Effects of Exercise on Persons with Metastatic Cancer

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Outline

- Background
- Methods
- Results
- Discussion
- Conclusion
- Acknowledgements
Background
Cancer Statistics

- The Canadian Cancer Institute estimates that in 2008, in Canada there will be:
  - 166,400 new cases of cancer
  - 73,800 cancer-related deaths

- Of persons with a new cancer diagnosis 30% will already have metastatic disease

- Once metastasis has occurred, prognosis is generally poor
Metastatic Cancer

- Creates different challenges than that of non-metastatic cancer as it is a palliative disease\(^4-8\)
- It causes declines in quality of life (QOL), psychological barriers and fatigue\(^4-8\)
- Persons with metastatic cancer are now living longer\(^9\)
- Suggest the need for research on interventions aimed at improving QOL
Previous Research

- Focused on exercise interventions for persons with local or regional cancer\textsuperscript{10-14}
- Many reviews investigated the impacts of exercise on fatigue\textsuperscript{7,10-15}
- Fatigue is a prevalent symptom
  - 90% of persons with cancer experience cancer-related fatigue\textsuperscript{6}
- Cancer-related fatigue has also been linked with symptoms of anxiety and depression\textsuperscript{6}
Previous Research

- Demonstrated physical exercise is an effective intervention to improve QOL & fatigue in persons with non-metastatic cancer\(^7,10-15\)

- Traditionally, persons with metastatic cancer were encouraged to rest\(^7\)

- Rest is no longer considered an appropriate intervention

- New literature is emerging regarding the potential benefits of exercise for persons with metastatic cancer\(^5,7,16,17\)
Purpose

To synthesize the available literature on the effects of exercise on QOL and physical measures in persons with metastatic cancer
Review Questions

1. What exercise interventions are being used for persons with metastatic cancer?

2. What is the effect of these interventions in respect to QOL and physical measures?

3. What research needs to be completed in the future?

4. Investigate the adverse effects and attrition rates documented in the studies.
Definition of Metastatic Cancer

- The spread of cancer from one part of the body to another\(^3\)

- For the purpose of this review it includes:
  - advanced cancer
  - palliative cancer
  - stage IV cancer

- Frequent sites of metastases include:
  - lung, liver, breast & bone\(^9\)
Quality of Life (QOL)

- Spirituality
- Environment
- Social relations
- Level of independence
- Physical health

QOL

QOL\textsuperscript{18}
Exercise

• “Any planned, structured, and repetitive bodily movement done to improve or maintain one or more components of physical fitness” 

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Methods
Search Strategy
Up to and including May 8, 2008

Databases:
- Medline, Embase, CINAHL, PsychInfo, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Databases of Systematic Reviews (EBM Reviews-Ovid) and PEDro

Keywords:
- metastatic OR palliative OR advanced
- cancer OR neoplasm
- exercise OR physical activity OR exercise therapy OR physical fitness
Inclusion Criteria

- **Population:** persons with metastatic or advanced or palliative cancer
- **Intervention:** exercise as the intervention or a component of the intervention
- **Publication:** in a peer-reviewed journal
- **Comparisons and outcome measures:** not screened at the initial stages to include all relevant studies
Exclusion Criteria

Population:
- Persons with lymphoma, melanoma or myeloma
- Less than 50% of the sample had metastatic or advanced cancer
- When results of those with metastatic cancer could not be separated from those with non-metastatic cancer

Type:
- Studies in a language other than English or French
- Newspaper editorials, single article reviews and qualitative research studies
Data Extraction

- Tool developed by reviewers
- Pilot tested by two reviewers
- Extraction was performed on each study by one reviewer and then checked by a second reviewer
- Data extracted from 12 studies: methods, participants, inclusion/exclusion criteria, intervention, attrition, adherence, and outcomes.
Quality Assessment

Randomized Controlled Trials (RCT’s)
- Modified van Tulder Criteria\textsuperscript{20}
  - One criterion added: “Was the study’s purpose clearly stated?”
  - Low = 0-4, Medium = 5-8, High = 9-12

Case Series
- Modified Case Series Criteria\textsuperscript{21}
  - Removal of criterion 6: comparison of sub-series
  - Low = 1-2, Medium = 2.5-3.5, High = 4-5

Case Reports
- Case Study Methodological Quality Assessment Tool\textsuperscript{22}
  - Low = 1-3, Medium = 4-5, High = 6-7
Data Synthesis

- Study characteristics were compiled in a table.
- Meta-analysis was not possible due to study heterogeneity in:
  - Study populations
  - Exercise interventions
  - Outcome measures
  - Study designs
Results
Titles reviewed after initial search of databases
Total = 674

Studies included after title screening
N = 224
(100% Agreement)

Articles found through hand searching
N = 1

Abstracts reviewed
N = 225

Full text reviewed
N = 27
(84.7% Agreement)

Studies included after evaluation of full text
N = 12
(96% Agreement)
12 Included Studies: 5 RCT’s

- **Rumans**\(^2^4\): 103 persons with advanced cancer of various primary sites participated in a multi-dimensional exercise program for 3 weeks.
- **Brown**\(^4\): 115 persons from the Rumans et al.\(^2^4\) study, followed for 4 weeks to investigate if improvements in quality of life (QOL) impact fatigue in patients.
- **Lapid**\(^2^3\): Geriatric subgroup of 33 persons from the Rumans et al.\(^2^4\) study followed for 4 weeks.
- **Headley**\(^1^6\): 38 women with advanced breast cancer completed seated exercises for 12 weeks.
- **Segal**\(^2^5\): 60 men with palliative prostate cancer completed resistance exercises for 12 weeks.
12 Included Studies:
5 Case Series

- **Oldervoll**\(^{26}\): 52 persons w/ metastatic cancer of various 1° sites completed circuit training, standing balance & aerobic endurance ex’s for 6 wks

- **Adamsen, 2003**\(^{27}\): 27 persons w/ advanced cancer of various 1° sites participated in a multi-dimensional intervention: resistance ex & stationary cycling for 6 wks

- **Adamsen, 2006**\(^{28}\): As per Adamsen 2003\(^{27}\) w/ 115 participants

- **Carson**\(^{29}\): 21 women with metastatic breast cancer performed yoga exercises for 8 wks

- **Porock**\(^{7}\): 9 persons w/ metastatic cancer of various 1° sites performed individual home exercises for 2-4 wks
12 Included Studies: 2 Case Reports

- **Crevenna**\(^{30}\): 1 female with metastatic breast cancer performed ergometric cycling for 1 year

- **Kelm**\(^{31}\): 1 male with metastatic adenocarcinoma of the rectum completed endurance training and strength exercises for 13 weeks
And then there were TEN

- Rummans et al.²⁴, Brown et al.⁴ & Lapid et al.²³ were based on the same study sample
- To demonstrate the breadth of literature all 3 studies were included in the characteristics table
- To prevent skewing of the results, only Rummans et al.²⁴ was included in the text of the results & discussion sections, resulting a total of 10 studies
Study Characteristics

Population

- *Cancer status*: five studies\textsuperscript{25,26,29-31} metastatic, four studies\textsuperscript{16,24,27,28} advanced and one study\textsuperscript{25} palliative

- *Primary cancer sites*: varied

- *Concurrent treatment*: eight studies included persons undergoing concurrent chemotherapy & four studies included persons undergoing radiation therapy
Characteristics of the Studies

Intervention
- **Type:** included yoga, balance, coordination, aerobic & strength training
- **Frequency:** generally 2-3 x/wk for 3-13 wk
- **Intensity:** strength @ 40-95% of 1RM $^{25,27,28,31}$ & aerobic @ low-moderate intensity $^{7,30,31}$

Most Frequent Outcome Tools
- **Physical measures:** 1RM$^{27,28,31}$ & VO2 max$^{27,28,30}$
- **QOL measures:** EORTC QLQ-30$^{26-28}$ & the SF 36 $^{27,28,30}$
Inclusion & Exclusion Criteria

Differed across studies in regards to:

- Life expectancy e.g. Porock\textsuperscript{8} versus Oldervoll\textsuperscript{26}
- Co-morbidities e.g. bone metastases/lesions
- Mental health status e.g. Adamsen\textsuperscript{28}
Attrition, Adherence & Adverse Effects

**Attrition:**
- RCT’s – ranged from 7-16%
- Case Series – ranged from 14-35%
- Case Reports – 0%

**Adherence:** ranged from 75-100%

**Adverse Effects:** no adverse effects were noted
Quality Assessment - RCT’s

- Three RCT’s assessed with the modified van Tulder Criteria²⁰
- All were rated as high quality (9/12)
- All failed to conceal the treatment allocation and blind the patient to the intervention (criterion C & D)
- Two studies²⁴,²⁵ did not blind the therapist to the intervention (criterion F)
- Headley et al.¹⁶ was able to blind the therapist to the intervention (criterion F)
Quality Assessment - Case Series

- Five case series were assessed with the modified Case Series Criteria\textsuperscript{21}
- All five studies were rated as medium quality
- None of the case series were able to fulfill blinding (criterion 5.2) or representative sampling (criterion 1)
- Carson et al.\textsuperscript{29} did not have explicit inclusion criteria (criterion 2)
Quality Assessment - Case Reports

- Two case reports were assessed using the Case Study Methodological Quality Assessment Tool.\(^\text{22}\)
- Crevenna et al.\(^\text{30}\) was rated high quality (6/7)
- Kelm et al.\(^\text{31}\) was rated medium quality (4/7)
- Both failed to clearly state their hypothesis (criterion B)
- The effect size in the Kelm et al.\(^\text{31}\) study was not clinically important (criterion F) and limitations were not identified (criterion G)
Levels of Evidence

Assigned using the Oxford Centre for Evidence-Based Medicine (CEBM) Levels of Evidence\textsuperscript{32}

- Three RCT’s = 2B
- Five case series = 4
- Two case reports = 5
Oxford CEBM Level 2B

**Improvements in physical measures including:**
- Increased upper and lower extremity muscle endurance \(^{25}\)

**Improvements in QOL measures including:**
- Improved quality of life \(^{16,24,25}\)
- Increased overall spiritual well being in the intervention group, and increased emotional distress in the control group \(^{24}\)
- The intervention group experienced a slower decline in total QOL \(^{16}\)
Oxford CEBM Level 4

Improvements in physical measures including:

- Increased strength and aerobic fitness\textsuperscript{27,28}
- Increased physical activity\textsuperscript{28}
- Increased walking distance and faster sit-to-stand\textsuperscript{26}
Oxford CEBM Level 4

Improvements in QOL measures including:

- Increased levels of invigoration and acceptance\(^{30}\)
- Decreased physical fatigue\(^{26}\)
- Increased role emotional, social and dyspnea subscales\(^{26}\)
- Improved role-physical score\(^{28}\)
- General increase in QOL\(^{29}\)
- Decreased anxiety\(^{8}\)
Oxford CEBM Level 5

Improvements in physical measures including:

- Increased aerobic fitness\textsuperscript{30,31}
- Improved respiratory function\textsuperscript{31}
- Increased or maintained 1 RM\textsuperscript{31}
Discussion
Limitations

Heterogeneity of:

- study samples
  - decreased external validity
- exercise interventions
  - unable to determine optimal frequency, intensity, exercise type and session duration
- outcome measures
  - No single measure for QOL$^{33}$
Limitations

Outcome Measures

- Reliable and valid outcome measures found to be most widely used\(^{25,34-37}\):
  - European Organization for Research and Treatment of Cancer QOL Questionnaire Core 30 (EORTC-QLQ-C30)
  - Functional Assessment of Chronic Illness Therapy (FACIT)
  - Symptom Distress Scale (SDS)
  - 36-Item Short Form (SF-36)
  - Multidimensional Fatigue Inventory (MFI)
  - Hospital Anxiety and Depression Scales (HADS)
Attrition

- Short life expectancy and debilitating symptoms make retention of participants challenging.
- It could be expected that attrition rates would be higher than normal for this population\(^{33}\).
- However, all 10 studies have attrition rates well below normal range.
Adherence & Adverse Effects

- Documented adherence rates ranged from 75% to 100%
- No comment on potential reasons
- Speculation: individualized programming, group participation or even noticeable improvements as motivators?
- No adverse effects documented
Implications for Future Practice

- Provides evidence to support exercise as a safe and effective intervention for persons with metastatic cancer
- Unable to direct a specific exercise prescription
- Exercise has a positive effect on QOL and physical status
- Important to communicate benefits and goals of exercise to patients and their families
Recommendations for Future Research

- Conduct larger and more rigorous RCT’s
- Investigate metastatic cancer sub-groups
- Use consistent terminology to define cancer status
- Determine acceptable attrition rates
- Clarify optimal (or minimal) exercise prescription
- Use consistent outcome measures
Conclusions
Concluding Statements

1. There is a **positive association** between exercise and changes in both QOL and physical status.

2. Clinicians working with persons with metastatic cancer should **use caution** with exercise prescription, as there is currently no agreement upon optimal exercise parameters.

3. Further research in the area should focus on **large-scale RCT’s** to identify optimal and safe exercise parameters for this population.
Acknowledgments

- Susan Harris - Clinical Faculty, Department of Physical Therapy, UBC
- Charlotte Beck - Health Sciences Reference Librarian, UBC
- Angela Busch - Associate Professor, School of Physical Therapy, University of Saskatchewan
- Elizabeth Dean - Professor, Department of Physical Therapy, UBC
- Physiotherapy Canada for considering our review for publication (submitted July 1, 2008)
References


Questions and Discussion
Thank You!