newsround

Selected reports edited by Janet Fricker

Study defines optimum exercise level in breast cancer

■ JNCI

Undertaking higher volumes of aerobic exercise or combining aerobic exercise with resistance exercise improves physical functioning and symptoms for breast cancer patients more than standard volumes of exercise, the Canadian CARE trial has found.

For patients undergoing chemotherapy, aerobic and resistance exercise – either separately or in combination – have been shown to improve physical functioning and manage symptoms. Few studies, however, have compared different doses or types of exercise to identify optimal exercise prescriptions for given outcomes.

In the Combined Aerobic and Resistance Exercise (CARE) trial, between April 2008 and September 2011, Kerry Courneya and colleagues, from the University of Alberta, Edmonton, randomised 301 breast cancer patients in a 1:1:1 ratio to thrice-weekly supervised exercise during chemotherapy consisting of either a standard dose of 25–30 minutes aerobic exercise (STAN; *n*=96); a higher dose of 50–60 minutes aerobic exercise (HIGH, *n*=101); or a combined dose of 50–60 minutes of aerobic and resistance exercise (COMB, *n*=104). The strength exercises used were leg extensions, leg curls, leg presses, calf raises, chest presses, seated rows, triceps extensions, biceps curl, and modified curl-ups; while aerobic exercise could be completed on a cycle ergometer, treadmill, elliptical, rowing ergometer, or combination.

The primary outcome was patient-reported physical functioning assessed by the physical functioning subscale of the Medical Outcomes Survey Short Form (SF)-36; with secondary outcomes including physical component subscales of SF-36.

Results show that, for the primary outcome, neither the HIGH nor the COMB regimens proved superior to the STAN regimen (P=0.30 and P=0.52, respectively). However, for secondary outcomes HIGH was superior to STAN for the SF-36 physical component summary (P=0.04), SF-36 bodily pain (P=0.02), and endocrine symptoms (P=0.02). COMB was superior to STAN for endocrine symptoms (P=0.009) and superior to STAN (P<0.001) and HIGH (P<0.001) for muscular strength. HIGH was superior to COMB for the SF-36 bodily pain (P=0.04) and aerobic fitness (P=0.03).

"The CARE Trial did demonstrate that higher doses of aerobic or combined exercise of up to 50 to 60 minutes per session are safe and feasible and do not interfere with chemotherapy completion or exacerbate any symptoms," write the authors.

Moreover, they add, a higher dose of aerobic exercise, curbs some of the negative effects of chemotherapy on aerobic fitness, patient-reported physical functioning, bodily pain, fatigue and endocrine symptoms, while combined exercise improves muscular fitness and partly mitigates worsening of endocrine symptoms.

With regard to the primary SF-36 physical functioning outcome, the authors speculate that the scale may not have been sufficiently sensitive to detect differences in high-functioning young patients.

■ K Courneya, D McKenzie, J Mackey et al. Effects of exercise dose and type during breast cancer chemotherapy: Multicenter randomized trial. *JNCI* 4 December 2013, 105:1821–32

No role for calcium/magnesium in neurotoxicity prevention

■ Journal of Clinical Oncology

The use of calcium/magnesium (CaMg) to protect against oxaliplatin-induced neurotoxicity was not supported by a US randomised trial.

Cumulative neurotoxicity, which commonly consists of cold intolerance, muscle cramps and throat discomfort, represents a prominent toxicity for oxaliplatin-based therapies. The rationale for using CaMg to prevent oxaliplatin-induced neuropathy comes from observations that oxalate is metabolised from oxaliplatin, and that oxalate is known to chelate Ca and Mg elements involved in the function of ion channels in nerve membranes. Therefore it was reasoned that CaMg might prevent or ame-

liorate oxaliplatin-induced neurotoxicity.

Two studies – CONcePT and N04C7 – recently investigated CaMg in the setting of neurotoxicity, but were both stopped early after the CONcePT trial showed patients receiving CaMg had significantly lower response rates than those receiving placebo. Results from the CONcePT study suggest that CaMg does not decrease either acute or chronic oxaliplatin-associated neuropathy; while the results of N04C7 suggest that CaMg decreases the cumulative sensory neurotoxicity seen in the first 100 days of therapy. Additionally, three small published observational studies of the utility of CaMg as a potential neuro-protectant for oxaliplatin proved negative.

Given the early discontinuation of two of the clinical trials, and their divergent results, Charles Loprinzi and colleagues, from the Mayo Clinic, Rochester, Minnesota, set out to undertake a new study to determine the value of CaMg in preventing oxaliplatin-induced neuropathy.

For the study, which took place between June 2010 and June 2012, 353 patients with colon cancer undergoing adjuvant therapy with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) were randomly assigned to intravenous CaMg before and after oxaliplatin (*n*=118), a placebo before and after (*n*=119), or CaMg before and placebo after (*n*=116).

Results using the EORTC Quality of Life Questionnaire-Chemotherapy-Induced Peripheral Neuropathy 20 tool for patient-reported acute neuropathy data show there were no statistically significant neuropathy differences among the three study arms regarding acute sensitivities to touching cold items (*P*=0.7978); discomfort swallowing cold liquids (*P*=0.4274), throat discomfort (*P*=0.0366) and muscle cramps (*P*=0.5501). Furthermore, no differences were found for clinician-determined measurement of the time to grade 2 neuropathy using the NCI Common Terminology Criteria for Adverse Events scale or an oxaliplatin-specific neuropathy scale.

"Given the more definitive results of this trial and the lack of observed benefit in the CONcePT trial and the other three small, randomized, placebo-controlled trials, the bulk of available data do not support the continued use of intravenous CaMg to prevent oxaliplatin-induced neuropathy," write the authors, who add that results from the current trial may change recommendations for future patients, resulting in savings in both time and expense.

Since CaMg does not appear to provide the solution for oxaliplatin-induced neuropathy, studies are now needed, they suggest, to define patients' risks for developing neuropathy on the basis of genetic factors and to explore the potential for other agents to prevent toxicity.

■ C Loprinzi, R Qin, S Dakhil et al. Phase III randomized, placebo-controlled, double-blind study of intravenous calcium and magnesium to prevent oxaliplatin-induced sensory neurotoxicity. *JCO* published online 2 December 2013, doi: 10.1200/JCO.2013.52.0536

Age represents no barrier for pelvic exenteration

■ Gynecologic Oncology

No concerns regarding duration of surgery, blood loss, length of hospital stays or complications rates were revealed for older women undergoing pelvic exenteration procedures, a retrospective US study has found.

Pelvic exenteration is a salvage procedure performed for centrally recurrent gynaecologic cancers that involves, to a greater or lesser degree, en bloc resection of pelvic structures, including the uterus, cervix, vagina, bladder and rectum. Advanced age has been considered a relative contraindication, due to the complexity and significant co-morbidities. Published data, however, suggests that carefully selected elderly patients with gynaecologic cancers can receive treatment without significant morbidity or mortality.

With limited studies exploring the influence of age in patients undergoing exenterative surgery, Pamela Soliman and colleagues, from the MD Anderson Cancer Center, Houston, Texas, set out to determine whether age at the time of the procedure has an independent impact on surgical complications or overall survival.

For the study, all women who underwent pelvic exenteration for any gynaecological indication at the centre between 1993 and 2010 were identified, and stratified into three age groups: young (≤50 years); middle (51 to 64 years) and senior (≥65 years). Altogether 161 patients were included in the analysis – 58 young, 62 in the middle age group and 41 in the senior group.

Results show that operative times were significantly shorter for women in the senior group (8.5 hours) compared with 9.5 hours for women in the middle group and 10.1 hours for women in the young group (*P*=0.0089). The overall incidence of post-operative complications for young, middle and senior age groups was 89.7%, 87.1%, and 87.8% respectively, with no significant differences found between the groups (*P*=0.8863). Overall recurrence rates following exenteration in the young, middle, and senior age groups were 68.4%, 46.7%, and 42% respectively (*P*=0.0165).

Furthermore, overall survival did not differ between age groups (*P*=0.3760). Senior women were more likely to have hypertension (*P*=0.0001) and pulmonary disease (*P*=0.040), but there were no differences between the cohorts for diabetes.

"In conclusion, advanced chronological age should not be considered a contraindication to a potentially curative surgical procedure. When patients are stratified by age, the duration of surgery, blood loss, length of hospital stay, and complication

rates do not increase with increasing age," write the authors.

The study indicates, they add, that pelvic exenteration can be offered to select patients without considerable increase in morbidity due to age alone. Several factors, write the authors, may contribute to higher recurrence rates in young patients, including tumour biology and selection bias.

■ M Huang, D Iglesias, S Westin et al. Pelvic exenteration: Impact of age on surgical and oncologic outcomes. *Gynecol Oncol* January 2014, 132:114–118

Rehabilitation programme improves urinary symptoms in prostate cancer

■ British Journal of Cancer

Multidisciplinary rehabilitation programmes in prostate cancer patients following completion of radiotherapy improved urinary and hormonal symptoms, and quality of life, a Danish study has found.

Occurring in tandem with developments in locally advanced or high-risk prostate cancer treatment – where radiotherapy combined with androgen deprivation therapy (ADT) has increased 10-year survival rates from 60% to 70% – has been recognition of the need to evaluate the impact of treatment on overall quality of life. Clinical attention has focused on how the adverse effects of treatment, such as urinary irritative problems causing frequency, nocturia, urgency or urge incontinence, might be counteracted.

In the current study, Karin Dieperink and colleagues, from Odense University Hospital, Denmark, investigated a multidisciplinary rehabilitation programme comparing usual care against psychosocial support from nurses together with counselling in pelvic floor exercises to reduce urinary irritative problems.

After completion of chemotherapy 161 patients were randomly assigned 1:1 to the intervention group (n=79) or to the usual care control group (n=82).

Patients in the intervention group received two nursing counselling sessions and two sessions with a physical therapist. Physical therapy sessions evaluated the individual patient's need for increased pelvic floor muscle function and general physical activity, and if necessary patients were guided to use biofeedback visual presentations to strengthen their pelvic floors. The self-training home programme consisted of pelvic floor muscle exercises integrated in daily activities, for example, during driving the car, walking, or working in the garden.

The primary outcome was urinary irritative sum score, based on the Expanded Prostate Cancer Index Composite (EPIC-26) using four items regarding pain, bleeding, weak stream, or frequent urination. Secondary outcomes included quality of life arising from the Medical Outcome Study Short-Form-12 (SF-12).

Results show that, in comparison to controls, men in the intervention group demonstrated improvements in the urinary irritative sum score (P=0.011), urinary sum score (P=0.023), hormonal sum score (P=0.018) and SF-12 physical component summary (P=0.002). Furthermore, patients with more severe impairment gained most.

A sub analysis showed that improvements of the urinary sum score were most pronounced in patients living alone (P=0.021), that men with pre-intervention urinary scores indicating moderate to severe problems gained the most (P=0.034), and that pre-intervention urinary irritative sum scores below the study mean value of 68 points predicted a higher effect of intervention (P=0.031).

"Based on the results of this study, it can be recommended that patients treated with radiotherapy of the prostate may be offered a combined nurse–physiotherapist intervention programme, especially patients with impairments within urinary irritative function," write the authors.

Timing, duration, and focus on the empowerment aspects of this intervention, write the authors, require further study.

■ K Dieperink, C Johansen, S Hansen et al. The effects of multidisciplinary rehabilitation: RePCa – a randomised study among primary prostate cancer patients. *Br J Cancer* 10 December 2013, 109:3005–13

Residents trained to include relatives

■ British Journal of Cancer

Training programmes for medical residents that focus on including relatives in the breaking bad news (BBN) consultation improved the communications skills of participants, a Belgian study has found.

Relatives frequently accompany patients to BBN consultations in order to provide support or to serve as the patient's advocate. Their presence, however, often introduces a new level of complexity, since physicians need to deal with two people who have differing needs, knowledge, concerns, distress levels and expectations.

In the current study, Darius Razavi, from the Institut Jules Bordet, Brussels, and colleagues, explored the efficacy of training programmes designed to teach residents the communication skills needed to break bad news to both patients and their relatives.

The study residents, who had a mean age of 28 years, were randomly assigned to undergo a 40-hour dyadic (two way) or triadic (three way) communication skills training programme (n=48) or to be placed on a waiting list (n=47). The investigators utilised the Belgian Interuniversity Curriculum – Communication Skills Training (BIC-CST) consisting of a 17-hour commu-

nication skills training programme focusing on dyadic consultations and a 10-hour programme on triadic consultations.

For each resident, communication skills were evaluated using a simulated BBN triadic consultation consisting of a 20-minute first medical encounter, with an actress playing a 37-year-old woman and an actor playing her 40-year-old husband. During the consultation, residents had to deliver a breast cancer diagnosis and discuss treatment (i.e. surgery, chemotherapy and radiotherapy). Transcripts from the consultation were analysed using content analysis software, with three dictionaries constructed for medical, emotional and social utterance content. For the analysis the consultation was divided into three phases: the pre-delivery phases devoted to preparing the patient and relative for the delivery of bad news by assessing what they know, understand and feel about the current situation; the delivery phase spent delivering the bad news; and the post delivery phase providing emotional support and additional information to both the patient and their relatives.

Results showed that, following training, the duration of the pre-delivery phase was longer for trained residents (RR=3.04; $P<0.001$). Furthermore, the simulated relative's first turn of speech about the bad news came more often during the pre-delivery phase (RR=6.68; $P=0.008$), and was more often initiated by the trained residents (RR=19.17; $P=0.001$). Trained residents also used more assessment (RR=1.83; $P=0.001$) and supportive utterances (RR=1.58; $P=0.001$).

"The results obtained demonstrate that the training programme did have a positive impact on the simulated BBN process, with residents exhibiting improved communication skills, improved inclusion of a simulated relative, and improved expression of the concerns by the simulated patient and relative," write the authors.

While the pre-delivery phase increased from approximately one minute before training to two minutes after training, the increase represented the time required for residents to assess what the patients and relatives felt, knew and understood about their situation.

■ I Merckaert, A Lienard, Y Libert et al. Is it possible to improve the breaking bad news skills of residents when a relative is present? A randomised study. *Br J Cancer* 12 November 2013, 109:2507–14

Wait times influence survival in uterine cancer

■ Journal of Clinical Oncology

Longer wait times from diagnosis of uterine cancer to definitive surgery have a negative impact on patient overall survival, a Canadian retrospective study has found. To the best of their knowledge, the authors state, the investigation represents the first large population-based study to have examined the impact of wait times for uterine cancer surgery on survival.

For patients the wait for surgery is anxiety provoking, with evidence suggesting that long waiting times can have a negative impact on survival, decrease patient satisfaction and result in poorer quality of life. Previous researchers have found longer wait times to be related to shorter survival in breast cancer, rectal cancer, pT2 bladder cancer, and melanoma, although the relationship has been less clear for cancers of the oesophagus, stomach, pancreas, lung, colon, kidney, and cervix.

In the current study Lorraine Elit and colleagues, from Juravinski Cancer Centre, Hamilton, Ontario, Canada, set out to determine whether wait time from the histological diagnosis of uterine cancer to time of definitive surgery by hysterectomy had an impact on all-cause survival.

For the study 14,225 women were identified from the Ontario Cancer Registry who received a diagnosis of uterine cancer between April 2000 and March 2009. Of these 4,808 were excluded because their hysterectomies occurred on the same day as diagnosis or patients did not have a hysterectomy, leaving a final study population of 9,417 women. For the study, wait time was evaluated in a multivariable model after adjusting for other significant factors.

Results show that the five-year survival of women with wait times of 0.1–2 weeks was 71.1%, of 2.1–6 weeks was 81.8%, of 6.1–12 weeks was 79.5% and more than 12 weeks was 71.9%. Compared with patients having wait times of <2.0 weeks, women having wait times of 2.1–6.0 weeks had a hazard ratio (HR) of 0.64 (95%CI 0.55–0.75), those with a wait time of 6.1–12.0 weeks had an HR of 0.65 (95%CI, 0.55–0.77), and those with a wait time of >12 weeks had an HR of 0.80 (95%CI, 0.67–0.97).

"From a regional or provincial perspective, given our data, which demonstrate a strong association between longer wait times and decreased survival, future policies might aim to provide hysterectomies within 6 weeks of diagnosis to optimize survival rates," write the authors, adding that surgery within two weeks of diagnosis is generally believed to be related to acute issues, such as anaemia associated with the need for blood transfusions.

Policies that affect access to hysterectomies for uterine cancer such as access to operating rooms and skilled surgeons, they add, should be examined. "Given that different neoplasms have different degrees of aggressiveness, future research should examine the relationship between wait times and survival for each type of neoplasm to determine appropriate cancer specific wait times," they write.

■ L Elit, E O'Leary, G Pond et al. Impact of wait times on survival for women with uterine cancer. *JCO*, published online 25 November 2013, doi:10.1200/JCO.2013.51.3671