Surveillance versus ablation for incidentally diagnosed small renal tumours: the SURAB feasibility RCT

Naeem Soomro,1* Jan Lecouturier,2 Deborah D Stocken,2,3 Jing Shen,2 Ann Marie Hynes,3 Holly F Ainsworth,2 David Breen,4 Grenville Oades,5 David Rix1 and Michael Aitchison6

1The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK
2Institute of Health and Society, Newcastle University, Newcastle upon Tyne, UK
3Newcastle Clinical Trials Unit, Newcastle University, Newcastle upon Tyne, UK
4University Hospital Southampton NHS Foundation Trust, Southampton, UK
5NHS Greater Glasgow and Clyde Health Board, Glasgow, UK
6Royal Free London NHS Foundation Trust, London, UK

*Corresponding author naeem.soomro@nuth.nhs.uk

Declared competing interests of authors: none

Published December 2017
DOI: 10.3310/hta21810

Scientific summary

The SURAB feasibility RCT
Health Technology Assessment 2017; Vol. 21: No. 81
DOI: 10.3310/hta21810

NIHR Journals Library www.journalslibrary.nihr.ac.uk
Scientific summary

Background

Kidney cancer is the eighth most common cancer in the UK and the number of people diagnosed has more than doubled over the past 20 years. Most of these tumours are < 4 cm in size and are discovered when patients are undergoing abdominal scans. Despite their small size, > 80% of these tumours are malignant. The exact future growth pattern for small kidney tumours is not clear, especially for each individual patient. Small tumours, even if cancerous, may not grow or spread, so some patients may never need any treatment. For those tumours that do grow after a period of active surveillance, delayed treatment is generally offered and is usually successful.

In clinically fit patients, the standard treatment is surgical removal of the diseased part of the kidney (partial nephrectomy). Less invasive procedures are now available: radiofrequency ablation (RFA), which kills the cancer by heat generation, and cryoablation (CRYO), which kills the cancer by freezing the cells. Although surgery treats the kidney cancer effectively, there can be complications. Ablative techniques do not require a long hospital stay but they may not completely kill the cancer the first time and, in some cases, follow-up and possible retreatment are required.

Active surveillance is when patients do not receive any treatment but are followed up regularly and their condition monitored. With the support of the National Cancer Research Institute, surgeons and radiologists around the UK have agreed to participate in this pilot trial. However, there is uncertainty as to whether or not, in reality, clinicians would randomise their patients to this trial and whether or not patients would be willing to be randomised. Therefore, we carried out a feasibility study to determine this.

The key questions to answer in our research were:

1. Are patients with kidney cancer willing to take part in a trial in which they will be randomly assigned to have ablation of the tumour or be actively monitored (active surveillance)?
2. Are clinicians willing to approach their patients with kidney cancer and ask them to take part in a trial in which they will be randomly assigned to have ablation of the tumour or be actively monitored (active surveillance)?

We planned to conduct a small-scale pilot trial in eight centres in the UK to look at our ability to randomise the process of decision-making by patients and the suitability of the measures we proposed to assess quality of life (QoL), anxiety, general health and well-being. Beforehand, we carried out some exploratory work: (1) a survey of clinicians to find out what type of patients (in terms of size of tumour and other medical conditions) they would consider suitable to enter into a trial of this kind and (2) a survey of patients to develop and test the information that will be provided to patients in a trial of this kind.

Objectives

Our aim was to determine if a definitive randomised controlled trial (RCT) comparing ablative treatment with active surveillance in patients with small renal mass (SRM) was possible. The aim of this study [a two-stage randomised feasibility study of SURveillance versus ABlation (SURAB) in the management of incidentally diagnosed SRMs] specifically was to determine the feasibility, based on recruitment and retention, of whether or not a sufficient proportion of eligible patients could be recruited into this study.
The objectives were:

- to assess factors that promote or inhibit recruitment and retention in the trial through qualitative research
- to assess potential bias in recruitment and retention, and systematic differences between those willing to be randomised and those eligible but unwilling
- examine the mechanism of data collection and assess the completion rates of data collection instruments to inform a definitive trial.

Secondary exploratory objectives were:

- to determine short-term morbidity and complications associated with ablative techniques (RFA/Cryo)
- to establish oncological outcome, including the prevalence of biopsy at 6 months in the ablative arm
- to assess QoL tools
- to test the feasibility of collecting data on the use of the health service and costs to patients and their families for the RCT.

Methods

This trial included an exploratory pre-pilot phase and a pragmatic multicentre randomised pilot feasibility trial with parallel qualitative process evaluation. We aimed to randomise 60 participants to the two arms of the study (1 : 1 ratio) in eight centres in the UK currently offering either RFA or CRYO for SRM among patients with SRMs (< 4 cm).

The primary outcome was feasibility, defined quantitatively in terms of recruitment and retention rates. Baseline data included patient demographics, disease characteristics and treatment plan. Questionnaires were requested at 3 and 6 months. Data for measuring return-to-normal activities (physical, social and occupational) included the Short Form questionnaire-36 items (SF-36) (from which the Short Form questionnaire-6 Dimensions health status measures were derived), Functional Assessment of Cancer Therapy – General and State–Trait Anxiety Inventory.

A qualitative process evaluation investigating patient, clinician and staff experiences of trial participation, as well as identifying barriers to, and facilitators of, participation, was conducted. Patient interviews were conducted within 2 weeks of recruitment discussions. The focus of these interviews was on participants’ experiences and understandings of trial processes and the intervention (i.e. ablation techniques, active surveillance protocols). When possible, follow-up interviews were conducted approximately 6 months after recruitment, in order to explore the acceptability of assessment tools and their experiences of the intervention. Clinicians were interviewed to understand and map existing processes of care in relation to management of patients with SRMs and to explore experiences of, and perspectives on, the SURAB trial and the study interventions.

The economic component of the study developed and tested the health economic data collection tool and the participant costs questionnaire (PCQ), and assessed the ease of health economic data collection.

Results

The trial was conducted across eight kidney cancer centres, with a site-specific period of recruitment ranging from 3 to 11 months. A total of 154 patients were screened as part of the trial. Of these, 36 were eligible to be entered into the trial and were provided with study details. Of these eligible patients, seven agreed to be randomised; however, one patient was found ineligible following biopsy results. Six patients were randomised: three patients received ablation and none of them experienced perioperative
complications. The 3-month data were collected for four of the six patients and 6-month data were collected for three of the six patients.

Ten patients agreed to be contacted about the qualitative substudy when approached by recruiting staff at the sites. Six declined to take part in the trial and the other four agreed, of whom three were randomised to active surveillance and one to ablation. The remaining eight patients were contacted and took part in an interview, all but one by telephone. The four interviewees randomised to active surveillance or ablation remained in the trial until it closed.

Pre-trial work with patients and a clinician survey helped us make changes in the conduct of the trial. The qualitative substudy identified factors that had an impact on recruitment to the trial, many of which could be improved. Clinical and organisational arrangements within participating centres were critical in the implementation of SURAB. There were variations in clinician preferences and practices, and also in operational set-up, which adversely impacted on the study. The eligibility criteria and variation in interpretation were seen as potential barriers. Integrating research and clinical pathways, particularly in renal biopsy, was challenging.

The main reason for the variation in recruitment between sites was reflective of the multidisciplinary team as a whole and their demonstration of equipoise about ablation versus active surveillance in the absence of surgical option within the trial. Some patients had strong preferences whereas others were ambivalent about randomisation and the treatment option offered within the trial. There were concerns regarding whether or not participation in the SURAB trial could affect the timing of their care pathway in the ablation arm.

The health economic component of the study developed and tested the health economic data collection tool, the PCQ. We also collected information on resource use of the intervention from case report forms and on patients’ health-related QoL from the administration of the SF-36. The aim was to examine the completeness and ease of collection of the above data, assess feasibility and inform the design of a future definitive trial. Owing to the early termination of the trial, only six patients were recruited and we obtained analysable information on only four of the six patients. As a result, the above aim could not be achieved because of the inadequate sample size. However, it is not an indication of the feasibility of the health economics component, as the study was terminated early for clinical reasons, which led to recruitment issues.

Conclusions

The SURAB trial has highlighted a range of issues that affected the feasibility of this study, specifically affecting recruitment to an ablation versus active surveillance design. We have identified organisational and operational issues within each of the recruiting centres, which required attention to improve recruitment for such a surgical trial for which multiple professionals had a stake in whether or not to consider the trial for their patients, driven by their clinical experience and personal views. Only 17% of the eligible patients were recruited to this trial. Any future trial needs to consider and address the clinical and organisational variation among centres to be successful. This trial has shown that a full trial is not presently possible without the major changes that have been highlighted.

Although we have not been able to assess feasibility of the health economics component, we have developed a workable health economic data collection tool. Based on the data that we have been able to collect, it is reasonable to assume that it would be feasible to collect relevant health economic data in a future trial.
Trial registration

The trial is registered as ISRCTN31161700.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.
Health Technology Assessment

ISSN 1366-5278 (Print)
ISSN 2046-4924 (Online)
Impact factor: 4.236

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the Health Technology Assessment journal

Reports are published in Health Technology Assessment (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in Health Technology Assessment are termed ‘systematic’ when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

The HTA programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS.

‘Health technologies’ are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

For more information about the HTA programme please visit the website: http://www.nets.nihr.ac.uk/programmes/hta

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 11/107/01. The contractual start date was in April 2014. The draft report began editorial review in September 2016 and was accepted for publication in September 2017. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors’ report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health.

© Queen’s Printer and Controller of HMSO 2017. This work was produced by Soomro et al. under the terms of a commissioning contract issued by the Secretary of State for Health. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).
Health Technology Assessment Editor-in-Chief

Professor Hywel Williams  Director, HTA Programme, UK and Foundation Professor and Co-Director of the Centre of Evidence-Based Dermatology, University of Nottingham, UK

NIHR Journals Library Editor-in-Chief

Professor Tom Walley  Director, NIHR Evaluation, Trials and Studies and Director of the EME Programme, UK

NIHR Journals Library Editors

Professor Ken Stein  Chair of HTA and EME Editorial Board and Professor of Public Health, University of Exeter Medical School, UK

Professor Andrée Le May  Chair of NIHR Journals Library Editorial Group (HS&DR, PGfAR, PHR journals)

Dr Martin Ashton-Key  Consultant in Public Health Medicine/Consultant Advisor, NETSCC, UK

Professor Matthias Beck  Professor of Management, Cork University Business School, Department of Management and Marketing, University College Cork, Ireland

Dr Tessa Crilly  Director, Crystal Blue Consulting Ltd, UK

Dr Eugenia Cronin  Senior Scientific Advisor, Wessex Institute, UK

Dr Peter Davidson  Director of the NIHR Dissemination Centre, University of Southampton, UK

Ms Tara Lamont  Scientific Advisor, NETSCC, UK

Dr Catriona McDaid  Senior Research Fellow, York Trials Unit, Department of Health Sciences, University of York, UK

Professor William McGuire  Professor of Child Health, Hull York Medical School, University of York, UK

Professor Geoffrey Meads  Professor of Wellbeing Research, University of Winchester, UK

Professor John Norrie  Chair in Medical Statistics, University of Edinburgh, UK

Professor John Powell  Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), UK

Professor James Raftery  Professor of Health Technology Assessment, Wessex Institute, Faculty of Medicine, University of Southampton, UK

Dr Rob Riemsma  Reviews Manager, Kleijnen Systematic Reviews Ltd, UK

Professor Helen Roberts  Professor of Child Health Research, UCL Institute of Child Health, UK

Professor Jonathan Ross  Professor of Sexual Health and HIV, University Hospital Birmingham, UK

Professor Helen Snooks  Professor of Health Services Research, Institute of Life Science, College of Medicine, Swansea University, UK

Professor Jim Thornton  Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

Professor Martin Underwood  Director, Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, UK

Please visit the website for a list of members of the NIHR Journals Library Board: www.journalslibrary.nihr.ac.uk/about/editors

Editorial contact:  journals.library@nihr.ac.uk