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

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Scientific summary

The SURAB feasibility RCT

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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.

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