Synthetic sling or artificial urinary sphincter for men with urodynamic stress incontinence after prostate surgery: the MASTER non-inferiority RCT

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Disclaimer: This report contains transcripts of interviews conducted in the course of the research and contains language that may offend some readers.

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Scientific summary

MASTER non-inferiority RCT

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Scientific summary

Background

Stress urinary incontinence (SUI) is common in men after prostate surgery and it can be difficult to improve. It has a major impact on quality of life, including profound loss of self-esteem and restrictions on work, social interaction and personal relationships, including sex life.

Surgery for persistent and bothersome SUI remains the only option for active management for some men. Implantation of an artificial urinary sphincter (AUS) is recommended for those still affected by troublesome SUI > 12 months after their prostate surgery. Despite this, some men continue to suffer with disabling incontinence, remaining reliant on containment measures.

Newer surgical approaches have been developed, and the male synthetic sling has emerged as a possible alternative to AUS implantation. However, robust data, derived from randomised controlled trials (RCTs), on the relative safety and efficacy of the male sling compared with those of the AUS are lacking.

Objectives

We aimed to compare the clinical effectiveness and cost-effectiveness of the male synthetic sling and AUS in men with persistent SUI after prostate surgery.

Methods

Design

This trial was a multicentre, non-inferiority RCT, with a non-randomised cohort (NRC) and an embedded qualitative component.

Setting

Twenty-eight urological centres in the NHS.

Participants

Between January 2014 and December 2017, centres recruited men who had undergone prostate surgery and decided to have surgery for urodynamic stress incontinence in discussion with their urologist.

Recruitment into the NRC stopped in October 2015.

Men were excluded if they had previously undergone male sling or AUS surgery, had unresolved bladder neck contracture or urethral stricture after prostate surgery, had insufficient manual dexterity to operate an AUS or were unable to give informed consent or complete trial documentation.

Intervention

Men in the RCT were randomised to receive a male synthetic sling or an AUS in a 1 : 1 allocation ratio using a web-based randomisation service. The minimisation algorithm was based on the type of previous prostate surgery (radical prostatectomy or transurethral resection of prostate), previous radiotherapy (or not) for prostate surgery and centre.

Men in the NRC chose, in discussion with their surgeon, to receive either the male sling or an AUS.

Blinding
Attempts were made to ensure that participants remained blinded prior to surgery, but necessary surgical consent limited blinding prior to surgery. Participants and surgeons could not be blinded to the treatment received. Outcome assessors were asked to remain blinded to the treatment received, where possible.

Sample size
Evidence from previous studies suggested that 20% of men would still be incontinent 12 months after receiving an AUS whereas 35% of men would still be incontinent after receiving a male sling. The sample size calculation was carried out by simulation. Assuming no difference between the groups of the trial, 310 participants would give 90% power to show that male slings were non-inferior to AUS by a margin of 15% or less. To allow for approximately 15% loss to follow-up, the sample size was increased to 360 participants.

Statistical analysis
The primary outcome in the RCT was analysed using a generalised model, clustering by centre and with adjustment for previous radiotherapy and 24-hour pad test weight at baseline as fixed effects. Statistical significance was at 5%, with a corresponding confidence interval (CI) equivalent to a one-sided 2.5% test for non-inferiority. An intention-to-treat analysis was carried out, with all participants remaining in their randomised group. Only descriptive data are provided for those in the NRC.

Health economics
The main economic evaluation used data collected alongside the RCT. An additional modelling analysis over the longer term was conducted to provide additional information for policy-makers. Analyses assessed costs and cost-effectiveness of the sling and AUS from the perspectives of the NHS and Personal Social Services in accordance with National Institute for Health and Care Excellence recommendations. Data were collected on resource use; broader health-care and societal care use of primary and secondary NHS services over 24 months, including further referral for additional specialist management; and broader societal resource use, including personal costs for containment products, private medical costs and lost productivity costs, mainly lost income. The economic evaluation was based on a cost–utility analysis in terms of incremental cost per quality-adjusted life-year (QALY) gained.

Qualitative evaluation
To fully understand the experience of both the participants and the clinicians, a comprehensive programme of qualitative studies was included. The principal aims were to establish the importance of the main trial outcomes to those receiving treatment for post prostate incontinence surgery and to explore patient and clinical experiences. Potential participants in the main study were identified using purposive sampling. Interviews were conducted face to face or over the telephone. Recruitment continued until data saturation was reached and no new themes emerged. Interviews were audio-recorded and transcribed verbatim, and data transcripts coded and analysed using a thematic analysis. Qualitative data management software (NVivo 10, QSR International, Warrington, UK) was used to facilitate data analysis.

Main outcome measures

Primary outcome
The clinical primary outcome was participants' self-report of continence following male sling or AUS surgery 12 months after randomisation [a composite outcome derived from responses indicating any loss of urine to one of the two questions ('How often do you leak urine?' and 'How much urine do you leak?') from the validated International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form].

The economic primary outcome was the cost-effectiveness of the male sling compared with that of the artificial urinary sphincter, measured as the incremental cost per QALY 24 months after randomisation.

A less strict definition of the primary outcome that included 'once a week or less often' and 'a small amount' for the definition of continence was agreed at the recommendation of the Data Monitoring Committee.

Secondary outcomes

Key secondary outcomes included a comparison of adverse events (AEs), costs of benefits and harms, need for further treatments, quality of life and general health, participant satisfaction and willingness to 'recommend surgery to a friend' up to 24 months after randomisation.

Other secondary outcomes were the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form score; the International Consultation on Incontinence Questionnaire-Urinary Incontinence Male Lower Urinary Tract Symptoms voiding, continence and sexual matters scores; operating time; length of hospital stay; and time to further surgery.

Participant questionnaires were issued at baseline (before surgery), 6 months after surgery and 12 and 24 months after randomisation. Men in the RCT were also reviewed in clinic 12 months after surgery.

Results

Recruitment

A total of 940 potentially eligible men were screened: 125 (13.3%) failed to meet the eligibility criteria and 335 (41.1%) of those remaining were excluded (the majority because the man did not want surgery, or because the patient or the urologist preferred the sling or the AUS). One man was excluded from the NRC after consenting because he was found not to have any incontinence. Therefore, 380 men (190 in each group) were included in the RCT and 99 men were included in the NRC.

Baseline

At baseline, the characteristics of participants in each group were similar. The average age was between 67 and 68 years. All men had received a previous prostate operation and > 90% were not leaking urine prior to their prostate operation.

In the RCT, 94% of men had undergone their original prostate surgery for prostate cancer. Approximately 50% had received physiotherapy for SUI and around 20% had received radiotherapy for prostatic disease. More than 90% of men leaked at least once per day, with more than one-third reporting that they leaked 'a large amount'. At least 90% of men had used pads or protection since their prostate surgery because of leaking urine. Incontinence, voiding and sexual functioning scores were similar across the groups in the RCT and the NRC.

In the RCT, 93% of men (180/190 in the male sling group and 175/190 in the AUS group) underwent surgery, with 91% (178/180 in the male sling group and 166/175 in the AUS group) receiving their allocated intervention. In the NRC, 86% of men underwent surgery (42/46 received a male sling and 43/46 received an AUS). AUS surgery took approximately 20 minutes longer than sling surgery. The length of hospital stay was similar (2 days) in both of the randomised groups and in the NRC.

Further surgery was more common in the male sling group (20/190, 10.5%) than in the AUS group (4/190, 2.1%): 18 men had their sling replaced by an AUS and two had a new sling inserted. Three men in the AUS group had another AUS inserted and one had his AUS removed but not replaced. In the NRC, eight men required further surgery: six (14%) had a sling replaced by an AUS and two (5%) had their AUS replaced

with another AUS. The length of time to re-admission is right skewed, but the median time to re-admission in the randomised groups and the NRC was between 10 and 13 months.

More men in the sling group than in the AUS group required postoperative catheterisation and catheterisation for longer than 24 hours. Otherwise, the rates of AEs were low and similar in both groups. In the RCT, 8 out of 180 men in the sling group experienced a serious adverse event (SAE) (recatheterisation requiring/prolonging hospital stay, $n = 3$; mesh erosion, $n = 3$; infection urosepsis, $n = 1$; developed coffee ground vomit, $n = 1$), compared with 13 out of 175 men in the AUS group (recatheterisation requiring/prolonging hospital stay, $n = 3$; infection, $n = 3$; erosion of device, $n = 2$; haematoma, $n = 1$; bruising and inflammation, $n = 1$; urinary retention/voiding difficulties, $n = 1$; pain, $n = 1$; transient hypotension, $n = 1$; thrombosis, $n = 1$; and exacerbation of asthma, $n = 1$). One man in this group experienced three SAEs. Six men in the NRC (male sling, $n = 5/42$; AUS, $n = 1/43$) experienced a SAE (anaphylaxis, $n = 1$; haematuria, $n = 1$; recatheterisation requiring/prolonging hospital stay, $n = 2$; dysuria, $n = 1$; and wound infection, $n = 1$).

Primary outcome

The primary clinical outcome was the proportion of men continent at 12 months post randomisation (male sling group 20/154, 13%; AUS group 25/158, 15.8%), defined as the combined responses of 'never' and 'none' to the questions 'How often do you leak urine?' and 'How much urine do you leak?' in the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form participant-reported questionnaire. Using the less strict definition, 52 out of 154 (33.8%) men in the male sling group and 55 out of 158 (34.8%) men in the AUS group were continent 12 months after randomisation.

The intention-to-treat estimated absolute risk difference was –0.034 (95% CI –0.117 to 0.048; non-inferiority $p = 0.003$), indicating a lower success rate in those randomised to receive a male sling than in those randomised to receive an AUS, but with a CI that excluded the predefined non-inferiority margin of –15%, implying that the sling was non-inferior to the AUS.

Secondary outcomes

Pad use fell from baseline, but there was no difference between the two randomised groups in those still using pads. Daily pad use was consistently slightly higher in the sling group than in the AUS group.

Significantly more men randomised to the sling group than those randomised to the AUS group reported that the effect of incontinence on everyday life was worse at all three time points. The International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form score (combining frequency, volume and effect of incontinence) was highest (and, therefore, worst) at 12 months. The difference between the two randomised groups was significant at all three time points, with a poorer outcome in the sling group than in the AUS group.

Voiding and continence scores were worse in the sling group than in the AUS group and, although the continence score showed improvement from baseline, the voiding score did not change over time. There was no difference between the groups in sexual function and there was a small improvement from baseline across the groups.

Of those randomised to receive the sling, 75 (40%) reported that they were very much better, compared with 99 (52%) in the AUS group. The volume of urine leakage at 12 months was reported to be worse than at baseline by 12 men in the sling group and five in the AUS group. The odds ratio shows a significant difference between the groups, with men in the sling group worse off (0.39, 95% CI 0.24 to 0.62; $p < 0.001$).

Men randomised to receive a male sling were less likely than those in the AUS group to be satisfied with the results of their surgery (odds ratio 0.44, 0.28 to 0.69; $p < 0.001$) and less likely to say that they would recommend their surgery to a friend (male sling group, $n = 108$, 79%, vs. AUS group, $n = 123$, 95%; odds ratio 0.18, 0.07 to 0.48; $p = 0.001$).

There were no statistically significant differences in the generic quality-of-life outcomes between the two randomised groups.

Economic evaluation

The base-case analysis indicated that, on average, male slings cost less than an AUS (–£2497, 95% CI –£3167 to –£1875), but, on average, resulted in fewer QALYs (–0.006, 95% CI –0.06 to 0.054). The incremental cost per QALY in the slings group was £425,870, with a 99% chance of being considered cost-effective at the £30,000 willingness-to-pay threshold for a QALY. This means that the use of slings would save £425,870 for each QALY lost compared with AUS. Long-term extrapolation showed that over time the cost difference fell to £1511 (95% CI £4597 to £5577), the QALY difference increased (–0.133, 95% CI –0.782 to 0.488) and the incremental cost-effectiveness ratio decreased to £11,385. This means that the cost saving for each QALY lost was £11,381 and the probability that slings are cost-effective decreased to 42%.

Qualitative evaluation

Qualitative enquiries provided in-depth perspectives from men undergoing both procedures and valuable insights regarding expectations and perceived treatment success. Men reported that, although complete continence was desired, they considered a reduction in leakage episodes and a reduction in the use of pads a successful outcome. A return to 'some level of normality' was the factor driving the desire for treatment. Both patients and the surgeons providing care expressed multifactorial preferences, which were derived through a variety of sources. Surgeons' opinions had the greatest influence on preference for a particular procedure, but men also considered lifestyle factors, perceived longevity of outcome and variable experiential factors, such as online resources and the experiences of others. Surgeons reported that they based their preference for one surgery over the other on the level of incontinence. It was anticipated that, in the future, this decision would be informed by the study outcomes. The range of inpatient and postoperative experiences described were similar for both procedures. Men said that successful outcomes were 'life-changing', even if they did not achieve complete dryness. Conversely, significant disappointment was reported when the procedure was deemed to have been unsuccessful and patients felt that they 'were back to square one'. The need for realistic information prior to surgery, to enable participants to fully understand the experience and recovery period, was highlighted. Clear information provision, potentially using data provided by the men in MASTER (Male synthetic sling versus Artificial urinary Sphincter Trial: Evaluation by Randomised controlled trial), is required to fully prepare patients for the entire experience and make them aware of the likelihood of success. Clear preferences that exist among men and surgeons should reflect the evidence provided in MASTER to ensure robust decision-making.

Conclusions

The majority of men reported improved continence levels from baseline, with the sling being non-inferior to AUS. Symptoms and quality of life significantly improved in both groups. Men were generally satisfied with both procedures. Overall, secondary and post hoc analyses favoured AUS over the sling.

Future work

Further surgery, satisfaction and quality of life at 5-year follow-up will inform longer-term outcomes and cost-effectiveness. An additional pain questionnaire will inform pain levels after both surgeries.

Trial registration

This trial is registered as ISRCTN49212975.

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