PACE: Predicting Adverse Cardiac Events in Breast Cancer Patients

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ABSTRACT

Background:
Breast cancer (BCA) affects one in eight women in the US. Doxorubicin (Dox) and Trastuzumab (Tsz) remain prevalent chemotherapies for breast cancer, but cause cardiotoxicty with significant morbidity and mortality in a subset of patients. The current study is a sub-study of an ongoing prospective observational study investigating if specific cardiac factors, growth factors, genetic polymorphisms and self-reported physical activity can predict which women will develop cardiac dysfunction from chemotherapy. The sub-study of PACE was aimed at characterizing the self-reported physical activity during first three months of chemotherapy.

Methods:
In a prospective, longitudinal study, 132 newly diagnosed breast cancer women receiving either AC or Tsz were enrolled over a 4-year period. Baseline data on age, BMI, personal history of hypertension, hyperlipidemia, diabetes mellitus, tobacco use, and coronary artery disease, family history of cardiomyopathy and self-reported physical activity at enrollment and at 4 time-points during first three-months of chemotherapy were ascertained. Enrolled participants were given baseline physical activity questionnaire and 4 additional CHAMPS questionnaire during chemotherapy (validated International Physical Activity Questionnaire – IPAQ and CHAMPS questionnaire respectively). CHAMPS questionnaire reported the various forms of physical activity in metabolic equivalent for task per hour per week (MET-hrs/wk). Complete questionnaires from 86 patients were analyzed.

Results:
The mean age of this cohort was 50 years old with a Caucasian predominance. Women average stage of breast cancer was Stage II. Physical activity significantly decreased in during Dox treatment in compared to TSZ. However looking at the combined group of Dox and TSZ there were a statically significant trend showing a overall decrease in self-reported physical activity.

Conclusions
Women enrolled in PACE have a high number of cardiovascular risk factors (hypertension, hyperlipidemia, and overweight). Our study demonstrates that most women describe a decrease in their physical activity during chemotherapy. It remains unknown if an exercise prescription decreases the likelihood of developing cardiotoxicity. Further work is needed with ongoing prospective studies.
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INTRODUCTION

Adequate exercise for patients undergoing chemotherapy for cancer treatment is critical. Many studies have revealed that patients undergoing cancer treatment who exercise more than their counterparts report decreases in depression and fatigue with concurrent increases in muscle strength, aerobic capacity, mental health, and overall immune function[1-9]. Some longitudinal studies have also found overall decreases in long-term mortality rates in patients who exercise during chemotherapy[10-12]. The long-term benefits of exercise on the cardiovascular system have been well documented and include prevention of systolic and diastolic dysfunction and mitigation of elevated blood pressures[13]. The purpose of this study was to characterize the natural trend of self-reported physical activity during breast cancer treatment.
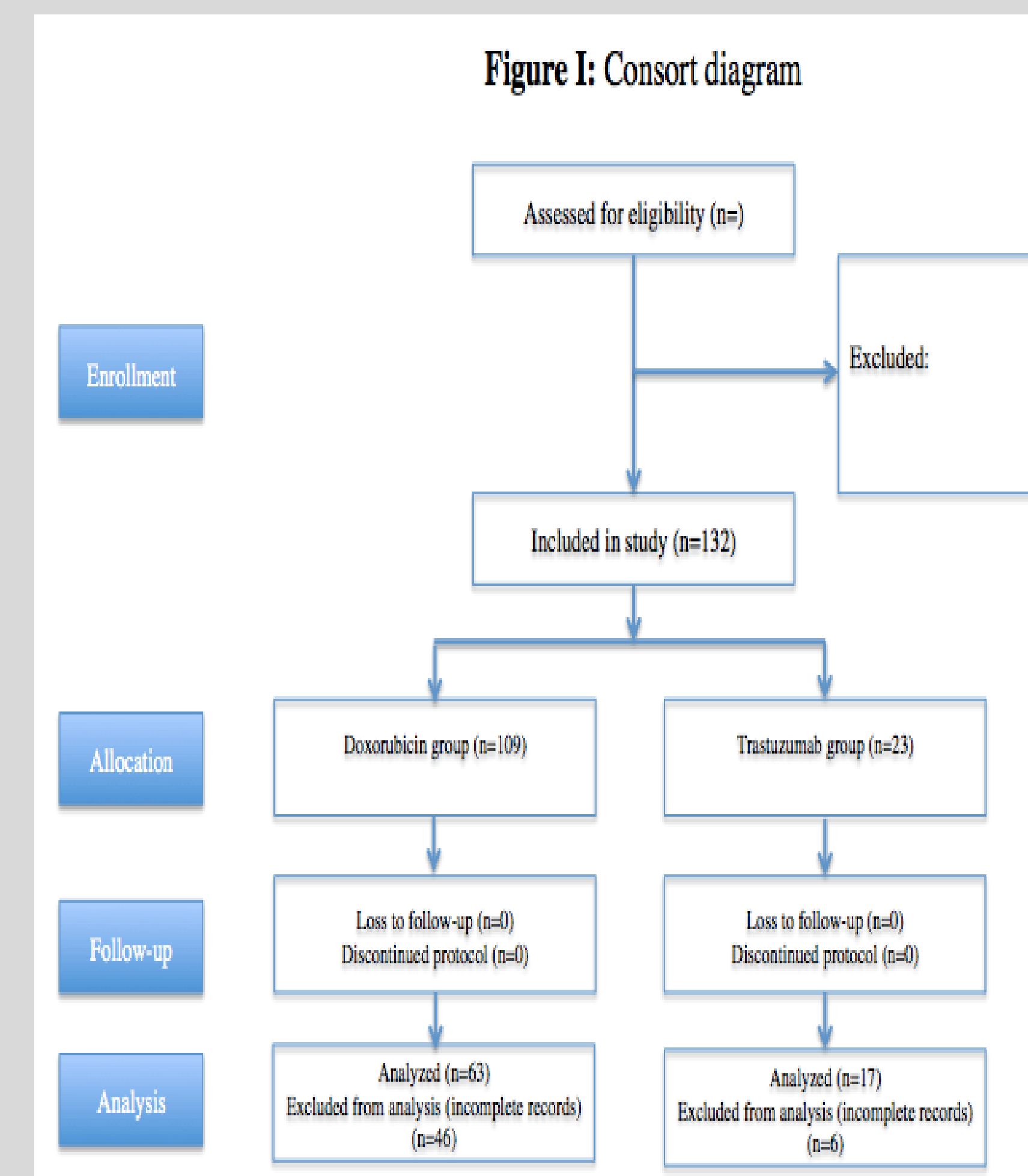
METHODS

Fig. 1: Flow diagram for patient enrollment
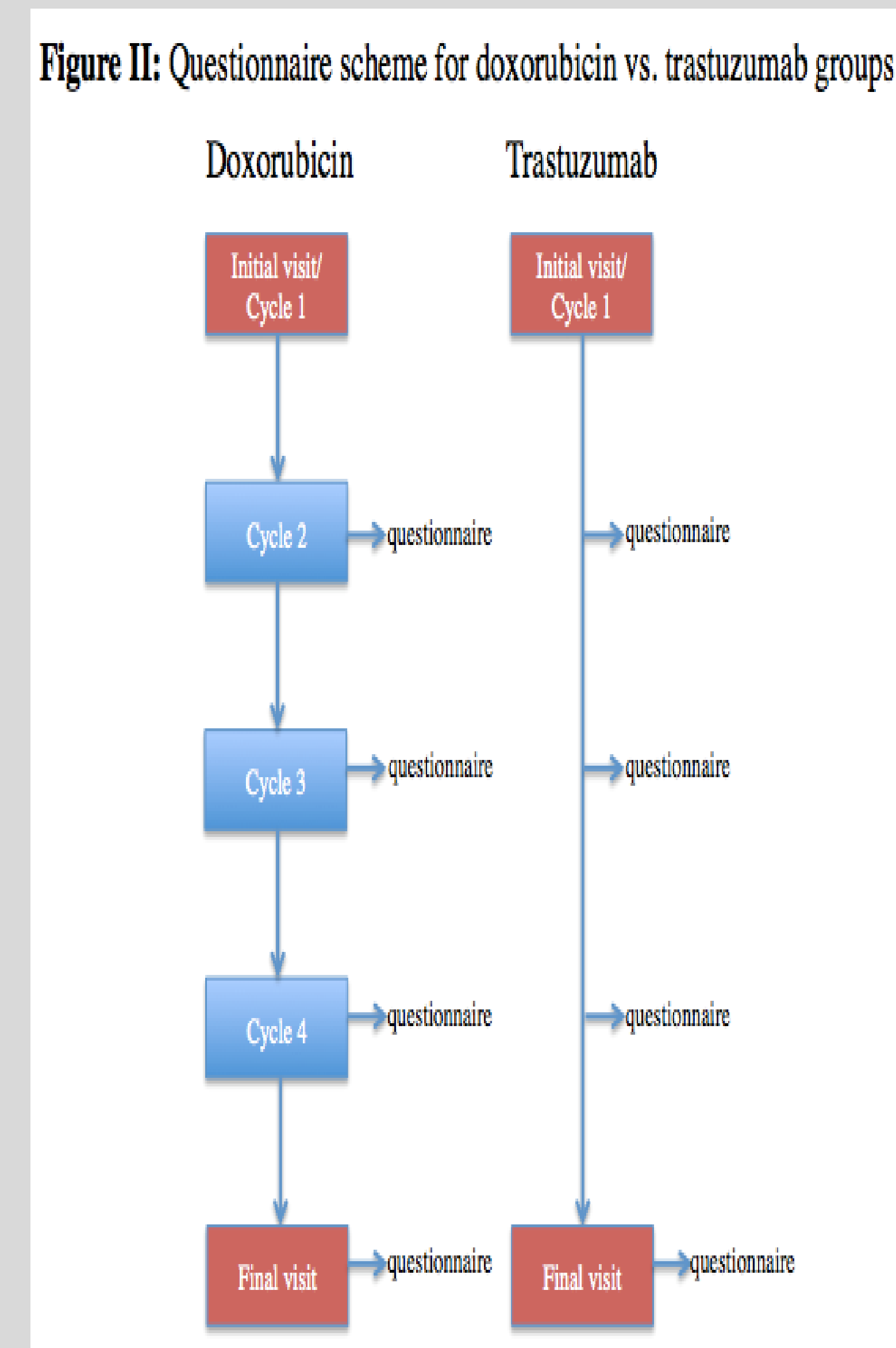
METHODS – QUESTIONNAIRE SCHEME

Fig. 2: IPAC and CHAMPS Questionaires were given at these corresponding times.
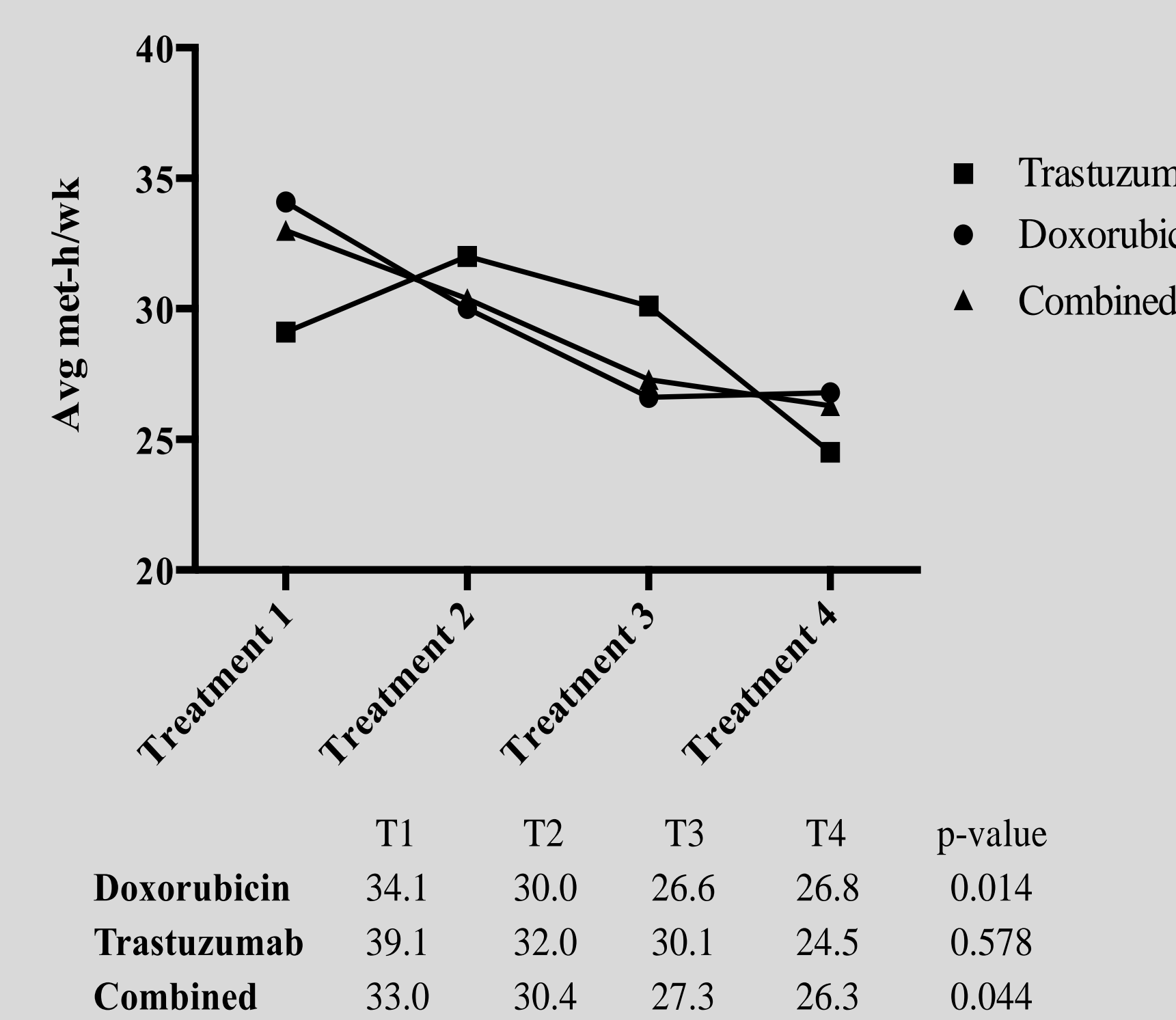
RESULTS – PATIENT CHARACTERISTICS

Table I: Baseline demographics and cancer characteristics

	Trastuzumab	Doxorubicin	p-value
Average age			
Gender			
Female	17 (100.0%)	63 (100.0%)	0.999
Male	0 (0.0%)	0 (0.0%	
Race			
Caucasian	16 (94.1%)	54 (85.7%)	0.801
African-American	1 (5.9%)	7 (11.1%)	
Other	0 (0.0%)	2 (3.2%)	
Cancer stage			
Stage I	8 (47.1%)	7 (11.1%)	0.006
Stage II	4 (23.5%)	37 (58.7%)	
Stage III	4 (23.5%)	14 (22.2%)	
Unknown	1 (5.9%)	5 (7.9%)	
Tumor stage			
T1	10 (58.8%)	22 (34.9%)	0.1
T2	2 (3.2%)	25 (39.7%)	
T3	3 (4.8%)	8 (12.7%)	
T4	1 (5.9%)	1 (1.6%)	
Unknown	1 (5.9%)	7 (11.1%)	
Nodal stage			
N0	9 (52.9%)	18 (28.6%)	0.455
N1	6 (35.3%)	33 (52.4%)	
N2	1 (5.9%)	6 (9.5%)	
N3	0 (0.0%)	2 (3.2%)	
Unknown	1 (5.9%)	4 (6.3%)	
Metastatic stage			
M0	16 (94.1%)	55 (87.3%)	0.676
Unknown	1 (5.9%)	8 (12.7%)	

Table II: Baseline medical and medication history

	Trastuzumab	Doxorubicin	p-value
Medical history			
Hx hypertension	6 (35.3%)	20 (31.7%)	0.778
Hx ventricular dilation	0 (0.0%)	0 (0.0%)	0.999
Hx systolic dysfunction	0 (0.0%)	0 (0.0%)	0.999
Hx heart failure	0 (0.0%)	0 (0.0%)	0.999
Hx hyperlipidemia	2 (3.2%)	18 (28.6%)	0.214
Hx coronary artery disease	0 (0.0%)	0 (0.0%)	0.999
Hx arrhythmia	1 (5.9%)	7 (11.1%)	0.999
Hx diabetes	1 (5.9%)	4 (6.3%)	0.999
Hx family cardiomyopathy	2 (11.8%)	21 (33.3%)	0.130
Medication history			
Beta-blocker	1 (5.9%)	11 (17.5%)	0.444
ACE-I/ARB	3 (17.6%)	9 (14.3%)	0.711
Diuretic	1 (5.9%)	10 (15.9%)	0.441
Aspirin	0 (0.0%)	2 (3.2%)	0.999
Substance history			
Tobacco			
Never	14 (82.4%)	45 (71.4%)	0.577
Ex-smoker	2 (11.8%)	16 (25.4%)	
<1 PPD	0 (0.0%)	1 (1.6%)	
>1 PPD	0 (0.0%)	1 (1.6%)	
Alcohol			
None	8 (47.1%)	22 (24.9%)	0.467
<1 per day	7 (41.2%)	38 (60.3%)	
1-2 per day	1 (5.9%)	2 (3.2%)	
3-5 per day	0 (0.0%)	1 (1.6%)	

RESULTS – CHANGE IN EXERCISE

Figure III: Average MET-h/week based on treatment protocol

	T1	T2	T3	T4	p-value
Doxorubicin	34.1	30.0	26.6	26.8	0.014
Trastuzumab	39.1	32.0	30.1	24.5	0.578
Combined	33.0	30.4	27.3	26.3	0.044

RESULTS – CHANGE IN WEIGHT

Figure IV: Change in weight based on treatment protocol

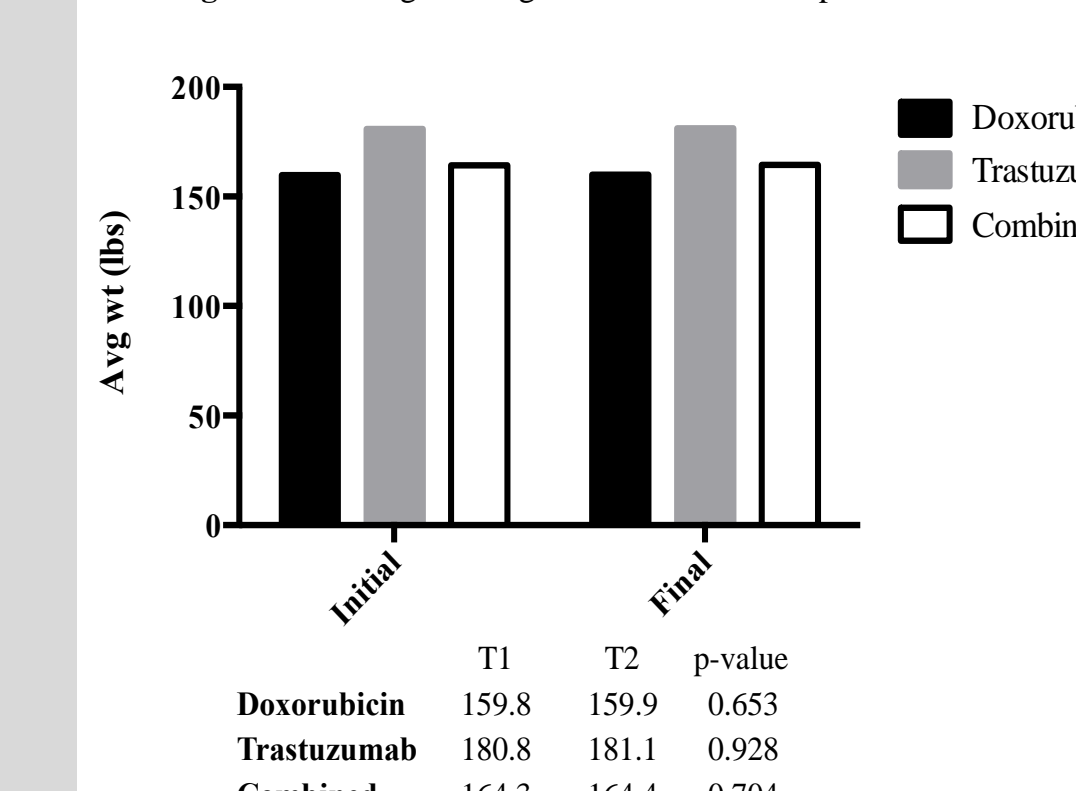|	T1	T2	p-value
Doxorubicin	159.8	159.9	0.653
Trastuzumab	180.8	181.1	0.928
Combined	164.3	164.4	0.704

Figure IV illustrates the average weights of patients at the initial study visit and the final study visit (~12 weeks after the initial visit). For all patients in the study, there was almost no change in the average weight from start to end of the study (p=0.704). This trend was also seen in sub-group analyses for patients in the doxorubicin and trastuzumab groups (p=.653 and p=.928 respectively).

CONCLUSION

- Women enrolled in PACE have a high number of cardiovascular risk factors (hypertension, hyperlipidemia, and overweight).

- Our study demonstrates that most women describe a decrease in their physical activity during chemotherapy.

- It remains unknown if an exercise prescription decreases the likelihood of developing cardiotoxicity.

- Further work is needed with ongoing prospective studies to investigate the effect of exercise on cardiac function during chemotherapy treatment.

ACKNOWLEDGEMENTS

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