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CAMERA - Complete Assessment of Older Patients with Cancer: A Non-randomised Feasibility Study.

Gillian Jackson¹, Rhian Gabe², Miriam Johnson¹, Kathryn
Date¹, Daniel Harman³, Anthony Maraveyas⁴, Rajarshi Roy⁴,
Michael J Lind¹.

1. Hull York Medical School

University of Hull

Cottingham Road

Hull

HU6 7RX

2. University of York

Heslington

York

YO10 5DD

3. Hull Royal Infirmary

Anlaby Road

Hull

HU3 2JZ

4. Castle Hill Hospital

Castle Road

Cottingham

HU16 5JQ

Dear Editor

One of the primary risk factors in the development of cancer is older age. The demographic shift to an ageing population has given rise to an increased number of older patients with cancer.

The extreme heterogeneity within this population renders applying standardised treatment pathways hazardous¹.

Disparities in physiological reserve and an increased risk of multiple comorbidities further exacerbates the complexity of cancer treatment management in older patients². Individual modifications to tailor treatment for each specific patient would be the gold standard; thus, detailed patient assessment providing a comprehensive health profile in addition to existing diagnostic test results are paramount when devising a personalised treatment care approach³.

Recognition of this has led to interest in the potential value of the Comprehensive Geriatric Assessment (CGA), to guide appropriate treatment selection in this patient cohort. CGA is a multidimensional tool to assess individual domains. These domains typically include: functional status (FS), comorbidities, nutrition, performance status (PS), psychological, cognition, social support, and medication, and collectively determine the functional status of the patient⁴.

Although CGA has been validated in a geriatric setting, it has not yet been validated in an oncological setting. A number of assessment tools have been designed to assess each of the

domains but there is no agreed format for CGA in oncology⁵. In addition to the lack of standardised format, CGA has also been criticised for being too time-consuming to complete and therefore difficult to incorporate routinely into a busy oncology setting⁶. Other screening tools have been developed to address this problem, such as the Vulnerable Elders Survey-13 (VES-13). The VES-13 is a patient self-rated, questionnaire with a total of 13 items to identify vulnerable older patients that require further assessment with CGA⁷.

Although significant feasibility work by leading experts in this field has already been completed^{8,9}, much of this research was in the US; we propose further feasibility work in UK hospitals is necessary, since implementation is likely to differ considerably. The aim of this study therefore, was to address the feasibility of using CGA and VES-13 in outpatient older adults with cancer, in England. Providing data to inform the design of a definitive randomised controlled trial (RCT), where these tools will be tested as an intervention to guide cancer treatment with regard to patient relevant outcomes.

Methods

Study population

This single centre, feasibility study was conducted in the oncology outpatient department of the Queen's centre, Castle Hill Hospital, Hull, from October 2014 until July 2015 in

patients aged 70 and older with a newly diagnosed cancer. A conservative eligible: consent ratio of 4:1 was considered feasible in terms of a subsequent trial given the age of the population. This study, including method of consent, was approved by Research Ethics Committee (REC) and Hull and East Yorkshire (HEY) trust R&D and was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki. Written informed consent was obtained from all participants.

Data collection

All consenting patients completed both assessment tools in full, consecutively in clinic with the help (if required) from a research nurse, starting with CGA and then the VES-13. Briefly, our CGA comprised of: Lawton's Instrumental Activities of Daily Living (IADL) to assess FS, diagnosed comorbidities according to Charlson comorbidity index, an internal screening questionnaire used routinely in the cancer centre was used to assess nutrition (see online supplemental appendix 1), Eastern Cooperative Oncology Group (ECOG) was used to assess performance status (PS), Geriatric Depression Scale (GDS) to assess psychological status, cognitive impairment was assessed in a two step process (as advised by our geriatrician team member (DH)), all 100 patients completed the Abbreviated Mental Test Score (AMTS), since a score of ≤ 8 is indicative of likely impairment,

patients with this score were also assessed using Folstein's Mini-Mental State Examination (MMSE), finally, participant medication information was obtained through medical notes and patient self-report. In accordance with previously published values, a cut-off score of impairment in two or more CGA domains signified vulnerability of an increased risk of poor treatment outcome⁸. Further detail on individual assessment scores can be obtained from the authors. The VES-13 screening tool has a maximum score of ten, the total overall score range in our study was zero (lowest risk) and ten (highest risk). In order to categorise participants in to vulnerable and not vulnerable, a cut-off score of three was used, whereby participants scoring three or more with the VES-13 tool were classified vulnerable⁷.

Statistical analysis

Descriptive analyses are presented to describe patients and clinical baseline characteristics, assessment outcomes and patient clinical outcomes after six month follow-up. *Post hoc* analyses to test inter-rater reliability between CGA and VES-13 was tested with Cohen's kappa. STATA software (version 14.0) was used for all statistical analyses.

Results

A total of 100 patients were recruited (mean age 78 years, SD 6, range 70-97 years; 50 (50%) were women. There were

sixteen different cancer types, colorectal cancer was the most frequent (26%). Almost 50% of patients had late stage cancer at diagnosis. Over half (66%) of the study population's intended treatment plan included chemotherapy. According to IADL, 60% of participants achieved a perfect score of eight, indicative of fully independent living, however, ECOG PS differed in that 47% of patients were rated as ECOG Zero indicating they were fully active. A quarter of patients (25%) scored high risk for depression with the GDS (further assessment outcomes detailed in table one). Primary outcomes for this study were recruitment and assessment times (secondary outcome results detailed in online supplemental). Average monthly recruitment rate was 11.1 and screen to consent ratio was 2.39:1 (details of study phase progression in figure one). The mean assessment completion time for the CGA was 16.3 minutes (SD 9.2, range 5-80 minutes). The mean assessment completion time for the VES-13 was 5.2 minutes (SD 3.6, range 1-35). Over half, 54 (54%), of participants were classed as vulnerable according to CGA, whilst almost half, 46 (46%) were classed as vulnerable according to VES-13 (score of 3 or more). Moderate agreement was observed between the CGA and VES-13 (Cohen's kappa value 0.52, 95% CI 0.35 to 0.69, $p = <0.001$).

Discussion

This feasibility study shows that recruitment to a trial using CGA and VES is feasible with only fifteen percent of approached patients declining consent. Time to complete the tools is reasonable in the context of routine clinical practice. The assessment tools selected for this study were brief in nature and could be self-completed during clinical waiting times, factors which may have contributed to our high participation rates. Other study data were collected from clinical records; thus minimising participant burden. Time constraints in busy routine cancer practice is a major concern regarding use of CGA in older adults. As there is no agreed CGA format, completion time depends on the format chosen. Mean completion time for the CGA in this study was consistent with previous studies using a similar format^{8,9}.

Currently, performance status as measured by the ECOG or Karnofsky Performance Status (PS) tools are widely used in oncology and used as a guide to treatment decisions. In our study, 83% of our participants had an ECOG PS of less than one; however, only half of the studies patients were classed as non-vulnerable by the CGA or VES-13. This supports findings from another study, suggesting CGA can help identify issues not necessarily identifiable by PS alone¹⁰. This prospective, consecutive study provides real-life out-patient data and included older patients with a variety of different solid cancer

types in order to test broad feasibility of CGA use. However, the study was not designed to detect any particular effect size, and the observations therefore support investigation in an appropriately powered study.

Strengths and limitations

The study population was derived from a single centre. Recruitment from outpatient clinic may have caused unintentional selection bias to yield a healthier population of older patients with cancer; consistent with a high percentage (66%) of participants with a treatment plan including chemotherapy. In future studies, effort should be made to recruit a cross section of participants with a range of health profiles.

Implications for future practice and research

Study design of a future RCT was not tested (no randomisation) and thus willingness to be randomised needs further assessment prior to progression to a definitive trial. The assessments were carried out by a study research nurse (RN). In order for the CGA or VES-13 to be tested in an RCT in a manner which could provide a new standard of care, the assessments need to be carried out by a clinical nurse as part of routine care.

Therefore, further work is needed to identify the time needed for clinical nurses to be trained and to deliver the assessment, and the acceptability of doing so. A comparison between RN and physician assessment was not made; this would be interesting to

examine in future work. The CGA results can be made available to the consultant rapidly, for both discussion with the patient and to assist with treatment decisions. Further work to determine whether and how the results of the CGA can influence treatment decisions is ongoing. The shorter questionnaire, the VES-13, may be useful as a screening tool.

Conclusion

This feasibility study is the first in a series of preparatory research studies aimed at informing the design and construct of a definitive RCT to test whether routine CGA assessment improves clinical outcomes in the older adult with cancer. We have shown recruitment is feasible in terms of willingness to be assessed and complete study questionnaires. CGA completion times in an outpatient clinic setting are reasonable.

Authors' disclosure

The authors declare no conflict of interest.

Authors' contributions

Study conception and design: Lind; Gabe; Johnson; Date; Maraveyas; Roy; Harman

Acquisition of data: Jackson; Lind; Gabe

Analysis and interpretation of data: Jackson; Gabe; Fairhurst

Drafting/revising of manuscript: Jackson

Critical revision: All authors

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