Anal fistula plug versus surgeon's preference for surgery for trans-sphincteric anal fistula: the FIAT RCT

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Scientific summary

The FIAT RCT

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Scientific summary

Background

Fistula-in-ano is a common proctological condition that affects mostly younger people and is a source of chronic morbidity. The aim of fistula surgery is to eradicate the disease while preserving anal sphincter function. The efficacy of the Surgisis® anal fistula plug (Cook Medical, Bloomington, IN, USA) in the treatment of trans-sphincteric fistula-in-ano has been variably reported. A 2007 National Institute for Health and Care Excellence review of the evidence on the fistula plug concluded that 'evidence of the efficacy and cost-effectiveness of the [fistula plug] is not adequate for it to be used without special arrangements for consent and for audit or research' (National Institute for Health and Care Excellence. *Closure of Anorectal Fistula Using a Suturable Bioprosthetic Plug. Interventional Procedures Guidance [IPG221]*. London: National Institute for Health and Care Excellence; 2007. Reproduced with permission). The Fistula-In-Ano Trial (FIAT) was commissioned by the National Institute for Health Research Health Technology Assessment programme in 2009 to undertake a rigorous valuation of the safety, efficacy and cost-effectiveness of the fistula plug in comparison with existing surgical techniques to treat trans-sphincteric fistula-in-ano.

Objectives

To undertake a randomised comparison of the safety, efficacy and cost-effectiveness of the Surgisis anal fistula plug with surgeon's preference for treatment of trans-sphincteric anal fistulas. Surgeon's preference included the use of one of several established surgical techniques used to treat trans-sphincteric fistula-in-ano: fistulotomy, cutting seton, advancement flap and ligation of intersphincteric fistula tract (LIFT). The research questions included:

i. What is the efficacy of the fistula plug in terms of disease-specific and generic quality of life (QoL) at 12-month follow-up in comparison with surgeon's preference?
ii. What are the clinical and radiological healing rates associated with the fistula plug, compared with surgeon's preference, at 12-month follow-up?
iii. What are the incontinence rates associated with the fistula plug, compared with surgeon's preference, at baseline and at 6- and 12-month follow-up?
iv. What are the complication rates associated with the fistula plug, compared with surgeon's preference, at 6-week, 6-month and 12-month follow-up?
v. What are the reintervention rates associated with the fistula plug, compared with surgeon's preference, at 6- and 12-month follow-up?
vi. What is the cost-effectiveness of the fistula plug, compared with surgeon's preference, in the treatment of trans-sphincteric fistula-in-ano?

Methods

A multicentre randomised controlled trial was undertaken across 53 NHS hospital trusts comparing the Surgisis anal fistula plug and the surgeon's preference of advancement flap, cutting seton, fistulotomy and the LIFT procedure in patients with a confirmed high trans-sphincteric fistula at risk of incontinence with fistulotomy (high trans-sphincteric was defined as involving approximately one-third or more of the external sphincter complex). Patients aged $\geq$ 18 years with a clinical diagnosis of high trans-sphincteric cryptoglandular fistula-in-ano were eligible if they had previously undergone examination under anaesthesia (EUA) to characterise the fistula, the fistula tract was $\geq$ 2 cm in length, only a single internal fistula opening was present at EUA, they had been treated with a draining seton for a minimum period of 6 weeks prior to

randomisation and provided informed consent. Patients with low trans-sphincteric, non-cryptoglandular (e.g. Crohn's disease, obstetric, irradiation, malignant) or other perineal fistulas (e.g. rectovaginal fistulas, pouch-vaginal fistulas) were excluded. Patients were also excluded if they had complex disease with more than one internal fistula opening, if there was clinical evidence of active perianal sepsis or if they had recurrent anal fistulas previously treated with a fistula plug. Patients with a contraindication to general anaesthesia, an absolute contraindication to magnetic resonance imaging (MRI) scan or a cultural or religious objection to the use of pig tissue were excluded.

Participants were randomised in a 1 : 1 ratio to either the Surgisis anal fistula plug group or the surgeon's preference group in accordance with a minimisation algorithm to ensure balance of age (< 30, 30–39, 40–49, 50–59, 60–69, ≥ 70 years), American Society of Anesthesiologists (ASA) grade (P1, P2, P3, P4), planned type of surgery (advancement flap, cutting seton, LIFT procedure, fistulotomy) and presence of extensions (yes, no).

The primary outcome measure was QoL measured using the validated, symptom-specific Faecal Incontinence Quality of Life (FIQoL) questionnaire. QoL was assessed at baseline and at 6 weeks, 6 months and 12 months post randomisation. Secondary outcomes were fistula healing rate at 12 months; faecal incontinence rates (St Mark's incontinence score) at baseline, 6 and 12 months; complication rates at 6 weeks, 6 months and 12 months; and reintervention rates at 6 and 12 months. A trial-based cost–utility analysis was undertaken.

Participants were followed up at the time of discharge following surgery and then at 6 weeks, 6 months and 12 months post randomisation. The trial ended when the last participant had completed 12-month follow-up. At all follow-up visits, information was collected on complications, reinterventions, serious adverse events and use of health services. At the 6-week and 6- and 12-month follow-up time points, the St Mark's incontinence score was measured and patients completed the FIQoL questionnaire to assess the impact of faecal incontinence on lifestyle, coping/behaviour, depression/self-perception and level of embarrassment. All patients underwent MRI at the 12-month time point or at the time of clinical relapse.

Analyses used the intention-to-treat principle, analysing participants in the treatment group to which they had been assigned at randomisation.

Results

Between May 2011 and March 2016, 304 participants were recruited to the FIAT. The majority had fistulas classified as ASA I and were aged between 30 and 60 years, and there was a slight predominance of males (55%). One hundred and fifty-two participants were randomised to the fistula plug group and 152 to the surgeon's preference group. The two groups were balanced in terms of baseline age, sex, smoking status, comorbidities, fistula characteristic and FIQoL score. St Mark's incontinence scores and EuroQol-5 Dimensions, three-level version, utility scores were marginally higher at baseline in the surgeon's preference group. No differences were seen in FIQoL between the fistula plug and surgeon's preference groups at 6-week, 6-month or 12-month follow-up. Clinical evidence of fistula healing was reported in 66 of 122 (54%) participants in the fistula plug group and in 66 of 119 (55%) participants in the surgeon's preference group at 12 months. MRI showed fistula healing in 54 out of 110 (49%) participants in the fistula plug group and in 63 out of 112 (56%) participants in the surgeon's preference group. The clinical healing rate at 12 months varied depending on the type of surgical procedure performed, being 55%, 64%, 75%, 53% and 42% for fistula plug, cutting seton, fistulotomy, advancement flap and LIFT procedure, respectively. Faecal incontinence rates were low at baseline, with marginal improvement in both groups post treatment. Complications were frequent, with 49 out of 142 (35%) participants in the fistula plug group and 25 out of 137 (18%) participants in the surgeon's preference group having experienced complications by the 6-week follow-up, and 28 out of 124 (23%) participants in the fistula group and 24 out of 121 (20%) participants in the surgeon's preference group having experienced complications by the 12-month follow-up. The only significant difference between the groups was in the

complication rate at 6 weeks ($p = 0.002$), influenced by a higher rate of unexpected pain in the fistula plug group. Treatment-specific complications included fistula plug extrusion (16%), cutting seton extrusion (18%), fistulotomy wound complications (15%), LIFT-related wound complications (15%) and advancement flap complications (18%). Reinterventions were similarly frequent, having been required in 30 out of 142 (21%) participants in the fistula plug group and 16 out of 137 (12%) participants in the surgeon's preference group by the 6-week follow-up, and in 28 out of 124 (23%) participants in the fistula plug group and 27 out of 121 (22%) participants in the surgeon's preference group by the 12-month follow-up. There was no difference between the two groups in time to reintervention. The majority of reinterventions involve surgical intervention, rather than medical care. The mean total costs were £2738 [standard deviation (SD) £1151] in the fistula plug group and £2308 (SD £1228) in the surgeon's preference group (mean difference £430; $p = 0.0174$). The average total quality-adjusted life-years (QALYs) gained was marginally higher in the fistula plug group (0.829, SD 0.174) than in the surgeon's preference group (0.790, SD 0.212), but this difference was not statistically significant ($p = 0.182$). Using multiple imputation and probabilistic sensitivity analysis, and adjusting for differences in baseline EQ-5D-3L utility, the fistula plug was 35–45% more likely than surgeon's preference to be cost-effective at a range of thresholds of willingness to pay for one QALY of £20,000–30,000.

Conclusions

The Surgisis anal fistula plug was associated with similar FIQoL to surgeon's preference at the 12-month follow-up. The clinical healing rates associated with the fistula plug and surgeon's preference groups were 54% and 55%, respectively, at the 12-month follow-up. The higher costs and highly uncertain QALY gains associated with the fistula plug mean that this technology is unlikely to be considered a cost-effective treatment in the UK NHS. The overall poor healing rates associated with the surgical treatment of trans-sphincteric fistula-in-ano demand that further research be undertaken to better understand the pathophysiology underlying this common disease. Further analysis of the FIAT data should help to identify clinical and radiological predictors of fistula response to treatment.

Trial registration

This trial is registered as ISRCTN78352529.

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This report

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