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Research paper

Research summary of poster presentations at the 2023 Florida cardio-oncology symposium

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1. Introduction

On March 1, 2023, the University of Florida (UF) Health Cancer Center (UFHCC) Cardio-Oncology Working Group hosted the inaugural UF Health Cardio-Oncology Symposium, "Emerging Topics in Cardio-Oncology". The goal of this symposium was to bring together UF researchers including clinical and research faculty and trainees who are interested in cardio-oncology to foster collaboration in this emerging multidisciplinary field. There were three external speakers with expertise in the cardio-oncology field and four internal UF speakers who currently focus on cardio-oncology in their respective research. The symposium ended with poster presentations, which provided a great opportunity for researchers from six UF colleges to not only present their cardio-oncology findings but also to network with each other, potentially leading to future collaborations and fostering new ideas for their own work. The detailed information of the symposium including the external and internal speakers are summarized in the other publications in this special issue. The purpose of this article is to summarize the findings presented in the posters.

2. Summary of topics presented in the poster session

A total of thirteen posters were presented by graduate students, postdoctoral fellows, and/or faculty members from six different UF colleges (Table 1). The topics ranged from basic science research focusing on the mechanisms of cardiotoxicity, to translational research focusing on identifying biomarkers for risk stratification, to using exercise for cardioprotection from cardiotoxicity as well as racial and

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Table 1
Posters abstracts.

Poster no.	Presenter	College	Department/ division	Abstract title
1[a]	Katelyn Bruno	Medicine	Cardiovascular Medicine	Trpc6 promotes doxorubicin-induced cardiomyopathy in male mice with pleiotropic differences between males and females [1]
2	Camara Casson	Herbert Wertheim College of Engineering	Biomedical Engineering	Integrative control of cardiac tissue biomechanical and biomolecular changes due to doxorubicin
3[a]	David DeRemer	Pharmacy	Pharmacotherapy and Translational Research	Racial and ethnic differences in cardiac surveillance evaluation of patients treated with anthracycline-based chemotherapy [3]
4	Jennifer Dungan	Nursing	Biobehavioral Nursing Science	Candidate genes for survivorship with coronary heart disease include cancer and tumor suppressor genes [7,8]
5[a]	Branden Nguyen	Health and Human Performance	Applied Physiology and Kinesiology	The effects of moderate intensity and high-intensity interval training on cardiorespiratory capacity and body composition during doxorubicin treatment [2]
6	Walter O'Dell	Medicine	Radiation Oncology	Effects of uncertainty in left ventricular border delineation on global longitudinal strain and versus LV ejection fraction calculations
7	Walter O'Dell	Medicine	Radiation Oncology	Detection of radiation-induced defects in heart perfusion in breast cancer patients
8	Walter O'Dell	Medicine	Radiation Oncology	Proton therapy preserves acute left ventricular ejection fraction relative to conventional X-ray therapy in breast cancer
9	Nathalie Roumi	Pharmacy	Pharmacotherapy and Translational Research	Dexrazoxane and all-cause mortality in anthracycline-treated cancer patients
10[a]	Samia Shabnaz	Pharmacy	Pharmacotherapy and Translational Research	Proteomic analysis of carfilzomib related heart failure in multiple myeloma (MM) patients from Prospective Observation of Cardiac Safety with Proteasome Inhibitor (PROTECT) study [4]
11[a]	Marwa Tantawy	Pharmacy	Pharmacotherapy and Translational Research	TMSB10/TRABD2A locus associated with carfilzomib related cardiotoxicity in patients with multiple myeloma: a whole-exome sequencing analysis [5]
12[a]	Marwa Tantawy	Pharmacy	Pharmacotherapy and Translational Research	MiRNA-125a association with carfilzomib-related cardiovascular adverse events in multiple myeloma patients: Prospective Observation of Cardiac Safety with Proteasome Inhibitor (PROTECT) study [6]
13	Melissa Vilaro	Agricultural and Life Sciences	Family, Youth, and Community Sciences	Planning, protocol, expected outcomes for a communal coping intervention to support DASH adherence among African American colorectal cancer survivors

[a] Abstracts 1, 3, 4, 5, 10, 11, 12 are excluded because they have already been published elsewhere.

ethnic differences in cardiotoxicity risk.

2.1. *Anthracycline-induced cardiotoxicity*

Five of the posters were related to anthracycline-induced cardiotoxicity (AIC) (posters #1, 2, 3, 5, and 9). Dr. Bruno and colleagues assessed *TRPC6*, a previously discovered gene associated with anthracycline-induced cardiotoxicity (AIC), as a therapeutic target for cardioprotection in cancer patients. They found that when treated with doxorubicin, male and female Trpc6-deficient mice had reduced vacuolation but only male mice showed improvement in markers of cardiac damage and had improved cardiac function echocardiogram compared to wild-type controls. They concluded that Trpc6 promotes cardiac damage following treatment with doxorubicin resulting in cardiomyopathy in male mice, while female mice were less susceptible to cardiotoxicity (poster #1) [1].

Graduate student Branden Nguyen from Dr. Smuder's team presented their research on the effects of moderate-intensity and high-intensity interval training on cardiorespiratory capacity and body composition during doxorubicin treatment in a clinically translational rodent model. The doxorubicin dosing protocol was administered in adult female Sprague-Dawley rats following a standard clinical treatment regimen. Rats prescribed exercise training followed current exercise guidelines for cancer patients. They found that moderate-intensity exercise and high-intensity interval training improved exercise tolerance, reduced fat mass, and increased lean mass in doxorubicin-treated rats. These findings mimic the clinical effects of doxorubicin on cardiorespiratory capacity and body composition in breast cancer

patients and demonstrate that exercise training during treatment can reduce these negative effects of doxorubicin chemotherapy (poster #5) [2].

Graduate student Camara Casson from Dr. Ferrall-Fairbanks's team created an *in vitro* model system to determine changes in the biomechanical and biomolecular properties after anthracycline treatment. Specifically, this model explored the development of a tissue-engineered cardiac construct of the left ventricle and its response to anthracycline treatment and determined the synergistic effects of the host environment on tissue degeneration of the cardiac tissue (poster #2, see abstract in the supplemental materials).

Multiple guidelines recommend cardiac surveillance such as echocardiography (ECHO) and serum cardiac biomarkers, B-type natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP), evaluation before and 6–12 months after anthracycline treatment. Dr. Deremer and colleagues evaluated the associations between racial and ethnic groups in cardiac surveillance of adult cancer survivors after exposure to anthracyclines in the OneFlorida Consortium. Among the 5430 participants included in this analysis, 63 % had a baseline ECHO, with 22.3 % receiving an ECHO at 6-month and 25 % at 12-month after the initiation of anthracycline treatment. Non-Hispanic black participants received significantly less cardiac surveillance compared to non-Hispanic white participants at baseline (odds ratio, OR = 0.76, 95 % confidence interval (CI): 0.64–0.89, $p = 0.001$). Compared to non-Hispanic white participants, Hispanic survivors of cancer received significantly less cardiac surveillance at 6-month (OR = 0.84, 0.72–0.98, $p = 0.03$) and 12-month (OR = 0.85, 0.74–0.98, p = 0.03) time points respectively (poster #3) [3].

PharmD student Nathalie Roumi evaluated the association of dexrazoxane treatment and all-cause mortality in over 6000 anthracycline-treated cancer patients in the OneFlorida Consortium. They found that even though mortality was lower in the overall analysis of all cancer patients treated with dexrazoxane + anthracycline compared to those treated with anthracyclines alone, there was no evidence of survival benefit of dexrazoxane in the adjusted analyses and by specific cancer types (adjusted hazard ratio of 0.89 and 95 % CI: 0.76–1.03, $p = 0.12$) (poster #9, see abstract in the supplemental materials).

2.2. Radiation-induced cardiotoxicity

Three posters were presented by Dr. O'Dell's team, with one poster focusing on the uncertainty in the measurement of global longitudinal strain and left ventricular ejection fraction (poster #6) and two posters focusing on radiation-induced cardiotoxicity (posters # 7 and 8). Specifically, Dr. O'Dell created custom software and tested the hypothesis that radiation to the heart wall caused decreased regional perfusion, which is measurable and predicted regional mechanical dysfunction in heart magnetic resonance images (MRI) in breast cancer patients (poster # 7, see abstract in the supplemental materials). They also performed a study to compare proton therapy and conventional radiotherapy in breast cancer patients and found that proton therapy preserves acute left ventricular ejection fraction in these patients with lower heart dose compared to conventional radiotherapy (poster # 8, see abstract in the supplemental materials).

2.3. Biomarkers of cardiotoxicity

Three poster abstracts investigated biomarkers for cardiotoxicity related to the proteasome inhibitor carfilzomib in patients with multiple myeloma using multi-omics approaches (posters # 10–12). If validated, these biomarkers could be used clinically to stratify patients according to their baseline risk for the development of cardiotoxicity prior to carfilzomib therapy.

Graduate student Samia Shabnaz in Dr. Gong's lab presented the OLINK proteomic analysis results of 28 patients with multiple myeloma including 14 patients with carfilzomib-related heart failure and 14 age-, sex-matched patients with no heart failure. β-NGF (beta nerve growth factor) and HB EGF (heparin-binding epidermal growth factor) were found to have lower intensity at baseline and post-treatment in the patients who developed heart failure compared to those who did not. β-NGF has a cardio-protective effect by activating the PI3K/Akt/NOS axis. HB EGF can decrease iNOS expression, increase nitric oxide (NO) production, and protect epithelial cells from apoptosis. This result suggested the importance of the PI3k/Akt/eNOS pathway and NO production in carfilzomib-related heart failure (poster #10) [4].

Postdoctoral Fellow Dr. Tantawy in Dr. Gong's lab reported the results of a whole-exome sequencing analysis of 219 patients with multiple myeloma treated with carfilzomib from the Oncology Research Information Exchange Network (ORIEN). A missense variant rs7148 in *TMSB10/TRABD2A* locus was found to be associated with an increased risk for carfilzomib-related cardiotoxicity, with OR of 10.94 ($p = 2.4*10^{-7}$). TMSB10 is a ubiquitous protein and member of the β-thymosin family and has been previously reported to be dysregulated in dilated cardiomyopathy. *TRABD2A* was previously associated with troponin elevation and heart failure (poster #11) [5].

Dr. Tantawy also presented her analysis of microRNA profiling of 60 carfilzomib-treated multiple myeloma patients including 31 patients with carfilzomib-related cardiovascular adverse events using TaqMan Open-Array Human MicroRNA panels. The relative expression level of miR-125a at baseline was significantly higher in patients who developed cardiovascular adverse events compared to those who did not, with OR of 1.25 and 95 % CI of 1.05–1.48 ($p = 0.014$) and fold change of 12.9. However, this miRNA was not significantly changed in post-treatment samples (OR = 1.12, 0.96–1.32, $p = 0.15$, and fold change of 3.87). MiR-125a has been reported to be upregulated in the plasma of humans and cardiac cells in rats with heart failure and acute ischemic stroke. Elevated baseline circulating miR-125a may be a biomarker for carfilzomib-related cardiovascular adverse events (poster #12) [6].

2.4. Genetics of cardioprotection

Genetic epidemiology work was also represented at this symposium. Dr. Dungan presented a slate of candidate genes for the study of cardio-oncology as identified in her genome-wide association studies (GWAS) [7,8] of longitudinal survivorship among large clinical cohorts of people with coronary heart disease. The candidates included genes such as *LSAMP, DAB2IP, TSSC1,* and *SLC9A9* etc., with some conferring increased risk of mortality and others providing evidence of potential cardioprotective effects, from which new hypotheses were discussed (poster # 4).

2.5. Survivorship in cancer patients

Dr. Vilaro presented her research evaluating communal coping (a process of cooperative problem-solving framing illness as a joint rather than an individual issue) as an intervention to support adherence strategies for cardiovascular disease risk reduction among African American colorectal cancer survivors (poster #13, see abstract in the supplemental materials).

3. Conclusion

There are a number of early and mid-career faculty at the University of Florida who are focusing their research programs on the cardio-oncology field. Their work encompasses all major realms of cardio-oncology from basic science research to translational research using different approaches including in vitro, in vivo, use of retrospective datasets, and prospective clinical trials and studies.

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Ethics statement

No animal of human studies are reported in this publication.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahjo.2023.100348.

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