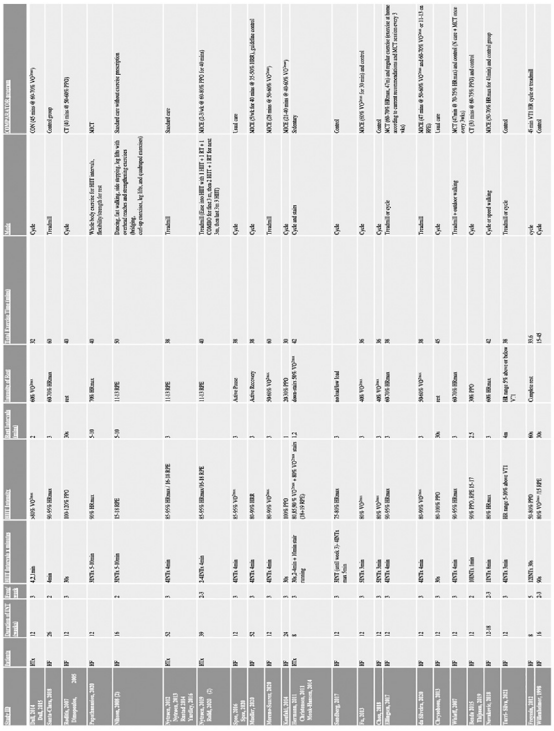

Figure 1. Summary of final findings. PPO= peak power output, HRQoL: health related quality of life, HIIT= high interval intensity training, MICE= moderate intensity continuous exercise, 6MWT= six minute walk test, HADS-A= hospital anxiety and depression scale- anxiety, VO2max= peak oxygen uptake

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P106
IS FLAXSEED EQUIVALENT AND/OR SYNERGISTIC WITH ACE INHIBITION IN THE TREATMENT OF CHEMOTHERAPY MEDIATED CARDIOTOXICITY?

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BACKGROUND: Breast cancer is a major public health concern in Canada. Although the current combination of surgery, radiation, and chemotherapy may lead to a cure in the breast cancer setting, the administration of the anti-cancer drugs Doxorubicin and Trastuzumab (DOX+TRZ) is associated with an increased risk of developing heart failure. Little is known, however, on whether flaxseed (FLX) is equivalent to angiotensin converting enzyme inhibition (ACEi) in the treatment of DOX+TRZ mediated cardiotoxicity.

METHODS AND RESULTS: In a chronic in vivo murine model of chemotherapy mediated cardiotoxicity, DOX+TRZ (8mg/kg and 3mg/kg, respectively) were administered weekly for a total of 3 weeks. Following this, mice were randomized to daily treatment with a 10% FLX supplemented diet, Perindopril (PER) (3mg/kg) via oral gavage, or a combination treatment of FLX+PER for an additional 3 weeks. Serial echocardiography was performed weekly. At the end of week 6, the mice were euthanized, and histological and biochemical analyses were performed on cardiac tissue. In mice treated with DOX+TRZ, the left ventricular ejection fraction (LVEF) decreased from 72±4% at baseline to 30±2% at week 6. Treatment with either FLX, PER, or FLX+PER improved LVEF to 52±4%, 54±4%, and 55±3%, respectively ($P < 0.05$) (Figure 1). Histological analyses confirmed significant disruption of myofibrils, vacuolization, and loss of sarcomere integrity in the DOX+TRZ treated mice. Treatment with FLX, PER, or FLX+PER, however, improved myofibril integrity at week 6 in mice receiving DOX+TRZ.

CONCLUSION: In a chronic in vivo murine model of DOX+TRZ induced cardiotoxicity, although FLX was equivalent to PER in the treatment of adverse LV remodeling, the combination of FLX and PER was not synergistic.

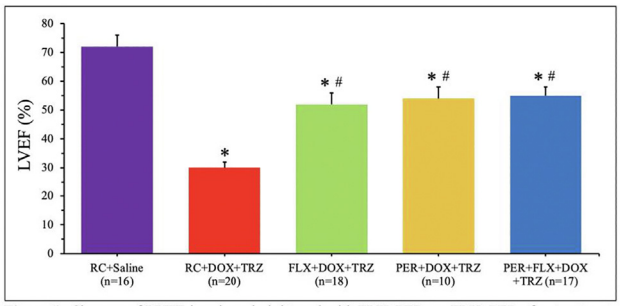

Figure 1: Changes of LVEF in mice administered with FLX, PER, or FLX+PER after treatment with DOX+TRZ. *p<0.05 RC+DOX+TRZ vs. RC+Saline. *#p<0.05 FLX+DOX+TRZ or PER+DOX+TRZ or PER+FLX+DOX+TRZ vs. RC+DOX+TRZ and RC+Saline.

Heart and Stroke Foundation of Canada

P107
MEDICAL MANAGEMENT OF HEART FAILURE WITH CONCURRENT DIABETES MELLITUS IN CANADIAN PRIMARY CARE

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BACKGROUND: Heart failure (HF) and diabetes (DM) often co-exist and are associated with increased mortality and hospitalization. Although most patients are managed in primary care, the disease intersection has mainly been studied in secondary care, ambulatory registries, and selected cohorts. We therefore assessed HF and DM management in primary care using the Canadian Primary Care Surveillance Network (CPCSSN).

METHODS AND RESULTS: CPCSSN is a primary care data repository consisting of 17 electronic medical record (EMR) systems, spanning all provinces in Canada except Saskatchewan. Data on over 2 million patients are contributed quarterly to the network. Patients with HF and DM were identified using validated case definitions. The sensitivity and specificity are 90% and 93% for identifying HF, and 96% and 97% for identifying DM. Prescription of all medical therapies increased from 2010 to 2020. In patients with HF alone (n=5,319 in 2010 and n=10,699 in 2020), renin-angiotensin blockade (RAASi) increased from 79.6% to 80.3%, beta-blockers from 29.3% to 47.2%, and mineralocorticoid receptor antagonists (MRA) from 6.4% to 17.3%. In those with concurrent DM (n=2,747 in 2010 and n=9,024 in 2020), the corresponding

rates were slightly higher at both time points for RAASi (88.6% to 83.5%) and MRA (9% to 19.3%), but lower for beta-blockers (24.5% to 44.8%). Sodium/glucose cotransporter 2 inhibitors (SGLT2i) were never prescribed in patients with HF alone. However, in patients with concurrent DM, prescription increased from 0.2% to 18.2%. Prescription of loop diuretics for symptom control increased for both HF with DM and HF alone groups, from 39.5 to 64.9%, and 33.4% to 58.4% respectively.

CONCLUSION: To our knowledge, this is the first study on primary care management of heart failure and diabetes in Canada. Our study showed an increase uptake of all HF therapies from 2010 to 2020, despite a lack of left ventricular ejection fraction (LVEF) information. There are ongoing prescription gaps in therapies potentially indicated across the spectrum of LVEF, such as MRA and SGLT2i. While the use of MRA was similar in HF with and without DM, SGLT2i uptake in patients with HF and concurrent DM was higher compared with those with HF alone. Further medical optimization of this complex patient population in primary care is needed.

P108
MYOCARDIAL RECOVERY AND SURVIVAL AFTER WEANING OF LEFT VENTRICULAR ASSIST DEVICE THERAPY IN PATIENTS WITH TOXIC AND NON-TOXIC CARDIOMYOPATHIES, A CANADIAN EXPERIENCE

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BACKGROUND: Left ventricular assist devices (LVAD) are increasingly used in advanced and refractory heart failure, mainly as a bridge to transplantation or as a destination therapy. LVAD unloading of the left ventricle (LV) can also promote myocardial recovery leading to improvement of the LV systolic function, allowing subsequent LVAD explantation. However, the parameters associated with LVAD weaning and the long-term outcomes of these patients are not well documented. The aim of this study was to assess the clinical and echocardiographic characteristics of weaned patients and to evaluate their event-free survival post-explantation.

METHODS AND RESULTS: We conducted a single-center retrospective study recruiting consecutive patients who underwent a second or third generation LVAD implantation at a Canadian cardiology center between November 2009 and October 2021. A total of 98 patients underwent an LVAD implantation at our institution during this period (Table 1). All patients were on guideline-directed medical therapy. Fourteen patients (14%) had significant LV recovery and were successfully weaned and explanted/decommissioned after a median support time of 309 days (range 55-595 days). Toxic cardiomyopathy, defined as an abuse of amphetamine (n= 2), energy drink (n=2) or mixed consumption (n= 6), was the most likely diagnosis for 10 of the weaned patients (71%). The LVEF was significantly higher (35% vs. 19%, p< 0.001) and the left ventricular end-diastolic diameter (LVEDD) was significantly smaller (51 mm vs. 60 mm, p=0.008) in weaned patients compared to non-weaned patients after 3 months of LVAD support (Figure 1). Myocardial recovery manifested by pump thrombosis in 4 of the 14 weaned patients (29%). After explantation, weaned patients were followed during a median time of 40 months (range 8-109 months). The mean LVEF was 44 +/- 6% at last follow-up and no patient had a LVEF below 35%. All patients were New York Heart Association class I or II. No death, heart transplantation, or mechanical support initiation occurred during follow-up.

CONCLUSION: LVAD therapy can induce significant LV reverse remodeling leading to myocardial recovery in a non-negligible proportion of patients, particularly young patients with toxic and non-ischemic cardiomyopathies. Early reverse remodeling with decreasing LVEDD and improving LVEF at 3 months following LVAD implantation is associated with successful subsequent mechanical support weaning. In a subset of patients pump thrombosis appears to be associated with LV reverse remodeling and weaning of mechanical support. Weaned patients maintain partial or complete LVEF recovery after LVAD explantation and have good long-term event-free survival.

Table 1. Baseline patient characteristics.

Characteristics	Weaned (n = 14)	Unweaned (n =84)	p value
Age - years			0.008
mean ± SD	40 ± 11	52 ± 16	
Median (range)	38 (24-59)	59 (22-73)	
Male sex, n (%)	8 (57)	69 (82)	0.035
Etiology of heart failure, n (%)			<0.001
Ischemic	1 (7)	35 (42)	
Toxic	10 (71)	1 (1)	
Amphetamine	2 (14)	0 (0)	
Energy drink	2 (14)	1 (1)	
Mixed consumption	6 (43)	0 (0)	
Toxic + other	2 (14)	5 (6)	
Idiopathic dilated cardiomyopathy	1 (7)	24 (29)	
Mixed (excluding toxic)	0 (0)	10 (12)	
Other	0 (0)	9 (11)	
Worsening heart failure duration in month, mean ± SD	2 ± 1	2 ± 2	0.600
Device type, n (%)			0.066
HeartMate II (axial-flow pump)	12 (86)	64 (76)	
HeartMate 3 (centrifugal-flow pump)	0 (0)	17 (20)	
HeartWare (centrifugal-flow pump)	2 (14)	3 (4)	
LVEF, mean ± SD	11 ± 3	14 ± 6	
INTERMACS profile – no. (%)			0.312
1	0 (0)	13 (15)	
2	3 (21)	12 (14)	
3	11 (79)	50 (60)	
4	0 (0)	9 (11)	
5 to 7	0 (0)	0 (0)	
Mechanical support pre LVAD, n (%)			0.096
Extracorporeal membrane oxygenation	0 (0)	12 (14)	
Intra-aortic balloon pump	2 (14)	3 (4)	
Other	0 (0)	0 (0)	
Pre LVAD inotropes, n (%)	14 (100)	74 (88)	0.173
Number of previous cardiac surgery, n (%)			0.054
0	13 (93)	64 (76)	
1	1 (7)	17 (20)	
2	0 (0)	3 (4)	
Laboratory values, mean ± SD			
Hemoglobin (g/L)	123 ± 21	114 ± 20	0.115
Serum creatinine (µmol/L)	78 ± 18	130 ± 60	<0.001
Serum alanine aminotrasnferase (ALT, IU/L)	70 ± 78	62 ± 90	0.747
Serum total bilirubin (µmol/L)	11 ± 10	16 ± 10	0.401
Serum albumine (g/L)	36 ± 5	36 ± 6	0.700
Comorbidities, n (%)			
Hypertension	1 (7)	33 (39)	0.015
Diabetes mellitus	0 (0)	25 (30)	0.011
History of atrial fibrillation	1 (7)	39 (46)	0.006
History of stroke	0 (0)	10 (12)	0.197
Chronic obstructive pulmonary disease	2 (14)	19 (23)	0.435
Renal replacement therapy	1 (7)	8 (10)	0.622
Implantable cardioverter-defibrillator	3 (21)	55 (65)	0.002
Cardiac resynchronization therapy	2 (14)	33 (39)	0.071
Hemodynamics parameters, mean ± SD			
Right atrial pressure (mmHg)	6 ± 5	10 ± 6	0.023
Mean pulmonary pressure (mmHg)	24 ± 8	36 ± 10	<0.001
Pulmonary capillary wedge pressure (mmHg)	18 ± 9	26 ± 8	0.001
Cardiac index (L/min/m²)	2.0 ± 0.5	1.9 ± 0.4	0.559
Pulmonary vascular resistance (Wood units)	1.9 ± 1.0	3.0 ± 2.0	0.073