selected for future experimental interventions or to serve as control without further notice. For the UMBRELLA FIT study, 168 physically inactive breast cancer patients (12-18 months post-baseline), who gave broad consent are randomised to a 12-week supervised exercise intervention or control. Endpoints are contamination, participation, generalizability and retention (methodological) and quality of life (effectiveness). In addition, instrumental variable analysis will be performed taking drop-out/non-compliance after randomisation into account.

Results

The UMBRELLA FIT trial recruitment started in October 2015, since then 130 patients have been randomised. Of 65 intervention patients, 55% agreed to participate. Reasons for non-participation were mainly time constraints, dislike of exercise, or avoidance of confrontation with their disease. Acceptance rate of the intervention has been lowest in the summer period.

Conclusion

It is anticipated that recruitment will be completed in 2017. Results on feasibility and effectiveness will be reported.

Trial registration

The Netherlands National Trial Register NL2006.041.15 / NTR5482

Acknowledgements

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A12

Patient-reported outcomes in routine care: impact for TwiCs

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Clinicians routinely collect information on patient-reported outcomes as a part of clinical care. For instance, a rheumatologist will want to understand a patient’s level of pain and functioning in order to consider the effectiveness of a new treatment; a cancer surgeon will want to know how a patient is recovering from surgery in order to determine whether persistent symptoms require attention. There are numerous reasons why the use of standardized questionnaires for such purposes is far superior to informal discussion.

At Memorial Sloan Kettering Cancer Centre (MSKCC) we have pioneered the use of electronic methods to gather patient-reported outcomes as part of standard care. Current clinical projects include urinary and erectile function after radical prostatectomy; pain and recovery after gynaecological surgery; bowel, urinary and sexual function after rectal surgery; patient satisfaction with breast reconstruction; gerontology; pain and discomfort during prostate biopsy. We ensure that clinical staff are involved in the development of the questionnaire, the design of the report given to clinicians summarising patient responses and its integration into clinical workflow. By optimizing the clinical value of patient-reported outcomes we ensure that patients do indeed complete them in routine practice. Data obtained to aid the clinical consultation can then be reused as the endpoints of randomised trials, facilitating the sort of clinically-integrated research associated with many TwiCs approaches. For instance, we are currently conducting a traditional randomized trial comparing two approaches to port-site closure after minimally-invasive surgery, using patient-reported hernia as an endpoint. The critical point is that all of our patients are asked to provide data on hernia, whether or not they take part in the trial. Hence, although our trial is not in a TwiCs context, it demonstrates how use of routinely collected patient-reported outcomes can facilitate the sort of low-cost, pragmatic trials common in TwiCs.
The cohort multiple randomised controlled trial (cmRCT) design facilitates multiple trials in an efficient cohort structure. The design poses some methodological and ethical challenges. Here we present an example of multiple sequential trials within a cmRCT colorectal cancer cohort (PLCRC) and the challenges that were encountered. PLCRC is a Dutch multicenter prospective cohort in which colorectal cancer patients of all stages are included. Within PLCRC, clinical data, patient reported outcome measures and biomaterials are collected. PLCRC was set up to facilitate multiple trials in a real-world setting according to the cmRCT-design. Currently, two trials are undertaken within PLCRC: the RECTAL BOOST study and the SPONGE trial. RECTAL BOOST evaluates the efficacy of boost radiation in addition to standard chemoradiation in patients with locally advanced rectal cancer [1]. SPONGE assesses the impact of the use of a retractor sponge in laparoscopic colorectal surgery on hospital stay and postoperative complication [2]. Both trials include rectal cancer patients from the same study population. Patients may therefore participate in both trials. Ethical issues arising from multiple trials within a cmRCT-design are related to the consequences of staged-informed consent [3] and include the following: (1) Participants who have not given consent for future random selection are considered ineligible for any trial within the cohort. However, at later points in time, they may want to reconsider their eligibility for future trials. Currently, no dynamic informed consent structure within PLCRC exists; (2) Aggregated

Fig. 2 (abstract A14). Flow charts of the VERTICAL trial and the competing classic RCT

A15

Multiple trials within the cmRCT design; an example within a colorectal cancer cohort

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Introduction

Many patients with cancer develop painful bone metastases which are a poor prognostic sign. About 60% of patients undergoing standard radiotherapy experience (partial) pain relief [1]. Stereotactic radiotherapy (SBRT) is able to deliver high-dose radiation precisely to the bone metastases and might achieve higher pain response rates [2]. In 2013, we initiated a cohort of patients with bone metastases – the PRESENT cohort – using the ‘cohort multiple Randomised Controlled Trial’ (cmRCT) design. The first randomised trial within the cohort is the VERTICAL study, comparing the effect of SBRT with standard radiotherapy in patients with metastatic bone disease [3].

Material and Methods

All patients with bone metastases visiting the Radiation Oncology or Orthopedic Surgery department of the UMC Utrecht are enrolled in a prospective cohort (PRESENT). Informed consent is obtained for being offered experimental interventions at random. Patients eligible for SBRT are randomised; patients allocated to the intervention group are offered the new treatment; control patients remain uninformed about the allocation. We compared inclusion rates and flow charts of the VERTICAL study with a competing classic RCT comparing SBRT with standard radiotherapy in patients with spinal metastases which started recruitment at the same time.

Results

Since January 2015, we have randomised 62 patients of which 27 patients were allocated to the SBRT arm (Figure). After randomisation, 6 patients were ineligible, e.g. due to too many painful lesions. Of the 21 remaining patients, 16 patients accepted SBRT. Due to rapid clinical deterioration, six patients were unable to undergo SBRT. In the competing classic RCT, 11 patients were randomised (Fig. 2) and all patients allocated to the intervention arm were able to undergo SBRT.

Conclusion

Comparing both trials (which are ongoing), the VERTICAL trial, using the cmRCT design, has a higher recruitment rate, and a more generalizable population as compared to the classic trial. The high drop-out rate in the intervention arm indicates that also the conduct of a cmRCT is challenging in this population.

Trial registration

The Netherlands Trials Register number NL49273.041.14 (PRESENT cohort) and NL49316.041.14 (VERTICAL trial). ClinicalTrials.gov registration number NCT02356497 (PRESENT cohort) and NCT02364115 (VERTICAL trial). Date of VERTICAL trial registration February 1, 2015.

References


A14

The ‘cohort multiple randomised controlled trial’ design for a fragile patient population

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References