant.

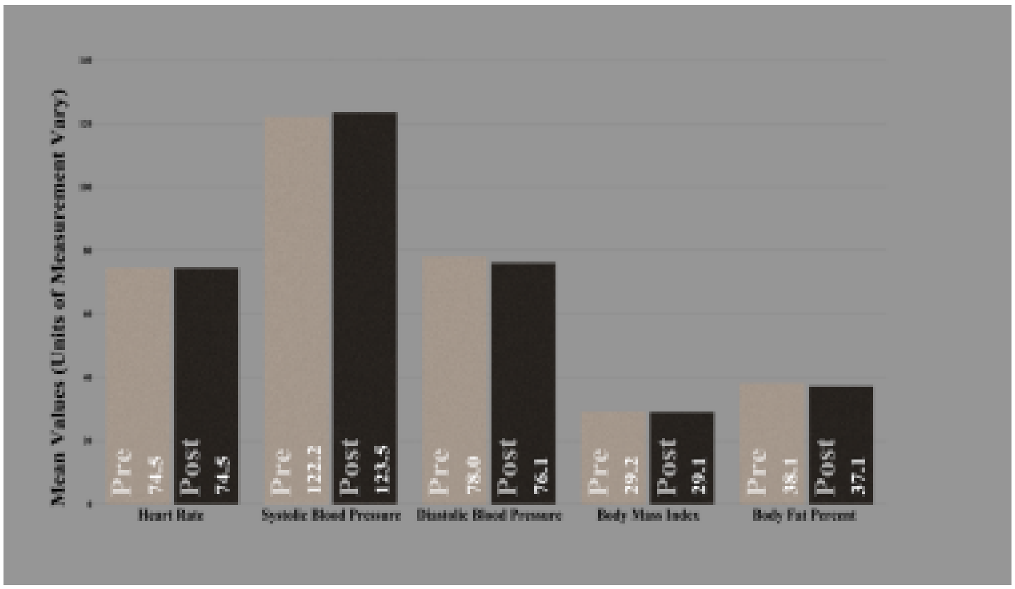

Figure 1. Cardiovascular and anthropometric assessment comparison of pre-and post- values.

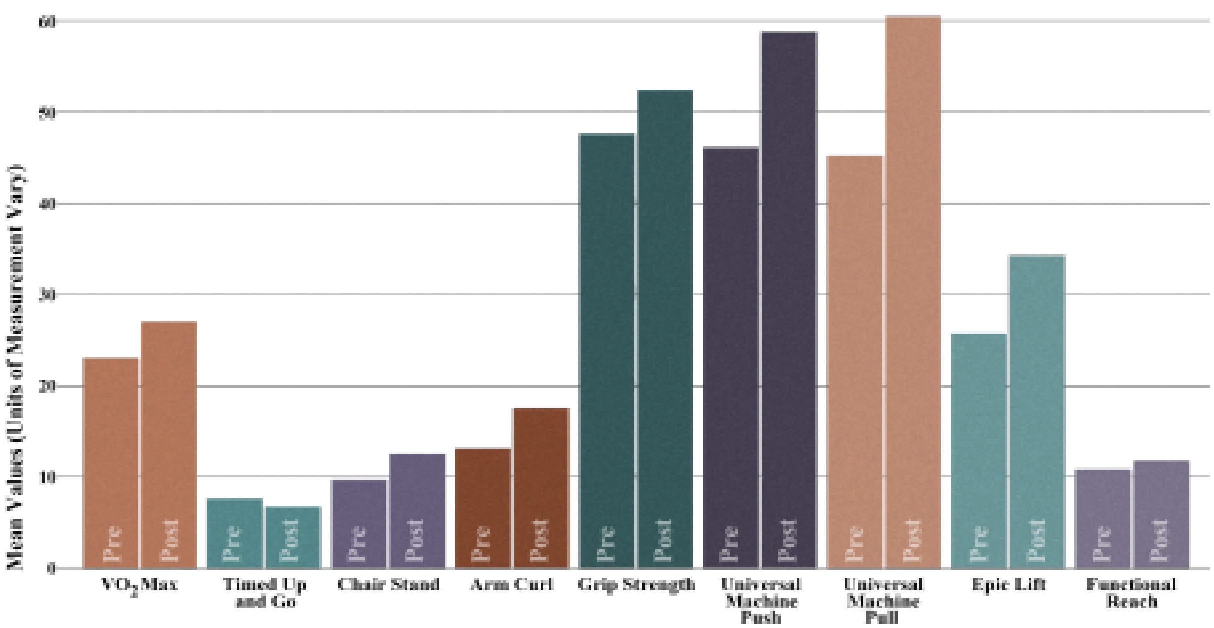

Figure 2. Physical function assessments comparison of pre-and post- values; displayed significant improvements (p<0.05)

Table 2

Physical functioning variables pre-and post- values using paired samples t-tests.

Physical Function Variables	Pre	Post	Sig.
Timed Up and Go (sec)	7.7 ± 2.8	6.8 ± 2.9	<0.001
Arm Curl (lbs)	13.1 ± 3.1	17.5 ± 3.7	<0.001
Grip Strength (kg)	47.6 ± 11.7	52.4 ± 11.5	<0.001
UTM Push (lbs)	47.7 ± 20.3	59.1 ± 25.0	0.001
UTM Pull (lbs)	44.8 ± 16.7	54.0 ± 18.5	<0.001
Epic Lift (lbs)	25.7 ± 13.4	34.3 ± 15.0	0.005
Functional Reach (cm)	10.8 ± 2.8	11.7 ± 3.4	0.002
Chair Stand	9.7 ± 2.4	12.5 ± 3.6	<0.001
Sit and Reach (cm)	-1.0 ± 5.8	-0.3 ± 4.0	0.321
Back Scratch (cm)	-3.3 ± 8.7	-2.6 ± 7.6	0.099
Timed Sit-to-Stand (sec)	14.4 ± 5.2	12.3 ± 4.6	0.005
Six-minute Walk (m)	399.9 ± 98.4	451.5 ± 104.5	<0.001

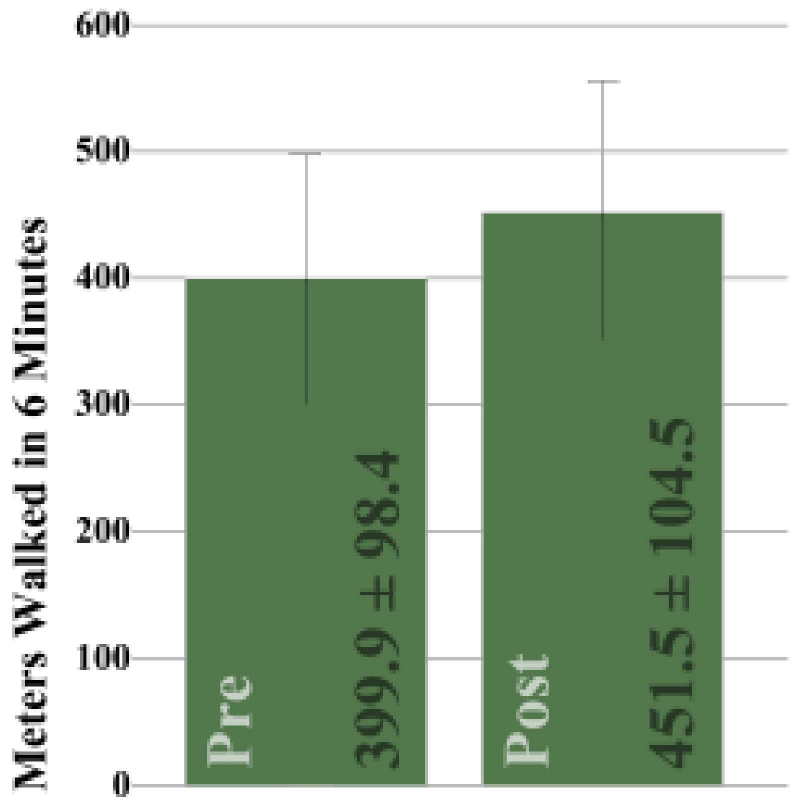

Figure 3. Six-minute walk pre- and post- values.

Table 3
Cardiometabolic variables pre- and post- values.

Cardiometabolic Variables	Pre	Post	Sig.
Resting Heart Rate	74.5 ± 13.3	74.5 ± 11.3	1.000
Weight (lbs)	171.4 ± 38.3	170.8 ± 36.4	0.585
BMI (kg/m^2)	29.2 ± 6.7	29.1 ± 6.4	0.477
Body Fat (%)	38.1 ± 7.2	37.1 ± 7.3	0.367
SBP (mmHg)	122.2 ± 14.6	123.5 ± 13.0	0.560
DBP (mmHg)	78.0 ± 9.9	76.1 ± 8.3	0.292
Mean Arterial Pressure	91.8 ± 8.4	92.3 ± 8.7	0.718
Pulse Pressure	44.5 ± 12.8	47.0 ± 10.8	0.177
VO_2 Max	22.6 ± 6.9	26.6 ± 4.0	0.008

Discussion

Since the mid-1970s decreases in cancer mortality rates have been improving in almost all cancer types, specifically in lung, breast, prostate, and colorectal (Siegel et al., 2021). Seigel et al. (2021) statistical analysis reported a decline of 31% translating to approximately 3.2 million fewer cancer deaths. Decline death rates are attributable to advancements in diagnosis, management, and treatment (Sherman et al., 2005). As survival rates have increased and continue to do so, so have interest in exercise programs for cancer patients. Exercise-oncology is a new field of cancer care clinicians acquire intending to introduce exercise programs in the management of cancer patients to receive benefits associated with exercises such as improvements in QOL, fatigue, cardiovascular fitness, and body composition (Pollán et al., 2020). Adopting exercise is becoming an important focus of attention because of the aid. In the National Cancer Institute Cancer Trends Progress Report, the section on Cancer survivors and physical activity stated in 2018 34% of cancer patients 18 years and older reported no physical activity as compared to over 50% in 1997.

Our study evaluated the effects of cardiovascular, anthropometric, and functional capacity of a 10-week exercise program that consisted of biweekly classes incorporating aerobic, flexibility, and resistance training. The results exhibited favorable improvements in strength, aerobic capacity, and flexibility at follow-up when compared to baseline. The duration of the exercise program totaling 20 supervised exercise sessions had a positive impact. The improvements in physical functioning align with prior meta-analysis and support the effectiveness of exercise for cancer patients. Juvet et al., (2017) systematic review reported short-term improvements in physical functioning and reduced fatigue in breast cancer patients from supervised exercise programs. The impact of exercise programs was also identified to have beneficial outcomes of treatment side effects, tolerance to cancer treatments, and physical function (Stout et al., 2005-2017).

Although our findings did not show a change in anthropometric variables, other interventions were longer in duration as demonstrated in the meta-analysis published by Strasser et al. The meta-analysis found that 2-3 days of whole-body resistance training 12 weeks to 6 months increases muscular strength, corrects muscular deficiencies, improves body composition in the short and long term, and it improves pain and range of motion (Strasser et al., 2013). This might explain why no change in body composition or fat percentage was found.

Conclusion

In conclusion, our findings illustrated significant physical functioning improvements at follow-up, 11 of the 13 domains showed improvements. It provides evidence that supervised exercise is safe and effective among cancer patients. These findings are useful to help guide clinicians in exercise prescription and planning for cancer patients. However, the intervention demonstrated no changes in body composition (weight, BMI, body fat percentage) or cardiometabolic parameters (heart rate or blood pressure). The high rate of attrition is a potential limitation. Further research is necessary to confirm our findings.

CHAPTER 3: THE ROLE OF ETHNICITY IN DEVELOPING CARDIOVASCULAR DISEASE IN AT-RISK POPULATIONS

Abstract

Background

In the U.S., cardiovascular disease (CVD) is responsible for 1 in 4 deaths. There are known predictors (e.g., obesity, hypertension, and dyslipidemia) that increase the odds of developing CVD; however, the risk is not proportionate among all ethnicities. While Hispanic Americans often display markers of elevated risk, they have longer life expectancies than their non-Hispanic counterparts. Further exploration of this phenomenon is necessary to elucidate how risk engenders disease in different ethnic groups.

Purpose. To evaluate CVD risk factors and the incidence of adverse cardiovascular events among at-risk Hispanic and non-Hispanic adults.

Methods. We enrolled 10 Hispanic and 41 non-Hispanic men and women with Type 2 diabetes in a 10-week exercise program. Prior to initiating exercise, we documented demographic data, collected a health history, conducted 7 tests of physical functioning, and measured cardiometabolic variables, including body mass index (BMI), body fat percent (BF%), blood pressure, heart rate, and HBA1C. We repeated all assessments following the intervention. Differences between ethnic groups in baseline values and exercise responses were evaluated with independent-samples t-tests and chi-squared tests.

Results. Hispanic subjects had fewer diagnoses of hypertension ($p=0.002$) and no history of heart attack, compared to 25% incidence among non-Hispanics ($p=0.077$). Hispanic subjects were 8.1 years younger ($p=0.032$), 40% of them smoked (compared to 0%; $p<0.001$), and they

had better body compositions as measured by BMI (p=0.038), BF% (p=0.021), and categorical obesity (p=0.030). Physical functioning was slightly better among Hispanic subjects as measured by the 6-minute walk (p=0.010) and functional reach (p=0.029). Participants who completed the exercise program experienced an improvement in all assessments but grip strength; there were no differences in improvement between ethnic groups.

Conclusion. We found exercise to benefit Hispanic and non-Hispanic subjects similarly. Hispanic adults with diabetes had a lower incidence of heart attacks. This may be attributable to observed anthropometric differences; however, if nutritional or behavior customs confer cardio-protective effects in this population, future researchers need to identify those variables.

Introduction

It is estimated that 92.1 million US adults have at least one type of cardiovascular disease (CVD) and by 2030 43.9% of the US adult population will have some form of CVD (Benjamin et al., 2017). Hispanics account for 18.5% of the US population based on the U.S. Census Bureau and are the fastest-growing ethnic group. They symbolize the diversity of the United States and are expected to constitute 30% of the US population by 2050 (Rodriguez et al., 2014). The U.S. Office of Management and Budget (OMB) defines Hispanics or Latino as “a person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin regardless of race”. Hispanic is an ethnic-based term that is independent of race (Aguayo-Mazzucato et al., 2019). “Race mainly alludes to physical characteristics that are genetically determined, while ethnicity relates to a perceived cultural distinctiveness, expressed in language, music, values, art, styles, literature, family life, religion, ritual, food, naming, public life, and culture” (Caballero, 2007). Despite their growing numbers Hispanics endure health disparities, specifically in categories that increase the prevalence of CVD.

In 2020, deaths attributed to CVD increased by 18.7% from 2010 to a total of approximately 19 million (Virani et al., 2022). But, risk factors are not proportionate among all ethnicities (Ferdinand et al., 2017). These risk factors that contribute to CVD are influential because depending on the level they can advance the prevalence of CVD. Knowing the level of risk factors present begins the prescription of treatment and management for preventative measures. There are fixed risk factors such as genetics and modifiable risk factors such as physical inactivity, unhealthful nutrition, dyslipidemia, hyperglycemia, high blood pressure, obesity, thrombosis/smoking, kidney dysfunctions, and hypercholesterolemia (Bays, 2020). The Center for Disease Control (CDC) presented an illustration of disparities among race and ethnic groups in the US with hypertension and results revealed that 28% non-Hispanic whites, 41.2% non-Hispanic blacks, 24.9% non-Hispanic Asians, and 25.9% of Hispanics had hypertension (Figure 4). The American Heart Association reported from 2015 to 2018 US Hispanic adults 20 years of age or older who had CVD were 52.3% females and 42.7% males. There is persistent evidence that shows Hispanics are affected by excessive rates of cardiovascular risk factors even after adjusting for age, body mass index, and socioeconomic status (Shaw et al., 2018). Interestingly, Hispanics have higher rates of life expectancy (Swenson et al., 2002). Thus, it is important to elucidate how risk factors engender disease in different ethnic groups. The identification of risk factors associated with different ethnic groups can help specify treatment interventions more appropriately and enhance our understanding of differences that could contribute to CVD. Such knowledge has implications for what behaviors should be modified that are crucial in sustaining low prerequisites of CVD.

We were interested in describing research findings on the differences in the contributions of CVD risk factors among at-risk Hispanics and non-Hispanics. The study is ongoing, so only the preliminary data were available for analysis.

Research Hypothesis

There will be significant differences in CVD risk factors among at-risk among at-risk Hispanic and non-Hispanic adults.

There will be significant differences in the incidence of adverse cardiovascular events among at-risk Hispanic and non-Hispanic adults.

Purpose

The purpose of this study is to evaluate CVD risk factors and the incidence of adverse cardiovascular events among at-risk Hispanic and non-Hispanic adults.

Null Hypothesis

There will be no significant differences in CVD risk factors among at-risk Hispanic and non-Hispanic adults.

There will be no significant differences in the incidence of adverse cardiovascular events among at-risk Hispanic and non-Hispanic adults.

Delimitations

Not at-risk Hispanic and non-Hispanic adults.

Patients not diabetic.

Limitations

The study is not a randomized control trial.

All subjects are permitted by their physician to participate in the study.

Subject honesty when reporting ethnicity.

Review of the Literature

Cardiovascular Disease

CVD is the leading cause of morbidity and mortality in developed and undeveloped countries regardless of race, gender, and ethnicity (Widmer et al., 2015). The CDC reported it is responsible for 1 of every 3 deaths and estimated annual costs are 273 billion and 444 billion. CVD is defined by the NHS as "a general term for conditions affecting the heart or blood vessels." It is a chronic disease that gradually develops throughout a lifetime (Francula-Zaninovic and Nola, 2018). The American Heart Association (AHA) explained CVD can refer to several conditions such as heart disease, heart attack, stroke, heart failure, arrhythmia, and heart valve problems. The CDC elucidated that the most common underlying cause of the development is atherosclerosis, a lipid storage disease where arteries become clogged with plaque, hardening and narrowing arteries which then restricts blood flow and oxygen supply to different parts of the body which can lead to blood clots and ultimately stroke and heart attack. Once symptoms begin to occur CVD has more likely to progress to an advanced stage where it causes the disability-adjusted life years leading to the loss of productivity (Perks et al., 2012).

Cardiovascular Risk Factors and Hispanics

CVD risk factors are separated into two categories, modifiable and non-modifiable risk factors. Modifiable risk factors include hypertension, tobacco use, diabetes mellitus, physical inactivity, obesity, unhealthy diet, cholesterol and lipids, depression and anxiety, and stress. Non-modifiable risks include age, gender, genetics, and family history (Balakumar et al., 2016). Hispanics have higher CVD risk profiles than non-Hispanics such as type 2 diabetes, obesity, lipid abnormalities, lower socioeconomic status, and lower levels of education and physical activity but according to death certificates, Hispanics have lower CVD mortality than non-Hispanics (Shaw et al., 2018). For instance, Latinos, a minority group, are 15% more likely to be obese and 65% more likely to have diabetes than non-Hispanic whites (Silfee et al., 2017).

Hispanics have higher rates of precursors of CVD and simultaneously have better life expectancies along with lower heart disease mortality, it is a phenomenon known as the Hispanic Paradox but why is not fully understood (Cortes-Bergoderi et al., 2013; Rodriguez et al., 2014). The reliance on death certificates for determining the reasons for mortality has the potential to be flawed (Cortes-Bergoderi et al., 2013). In the meta-analysis by Cortes-Bergoderi et al. (2013) they examined; data collected from 1950 to 2009 from 341 publications of which 17 fulfilled the inclusion criteria, 22,340,554 Hispanics, and 88,824,618 non-Hispanic whites, confirmed the existence of the Hispanic paradox regarding CVD mortality. There are theories explaining the paradox such as diets rich in fruit and legumes, more social support, the presence of family, Hispanics who migrate being healthier, and Hispanics are returning to their home country to retire or die (Shaw et al., 2017; Gallo et al., 2009). Another reason for the low mortality is a hypothesis theory called the “salmon bias,” this is when foreign-born Hispanics who have been living in the United States for some time leave and return to their country of origin when their health begins to deteriorate to live the remainder of their life, this migration leaves mortality of US Hispanics lower (Turra et al., 2008).

Prevention of Cardiovascular Disease

CVD prevention is defined as a co-oriented set of actions, at the public and individual level, aimed at eradicating, eliminating, or minimizing the impact of CVDs and their related disability (Perk et al., 2012). The World Health Organization (WHO) reported reduction should be based on three points: surveillance (map and monitor the epidemic of CVDs), prevention (reduce exposures to risk factors), and management (equitable health care for people with CVDs) (Alwan, 2011). Furthermore, the WHO stated mortality from CVD can be prevented by over three-quarters by sufficient lifestyle changes. Nonmodifiable risk factors that are invariable are age, genetics, and gender. Since those risk factors are fixed we considered the variables we can adjust and the effect of adjustments.

Modifiable risk factors are those variables that can be affected by altering behaviors such as terminating smoking, inadequate physical activity, obesity, high cholesterol, high triglycerides, stress, and type 2 diabetes Metellus (Francula-Zaninovic and Nola, 2018). CVD has been difficult to encounter and sustain improvements because of its unceasing advancement over the years. According to Lavie et al. (2019), the leading modifiable risk factors are physical inactivity and sedentary behavior. Increasing levels of exercise improve cardiorespiratory fitness levels for all ages, races, ethnicity, and both sexes which is effective in the prevention of CVD (Lavie et al., 2019). In the observational cohort study by Blair et al. (1996), it was discovered that fit persons with a combination of smoking, high blood pressure, or elevated cholesterol had lower mortality rates than low-fit persons with none of the combination of factors. Hence, exercise has an impact but adherence to it is essential to obtain the benefits. Exercise is low cost and accessible to all. Cardiorespiratory fitness has substantial evidence supporting physiological benefits including reduced blood pressure, improved heart rate variability, improved insulin sensitivity, reduction in hypertension, and reduction in depression that goes well beyond the obviation of the progression of CVD (Nauman et al., 2017).

Another strategy for encountering CVD is pharmacological measures. Data from clinical trials have proven the effectiveness of reducing CVD and total mortality by the use of statins, aspirin, and blood pressure-lowering agents (Bansilal et al., 2015). But, as categorized by the WHO there are barriers to medications that source nonadherence, being patient, condition, treatment, socioeconomic, and health system-related factors (Burkhart and Sabaté, 2003). A randomized control trial to assess the effectiveness of the polypill-based strategy in a population with low socioeconomic status led to reductions in systolic blood pressure and low-density lipoprotein (LDL) cholesterol (Muñoz et al., 2019). Yet, medication treatment has a substantial proportion of subjects who do not adhere to all cardiovascular medications as presented in the systematic review and meta-analysis by the European Heart Journal (Chowdhury et al., 2013).

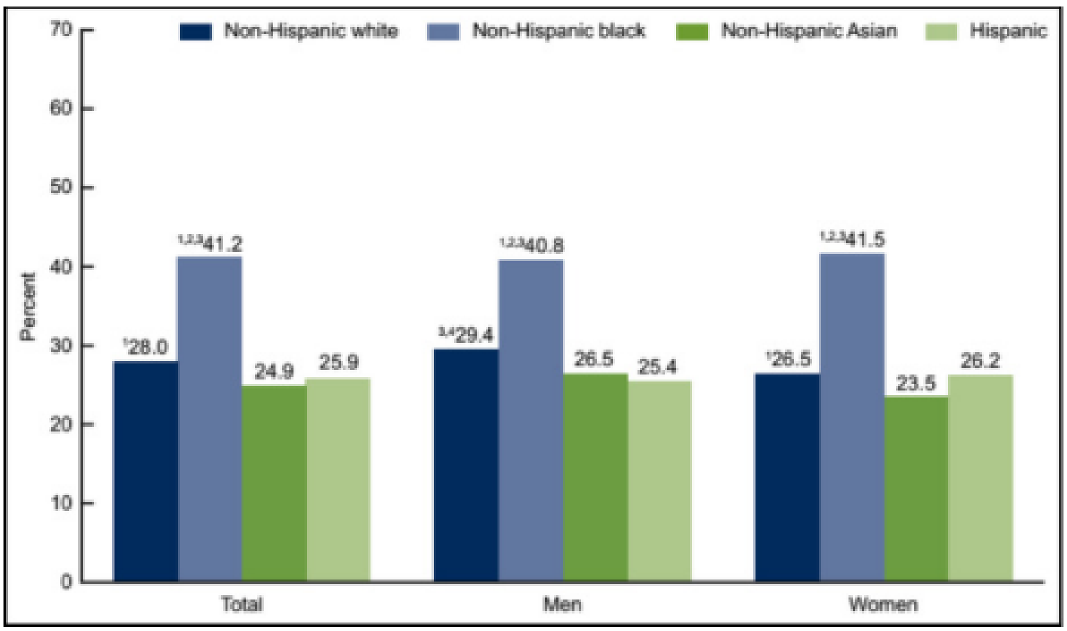

Figure 4. Prevalence of hypertension among adults aged 18 and over, by sex and race and Hispanic origin: the United States, 2011-2014. Source: Centers for Disease Control and Prevention/National Center for Health Statistics, National Health, and Nutrition Examination Survey, 2011-2014. https://www.cdc.gov/nchs/data/databriefs/db220.pdf

Methodology

Subjects

The subjects in the study were all diagnosed with diabetes and were offered an exercise and education class to treat their illness. We evaluated the effect of an exercise program consisting of cardiovascular training, strength training, and flexibility on 67 diabetic patients. Of the 67 subjects, 51 reported their ethnicity. Out of the 51 subjects in the program who reported their ethnicity, 10 Hispanic and 41 non-Hispanic men and women with Type 2 diabetes were used in the comparative analysis. The other 16 subjects that failed to report their ethnicity were randomly assigned to one of two groups; Group 1: Attend exercise class 2x/week and prescribed to walk for an hour 3x/week then log it, Group 2: Attend exercise class 2x/week with no prescribed walking.

Pre-Evaluation

Patients were randomly assigned to groups and evaluated by a single clinician for demographic and health history, anthropometric assessment (body mass index (BMI) and body fat percentage), cardiometabolic risk factors (blood pressure, heart rate, HbA1c), tests of physical functioning (six-minute walk test, timed up-and-go, chair stand test), strength (arm curl and handgrip), flexibility (functional reach, sit-and-reach, back scratch). After the domains of tests, patients completed a quality of life inventory encompassing numerous domains of life.

Exercise Program

For 10 weeks exercise classes were conducted twice per week by the clinician who did baseline testing and assisted by student interns with expertise in group exercise classes. Each day consisted of check-in, exercise, and cool down.

Check-in

Upon arrival, all patients signed in and retrieved their exercise cards that displayed the exercise program, blood pressure, blood glucose, and goal heart rate. Each patient was instructed to obtain and report their blood glucose level according to the reading of their device. A student intern measured patients' systolic and diastolic blood pressure.

Aerobic Exercise

Each aerobic exercise was performed for 6 minutes. The aerobic exercise included: an upper body extremity bike, treadmill, recumbent bike, and the Nu-Step. If the patient was not currently on heart medication, their heart rate was reported by a fingertip oximeter following the completion of each aerobic exercise. Patients were encouraged to exert themselves between 60-75% of maximum heart rate. If the patient was currently on heart medications, the patient reported his or her level of exertion dependent on the Borg Rating of Perceived Exertion (range 6-20). Such patients were encouraged to exert themselves at a score between 12-14.

Resistance Exercise

Resistance exercises consisted of chest press, latissimus dorsi pulldowns, tricep extensions, standing rows, bicep curls, wall squats, and step-ups. On the first day, each patient was required to do one set of ten repetitions, the second day increased to two sets of ten repetitions, and the third day increased to three sets and ten repetitions. Patients continued performing three sets of 10 repetitions for the remainder of the program.

Cooldown

All patients participated in the cool down following the completion of aerobic and resistance exercises. Major muscles of the upper and lower body were stretched for approximately 45 seconds each. Yoga poses were incorporated during the cooldown. The session was concluded with deep breathing exercises.

Post-Evaluation

At the end of 10 weeks, all subjects were reevaluated for anthropometric assessments, cardiometabolic risk factors, physical functioning, strength, and flexibility. Patients in Group 1 submitted a written walking log, quantifying their participation with the walking recommendation throughout the study. All tests were repeated by the same physician who conducted them at baseline.

Statistical Analysis

All statistical analyses were conducted using SPSS version 24 (IBM SPSS Statistics, IBM Corporation, Chicago IL, USA). Differences between Hispanic (n=10) and non-Hispanic (n=41) subjects' baseline values were evaluated using mean comparative analyses. Independent-samples t-tests were run to compare mean differences using the continuous variables; baseline BMI, body fat percent, baseline 6-minute walk, and baseline functional reach. Chi-squared tests were run to identify mean differences using the categorical variables; diagnosis of hypertension, smoking status, and categorical obesity. Subjects that failed to report their ethnicity were excluded from the comparative analysis. Later, frequency and descriptive statistical analyses were run using only excluded subjects. The results from the aforementioned analyses are presented in Table 4.

Results

Overall, Hispanic subjects had greater physical functioning. The remaining variables were higher in both mean and proportion for non-Hispanics. Previous heart attack (p=0.077) and baseline HbA1C (p=0.153) were not statistically significant (Table 4). Categorical variables between Hispanics and non-Hispanics included the diagnosis of hypertension, previous heart attack, smoking status, and categorically obese. There were significant differences between the two subject groups for the following categorical variables; diagnosis of hypertension (p=0.002), smoking status (p<0.001), and categorically obese (p=0.030).There were significant differences between the two subject groups for the following continuous variables seen in Figures 6 and 7. Analysis included baseline BMI (p=0.038), body fat percentage (p=0.021), baseline 6-minute walk (p=0.010), and baseline functional reach (p=0.029). Of these variables smoking status, 6-minute walk, and functional reach were higher in Hispanic subjects.

Table 4

Independent samples t-test and Chi-squared test between Hispanic and Non-Hispanic patients.

Variable	Hispanic	Non-Hispanic	Did Not Report	Significance
N	10	41	16	
Diagnosis of Hypertension	30%	80%	56%	p = 0.002
Previous Heart Attack	0%	25%	13%	p = 0.077
Smoking Status	40%	0%	6%	p < 0.001
BMI (baseline)	29.4 ± 4.2	34.8 ± 6.6	29.6 ± 7.0	p = 0.038
Body Fat % (baseline)	34.8 ± 8.4	40.7 ± 6.6	38.6 ± 5.5	p = 0.021
Categorically Obese	40%	75.6%	31.0%	p = 0.030
6-min walk (baseline)	476.6 ± 83.3	369.4 ± 119.5	408.7 ± 84.4	p = 0.010
Functional Reach-inches (baseline)	12.5 ± 3.4	10.3 ± 2.7	10.6 ± 3.1	p = 0.029
HbA1C (baseline)	7.6 ± 1.4	6.9 ± 1.1	6.8 ± 1.0	p = 0.153

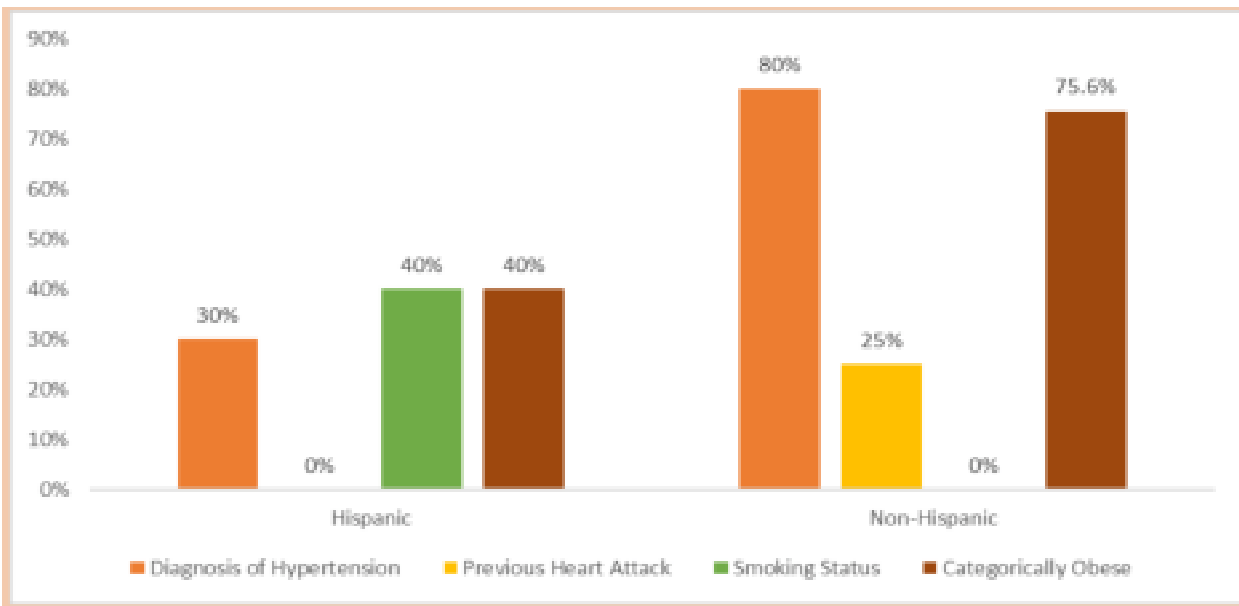

Figure 5. Difference between Hispanic and Non-Hispanic patients for categorical variables using Chi-squared tests.

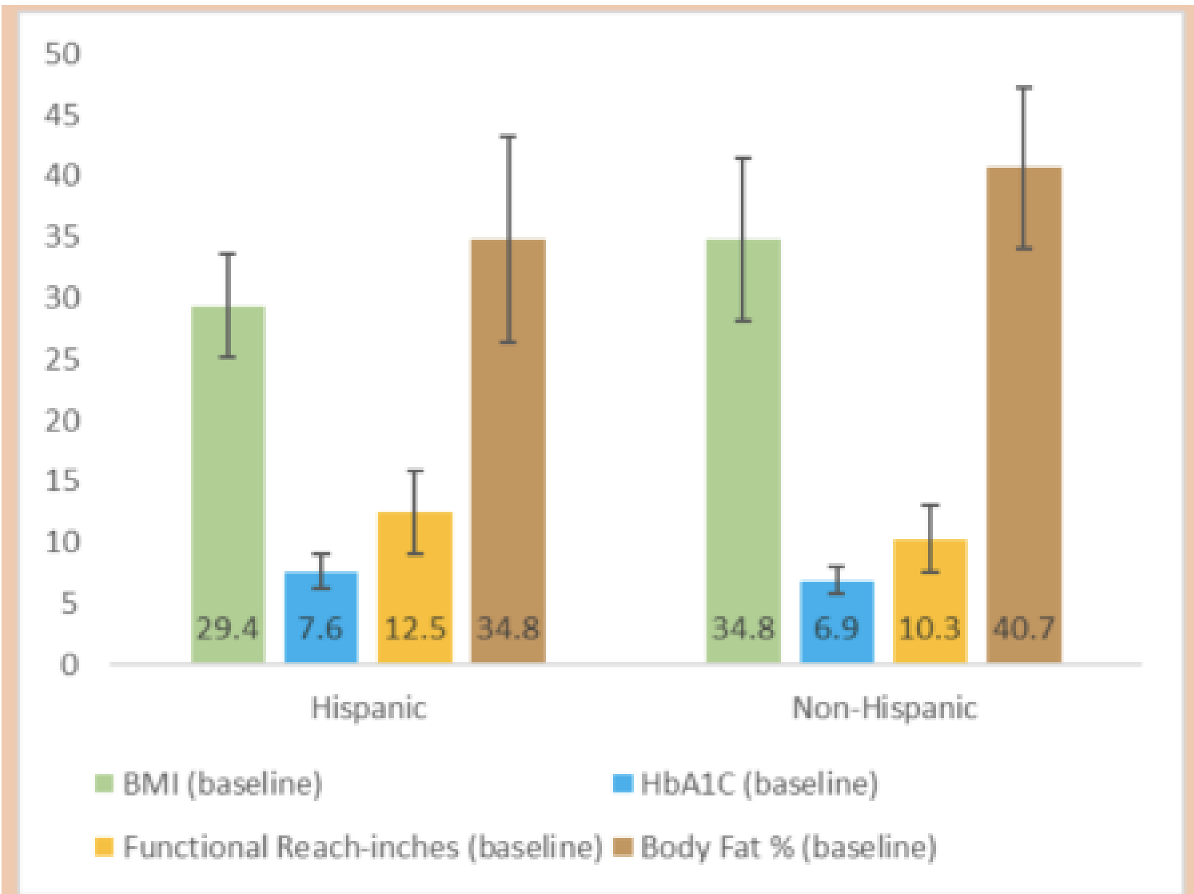

Figure 6. Differences between Hispanic and Non-Hispanic patients for continuous variables using Independent-samples t-tests.

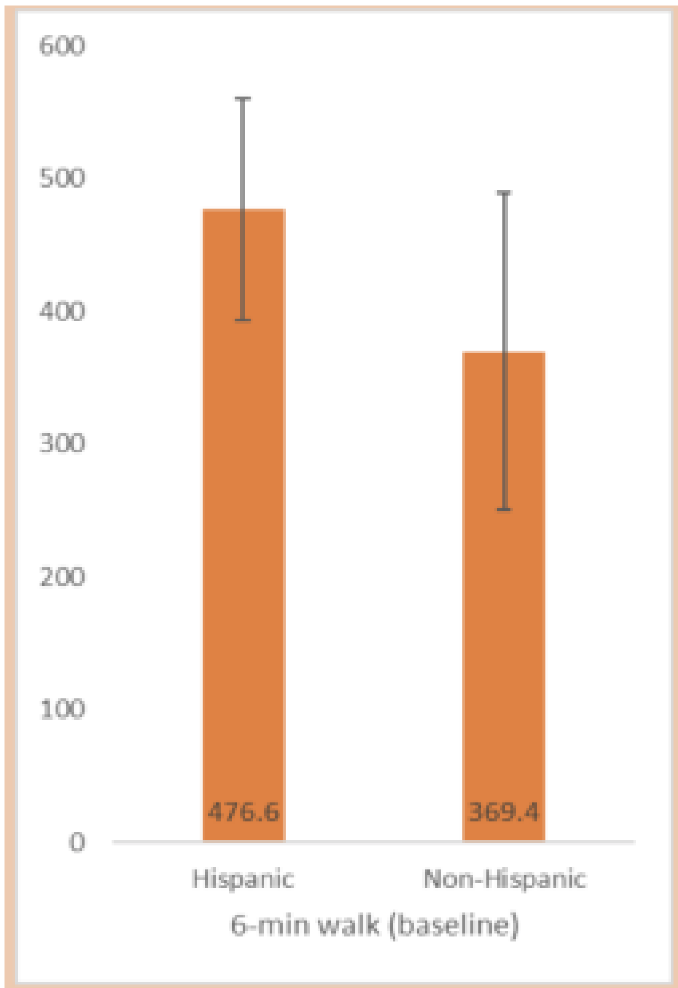

Figure 7. Differences between Hispanic and Non-Hispanic patients for the continuous variable of the 6-minute walk test.

Discussion

Hispanics have suffered from a tendency to have a high incidence of very high rates of type 2 diabetes, obesity, metabolic syndrome, and multiple vascular complications (Caballero, 2007). The same study by Caballero (2007) also identified Hispanics to have a genetic tendency to develop insulin resistance and metabolic syndrome influenced by cultural, socioeconomic, nutritional, and lifestyle factors. Hispanics have trailed behind non-Hispanics in treatment and are less likely to achieve well-care for diabetes and hypertension (Balfour et al., 2016). Kau et al. (2003) examined the misuse of diabetes drugs due to the lack of health insurance and old age. High-risk profiles in Hispanics led to attention in finding the reason for the occurrence because of the lack of data among all Hispanic groups in the United States regarding the overall prevalence (Rodriguez et al., 2014).

Our findings of 67 subjects indicate that ethnicity is not a factor in the control of Type 2 diabetes, a precursor of CVD. We identified differences in smoking status, the incidence of hypertension, obesity, and physical functioning in Hispanic adults compared to non-Hispanic adults. In the present sample of diabetic patients enrolled in the exercise program, there appeared to be no difference in glycemic control between Hispanic and non-Hispanic subjects. A difference we discovered was Hispanics had a lower incidence of heart attacks. This trend may be attributable to observing anthropometric differences. However, if nutritional or behavioral customs confer cardio-protective effects in this population, it is important for future researchers to identify those variables.

The diabetic population is already at an increased risk of developing cardiovascular disease. However, looking into our sample of diabetic patients there appears to be a lower risk for developing CVD in the Hispanic population than for non-Hispanics when using the baseline values collected before the exercise program. Our study supports the finding that the overall prevalence of CVD for Hispanics is lower than non-Hispanics (Rodriguez et al., 2014).

Our findings do not support higher rates of CVD risk factors among Hispanics. We contradict the notion that Hispanics are 15% more likely to be obese and 65% more likely to have diabetes than non-Hispanic Whites (Silfee et al., 2017). Yet, our findings support that Hispanics experience lower CVD prevalence and mortality than non-Hispanics. As a group that makes up a large share of the population, the National Research Council (US) Panel on Race, Ethnicity, and Health in Later Life evaluated how the levels are perplexing since Hispanics have lower socioeconomic status and lesser access to healthcare than non-Hispanics. Corresponding to other literature, we observed no difference in risk of all-cause mortality (Clements et al., 2018). Balfour et al. (2016) also found conclusions of Hispanics have low CVD prevalence and mortality. Our similar assessment of lower levels in Hispanics can be related to the salmon bias and contribute to the hypothesis (Guadamuz et al., 2021). This suggests that ethnicity is not a factor in developing CVD or adverse cardiovascular events. We found this also applies to if one is to have CVD prerequisites it is less likely of resulting to death if Hispanic. In addition, the study points to the complexity of the Hispanic paradox and the importance of understanding it to determine why mortality rates are low in this group.

Conclusion

There was no significant difference in CVD risk factors and the incidence of adverse cardiovascular events among at-risk Hispanic and non-Hispanic adults. Using the baseline values collected before the exercise program there appeared to be a lower risk for developing cardiovascular disease in the Hispanic population than for non-Hispanics. Understanding differences in risk factors between various ethnicities can help identify appropriate interventions for treatment and delimit variables of interest during treatment. The present study was limited to a population-based sample of Hispanics within driving distance of St Joseph's Hospital. The sample size in this study may not be sufficient enough to present a discrepancy across both groups. Further research is important to consider a larger sample size to evaluate.

CHAPTER 4: THE EFFECT OF RADIATION THERAPY ON CANCER PATIENTS PARTICIPATING IN STRUCTURED EXERCISE

Abstract

Background

Radiation therapy was first attempted as a treatment for cancer in 1896. Since then, it has become a common modality, and the survival rate among diagnosed patients has increased drastically. While radiation can prolong life expectancy, it can be deleterious to the patient's health. Exercise has consistently demonstrated improvement in anthropometric, cardiometabolic, and functional capacities of cancer survivors, but data concerning the effect of radiation on exercise outcomes are limited.

Purpose. To evaluate the effect of radiation therapy on exercise outcomes in cancer survivors.

Methods. Patients participated in a 10-week exercise intervention involving aerobic, resistance, and flexibility training. 59 patients had never used radiation (NR), 63 had complete radiotherapy (HR), 18 currently undergoing treatment (CR), and 17 failed to report their status. We analyzed differences among the three radiation exposure groups (NR, HR, and CR) in baseline characteristics, exercise adherence, and improvement in several parameters of health and function using chi-square and multivariate tests; posthoc analyses tested specific group differences.

Results. There were no baseline differences between groups in age, health history, body composition, cardiovascular parameters, fatigue, insomnia, or depression. Patients in the NR group performed better on the five times sit-to-stand test than HR patients (p=0.013) and better

on sit-and-reach (p=0.037) and functional reach (p=0.059) than CR patients. There were no differences in program completion based on the use of radiation (p=0.404). Although there were no baseline differences in the six-minute walk (p=0.987), CR patients improved more than HR patients (p=0.038) and NR patients (p=0.051). There were no baseline differences in systolic blood pressure (p=0.957) but CR patients experienced greater reductions than patients in the HR group (p=0.011) and NR group (p=0.035).

Conclusion. Exercise may be an effective way to mitigate some of the health consequences associated with radiation therapy. In our sample, exercise improved blood pressure and a six-minute walk more in patients who were currently undergoing treatment; however, our low retention rate may create potential bias and fail to accurately characterize expected results.

Introduction

Cancer is one of the leading causes of death worldwide and the number of diagnoses is expected to increase in the coming years. Along with the continuous increase is the expected rise of cancer survivors (Siegel et al., 2021). Approaches for cancer treatment comprise of radiation therapy, chemotherapy, surgery, immunotherapy, and hormonal therapy (Wang et al., 2018). Radiation therapy (RT) also known as radiotherapy, is subject to the use of high-energy rays or radioactive substances to damage tumoral cells and halt their growth and division (Gianfaldoni et al., 2017). RT was first attempted by Emil Grubee as a treatment for breast cancer in 1896 after x-rays were first discovered by Wilhelm Conrad Röntgen from Germany in 1895. Since then, it has become an essential and effective modality implemented in worldwide cancer care, treating approximately 50% of cancer patients (Baskar et al., 2012).

RT is the most cost-effective accounting for about 5% of total care costs (Ringborg et al., 2003). It has been recognized as an essential element in cancer patients' treatment for the reason that it has the potential to improve the rates of cure of 3.5 million people each year (Jaffray and Gospodarowicz, 2015). While RT can prolong life expectancy and aid against cancer it is deleterious to a patient's health. RT is associated with a negative impact on quality of life and multiple complications in multiple health domains (Liu et al., 2017; Żmijewska-Tomczak et al., 2014). Exercise during and after adjuvant cancer therapy serves as an effective method to subdue negative psychological and physical side effects and symptoms, limit disease progression, and directly benefit cancer treatment (Schmitz et al., 2010; Brown et al., 2012).

The American College of Sports Medicine (ACSM) encourages cancer survivors to participate in 150 minutes of moderate-intensity exercise with the addition of resistance training twice a week (Schmitz et al., 2010). A cancer survivor refers to "any person who has been diagnosed with cancer, from the time of diagnosis through the remainder of life," but it is important to recognize that not all people with a history of cancer identify as survivors (Berry et al., 2019). Only one-third of cancer survivors meet ACSM guidelines (Brown et al., 2012). Numerous studies have explored the effect of exercise on cancer survivors, consistently discovering that the incorporation of exercise promotes improvements in anthropometric, cardiometabolic, and functional capacities of individuals at all stages of their cancer continuum (Brown et al., 2012). On the contrary, data concerning the effect of radiation therapy on exercise outcomes are limited and require further research.

With regards to the above, the study evaluated the effect of RT on exercise outcomes in cancer survivors in a 10-week structured program.

Research Hypothesis

Radiation therapy will have a significant effect on exercise outcomes in cancer survivors.

Purpose

To evaluate the effect of radiation therapy on exercise outcomes in cancer survivors.

Null Hypothesis

Radiation therapy will not have a significant effect on exercise outcomes in cancer survivors.

Delimitations

People not cancer survivors or cancer patients.

Limitations

The study is not a randomized control trial.

All subjects are permitted to participate in the study.

Subject honesty when completing the Fatigue Symptom Index, Athens Insomnia Instrument, and Zung-Self Rating Depression Scale surveys.

Review of the Literature

Overview of Cancer and Treatment

Cancer is a "multigenic and multicellular disease that can arise from all cell types and organs with a multi-factorial etiology," (Baskar et al., 2012). The foundation of cancer is cancer cells, they proliferate rapidly and initiate tumors and drive tumor progression forward (Hanahan and Weinberg, 2011). Cancer cells are resistant to anti-growth signals that prevent abnormal cell division (Baskar and Itahana, 2017). Traditionally treatment targets those highly proliferating mutated tumor cells and new advancements are analyzing tumor microenvironment (TME). TME is the cellular environment in which the tumor exists in the human system and describes the non-cancerous cells in the tumor that affects cancer progression and is vital for identifying cell or protein targets for cancer prevention and therapeutic purposes (Wang et al., 2018). Methods of treatment are surgery, RT, immunotherapy, hormonal therapy, and chemotherapy (Mun et al., 2018). Treatment is dependent on the type of cancer and what stage it is advanced and may be combined to completely remove cancer tissues (Wang et al., 2018). It kills tumor tissues but can also damage normal tissue leading to toxicity (De Ruysscher et al., 2019).

Radiation Therapy and its Effects

RT is the most effective cytotoxic treatment and has trifold benefits of cost-efficiency, patient care, and organ preservation (Thariat et al., 2013). RT is delivered in different fractions either by linear energy transfer (LET) primarily as high energy sources like photons (gamma and X-rays), charged particles (electrons), and protons or external radiation from outside the body to the tumor via radiation beam (Baskar and Itahana, 2017). Radiation functions as a physical agent that damages DNA directly or indirectly produce free radicals (charged particles) that damage the cellular DNA (Baskar et al., 2008). DNA damage is achieved by single-strand breaks or double-strand breaks which affect signaling pathways (Baskar et al., 2014).

RT has a significant impact on survival, disease control, and treatment-related mortality (Bradley & Mendenhall, 2018). RT has made many technological improvements since the discovery of the x-ray in 1895 which translate to better clinical results and patient care over time (Thariat et al., 2013). Despite advancements cancer patients have common side effects from treatment including taste alterations, eating problems (chewing and swallowing), xerostomia, dysphagia, trismus, hoarse voice, bone necrosis, fibrosis of soft tissue, and hearing and speech impairment (Żmijewska-Tomczak et al., 2014). Another impairment is reduced cognitive function for example exhibiting difficulties with learning, memory, attention, processing speed, and executive function (Falleti et al., 2005 & Ahles et al., 2012). As a result of treatment side effects are negative changes to the patient's quality of life (QoL) (Żmijewska-Tomczak et al., 2014). The World Health Organization defines QoL as "an individual's perception of their position in life in the context of the culture in which they live and in relation to their goals, expectations, standards, and concerns." According to Siegrist and Junge, it includes physical indicators, mental determinants, and social indicators.

Another common and distressing symptom of cancer and cancer treatment is cancer-related fatigue (CRF) (Hilfiker et al., 2018). The National Comprehensive Cancer Network defines CRF as "a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning." Cancer-related fatigue is contributed by oxidative stress, which is meticulously linked to tumor hypoxia, and acidic environments (Ashcraft et al., 2019). Treatments to eradicate cancerous tumors can activate the proinflammatory cytokine network in response to tissue damage from RT leading to fatigue through cytokine signaling in the central nervous system (Bower et al., 2014).

Exercise and the Cancer Patient

In the past cancer patients were encouraged to rest if they felt adverse symptoms like fatigue but positive findings from the first generation of oncology studies for exercise have shifted that for its contributions to improved health, prevention of cancer regrowth, and functional outcomes (Stout et al., 2017). Exercise is defined as "a subset of physical activity that is planned, structured and repetitive and that has a final or an intermediate objective of improving or maintaining physical fitness" (Pollán et al., 2020). Exercise is not only safe and feasible for cancer patients during and after treatment but also has direct beneficial effects linked to the general health-promoting properties of exercise (Christensen et al., 2018). It is a relevant intervention for patients to mitigate or prevent adverse psychological or physiological outcomes that can lead to mortality (Mishra et al., 2012). Exercise decreases pain whereby increases strength, cardiorespiratory fitness, and flexibility and decreases hospital stay, stress, anxiety, insomnia disorders, and depression (Reis et al., 2018). Growing support for cancer patients and survivors to engage in exercise led the American College of Sports Medicine (ACSM) to assemble guidelines on exercise that are in accordance with the recommendations of the US Physical Activity Guidelines for Americans (PAGA), which suggests at least 150 minutes a week of moderate-intensity activity or 75 minutes a week of vigorous-intensity or an equivalent combination (Wolin et al., 2012). It is important to note this recommendation is a long-term goal and should not be the initial prescription for a sedentary patient (Jones et al., 2010). Sedentary behavior and low exercise levels are associated with deconditioning, poor symptom control, and poor clinical outcome after diagnosis (Jones et al., 2010). Silver and Gilchrist's review discusses how exercise improves pain and musculoskeletal issues, deconditioning and endurance effects, fatigue, balance and falls, and psychosocial problems. The research on the association between exercise, recurrence, and survival is limited. The summary of research by Schwartz (2012) included 3 studies that were the first to examine the role of exercise in preventing reoccurrence and improving survival and it provides the strength of including exercise in cancer patients' daily routine.

Although many of the studies don't demonstrate the maintenance of physical activity to prevent adverse symptoms and side effects on many uncommon cancers there are numerous significant studies on the most common within the population such as breast, prostate, and colorectal, and these studies either focus on a single cancer-related impairment or a broad range of symptoms (Stout et al., 2017). This inconsistency may be due to these cancers having the highest percentage of diagnosis within the US population, the decreasing rate of death, and the ability to counteract the progression of cancer within these cancer types (Siegel et al., 2019). Even so, data is insufficient to suggest specific exercise recommendations for different cancer groups at different stages of the cancer trajectory (Speed-Andrews et al., 2009).

It is important to note exercise eliciting beneficial changes in insulin-related pathways, reducing inflammation and serum estrogen levels, and enhancing oxidative, immune, and cellular repair pathways are areas of controversy because the evidence remains preliminary (Thomas et al., 2021). Minimal evidence is known about protection against the progression of tumor growth but possible mediators are changes in body composition, sex hormone levels, systemic inflammation, and immune cell function (Pedersen et al., 2016). For instance, Pedersen et al. (2016) showed a 60% reduction in tumor growth and incidence across five different tumor models in voluntarily wheel-running tumor-bearing mice by upregulating pathways associated with immune function, distinctively by exercise significantly increasing natural killer (NK) cell infiltration through beta-adrenergic signaling. Exercise can regulate oxidative stress and affect vascular normalization by increasing blood flow, metabolic programming by reducing tumors' glucose consumption rate, and immune cell mobilization (Ashcraft et al., 2019).

The challenge oncologists encounter is tailoring the prescription of exercise such as; the type of exercise program suitable for the cancer type, treatment type, and how to meet FITT (frequency, intensity, type, and time) principles while considering the functional status of the individual (Stout et al., 2017). The most effective form of exercise for cancer patients is one that is individually prescribed and supervised as a therapeutic program as it happens for drug treatments (Ferioli et al., 2018). Yet, recommendations alone aren't enough to get cancer patients or survivors to exercise, another strategy like an exercise packet or referral can further increase retention to exercise (Park et al., 2015). So, maybe by strengthening the impact of exercise, it can be established to become the norm as a means of cancer treatment modalities in addition to treatment for oncologists to prescribe.

When examining the literature to determine what type of exercise (aerobic or resistance training) is best for the most benefit, the data is supportive to combine both aerobic and resistance training (Luan et al., 2019). Correspondingly, emerging studies continue to agree that exercise improves physical functioning, symptoms of fatigue, and quality of life but evidence on the intensity of exercise is warranted. A more specific guide for an exercise prescription can provide transparency and stability to aid from adverse effects or comorbidities and acquire the benefits from exercise. Determining the type is dependent on the patient's needs, stage of cancer, current exercise behavior, and the pre-screening outcome (Jones et al., 2010). Optimizing these categories of an exercise program will propose to initiate high adherence, recruitment, and retention (Speed-Andrews et al., 2009).

The variation of studies analyzes how exercise affects cancer patients acutely and chronically. Therefore, the aim of this study was not only to contribute to the benefit of exercise but to illustrate the impact of RT on exercise outcomes in cancer patients.

Methodology

Subjects

157 cancer survivors participated in an exercise intervention involving aerobic, resistance, and flexibility training. The study contained 59 patients who never used radiation (NR), 63 who previously completed radiotherapy (PR), 18 currently undergoing treatment (CR), and 17 individuals with an unknown radiation status. Individuals with unknown radiation status were excluded from data analysis. Participants attended an initial evaluation, completed ten weeks of exercise, and were retested during a post-evaluation assessment. We then compared initial evaluation measures between post evaluations. All participants completed a form of consent and returned a signed consent from their physician to participate in the study.

Initial Evaluation

During the initial evaluation, patients completed multiple questionnaires that established their demographics and health history. Additionally, multiple tests determined cardiometabolic risk factors (blood pressure, VO2 max, heart rate), anthropometric measurements (BMI and body fat percentage), physical fitness, and psychological well-being of the individual. Four domains of physical fitness were tested; physical functioning, endurance, strength, and flexibility. Timed up-and-go and chair stand test determined physical functioning. The six-minute walk determined endurance. Arm curls, handgrip, UTM push, UTM pull, and Epic Lift determined strength. Functional reach, sit-and-reach, and back scratch determine flexibility. The Fatigue Symptom Index, Athens Insomnia Instrument, and Zung-Self Rating Depression Scale survey determined psychological well-being.

Exercise Program

Patients exercised biweekly for one-hour sessions. Each exercise session consisted of three phases: check-in, exercising, and cool down. All patients initiated training simultaneously but followed their personalized exercise program throughout the session. Each patient had exercise cards containing a personalized exercise program and goal heart rate for the individual. Following rest periods, student interns performed blood pressure tests. Patients were instructed to record their blood pressure on their exercise cards.

Check-in

Patients retrieved their exercise cards and were advised to sit in the waiting room for 5 minutes until called to enter the gym to begin exercise.

Aerobic Training

Patients exercised for six minutes at each aerobic-based exercise; treadmill, Nu-Step, recumbent bike, and Upper Body Extremity bike, for a total of 24 minutes. Each patient was encouraged to exert themselves to their goal heart rate, which was determined by a fingertip pulse oximeter following the six minutes at each station. If the patient was on heart medications, the Rating of Perceived Exertion (RPE) was recorded based on the Borg Scale.

Strength Training

Patients gradually performed resistance exercises. Ten repetitions were completed on the first day, twenty repetitions on the second day, and thirty repetitions on the third day of exercise. The patient continued to perform thirty repetitions (3 sets of 10) per exercise for the remaining of the program. The exercises included chest presses, latissimus dorsi pull downs, bicep curls, standing rows, triceps extensions, squats, and step-ups.

Cooldown

Upon completion of all aerobic and strengthening exercises, patients recollected for the group to cool down. Led by a head clinician or student interns, patients performed multiple stretches of major muscle groups, yoga poses, and deep breathing exercises.

Post Evaluation

After completion of the ten weeks, all individuals were retested in all domains tested during the initial evaluation and surveys determining psychological well-being.

Statistical Analysis

All statistical tests were conducted using SPSS version 24 (IBM SPSS Statistics, IBM Corporation, Chicago, IL, USA). Descriptive statistics of the total sample (means, percentages, and standard deviations) were conducted to determine patient characteristics at baseline. We analyzed differences among the three radiation exposure groups (NR, PR, and CR) using a one-way analysis of variance (ANOVA) in baseline characteristics and exercise adherence ($p<0.05$). Post-hoc analyses tested specific group differences. Multivariate tests analyzed improvements for pre and post-exercise programs in several parameters of health and function.

Results

Subjects

As seen in Table 5, when comparing the PR, NR, and CR groups there were no baseline differences in age, health history, body composition, cardiovascular parameters, fatigue, insomnia, or depression. Based on posthoc analyses, patients in the NR group performed better on the five times sit-to-stand test than PR patients ($p=0.013$) and better on sit-and-reach ($p=0.037$) and functional reach ($p=0.059$) than CR patients.

Exercise Adherence

There were no differences in program completion based on the use of radiation ($p=0.404$).

Subjects Who Completed the Ten Weeks

Although there were no baseline differences in the six-minute walk ($p=0.987$) figure 8 shows CR patients improved more than PR patients ($p=0.038$) and NR patients ($p=0.051$). There were no baseline differences in systolic blood pressure ($p=0.957$) but CR patients experienced greater reductions than patients in the PR group ($p=0.011$) and NR group ($p=0.035$).

Table 5

Subject baseline characteristics and exercise adherence between the never used radiation (NR), currently using radiation (CR), and previously used radiation (PR) groups.

	TOTAL	PR	NR	CR	Sig.
N	140	63	59	18	
Age (years)	61.1 ± 10.7	61.2 ± 10.8	61.00 ± 10.8	60.9 ± 10.7	.994
Weight (lbs)	179.1 ± 56.0	181.6 ± 67.4	179.8 ± 48.7	168.5 ± 33.1	.713
BMI (kg/m^2)	29.8 ± 8.6	30.1 ± 9.3	30.2 ± 8.4	27.5 ± 6.7	.536
BF%	35.9 ± 8.5	37.5 ± 9.1	36.0 ± 7.3	32.0 ± 10.2	.375
6 Minute Walk (m)	379.9 ± 100.8	378.0 ± 94.2	381.6 ± 110.0	380.5 ± 100.1	.987
Functional Reach (cm)	11.1 ± 2.8	10.9 ± 3.0	11.0 ± 2.6	12.5 ± 2.7	.121
Timed-up-and-go (sec)	7.8 ± 2.4	8.0 ± 2.6	7.9 ± 2.4	7.2 ± 1.5	.544
Sit and reach (cm)	-3.0 ± 5.6	-3.0 ± 5.8	-2.1 ± 5.5	-6.3 ± 4.0	.112
Back scratch (in)	-4.0 ± 8.0	-5.2 ± 8.2	-3.2 ± 7.5	-3.6 ± 9.1	.624
Grip average (kg)	51.8 ± 15.1	51.1 ± 15.6	52.1 ± 14.5	53.4 ± 16.2	.829
Systolic (mmHg)	122.9 ± 14.8	123.3 ± 15.0	122.5 ± 14.5	122.5 ± 16.2	.957
Diastolic (mmHg)	77.5 ± 9.7	77.0 ± 10.4	78.2 ± 9.5	77.1 ± 8.6	.807
MAP	92.4 ± 9.9	92.4 ± 11.0	92.5 ± 9.0	92.3 ± 9.2	.998
Pulse Pressure	45.7 ± 11.7	46.3 ± 10.8	45.1 ± 11.6	45.4 ± 14.3	.863
Heart Rate	79.1 ± 15.8	78.9 ± 15.1	79.1 ± 17.7	79.8 ± 12.8	.984
VO2 Max (L/kg)	22.8 ± 6.2	22.2 ± 3.8	23.3 ± 9.2	23.9 ± 0.8	.881
UTM Push (lbs)	50.7 ± 23.1	50.0 ± 25.1	52.5 ± 23.5	48.0 ± 14.4	.891
UTM Pull (lbs)	46.1 ± 17.4	44.4 ± 16.3	48.9 ± 19.7	44.2 ± 15.5	.660
Epic Lift (lbs)	25.3 ± 12.3	27.1 ± 12.7	21.8 ± 13.3	25.0 ± 5.8	.521
Fatigue	60.9 ± 26.1	62.5 ± 28.8	59.2 ± 24.6	60.5 ± 21.3	.820
Insomnia	8.6 ± 4.6	7.6 ± 2.6	10.0 ± 6.9	12.5 ± 9.2	.282
Depression	37.5 ± 6.3	37.8 ± 6.0	39.4 ± 4.2	30.5 ± 12.0	.241
Completion of Program	37.7%	40.6%	45.6%	27.8%	.404

Note. Using one-way analysis of variance (ANOVA) in baseline characteristics and exercise adherence ($p<0.05$). The individuals (n=17) who failed to report their status are excluded from the analysis.

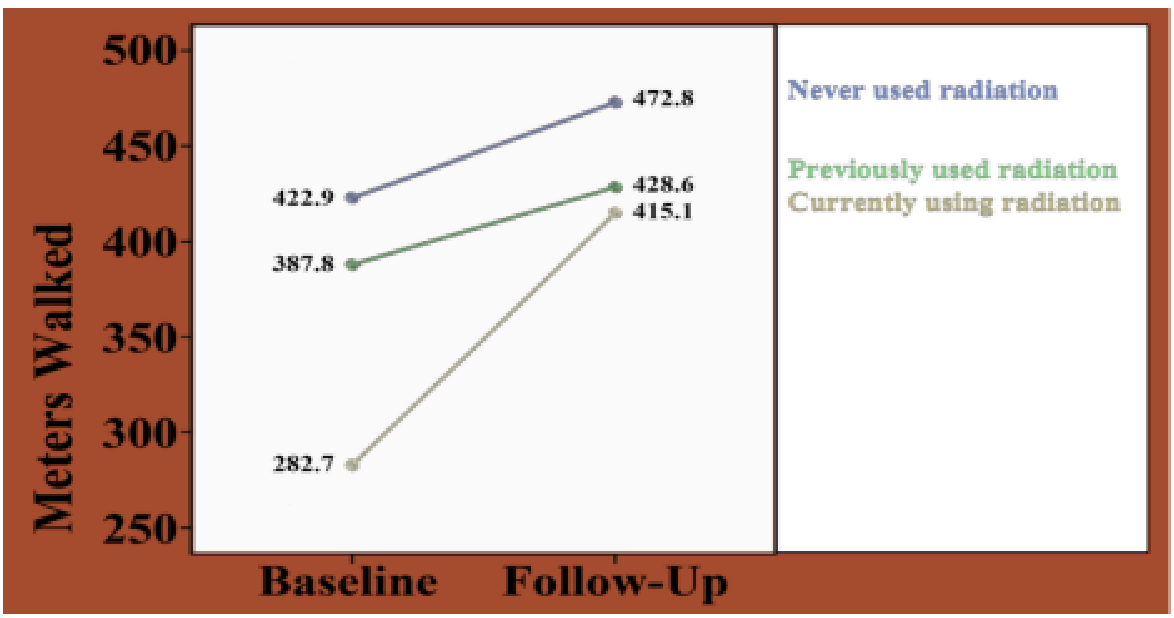

Figure 8. Changes in pre to post-6-minute walk distances between NR, CR, and PR groups are presented

Discussion

Exercise for the overall care and management of cancer patients has been an expanding interest in the strength of the benefits presented through data (Pollán et al., 2020). In our research, we found that subjects currently using radiation (CR) had greater exercise outcomes compared to those that never used radiation (NR) and previously used radiation (PR). RT is linked to adverse effects and side effects, fatigue being the most frequent (Lipsett et al., 2017). So, including exercise in an individual's daily routine can alleviate those side effects that decrease quality of life and function. Our study is significant because it demonstrates the impact exercise has on cancer patients. We also justify it as a useful adjuvant treatment at different points of the course of cancer.

Exercise during treatment may be illustrated as not being sufficiently beneficial since there is still vagueness in its relation to cancer-related fatigue (Kelley & Kelley, 2017). During and after treatment cancer patients are underdiagnosed and undertreated from cancer-related fatigue so obtaining benefits from exercise may be limited because they are negatively impacted by treatment such as RT but the literature is uncertain (Thong et al., 2020). Our study displays that belief is not completely appropriate to state. We differ because patients during treatment in our study had the greatest improvements in blood pressure and the 6-minute walk test reflected physical improvements. The six-minute walk test is an indicator of peak oxygen consumption, a measurement of cardiorespiratory fitness which is an impairment cancer patients encounter (Jones et al., 2012). Yet, in other research studies, it was determined that some subgroups of cancer patients are too ill to adhere to prescribed exercise (Scott et al., 2018). Our low retention rate may be parallel to those findings and be because of the illness of the cancer patient. Our results may be interpreted with caution given we did not include the stage of cancer development in subjects currently undergoing RT. Nonetheless, our data support the findings that exercise is advantageous considering that exercise prescription is individualized based on the identified ability of the subject.

Systematic reviews, like that of Schumacher et al. (2021) stated all studies included had an increase in performance in at least 1 domain of a physical function. However, more recent a systematic review of 1563 cancer patients completed trials of combining exercise and RT and concluded that combining both was safe and well-tolerated with improvements in patient-reported outcomes for patients with breast, prostate, and head and neck cancer (Zaorsky et al., 2021). In agreement with previous findings, we found that there is positive gain to have from exercise at every level of cancer diagnosis, during radiation being the greatest. This allows cancer patients and survivors to be independent and perform daily activities without restrictions.

Poor outcomes of physical fitness tests have been associated with reduced survival, poor surgical outcomes, and treatment-related complications (Verweij et al., 2016 & Loughney et al., 2016). For that reason exercise is recognized as essential for the cancer patient. Effects of exercise have demonstrated better symptom-related outcomes, reduced inflammatory biomarkers, declined fatigue, increased quality of life, and increased physical function, while also playing a role in preventing tumor progression (Ashcraft et al., 2019).

Conclusion

A structured, comprehensive exercise program of aerobic and strength training performed at moderate intensity improved blood pressure and six-minute walk more in patients who were currently undergoing radiation treatment in comparison to an individual not undergoing radiation therapy at the time and individuals who never used radiation. This further solidifies the incorporation of exercise as an essential adjunct therapy for cancer patients or survivors, and an effective way to mitigate some of the health consequences associated with radiation therapy. However, we recognize that our low retention rate may create potential bias and fail to accurately characterize expected results.

CHAPTER 5: CONCLUSION

I specified my objective for this thesis was to bring additional findings to 3 questions with limited data. The questions included are is structured exercise effective in improving cardiovascular, anthropometric, and functional capabilities in cancer survivors, are Hispanics more vulnerable to CVD risk factors and the incidence of adverse cardiovascular events, and how does RT affect structured exercise outcomes in cancer survivors. Cancer and CVD, are the two utmost impactful diseases people encounter worldwide. These findings allow for the significance of the interrelationship of ethnicity, treatment, and structured exercise in these populations to illustrate the positive impact on disease risk and consequences.

In the study examining cancer patients' effects of participating in a structured exercise program exercise did not affect anthropometric or cardiovascular profiles, but improved physical functioning in 11 of 13 domains. These findings are useful to help guide clinicians in exercise prescription and planning for cancer patients. The results exhibited favorable improvements in strength, aerobic capacity, and flexibility at follow-up when compared to baseline. Findings align with current research on the benefits of exercise.

When evaluating the role of ethnicity in developing CVD we used a structured exercise program to identify risk factors and adverse events. We found exercise to benefit Hispanic and non-Hispanic subjects similarly. Our study demonstrated Hispanics may not be more vulnerable to CVD risk factors or adverse cardiovascular effects. There was no significant difference in CVD risk factors and the incidence of adverse cardiovascular events among at-risk Hispanic and non-Hispanic adults. Using the baseline values collected before the exercise program there appeared to be a lower risk for developing cardiovascular disease in the Hispanic population than for non-Hispanics, which contradicts some of the current literature. Understanding differences in risk factors between various ethnicities can help identify appropriate interventions for treatment and delimit variables of interest during treatment.

The final study analyzed cancer patients undergoing radiation treatment and exercise outcomes. Cancer treatment includes exposure to consequences and adverse events. Our results concluded exercise may be an effective way to mitigate some of the health consequences associated with the treatment of radiation therapy. We also display support for the prescription of exercise during all stages of cancer since there was an improvement for all groups in the study. Additionally, support for the incorporation of exercise as an essential adjunct therapy for cancer patients or survivors.

The findings allude to the assumption that these clinical populations of type-2 diabetics and cancer patients face consequences, which are not expressed disproportionate based on ethnicity. The consequences are detrimental to their health and daily routines, but structured exercise similarly improves functional abilities and mitigates those consequences to allow for independence.

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