

PE1517/GG

Scottish Government Letter of 1 July 2016

Dear Ms Lamont

The Cabinet Secretary and I appeared before the Petitions Committee in October last year to discuss the Interim Report of the Independent Review of transvaginal mesh implants. While giving evidence I was asked for our view on the approach to the Single Incision Mini-Slings (SIMS) trial in the light of the recommendations of the Independent Review and agreed that we should contact the trial team to review the trial protocol.

The Scottish Government has concluded its review and I have enclosed a report setting out the findings, concluding that there is no evidence to support stopping the trial. However, in line with the current position on transvaginal mesh procedures in Scotland, the report recommends that recruitment to the trial is deferred until the improved standards of care, recommended by the Independent Review, are implemented.

The trial team has also confirmed that it is happy to recommend to all Scottish sites participating in the trial that for the standard mid-urethral sling procedure, the retropubic approach is preferred over the transobturator approach.

Yours sincerely,

Catherine Calderwood
Chief Medical Officer

TRANSVAGINAL MESH IMPLANTS

Single Incision Mini-Slings (SIMS) - Review of Trial Protocol

Introduction

In light of concerns raised about the surgical treatment of stress urinary incontinence (SUI) and pelvic organ prolapse (POP) involving synthetic mesh, the Scottish Government commissioned an Independent Review of evidence. The findings of the review published as an Interim Report (IR), were considered at a meeting of the Public Petitions Committee in October 2015. While giving evidence, the Cabinet Secretary was asked about the SIMS trial and if it could continue in the light of conclusions contained in the IR. The Chief Medical Officer agreed that the Scottish Government would oversee a review of the trial protocols. This review is now complete and the outcome, based on information gathered from a number of sources (the IR itself and its Chair, National Institute for Health Research (NIHR), Trial Chief Investigators and Chief Scientist Office), is contained here.

Background

i. What is the SIMS trial?

The SIMS trial is a pragmatic multicentre randomised controlled trial (RCT) conducted with the aim of determining both the clinical and cost-effectiveness of adjustable anchored Single Incision Mini-Slings (SIMS) compared to tension-free Standard Mid-Urethral Slings (SMUS) in the surgical management of female stress urinary incontinence (SUI). This is a national (United Kingdom) health technology assessment (HTA) funded study and conducted under the auspices of the NIHR.

The hypothesis being tested is that the patient-reported success rate following surgical treatment with adjustable anchored SIMS procedures is non-inferior to tension-free SMUS while the former is associated with less post-operative pain, shorter hospital stay, earlier recovery and consequently earlier return to usual activities/work and is more cost effective than SMUS.

In the SIMS trial protocol, SMUS are described as the most commonly performed surgical procedures for the treatment of SUI and involve insertion of tension-free slings (mesh) via either the retropubic or transobturator routes. SIMS is a third generation mid-urethral sling developed to allow true ambulatory treatment with reduced morbidity and earlier recovery while maintaining similar efficacy to SMUS.

The study aims to compare existing conventional treatment (SMUS) with a newer approach (SIMS) in the NHS setting, utilising standard clinical practices and governance policies. The trial does not dictate the particular SMUS or SIMS product to be used, leaving this to clinical indication or clinician preference.

Women over 18 years of age who have completed their family are eligible for the trial. Identification of a patient as a possible candidate for the study should only occur after consideration by a multi-disciplinary team (MDT) and only then can it be discussed with her (this was not in the original trial protocol but is now practice advocated by the trial team).

Following surgery, patient follow-up takes place for 3 years. Primary outcome measures are patient reported success rates recorded at 1, 2 and 3 years. Secondary outcomes include complication rates, pain, urinary symptoms and an objective measurement of success, a 24 hour pad test over the same time course. The intended sample size is 650 patients. As of 4 February 2016, 411 patients have been randomized into the trial, 115 in Scotland. Information relating to the procedures performed is confidential and will remain so until the time of analysis. However, as a consequence of randomisation, approximately half will have undergone a SIMS procedure.

ii. Why is the SIMS trial controversial?

Conclusion 7 of the Independent Review (Interim Report) states: “A review of the different sources of evidence available to and considered by the Independent Review (patient experience, clinical expert opinion, research evidence and epidemiological evidence from routine information) has led us to express concern in this Interim Report at the use of the transobturator rather than the retropubic approach for routine surgery for stress urinary incontinence using mesh. The clinical governance arrangements that we have recommended will allow an individual case to be considered in the context of a multi-disciplinary assessment, including patient views. **We await the final publication of key research reports but wish to register these concerns and to recommend that the Expert Group in the following months before the publication of the final report explore further appropriate pathways to ensure the techniques chosen take the differential patient and clinical experience, as well as research evidence into account.**”

In the light of this recommendation, those opposed to the use of mesh contend that since SIMS is a transobturator device it should not be used in Scotland. Furthermore, the trial should be stopped.

iii. Is SIMS a transobturator device?

Section 3.1 of the trial protocol (Intervention to be evaluated) states that SIMS are “Robustly anchored to the Obturator Complex...” Later, in section 3.1.1, technical aspects of insertion are described including “...The applicator would then pivot slowly behind the (pubic) ramus and through the obturator complex allowing the fixed anchor to its position in the obturator membrane and muscles...”

Therefore, SIMS must at least be regarded as an “obturator” device and since insertion traverses the obturator membrane, then it could reasonably be regarded as “transobturator”. The SIMS device does not however traverse further into the groin/thigh and therefore it does not involve muscles beyond the obturator complex (adductors as well as gracilis). Standard transobturator SMUS do traverse and are anchored in these muscles, and this might explain the low incidence of pain associated with SIMS reported in a contemporary Scottish patient group (1/67- SIMS Trial Team).

Governance

This has two broad components:

i. Governance of the research (protocol, randomisation, data handling etc.)

The SIMS trial was recommended for funding following comprehensive independent expert scientific review and has Research Ethics Committee (REC) approval. RECs safeguard the rights, safety, dignity and well-being of research participants, independently of research sponsors and funders. These arrangements are part of the well-established and trusted governance standards for studies of this kind in the United Kingdom (as set out for Scotland in: Scottish Executive Health Department Research Governance Framework for Health and Community Care, 2006). The trial protocol includes on-going assessment by an independent data monitoring committee that has access to un-blinded trial data including serious adverse events.

ii. Governance of the treatment being assessed in the NHS setting (pathway of care, multi-disciplinary team working, informed consent, conduct of surgery etc.)

As noted above, the SIMS Trial seeks to determine the effectiveness of different treatments undertaken within standard NHS conditions and with standard NHS practices at participating sites. The IR revealed deficiencies in the current standards in Scotland and made recommendations for improvement (pathway of care, multi-disciplinary team working, informed consent, conduct of surgery, adverse event reporting and governance). An Expert Group has been formed to take these forward. This work is on-going and the new standards for care are not yet fully defined or implemented.

The SIMS trial following publication of the Independent Review

Concern is expressed in the IR at the use of the transobturator approach in routine surgery for SUI using mesh. Since the SIMS trial involves use of a device that can be described as “transobturator”, requests have been made to stop the trial since it is perceived by some to potentially represent an increased risk to patient safety. However, the IR makes no specific recommendations in relation to SIMS or the SIMS trial. Additionally, it would not be correct to advocate cessation of the SIMS Trial on the basis of the IR. In the IR, Conclusion 7 is derived from a number of sources of evidence including patient experience and clinical opinion, and does indeed express concern at the use of the transobturator rather than the retropubic approach for routine surgery. It does not however, state that the transobturator route should not be used and indeed available evidence reviewed in the IR does not support this. Instead the IR recommends that clinical governance arrangements should be in place to allow care to be individualized, taking into account the views of the patient, **the outcome of** assessment by the multi-disciplinary team and research evidence. In this context, a retropubic approach will be normal in most instances when surgery is necessary but it would also be accepted practice to advise patients of appropriate research studies so that they have choice and can make an informed decision to participate if they so wish.

Furthermore, the IR makes recommendations about the need for further research evidence. In this context the SIMS Trial is wholly consistent with the spirit of the IR. The SIMS trial is high quality research that seeks to answer important questions about the use of mesh in the treatment of SUI. SIMS devices are a new technology

and have attractive potential benefits to patients. As noted, the trial protocol includes on-going assessment by an independent data monitoring committee that has access to un-blinded trial data including serious adverse events. This committee can make recommendations about modifications to the protocol or termination of all or part of the trial. It has not done so. Furthermore, NIHR continues to be satisfied with both the scientific and ethical veracity of the trial as well as the conduct of the trial itself. NIHR and the trial team remain fully committed to this research.

Conclusion

In the light of available evidence, there are no objective grounds for the Scottish Government to request that the SIMS trial be stopped:

- The study has been approved following independent scientific and ethical scrutiny.
- The independent data monitoring committee has not raised any safety concern.
- The scientific questions the trial has set out to answer remain unanswered and answering them would provide important new evidence.
- NIHR as funder and the trial team are both clear that the trial is important and there are no grounds for the trial to be stopped.
- The trial is consistent with both the spirit and letter of the IR.

The Research Governance Framework indicates responsibility for the trial lies with the sponsor of the study (in this case the University of Aberdeen and Grampian Health Board) and the care provider. Neither the CMO nor CSO consider there is evidence to support stopping the trial.

However, the IR has recommended changes to standard practice in Scotland in light of short comings identified in the care provided for women undergoing surgical treatment for SUI and it is important these are corrected. The Expert Group is taking this work forward. Since the SIMS trial is conducted within standard NHS practice the Scottish Government believes recruitment to the trial should be in line with the current position on transvaginal mesh procedures in Scotland. Therefore the Scottish Government request the voluntary suspension of recruitment to the trial implemented by the trial team continues in Scotland until the work of the Expert Group has been developed and the new standard of care put in place at the Scottish trial site(s). It is conceded this will exclude women in Scotland from being offered an informed choice about entering this trial in contrast to their counterparts elsewhere in the UK however a temporary suspension, as suggested, will prevent women being exposed to unnecessary risk.