People with metastatic breast cancer taking part in a nine-month structured exercise programme report less fatigue and improved quality of life in comparison to controls. The study, <u>abstract GS02-10</u>, presented at the San Antonio Breast Cancer Symposium, held December 5–9, 2023, also showed the exercise group experienced less pain and shortness of breath than the control group, and furthermore, many continued to exercise beyond the nine months of the study.

"Optimising quality of life is, of course, important for everybody, but especially for patients living with metastatic disease who undergo continuous treatment," said study presenter Anne May, from the Julius Center for Health Sciences and Primary Care at the University Medical Centre, Utrecht, The Netherlands. "By improving quality of life through enhanced symptom management, we can help patients better enjoy their personal, social, and, if applicable, working life."

Patients with metastatic breast cancer often experience cancer- and treatment-related side effects that impair daily activities, including fatigue, decreased physical fitness, insomnia, depression, neuropathy and pain. While guidelines recommend exercise for breast cancer patients undergoing curative treatment for reducing side effects, little research has been undertaken into the effectiveness of exercise in patients with metastatic breast cancer. Given the expected increased risk of skeletal-related events, including pathological fractures and spinal cord compressions, exercise has been underutilised in this group of patients. A notable difference between curative and metastatic settings, write the authors, is that patients in the metastatic setting generally receive continuous treatment, leading to the need for longer durations of exercise programmes.

For the PREFERABLE-EFFECT trial (NCT04120298), between 2019 and 2022, May and colleagues randomised 357 patients with metastatic breast cancer, who had a life expectancy of at least six months, in a ratio of 1:1, to receive twice weekly supervised exercise sessions for nine months, (involving balance, resistance and aerobic exercises, n=178) or no supervised intervention (n=179). All patients in the study received a physical activity tracker and generic advice on exercise. The exercise programme was offered twice a week for six months; and then from six to nine months participants did one of the supervised sessions in their own homes. "We hypothesized that the transition from supervised to unsupervised exercise sessions will help participants to maintain a physically active lifestyle beyond the period of study participation," wrote the authors in a paper published in *Trials*, in 2022, outlining the study protocol. The primary outcomes of physical fatigue (using the EORTC QLQ-FA12) and health related quality of life (using the EORTC QLQ-C30) were assessed at baseline, three, six and nine months. Participants were recruited from healthcare centres in Germany, Poland, Spain, Sweden, the Netherlands and Australia. In cases of bone metastases, trainers were provided with specific instructions on adaptations that needed to be made to the prescribed exercise programmes.

Results show the patients, who included two men with metastatic breast cancer, were on average 55.4 years of age, with 73.9% having bone metastases.

At three, six, and nine months, patients in the exercise arm had average health-related quality of life scores that were 3.9, 4.8, and 4.2 points higher than patients in the control arm (indicating higher quality of life). Their EORTC-FA12 scores were 3.4, 5.3, and 5.6 points lower than patients in the control arm (indicating decreased fatigue).

At six months, patients assigned to the exercise intervention reported significantly better scores in comparison to the control arm, including a 5.5-point increase in social functioning, a 7.1-point decrease in pain, and a 7.6-point decrease in shortness of breath.

In the steep ramp test (evaluating cardiorespiratory fitness), patients in the exercise group reached an average maximum resistance that was 24.3 Watts (13%) higher than for patients in the control

group.

"We are excited about the results of our study because these are an important addition to current ASCO [American Society of Clinical Oncology] and ACSM [American College of Sports Medicine] guidelines that recommend exercise during curative treatment. Importantly, some patients with metastatic breast cancer worry exercise might worsen their fatigue and pain, but this study shows that exercise can actually improve these outcomes," says May. The fact that some patients continued to exercise after completing the nine-month programme, she adds, leads to the conclusion that it helped people to develop regular exercise habits.

Next, the investigators plan to look at the cost effectiveness of the exercise programme from a societal perspective (including healthcare costs and patient and family costs) and at the effect of exercise on overall survival and cancer-related survival. They also plan to explore the effect of exercise on inflammatory blood markers.

While the exercise programme was aimed at patients with breast cancer, the investigators believe that exercise plays a role in all types of cancer. In the Netherlands, a comparable study is currently being conducted in patients with metastatic colorectal cancer. When starting exercise initiatives in patients with metastatic disease, the authors stress, there will be a need for "good dialogue" between oncologists and physical fitness trainers on the condition of the patient, such as the location of bone metastases, so that the trainer can adjust the programme appropriately.