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1 **Fit for life after cancer: does exercise timing matter?**

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24 **Abstract**

25 **Objectives:**

26 To assess the effects of a single exercise session per week for 6 weeks on quality of life, fatigue
27 and exercise participation in male and female cancer survivors with follow up at 6-months. A
28 secondary aim was to identify if the timing of exercise delivery determined its effect.

29 **Methods:**

30 An exploratory prospective cohort study design was implemented. Twenty-five patients
31 undergoing, or who had completed cancer treatment (11 active treatment; 14 completed
32 treatment) undertook exercise and educational sessions (Fit for Life) 1x/week. The Brief
33 Fatigue Inventory (BFI), the European Organisation for Research and Treatment of Cancer
34 Quality of Life C30 (EORTC QLQ C-30), and the Godin Leisure Time Exercise Questionnaire
35 (GLTEQ) were used to assess fatigue, QoL and exercise levels respectively. Participants were
36 evaluated before and after the intervention, and after 6 months.

37 **Results:**

38 There was a significant group x time interaction for the GLTEQ at 6-month post in favour of
39 exercising during active treatment ($p=0.01$). No other group x time interactions were observed
40 across the EORTC QLQ C-30 or BFI. There was a significant main effect for time for EORTC
41 QLQ C-30 Global with a significant increase observed between pre-and 6-month post.

42 **Conclusions:**

43 Exercise 1x/week delivered during treatment may impact on long-term exercise participation
44 in adult cancer survivors. This lower volume programme may improve QoL, but has minimal
45 effect on fatigue suggesting an insufficient exercise dosage to impact this variable. This study
46 generates interesting proof of concept results and may be helpful in the development of larger
47 RCT's.

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49 **Keywords:** cancer; exercise; rehabilitation interventions; follow up; exercise timing.

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74 Cancer survivors often suffer from impaired quality of life (QoL), fatigue and reduced exercise
75 engagement [1–3]. Exercise has been shown to help combat the physical and psychosocial side
76 effects of treatment with both time of exercise delivery (during treatment (DT) vs post
77 treatment (PT)) and training frequency (sessions/week) highlighted as possible determinants
78 of the response noted. Recent reviews have suggested that exercise provides physical benefits
79 when delivered both during and after cancer treatment [4,5], but may have an additional
80 psychosocial impact when delivered during treatment [6]. In addition, a training frequency of
81 3x/week has been recommended as optimal for improving quality of life (QoL) and outcomes
82 associated with QoL such as aerobic capacity (VO_{2peak}) and fatigue [6]. However, exercise
83 participation amongst cancer survivors remains poor. In addition, the expectation that sedentary
84 cancer survivors can achieve ~150mins/week of exercise may be unrealistic with barriers to
85 participation such as lack of time commonly reported [7]. Therefore, we aimed to assess the
86 effects a single weekly exercise session (60mins) provided as part of a clinical service for
87 oncology patients on QoL, fatigue and exercise participation over 6-weeks with follow up at
88 6-months' post (6-m POST). A secondary aim was to identify if the timing of the delivery of
89 the exercise intervention determined its effect.

90

91 **METHODS**

92

93 **Experimental Design:** An exploratory prospective cohort study comprising of a 6-wk training
94 and education intervention. Outcomes were measured at PRE, POST and 6-m POST.

95

96 **Participants:** Following institutional ethical approval, 25 male and female cancer survivors
97 volunteered to participate (See *Table 1*. for clinical characteristics). Individuals were screened
98 for eligibility which included; 1) undergoing or having completed treatment for cancer; and 2)

99 an Eastern Cooperative Oncology Group status (ECOG) of 0-2. Individuals were excluded if;
100 1) they required assistance to mobilise; 2) were <6-wk post-surgery; or 3) had dementia or a
101 psychiatric illness which may preclude informed consent and/ or active exercise participation.
102 The intervention was provided as a clinical service to patients attending for cancer treatment
103 and physiotherapy services; therefore, allocation to the groups was not-randomised. Point of
104 commencement (DT vs PT) was self-selected, with patients offered access to the programme
105 at all treatment stages when attending hospital appointments. Participants were fully informed
106 of all experimental procedures prior to providing written informed consent.

107

108 **Training Intervention:** Supervised exercise and educational sessions (1x/week for 6-wks).
109 *Exercise sessions:* Cardiovascular, resistance and balance exercises. Sessions lasted 60-mins
110 (12 exercise stations – 2.5-min per exercise x 2). *Educational sessions:* Exercise pacing (x2),
111 healthy eating (x2), stress management (x1), and behaviour change (x1).

112

113 **Assessments**

114 *Fatigue:* Assessed by the Brief Fatigue Inventory (BFI), comprised of 9 questions under 4
115 headings. Each question was rated on a scale 1-10. A mean BFI score of 0, 1-3, 4-6 and 7-10
116 indicates no fatigue, mild fatigue, moderate fatigue and severe fatigue respectively (Mendoza
117 et al, 1999).

118

119 *Quality of life (QoL):* Assessed by the European Organisation for Research and Treatment of
120 Cancer QoL C-30 (EORTC QLQ C-30). A change in subscale score of >10 is acknowledged
121 as clinically meaningful.

122

123 *Exercise participation:* Assessed by the Godin Leisure Time Exercise Questionnaire (GLTEQ).
 124 Individuals self-report the frequency and duration of mild, moderate and strenuous exercise
 125 over a 1-wk period.

126

127 Table 1 Demographic and clinical characteristics of participants

Characteristics	N (%)
Age (years)	
20-40	1 (4)
40-65	20 (80)
>65	4 (16)
Sex	
Female	20 (80)
Male	5 (20)
Diagnosis	
Breast	20 (80)
Prostate	4 (16)
Lung	1 (4)
Treatment stage	
Active treatment	11 (44)
Completed treatment	14 (56)
Treated with chemotherapy	
Y	5 (5)
N	20 (80)

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129

130 **Statistical Analysis**

131 Data were analysed using a 2 x 3 repeated analysis of variance (ANOVA) with between-factors
132 “group” (i.e. DT vs PT) and within-factor “time” (i.e. PRE, POST, 6-m POST) using SPSS.
133 Significance was set at $p < 0.05$. Significant interactions and main effects were analysed using
134 Tukey post hoc tests.

135

136 **RESULTS**

137 Twenty-five participants completed the study (age= 57.24 ± 10.5 years). *Fatigue*: The BFI
138 demonstrated no significant main effect for time ($p=0.08$) or significant interaction for group
139 x time ($p=0.06$). At POST, fatigue increased (+49%) and decreased (-15%) in the DT and PT
140 groups respectively. Fatigue decreased at 6-m POST vs POST in both groups (DT, -48%; PT,
141 -7%). *QoL*: No significant main effect for time for Function-QoL ($p=0.08$) or Symptom-QoL
142 ($p=0.11$) was noted. However, there was a significant main effect for time for Global-QoL
143 ($p=0.015$). Pairwise comparison showed a significant increase between PRE-and 6-m POST
144 time intervals (57.89 ± 20.93 vs 70.13 ± 16.89 , +21%) ($p=0.01$). There was no significant
145 interaction for group x time ($p>0.05$). At POST, Global-QoL decreased by 13% and increased
146 by 19% in DT and PT groups respectively. At 6-m POST, Global-QoL increased by 35% in
147 the DT with no change in the PT compared to POST. *Exercise participation*: The GLTEQ
148 demonstrated no significant main effect for time ($p=0.12$). A significant interaction for group
149 x-time ($p=0.01$) was noted with the DT group showing a significantly greater GLTEQ score at
150 6-m POST (50.97 ± 26.57) vs PT group (35.62 ± 14.87) (*Figure 1*). At POST, GLTEQ
151 decreased by 22% and increased by 30% in DT and PT respectively. At 6-m POST, GLTEQ
152 increased by 70% and 2% vs POST in DT and PT respectively.

153

154 **DISCUSSION**

155 These results suggest that an exercise-based intervention delivered 1x/weekly for 6-wks may
156 have minimal impact on fatigue levels, but may lead to significant long-term improvements in
157 Global-QoL. Overall the intervention delivered demonstrated no long-term effect on exercise
158 participation but these preliminary results indicate that there was a significantly larger increase
159 in long-term exercise participation in those who began exercising during active cancer
160 treatment when compared to those who engaged after treatment.

161

162 Fatigue is a common side effect associated with cancer and can negatively impact QoL and
163 exercise participation (2). Therefore, strategies which can attenuate fatigue may positively
164 impact survivorship. In the current study, exercise delivered 1x/week for 6-wks had no
165 significant effect on fatigue levels irrespective of the timing of the intervention delivery. Of
166 note, while non-significant in this preliminary study, DT demonstrated an increase in fatigue
167 (+49%) from PRE-to POST, whilst fatigue levels fell in PT (-15%) over the same period.
168 Similar observations have previously been reported with better fatigue responses observed in
169 groups exercising post-treatment [8], most likely explained by increases in fatigue noted in
170 response to ongoing cancer treatment/s [9].

171

172 At 6-m POST, fatigue levels had fallen in both groups but this did not reach statistical
173 significance. Previously, an 8-week (60 mins 3x/week) deep-water exercise programme led to
174 reductions in fatigue when measured at 8-weeks and 6-months [10]. Current recommendations
175 for improving outcomes such as fatigue [6] suggest a training frequency of 3x/week. Therefore,
176 the training frequency in the current study may have been too low to exhibit an improvement
177 in this measure. Further research with adequate numbers to confer statistical power in outcomes
178 of fatigue are required to fully elucidate the exercise frequency/volume question.

179

180 The present study demonstrates that exercise and education delivered 1x/week for 6-weeks can
181 lead to long-term improvements in Global-QoL with significant improvements seen at 6-m
182 POST, independent of group. This is in line with findings from a recent systematic review [4]
183 which concluded that additional exercise, when compared with normal care can lead to
184 significant improvements in Global-QoL at 6 month follow-up. Interventions which exhibit
185 sustained and longer-term health benefits warrant careful consideration, particularly given the
186 increasing life expectancy in cancer survivorship [11].

187

188 In the current exploratory study, the prescribed exercise programme improved Global-QoL,
189 but had no impact on QoL subscales of function and symptom. This could be related to the lack
190 of change in fatigue, as fatigue may substantially impact QoL [12]. Indeed, a recent study in
191 prostate cancer survivors identified disruption of daily living and increased dependency on
192 others as negative factors associated with fatigue [13]. Therefore, exercise and educational
193 programmes developed to improve QoL should be sufficiently tailored to address fatigue to
194 impact on the multidimensional aspects of QoL.

195

196 Long-term exercise engagement is an important lifestyle choice and is considered essential for
197 the maintenance of long-term health [14]. The current study demonstrated that a low intensity
198 exercise and education based intervention completed during treatment led to greater long-term
199 lifestyle change (*Figure 1*). A cancer diagnosis is a period in which patients may show greater
200 motivation for lifestyle changes [15]. It is possible that participants who received an exercise-
201 based intervention during treatment were more receptive to the health promotion message, in
202 what has been previously referred to as the teachable moment [16], and therefore found it easier
203 to maintain lifestyle changes upon completion of treatment. In addition, increased
204 patient/doctor contact for the DT group may have encouraged continued exercise engagement.

205 The influence of the oncologist on exercise participation has previously been noted in the
206 literature [17]. However, in this study, oncologist contact time was not recorded so this
207 potential confounding factor cannot be controlled for in the analysis conducted.

208

209 **STUDY LIMITATIONS**

210 The main study limitations were the small number of participants and the non-randomised
211 allocation of the exercise timing. In addition, as the exercise intervention was provided as part
212 of oncology care services, individuals self-selected when to commence the intervention
213 suggesting that more motivated individuals may have chosen during “active treatment”.
214 However, despite these limitations, the results generate interesting, proof of concept results
215 that may be helpful in the development of larger RCTs in the area.

216

217 **CONCLUSION**

218 In summary, Global-QoL at 6-m POST increased following 6-wks of exercise 1x/week,
219 independent of treatment stage. Beginning exercise during treatment appears to be more
220 effective for improving long-term exercise participation possibly due to greater motivation for
221 lifestyle changes, but increased fatigue levels during the intervention period were noted.
222 Further research in this area is warranted to confirm these findings.

223

224 **Competing Interests:** None declared.

225

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238 analysed the data and wrote the manuscript. OL critically reviewed the manuscript. All authors
239 have read and approved the final version of the manuscript.

240

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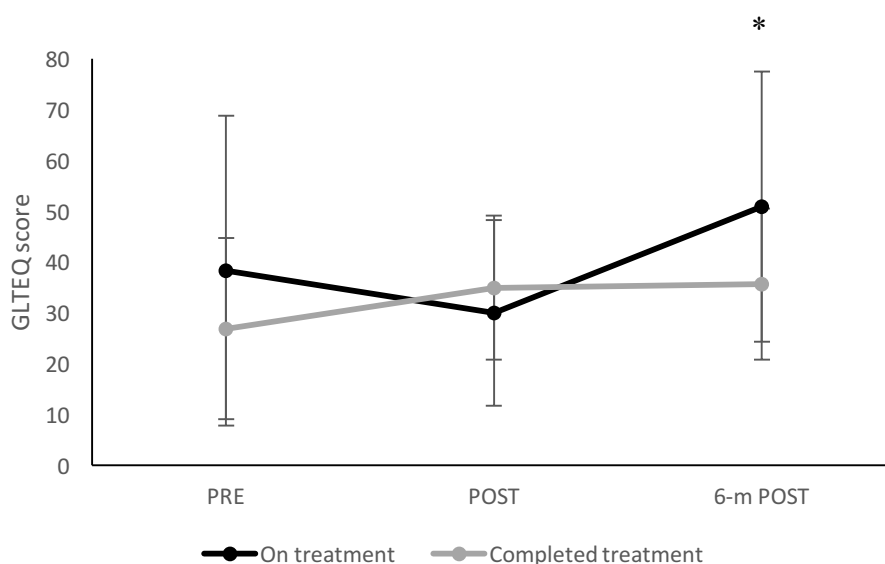
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Figure 1. Changes in GLTEQ scores. * indicates P<0.05 for interaction of group x time.

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