CANCER AND EXERCISE: IMPROVING PHYSICAL FUNCTION AND CARDIOPULMONARY HEALTH DURING AND AFTER TREATMENT

Community Medical School 2013
May 14, 2013
Kim Dittus MD & Susan Lakoski MD
TOPICS FOR DISCUSSION

- Status of Cancer Survivors
- Physical Fitness
  - Strength & Function
  - Cardiorespiratory Fitness
- Oncology Rehabilitation: A model to improve fitness of cancer survivors
13.7 MILLION AND GROWING

35,000 Survivors in Vermont

Am Cancer Society, 2013
CHARACTERISTICS OF CANCER SURVIVOR

- 64% of adults are expected to live at least 5 years after diagnosis
- 61% are over the age of 65
- Breast cancer survivors are the largest population (22%), followed by prostate (17%) and colorectal (11%)
- 50% have late treatment-related effects
IMPACT OF SURGERY & RADIATION

- Impaired range of motion
- Lymphedema
- Impaired organ function
- Fibrosis of tissue
- Pulmonary/Cardiac Dysfunction
- Cognitive change
ACUTE IMPACT OF MEDICAL ONCOLOGY THERAPY

- Fatigue
- Deconditioning
- Sarcopenia
- Cardiac/Pulmonary Dysfunction
- Nausea/Vomiting
- Anxiety/Depression
- Pain
- Cognitive Impairment
LONG TERM IMPACT OF CANCER & IT’S THERAPY

- Fatigue
- Functional Impairment
- Lymphedema
- Weight gain, muscle loss
- Cognitive impairment
- Diminished body image
- Heightened anxiety/depression
WHICH IMPACTS OF CANCER THERAPY IMPROVE WITH EXERCISE?

- Fatigue
- Functional Impairment
- Lymphedema
- Weight gain
- Cognitive impairment
- Diminished body image
- Heightened anxiety/depression

Gallavo, 2006
LONG TERM IMPACT OF CANCER & IT’S THERAPY

Diminished aerobic capacity, strength & function
TOPICS FOR DISCUSSION

• Status of Cancer Survivors
• Physical Fitness
  • Strength & Function
  • Cardiorespiratory Fitness
• Oncology Rehabilitation: A model to improve fitness of cancer survivors
COMPONENTS OF PHYSICAL FITNESS

Cardiorespiratory Fitness
Muscular Strength
Muscular Endurance
Flexibility
Body Composition
IMPACT OF CHEMOTHERAPY ON STRENGTH IN 14 WEEKS

Keilani et al 2012
Not Just Chemotherapy: Trajectory of Muscle Change in Prostate Cancer

Galvao DA et al 2007
CAN STRENGTH IMPROVE WITH EXERCISE: TRANSPLANT EXAMPLE

Objective: Determine the impact of autologous transplant on aerobic capacity, strength, and body composition

- Evaluate the effect of transplant
- Randomization into Exercise vs. Control

Hays et al ’03 and ‘04
SCHEMA

- **Phase I Pre Transplant**
- **Phase II Post Transplant**
- **Phase III F/u & Intervention**
  - Control
  - Exercise

Measurements:
- Body Composition
- Strength

Hays et al ’03 and ‘04
CHANGES WITH STEM CELL TRANSPLANT: LOWER EXTREMITY STRENGTH

Kg pressed/kg body weight with Leg Press

Hays et al ‘03 and ‘04
Diminished Physiologic Mechanisms Supporting Physical Function

- Decreased CV Fitness
- Diminished Strength

Impaired Physical Function

Morbidity & Mortality

Modifiers

- Individual physical capacity & reserves
- Weight & Diet
- EXERCISE

Cancer

Cancer Treatment
FUNCTIONAL IMPAIRMENT

- Cant walk 1/2 mile
- Problems with stairs
- Unable to prepare meals

% Distribution by cancer duration:
- No cancer
- 5 yrs
- 2-5 yrs
- <2 yrs

Sweeny et al JNCI 2006
IMPACT OF PHYSICAL FUNCTION ON SURVIVAL

No Decline at 27 mos
Decline in PF−10 > 0.8 SD at 27 mos

Proportion Surviving

Days

Sehl et al 2013
TOPICS FOR DISCUSSION

• Status of Cancer Survivors
• Physical Fitness
  • Strength & Function
  • Cardiorespiratory Fitness
• Oncology Rehabilitation: A model to improve fitness of cancer survivors
EXERCISE IS DANGEROUS
CORONARY HEART DISEASE EVENTS AMONG SEDENTARY VS. ACTIVE WORKERS MEN 35-64, IN LONDON 1949-1952

PHYSICAL ACTIVITY & SURVIVAL: BREAST CANCER

- Evaluated the impact of physical activity on rates breast cancer recurrence and death
- Approximately 3000 nurses diagnosed with Stage I-III breast cancer between 1984 and 1998
- Collected information about physical activity at least 2 years; Monitored for breast cancer outcomes

Holmes et al. JAMA, 2005.
PHYSICAL ACTIVITY AND SURVIVAL: BREAST CANCER

Recurrence *  Breast Ca Death  Total Death #
< 1hr/wk  1-3 hrs  3-5 hrs  5-8 hrs

*p=0.05, # p<0.004
PHYSICAL ACTIVITY ESTIMATED USING QUESTIONNAIRES

• Strengths
  • Inexpensive
  • Noninvasive

• Weaknesses
  • Self-report bias
  • Accuracy and reliability
CARDIORESPIRATORY FITNESS

• Index of functional capacity of hearts & lungs

• Reflects efficiency of $O_2$ uptake, transport, and utilization in muscles

• Excellent surrogate of chronic exercise exposure and reproducible measurement
Cardiorespiratory Fitness: Global Assessment of Health

DOES BEING LOW FIT IMPACT SURVIVAL?
FITNESS AND MORTALITY IN CAUCASIAN MEN (N= 6213 REFERRED FOR EXERCISE TESTING)

Myers, J. NEJM 2002;346:798-801
FITNESS AND MORTALITY RISK IN ASYMPTOMATIC WOMEN: 20-YR FOLLOW UP (N= 2994, 30-80 YEARS)

Mora, S. Lipid Research Clinic Study. JAMA 2003;290(12):1600-1607
LIFETIME RISK OF CVD DEATH ACCORDING TO BASELINE FITNESS LEVELS AT AGE 55

Berry, Lakoski, JACC, 2011
FITNESS AND 30-YEAR SURVIVAL IN “LOW-RISK ADULTS”

1-MET increase = 18% reduction in CVD Mortality

Lakoski, JAHA 2012
FITNESS AND FUTURE CANCER RISK
FITNESS AND SURVIVAL FROM BREAST CANCER (N=14,811)

\[
\chi^2 = 7.3, \text{ df}=2, \ P=0.03
\]

Peel et al. Med Sci Sports & Exercise, 2009
WHAT DETERMINES OUR ABILITY TO BE FIT?
THE NEXT FEW SLIDES ARE "EMBARGOED"
I.E. THEY ARE SO HOT OFF THE PRESS THAT WE CAN’T SHARE THEM
AGE, GENDER AND FITNESS:
THE BALTIMORE LONGITUDINAL AGING STUDY
(N=1513, AGE 21-87 YRS)

Fleg et al. Circulation. 2005;112: 674-682
FITNESS & BMI:
COOPER CENTER LONGITUDINAL STUDY (1990-2009; N=2553, 50 YRS)
7-YEAR CHANGE IN FITNESS & BODY WEIGHT (BASELINE & YEAR 7, N=2458, 18-30 YRS)

FITNESS AND PHYSICAL ACTIVITY INTENSITY: CCLS (1990-2009)

N=35,095

0 = sedentary
1 = non-running activities
2 = 0-10 miles/week running
3 = 11-20 miles/week running
4 = >20 miles/week running
30-YEAR FOLLOW-UP DALLAS BED REST AND TRAINING STUDY

Rationale for Cardiorespiratory Fitness Testing After a Cancer Diagnosis
Multiple CVD Hit in Cancer Patients

Direct Effects
- Surgery
- Radiation
- Systemic Therapy

Indirect Effects
- Physical inactivity / changes in body composition
- Aging
- Other CVD risk factors (HTN)

CV Risk Factors → Cancer Diagnosis → Decreased Cardiovascular Reserve → ↑↑CVD

Jones et al. J Am Coll Cardiol, 2007
Superiority of Measuring Fitness in Oncology Setting

- Pulmonary function (Systemic therapy, RT)
  +
- Cardiac function (DOX, Herceptin, RT, TKIs)
  +
- Vascular compliance (DOX, RT, TKIs)
  +
- Skeletal muscle function (decadron, ADT, chemotherapy)

II

↓↓↓↓ CV reserve

Fitness Following Breast Cancer Treatment with Normal Ejection Fraction

VO₂peak (mL·kg⁻¹·min⁻¹)

Post Tx

Age-Pred

↓ 31%

<table>
<thead>
<tr>
<th>Cohort</th>
<th>40yrs</th>
<th>50yrs</th>
<th>60yrs</th>
<th>70yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients After Therapy</td>
<td>21.05</td>
<td>19.51</td>
<td>17.97</td>
<td>16.44</td>
</tr>
<tr>
<td>(n=140)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy controls</td>
<td>29.82</td>
<td>26.32</td>
<td>22.82</td>
<td>19.32</td>
</tr>
<tr>
<td>(n=107)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Impaired fitness across Breast Cancer Continuum

VO$_{2peak}$ (mL·kg$^{-1}·$min$^{-1}$)

- **Pre-Tx**: VO$_{2peak}$ decreased by 28%
- **During Tx**: VO$_{2peak}$ decreased by 31%
- **Post Tx**: VO$_{2peak}$ decreased by 35%
- **Metastatic**: VO$_{2peak}$ decreased by 37%

Jones et al. *J Clin Oncol* 2012
Impaired Fitness 7 years after Breast Cancer Treatment

Lakoski, et al. in press, Breast Cancer Research and Treatment
Impaired Fitness 10 years after Cancer Treatment

- Ovarian (n=22)
- Endometrial (n=52)
- Cervical (n=122)

[Bar chart showing METs for different cancer types]
Importance of Measuring Fitness in Oncology Setting

- Early marker of cardiopulmonary limitations with therapy
- Marker of survival after breast cancer therapy
- Direct measurement allows for targeted interventions to improve fitness
Maximal exercise testing safe / feasible in cancer patients

Diminished Fitness is Reversible in Breast Cancer Patients
Exercise training to improve Fitness after Breast Cancer Txt

• Meta-analysis of RCTs evaluating cardiorespiratory fitness ($VO_{2peak}$)

• Six studies, 571 patients (exercise, n=344; usual care control, n=227)

• Exercise increased $VO_{2peak}$ 2.90 mL.kg.min (15%)

Jones et al. Oncologist, 2011
AMERICAN COLLEGE SPORTS MEDICINE & AMERICAN CANCER SOCIETY: EXERCISE RECOMMENDATIONS

- Weekly activity of 150 minutes of moderate intensity exercise or 75 minutes of vigorous intensity exercise
- Strength training 2 to 3 sessions weekly that includes exercises for major muscle groups
- Flexibility recommendations to stretch major muscle groups and tendons on days that other exercise is performed
PHYSICAL ACTIVITY AMONG CANCER SURVIVORS: CURRENT NHANES

• 87.3% without cancer DID NOT meet recommendations of 150 min/week
• 95.5% cancer survivors DID NOT meet recommendations
• Differences by cancer type:
  • 17.9% ovarian meeting
  • 3.8% prostate meeting
  • 3.7% breast meeting

Smith et al AM J Transl Res 2011
TOPICS FOR DISCUSSION

• Status of Cancer Survivors
• Physical Fitness
  • Strength & Function
  • Cardiorespiratory Fitness
• Oncology Rehabilitation: A model to improve fitness of cancer survivors
STEPS TO WELLNESS

Oncology and Hematology Rehabilitation at FAHC/UVM
CANCER SURVIVOR CONTINUUM

- Diagnosis
- Oncologic Therapy
- Initial Recovery
- Long Term Survival
- Palliation
Cancer Care Continuum

Prevention of Decline
Therapeutic Rehabilitation

Therapeutic & Restorative Rehabilitation

Diagnosis → Oncologic Therapy → Post Therapy → Long Term Survivors

- Pulmonary rehabilitation intervention prior to surgery
- Resistance training for individuals with cachexia
- Fatigue management
- Pain Control
- Preservation of CV fitness and strength
- Prevent functional decline during therapy
Cancer Care Continuum

Prevention of Decline
Therapeutic Rehabilitation

Diagnosis ➔ Oncologic Therapy ➔ Post Therapy ➔ Long Term Survivors

Therapeutic & Restorative Rehabilitation

- Interventions for deconditioned individuals
- Improved Aerobic Capacity & Strength
- Restore function (range of motion)
- Lymphedema management
- Fatigue management
- Lifestyle modifications

Started Here
Aug 2011
PIECES IN PLACE AT FAHC

• Support of Oncology & Physical Therapy services
• Access to cardiac rehabilitation space afternoons
• An Athletic Trainer with salary support from the Victoria Buffum Foundation
MODELED AFTER CARDIAC REHABILITATION

- System of referral
- Evaluation & testing pre & post
- Exercise component
- Lifestyle Education
INCREASED EMPHASIS ON PHYSICAL THERAPY

• Skills that address needs across the cancer continuum
• Can evaluate for many deficits
• Able to provide exercise assessments and prescribe exercise interventions
• Aware of other rehabilitation services
• Services can be reimbursed by insurance
Physical Therapy Evaluation

Additional PT services
- Lymphedema
- ROM
- Pain

Other Rehabilitation Services
- Occupational Therapy
- Memory Center

Exercise Intervention
- Aerobic & Resistance Training
- Focus on improving strength & endurance
- Fatigue Management

Weight Loss Interventions

1hr Eval & Testing

At Cardiac Rehab Tilley Dr & Shep 2
MD EVALUATION

• Summarize oncologic therapy received
• Identify continuing cancer-related symptoms that require intervention
• Determine if referrals are needed
• Help determine exercise goals
CANCER SURVIVORS RECEIVE:

- PT and MD evaluation
- Exercise Tolerance Test
- A personalized aerobic and resistance exercise program
- Opportunity to exercise at cardiac rehab site 2 days per week for 12 weeks
- Referrals as needed
- Education classes on site
RESEARCHERS GAIN A LIVING DATABASE

- Physical parameters
  - 6 minute walk test
  - 1 rep max (chest press, leg press)
- Anthropometrics
- VO2 max parameters
- Functional Measures
  - Range of motion
  - Strength shoulder
  - Balance
MEASURES INCLUDED IN THE DATABASE

- Late long term symptoms
  - Fatigue
  - Sleep
  - Quality of Life (SF36)
- Distress
  - Distress thermometer
  - Depression
  - Anxiety
FUNDING FOR ONCOLOGY REHAB

- NO Insurance coverage for Onc Rehab
- Insurance Reimbursement for PT & MD Evals
- Reimbursement for Exercise Tolerance Test

We Depend on Donated Funds
RESULTS SO FAR…

- 178 cancer survivors evaluated in the last year (2012-2013)
- 115 Started the program (65%)
- 100 Completed the program (87%)
  - Attended > 20 sessions – 40%
  - Attended 16-20 – 45%
  - Attended 10-15 – 13%
  - Attended < 10 – 2%
STRENGTH COMPARED TO NORMAL VALUES

72% < 10th percentile for UE 1 rep max strength before

25% < 10th percentile for UE 1 rep max strength after

68% < 20th percentile for LE 1 rep max strength Before

34% < 20th percentile for LE 1 rep max strength after
6 MINUTE WALK TEST

Pre

Post

Meters

500 520 540 560 580 600 620

*
DEPRESSION & ANXIETY SCORES

Mild Depression /Anxiety

Pre
Post

Depression
Anxiety
ADVANTAGES OF THIS MODEL

• Use cardiac rehab sites across the country
• Partially funded
• Inclusive
• Can provide a database to evaluate impact of cancer therapy and effect of rehabilitation
• Serve as a platform for research
ONCOLOGY REHABILITATION: A LABORATORY FOR TRANSLATIONAL RESEARCH

T1

Oncology Rehabilitation Interventions

T2

T3
Evaluate skeletal muscle *structure, function* and *metabolism* at the whole body, tissue, cellular and molecular level to determine the impact of cancer and cancer therapy on the development of physical disability.
UVM RESEARCH EXAMPLES

- Cancer patients have 12.6% absolute risk of blood clots at 1-year
- 50% occur during the first 3-months of chemotherapy
- Cancer patients with a blood clot have a 2.5-fold higher mortality

Expect Trial

Oncology population -- High-risk of Blood Clot
Timing -- During Chemotherapy
Training -- Moderate intensity aerobic exercise
Outcome -- Markers of Blood Clot Risk

Lakoski et al
UVM RESEARCH EXAMPLES

- 67% of Breast Cancer Survivors are overweight or obese
- Individuals with excess weight are more likely to have their cancer come back
- Weight loss results in changes in biomarkers of cancer risk and progression

IWEB Behavioral Weight Loss Intervention
Population -- BC survivors throughout New England
Intervention – Behavioral-based Weight Loss Intervention Delivered Online
Outcome – Feasibility & Change in Biomarkers
STEPS TO WELLNESS TEAM

• Oncology: Kim Dittus, Susan Lakoski, Patti O’Brien, Penny Gibson, Nate Kokinda, Kristie Grover
• Cardiology: Phil Ades, Patrick Savage, Jason Rengo
• Physical Therapy: Diane Stevens, Michael Laramee, Kim Woods, Natalie Bradford, Steve Eyler
• Trainers: Rebecca Reynolds & Elisha Crowley
• Quality: Joan Blondin
• Business: Susan Webber, Nick Jaidar
• Development Office for University of Vermont & FAHC
ONCOLOGY REHABILITATION: A LONG ROAD … BUT WE ARE GETTING THERE

Special Thank You:

Victoria Buffum Foundation
Estate of Jane Lande

UVM Foundation in Honor of Karen Meyer

FAHC Axillary

UVM College of Medicine & FAHC Marathon Teams