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Can depth of tumour invasion predict lymph node positivity in patients undergoing resection for early rectal cancer? A comparative study between T1 and T2 cancers

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Abstract

Objective The present study investigated the risk of lymph node metastasis according to the depth of tumour invasion in patients undergoing resection for rectal cancer.

Method The histology of patients undergoing oncological resection with regional lymphadenectomy for rectal cancer at St Marks Hospital from 1971 to 1996 was reviewed. Of the total number of 1549 patients, 303 patients with T_1 or T_2 rectal cancers were selected. The tumour type, grade, evidence of vascular invasion, depth of submucosal invasion (classed into 'sm1-3') were evaluated as potential predictors of lymph node positivity using univariate and multi-level logistic regression analysis.

Results Tumour stage was classified as T_1 in 55 (18.2%) and T_2 in 248 (81.2%) patients. The incidence of lymph node metastasis in the T_1 group was 12.7% (7/55), compared to 19% (47/247) in the T_2 group. The node positive and negative groups were similar with regard to patient demographics, although the former contained a significantly higher number of poorly differentiated ($P = 0.001$) and extramural vascular invasion tumours ($P = 0.002$). There was no significant difference in the number of patients with sm1-3, or T_2 tumour depths within the lymph node positive and negative groups. On multivariate analysis the presence of extramural vascular invasion (odds ratio = 10.0) and tumour grade (odds ratio for poorly *vs* well-differentiated = 11.7) were independent predictors of lymph node metastasis.

Conclusion Whilst the degree of vascular invasion and poor differentiation of rectal tumours were significant risk factors for lymph node metastasis, depth of submucosal invasion was not. This has important implications for patients with superficial early rectal cancers in whom local excision is being considered.

Keywords Early rectal cancer, tumour depth, lymph node, metastasis

Introduction

Curative surgery for rectal cancer aims to provide adequate oncological clearance whilst minimizing the morbidity and mortality associated with the procedure. This traditionally involves total mesorectal excision (TME) [1,2] with anterior resection and anastomosis, or abdominoperineal excision of the rectum with end colostomy formation. In addition to laparoscopic rectal cancer surgery which may minimize morbidity [3] without compromising the adequacy of excision [4,5], local excision has been proposed as an option for patients with early rectal carcinoma in whom radical surgery and its complications may be avoided, as well as for patients in high-risk groups such as the elderly and those with significant co-morbidity who may not be suitable for administration of general anaesthesia [6]. A locally excised specimen is appropriate only if it includes an adequate margin of resected normal tissue, if the tumour grade is not aggressive, and if the disease has not metastasized to loco-regional lymph nodes or distant sites.

Radiological techniques for staging rectal cancer including endo-anal ultrasound (EUS) [7,8] and pelvic

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magnetic resonance imaging (MRI) [7,9] have been used in determining selection patients for whom local excision is appropriate.

Commonly used techniques for local excision of low-lying rectal cancers include transanal resection [10] and transanal endoscopic microsurgery [11]. In addition to this, the use of adjuvant therapy in the form of chemo- and radiotherapy has the potential to provide added protection against disease recurrence in those undergoing local excision of early rectal cancers [12,13]. Despite these improvements in the local curative treatments for early rectal cancer, the main challenge remains the selection of suitable patients. Tumour grade, stage, size, and position are all known to be important determinants of success following local resection of early (T_1) rectal cancers [6], but despite close patient selection on the basis of these, recurrence rates have been reported to be as high as 18% [14]. In an attempt to review the factors that predispose to local recurrence and lymph node metastasis more closely, Nascimbeni *et al.* [15] studied histological specimens retrospectively from 353 patients undergoing colorectal resection for sessile T_1 lesions. The authors reported that the depth of invasion into the lower third of the submucosa (classified as 'sm3'), the presence of lymphovascular invasion, and lesions in the lower third of the rectum were significant predictors of lymph node metastasis. This prompted the authors to suggest that T_1 lesions extending to the lower third of the submucosa and located in the lower third of the rectum should be treated by oncological resection (TME) or, if treated by local excision, should also have adjuvant chemoradiation therapy. In a subsequent retrospective study comparing local excision to oncological resection in 144 patients, the same authors reported 10-year overall and cancer-free survival rates to be better in the latter group [16].

The present study aimed to further investigate the risk of lymph node metastasis with depth of tumour invasion in patients with early (T_1) rectal carcinoma, comparing this to those with T_2 lesions.

Method

The histopathological records of 1549 patients with rectal cancer who underwent oncological resections with regional lymphadenectomy at St Mark's hospital from 1971 to 1996 were retrieved from a prospectively collected pathology database. A single pathologist then reviewed the cancer specimen slides from these patients and further staged the depth of submucosal invasion in the case of T_1 tumours as described by Kikuchi *et al.* [17]. The study was approved by the local research ethics committee.

Criteria for inclusion

In order to be included in this study, the following were required of each case:

1. Adequate remaining tissue sample with which the new histopathological characterization could take place;
2. Operative information: type of operation (abdominoperineal excision or anterior resection of rectum);
3. Histopathological information: tumour size (maximum diameter), stage (TNM classification), grade, histological type, evidence of vascular invasion, microscopic resection margin involvement (circumferential and distal resection margin), and the number of tumour positive lymph nodes harvested.

Outcomes of interest and definitions

Depth of submucosal invasion was staged as 'sm1' if the cancer invaded into the upper third of the submucosa, 'sm2' if it invaded into the middle third and 'sm3' if it invaded into the lower third of the rectal submucosa, with involvement of the muscularis propria resulting in a staging of T_2. Other outcomes that were extracted from the histopathological report for each specimen included the presence of lymph node metastasis, tumour type, tumour grade and evidence of vascular invasion. Lymph node positivity was defined as the presence of metastatic tumour deposits in at least one lymph node in the resected specimen.

Statistical analysis

Univariate and multivariate logistic regression analysis were used to identify the relationship between risk factors for lymph node metastasis (including depth of penetration) and lymph node positivity. A P-value of <0.05 was considered as statistically significant. All statistical analysis was performed with 'Statistical Package for the Social Sciences' version 11 for Windows (SPSS, Chicago, Illinois, USA).

Results

A total of 1549 patients with rectal cancer were identified, of which 313 (20.2%) were classed as having T_1 or T_2 cancer. Of these, 11/313 (3.5%) patients with T_1 cancers were excluded from the study because of inadequate tissue sample for histopathological re-classification into sm1-3 level, with the results from the remaining 303 (19.6%) patients included. Tumour stage was classified as T_1 in 55 (18.2%) and T_2 in 248 (81.2%) of these patients. Table 1 summarizes the demographic and tumour characteristics of these patients. Between the four groups,

Table 1 Tumour and patient characteristics tabulated by the depth of tumour penetration.

	Tumour depth			
Outcome	sm1 (n = 15)	sm2 (n = 7)	sm3 (n = 33)	T2 (n = 248)
Demographics				
Age; mean (SD)	53.8 (15.7)	55.5 (8.7)	62.3 (11.3)	61.9 (12.4)
M:F ratio	10:5	5:2	18:15	138:110
Mean tumour size; cm (SD)†	2.8 (2.7)	1.5 (1.4)	3.5 (1.3)	4.0 (1.8)
Distance of cancer from dentate line; median (IQR)	2.5 (3)	3 (7)	2.4 (5)	2.2 (3)
Number of lymph nodes harvested; median (IQR)	7 (10)	8 (17)	8 (6)	11 (9)
Tumour type				
Adenocarcinoma	15 (100%)	6 (85.7%)	31 (93.9%)	230 (92.7%)
Mucinous/signet cell	0	1 (14.3%)	2 (6.1%)	18 (7.3%)
Tumour grade†				
Well differentiated	6 (40.0%)	1 (14.3%)	9 (27.3%)	56 (22.7%)
Moderately differentiated	8 (53.3%)	6 (85.7%)	21 (63.6%)	175 (70.9%)
Poorly differentiated	1 (6.7%)	0	3 (9.1%)	16 (6.48%)
Evidence of vascular invasion				
No vascular invasion	12* (92.3%)	7 (100%)	29 (87.9%)	204 (82.6%)
Intra-mural	1 (7.7%)	0	4 (12.1%)	35 (14.2%)
Extra-mural	0	0	0	8 (3.2%)
Co-existing pathology				
FAP†	4 (26.7)	1 (14.3)	3 (9.1)	9 (3.6)
UC	1 (6.7)	1 (14.3)	3 (9.1)	12 (4.8)
Synchronous lesion	1 (6.7)	1 (14.3)	1 (3.0)	9 (3.6)

FAP, familial adenomatous polyposis; UC, ulcerative colitis.
*Data on vascular invasion reported on 13 of 15 patients.
†$P < 0.05$.

patients were matched for age, sex, tumour distance from anal verge, number of lymph nodes harvested and tumour type. There was however, a significant difference between groups in tumour size, tumour grade, and the number of patients with familial adenomatous polyposis (FAP). Patients in the sm3 and T_2 groups were more likely to present with larger tumours and with a higher proportion of poorly differentiated cancers. Similarly, patients in the sm1 group contained a larger proportion of patients with FAP. It is also worth noting that the patients with FAP had a mean age of 45.9 years, which was significantly younger than the non-FAP patients ($P < 0.001$).

Lymph node metastasis

Fifty-four patients (17.8%) were found to have evidence of tumour spread to adjacent lymph nodes. In the T_1 group the incidence of lymph node metastasis was 12.7% (7/55), whereas in the T_2 group this was 19% (47/247). Table 2 presents the patient and tumour characteristics of the lymph node positive and negative group. Univariate analysis showed that there was no significant association between lymph node metastases and patient age or gender, tumour size, distance from the dentate line, and tumour type. The node positive group did however contain a significantly higher number of patients with poorly differentiated tumours ($P = 0.001$) and patients with evidence of extramural vascular invasion ($P = 0.002$). Finally there was no significant difference in the number of patients with sm1, sm2, sm3, or T_2 tumour depths within the lymph node positive and negative groups.

Tumour type, grade and evidence of vascular invasion

The type, grade and evidence of vascular invasion in patients with positive lymph nodes are shown in Table 3. Interestingly, despite having no evidence of lympho-

Table 2 Lymph node positivity by tumour characteristics.

	Lymph node status		
	N_0 (=249 patients)	N_1 (=54 patients)	*P*-value
Age	61.8 (11.8)	59.1 (15.1)	0.212
Gender			
Female	107 (81.7)	24 (18.3)	0.667
Male	140 (82.4)	30 (17.6)	
Tumour size	4.1 (1.9)	4.3 (1.9)	0.591
Distance from dentate line	3.0 (2.9)	3.0 (2.3)	0.900
Type of tumour			
Adenocarcinoma	232 (82.6)	49 (17.4)	0.645
Mucinous/signet cell	16 (76.2)	5 (23.8)	
Vascular invasion			
No invasion	213 (84.5)	39 (15.5)	0.002
Intramural	31 (77.5)	9 (22.5)	
Extramural	3 (37.5)	5 (62.5)	
Tumour differentiation			
Well	66 (91.7)	6 (8.3)	0.001
Moderate	172 (81.9)	38 (18.1)	
Poor	11 (55)	9 (45)	
Co-existing disease			
UC	15 (88.2)	2 (11.8)	0.388
FAP	14 (82.4)	3 (17.6)	0.642
Synchronous	11 (91.7)	1 (8.3)	0.336
Depth of tumour invasion			
Sm1	13 (86.7)	2 (13.3)	0.238
Sm2	6 (85.7)	1 (14.3)	
Sm3	29 (87.9)	4 (12.1)	
Combined T_1	48 (87.3)	7 (12.7)	
Muscularis propria (T_2)	201 (81.0)	47 (19.0)	

vascular invasion on histology, two patients (16.7%) in the sm1 group and one patient in the sm2 group (14.3%) presented with lymph node metastasis.

Risk factors associated with lymph node metastasis in early rectal cancer

The results of multivariate analysis to determine the effect of risk factors associated with metastasis on lymph node positivity the T_1 and T_2 rectal cancers are presented in Table 4. Whilst poorly differentiated tumour grade and evidence of vascular invasion did have a significant effect on the incidence of lymph node metastasis, tumour type did not affect this outcome. Interestingly, depth of tumour penetration did not have a significant effect on lymph node metastasis between sm1-3 and T_2 groups.

Discussion

The findings of this study suggest that whilst both the degree of vascular invasion and poor differentiation of rectal tumours were significant risk factors for lymph node metastasis, this was not the case when the depth of submucosal tumour invasion was considered. Both the degree of vascular invasion and tumour differentiation are well-known prognostic indicators of lymphatic spread and local recurrence in patients with rectal cancer. Although the depth of mucosal invasion has previously been suggested as being an important risk factor for lymphatic spread, the finding in this study that two patients with sm1 and one patient with sm2 rectal cancers had lymph node metastasis has important implications for patients with superficial early rectal cancers in whom local excision is being considered.

Closer inspection of the two sm1 patients with lymph node involvement in this study revealed that both had been diagnosed with FAP. This is an important finding not only because patients with familial polyposis syndrome have a high likelihood of developing colorectal cancer, but also because the tumours these patients can present with may be more advanced and aggressive at a

Table 3 Lymph node positivity by tumour stage and characteristics.

	Lymph node positivity by tumour depth				
	sm1 (n = 15)	sm2 (n = 7)	sm3 (n = 33)	T2 (n = 248)	*P*-value
Tumour type					
Adenocarcinoma	2/15 (13.3%)	0/6 (0%)	3/31 (9.7%)	44/230 (19.2%)	0.079
Mucinous/signet cell	0 (0)	1/1 (100%)	1/2 (50%)	3/18 (16.7%)	0.154
Tumour grade					
Well differentiated	0/6 (0%)	0/1 (0%)	0/9 (0%)	6/56 (10.7%)	0.149
Moderately differentiated	2/8 (25%)	1/6 (16.7%)	3/21 (14.3%)	32/175 (18.3%)	0.765
Poorly differentiated	0 (0)	0 (0)	1/3 (33.3%)	8/16 (50%)	0.150
Vascular invasion					
Nil	2/12 (16.7%)	1/7 (14.3%)	4/29 (13.8%)	32/204 (15.7%)	0.771
Intra-mural	0/1 (0%)	0 (0)	0/4 (0%)	9/35 (25.7%)	0.038
Extra-mural	0 (0)	0 (0)	0	5/8 (62.5%)	—

Table 4 Multivariate analysis of risk factors associated with lymph node metastasis in patients with early rectal cancer.

Risk factor	B	OR	95% CI	*P*-value
Depth of tumour penetration				
Sm1	0	1		
Sm2	−0.349	0.706	0.051–9.861	0.796
Sm3	−0.762	0.467	0.070–3.127	0.432
Muscularis propria (T_2)	−0.276	0.759	0.156–3.682	0.732
Tumour type				
Adenocarcinoma	0	1		
Mucinous/signet cell	0.302	1.352	0.386–4.733	0.637
Tumour grade				
Well differentiated	0	1		
Moderately differentiated	0.839	2.315	0.910–5.886	0.078
Poorly differentiated	2.459	11.696	3.262–41.945	**<0.001**
Vascular invasion				
Nil	0	1		
Intra-mural	0.399	1.490	0.630–3.523	0.363
Extra-mural	2.300	9.973	2.218–44.836	**0.003**

younger age. With regard to the grade, both sm1 tumours were moderately differentiated and therefore more aggressively growing than the other cancers in the group. It is, of course, also possible that these patients had synchronous lesions that went undetected in the specimen despite very careful histological re-examination. This is because in FAP the large number of polyps present can make it difficult to exclude synchronous lesions. Local treatment, therefore, ought not to be the preferred option for patients with polyposis syndromes who present with early rectal cancer.

Whilst the depth of mucosal invasion may be used as a guide to determine the likelihood of successful local curative surgery for rectal cancer, it must be used together with other prognostic indicators of success such as degree of tumour differentiation, and evidence of vascular invasion. Where the T_1 tumour is superficial (sm1 or sm2) but one of these additional risk factors are present, the clinician should consider either more aggressive curative resectional surgery, or the use of adjuvant oncological treatment in the form of chemo- or chemoradiotherapy. In addition, Chambers *et al.* [18] have suggested that rectal cancer morphology may be used as an additional factor to determine outcome. They showed that patients with exophytic (polypoid and sessile) carcinomas had better 5-year survival and local recurrence than patients with non-exophytic (ulcerated and flat) lesions.

Several studies have recently reported higher risk of tumour recurrence [19] and reduced overall long-term survival [16] following local excision of T_1 rectal cancers when compared to radical surgery, with tumour size and location in the rectum both considered to be important in determining success. Recently, Wirsing *et al.* reported a 34-year retrospective review of patients treated with transrectal excision for T_1 rectal cancer with clear margins and found a 26% rate of local recurrence with 13% of patients dying from metastatic rectal cancer [20].

Whether the use of chemo- or chemoradiotherapy improves the outcome following local excision however, is not at present clear, with some studies suggesting improved recurrence and disease-free survival [12,21], but others being less convincing [22].

Radiological staging of rectal cancer using either or both EUS [7] and pelvic MRI [7,9] is likely to be important in selecting patients for whom local excision is appropriate. Whilst preoperative staging of the primary tumour has advanced significantly in recent years, lymph node assessment has remained poor. Currently, mesorectal nodal enlargement (5 mm, 6 mm, 10 mm) is the only consistently used imaging criterion on which the diagnosis of metastasis is made. However, there is no definitive, validated size criterion for the assessment of malignancy in mesorectal lymph nodes. Nodal enlargement has major limitations in that metastases in small lymph nodes or lack of metastases in larger lymph nodes are wrongly described. A significant number (up to 45%) of malignant nodes have been shown to be smaller than 5 mm [23,24] and would not be correctly defined using presently used criteria. Indeed, lymph nodes smaller than 5 mm have been suggestive as prognostic indicators of local recurrence [25].

Combining preoperative staging with histological tumour grade and factors such as evidence of vascular invasion and tumour morphology will allow the clinician to determine which patients warrant adjuvant therapy, and may therefore improve the outcome from local surgery. In addition, new emerging techniques may also be employed in the future to detect lymph node involvement by tumour preoperatively such as ultrasmall particle iron oxide (USPIO) contrast enhanced MRI [26] which may contribute to the decision-making process as to which patients may be suitable for local excision of early rectal cancer.

It is important to acknowledge the limitations of this study. Firstly, the data was not collected prospectively. Having said this, due to the meticulous collection and storage of specimens by our Pathology Department, the retrospective material is of a very high quality with multiple paraffin-embedded blocks stored per patient. Multiple sections were taken for the purpose of this study

and we are confident about the determination of T stage and depth of submucosal invasion in the T_1 cases. Secondly, the patient group had undergone curative resection for rectal cancer and not local resection suggesting that despite stage, the operating surgeon felt the need for radical surgery to allow the best chance of curative treatment. Thirdly, the sample size of the T_1 group was relatively small, with the majority of cases in this study being T_2 cancers.

Another factor influencing the data is that St Mark's Hospital is a tertiary referral centre receiving patients of a more complicated nature and our dataset includes patients who may have been considered inoperable by other centres. In addition, St Mark's Hospital has a large number of patients with FAP in its Polyposis Registry and also receives FAP patients in whom a cancer has already developed.

Despite these limitations however, this study has shown that whilst the link between submucosal tumour depth of invasion and lymphatic spread for early rectal cancer may exist, it requires further investigation. This will allow the clinician to decide whether adjuvant therapy is indicated, and therefore perform an excision that offers the best chance of loco-regional control and increased cancer-specific survival. There is a need for further prospective research comparing not only local resection (with or without adjuvant oncological therapies) to radical surgery for early rectal cancer in patients with no other risk factors for lymphatic spread, but also for research on the use of chemo- and radiotherapy for locally excised rectal cancers. Long-term follow-up of these patients will subsequently allow for disease recurrence and survival data to be obtained for this treatment modality.

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Original article

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Predictive factors for successful sacral nerve stimulation in the treatment of faecal incontinence: a 10-year cohort analysis

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Abstract

Objective Sacral nerve stimulation (SNS) is an established treatment for faecal incontinence. We aimed to identify specific factors that could predict the outcome of temporary and permanent stimulation.

Method A cohort analysis was performed to identify potential predictive factors in 81 patients who underwent temporary SNS at a single institution over a 10-year period (June 1996 to June 2006). Data were obtained from prospectively collected patient symptom diaries and quality of life questionnaires, operation reports, anorectal physiological studies, endoanal ultrasound images and radiology of lead placement.

Results Clinical outcome of temporary screening was not affected by patient gender, age, body mass index, severity or length of symptoms. The need for a repeated temporary procedure was associated with subsequent failure during screening ($P = 0.008$). A low threshold to obtain a motor response during temporary lead insertion was associated with improved outcome ($P = 0.048$). Evidence of anal sphincter trauma was associated with a greater risk of failure ($P = 0.040$). However, there was no difference in medium-term outcome between patients with external anal sphincter (EAS) defects and patients with intact anal sphincter muscles.

Conclusion Variables have been identified that help to predict the outcome of SNS. The presence of an EAS defect should not preclude treatment.

Keywords Sacral nerve stimulation, neuromodulation, faecal incontinence, predictive value of tests, surgery, obstetric

Introduction

Sacral nerve stimulation (SNS) is an established first-line surgical treatment for patients with faecal incontinence (FI) resistant to medical and behavioural therapies [1]. Initially used in those with a structurally intact sphincter mechanism, the recent evidence suggests that those with sphincter muscle defects have a similar result from chronic stimulation [2–5].

One advantage of SNS over alternative surgical techniques is the ability to evaluate the efficacy of treatment prior to definitive permanent neurostimulator implantation. Percutaneous, peripheral nerve evaluation (PNE), performed under local or general anaesthesia, assesses the acute response to stimulation. The response can be variable depending on the nerve root being stimulated, the proximity of the electrode to the nerve and the amplitude of stimulation [6]. With stimulation of the third sacral nerve root at low amplitudes, a patient classically experiences a pulsing or vibrating sensation around the anus. At higher amplitudes, there is a reflex motor contraction of the anus or pelvic floor with flexion of the hallux [7]. Some patients do not exhibit this classical response but still achieve improved continence with temporary stimulation. This suggests that these signs cannot be entirely relied on to predict the outcome of therapy.

In patients showing an adequate response to PNE, a temporary wire electrode is inserted. This is connected to an external pulse generator. Patients then commence a screening evaluation that usually lasts between 1 and 3 weeks. Those who do not respond to acute stimulation do not proceed to the temporary screening phase.

Patients are deemed eligible for permanent implantation if temporary stimulation achieves a >50% reduction in incontinent episodes, as measured by baseline and temporary stimulation bowel habit diaries. After permanent implantation, one in 10 patients fail to have benefit from chronic stimulation and others fail to reach the same efficacy achieved during the trial period [8]. The reasons

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for this subsequent failure have yet to be identified. This study aimed to identify specific factors that may predict the success or failure of temporary and permanent SNS in the treatment of FI.

Method

A retrospective analysis was undertaken of all patients who had undergone temporary SNS for FI between June 1996 and June 2006 at St Mark's Hospital, London. The study population studied consisted of 81 patients, five men and 76 females with a median age of 53 years (range: 33–73). The length of time with symptoms of FI was a median of 7 years (range: 1–30). All had failed previous medical therapy with 69 patients having failed previous behavioural therapy.

Data had been collected prospectively by means of bowel habit diaries, the short form 36 (SF-36) quality of life questionnaire [9], the Rockwood faecal incontinence quality of life (FIQL) score [10] and subjective clinical evaluation in the outpatient setting. A review of number of sessions of biofeedback completed prior to neurostimulation, hospital operating notes, stimulation parameter settings, anorectal physiological studies at baseline and with stimulation and endoanal ultrasonography or magnetic resonance imaging performed prior to therapy was also performed.

To test for possible predictive factors, baseline demographics of sex, age, body mass index (BMI) and length of symptoms were compared with outcome of temporary and permanent stimulation. A successful result from temporary stimulation was defined as a reduction in episodes of total incontinence of >50%.

Baseline endoanal ultrasound examinations were reviewed by two investigators blinded to each other findings and Starck's score was determined based on the radial extent, depth and length of any external (EAS) or internal anal sphincter (IAS) defect [11]. The score ranges from zero, equal to no sphincter disruption, to a maximum score of 16 that equates to severe disruption to both the IAS and EAS. Operating data on temporary and permanent lead implantation was analysed, as were stimulation parameters of the temporary and permanent neurostimulators. Analysis of lead placement was made from intra-operative imaging.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences version 10.0 (SPSS^{TM}, Chicago, Illinois, USA). Qualitative data were compared using chi-squared test or two-tailed Fisher exact test. Continuous variables were analysed by nonparametric tests (Mann–Whitney *U*-test, Wilcoxon test and Kruskal–Wallis test). Statistical significance was indicated by a two-sided *P*-value ≤ 0.05.

A univariate and multivariate analysis was performed to identify potential predictive factors in which temporary and permanent failures were the dependent outcome variables. Independent variables with a *P*-value ≤ 0.2 by bivariate statistics were included in a forward stepwise logistic regression model. The results are reported as odds ratio (OR) and 95% confidence intervals (CI).

The long-term outcome of SNS was evaluated by Kaplan–Meier curves for which >50% clinical improvement was the end-point. The curves for patients with intact anal sphincter muscles and those with EAS defects were compared using a log rank test.

Results

Eighty-one patients underwent PNE followed by temporary screening. Six patients had two test procedures because of presumed lead migration and in one patient three test stimulations were performed. Having a repeated procedure was significantly associated with subsequent failure of temporary stimulation ($P = 0.008$). Of the seven patients that underwent more than one trial of screening, four failed to have clinical benefit and were not considered eligible for permanent implantation. All three patients deemed eligible underwent permanent implantation. However, on most recent follow-up, only one of these three subjects had >50% improvement in symptoms with chronic stimulation ($P = 0.052$).

Predictors of outcome of PNE and temporary screening

Outcome of temporary screening was stratified by eligibility for permanent stimulation. Sixty-nine (85%) of the 81 patients were eligible for implantation of a permanent pulse generator following temporary screening.

There was no significant difference between eligible and non-eligible groups in terms of age, BMI, length of symptoms, medication use, number of previous biofeedback sessions, baseline episodes of incontinence and baseline quality of life scores (Table 1). Subanalysis of those with a BMI ≥ 30, suggested a larger proportion of obese patients failed temporary screening compared with those with a BMI <30 (43% *vs* 15%; $P = 0.340$).

Endoanal ultrasonographic evidence of anal sphincter trauma (scarring, partial or full length defect) was present in 46 (57%) patients. A defined defect in either the IAS or EAS was present in 37 (46%) patients. Outcome did not relate to the structural integrity of the anal sphincter with the proportion of patients not eligible for permanent

Table 1 Median (range) baseline demographics of patients who were eligible (>50% reduction of incontinent episodes) and not eligible (<50%) for permanent neurostimulation after a 2-week screening period.

	Eligible ($n = 69$)	Not eligible ($n = 12$)	*P*-value
Baseline demographics			
Male/female	3/66	2/10	0.102
Age (years)	55 (33–73)	55 (38–67)	0.755
Body mass index (kg/m^2)	26.29 (19.78–41.77)	26.63 (22.67–46.39)	0.481
History of FI (years)	7 (2–30)	6 (1–17)	0.620
Biofeedback sessions (number)	3 (0–20)	4 (2–6)	0.403
Current medication use	60 (88%)	11 (91%)	0.841
Urge incontinence*	3 (0–52)	3 (0–82)	0.967
Passive incontinence*	7 (0–160)	11 (1–78)	0.496
Total incontinence*	12 (0–161)	16 (4–160)	0.580
Soiling*	9 (0–14)	10.5 (5–14)	0.703
Urgency score†	4 (1–5)	4 (3–5)	0.799
Rockwood (10) quality of life scores	($n = 40$)	($n = 5$)	
Lifestyle	2.00 (1.00–3.90)	2.50 (1.20–2.70)	0.986
Coping	1.44 (1.00–3.33)	1.38 (1.00–2.11)	0.744
Depression	2.14 (1.00–3.57)	1.86 (1.29–2.29)	0.212
Embarrassment	1.66 (1.00–3.33)	1.33 (1.00–2.00)	0.400
SF-36 quality of life scores	($n = 40$)	($n = 5$)	
Physical function	60 (0–100)	70 (35–90)	0.603
Role – physical	25 (0–100)	50 (0–100)	0.362
Bodily pain	51 (0–100)	84 (30–100)	0.395
General health	60 (0–100)	72 (20–77)	0.829
Vitality	45 (0–90)	30 (0–80)	0.692
Social functioning	50 (0–100)	50 (25–100)	0.817
Role – emotional	66 (0–100)	33 (0–100)	0.821
Mental health	60 (12–100)	52 (16–88)	0.319
Anorectal physiology and EAUS	($n = 56$)	($n = 12$)	
Anal canal length (cm)	2.5 (1–4.5)	2.0 (1–4)	0.111
Resting pressure (cmH_2O)	34.5 (8–115)	36.5 (9–105)	0.797
Squeeze increment (cmH_2O)	29.5 (5–199)	34 (7–193)	0.633
5 s squeeze increment (cmH_2O)	5 (0–75)	2 (0–133)	0.928
Involuntary increment (cmH_2O)	42 (6–140)	44 (10–122)	0.941
Threshold volume (ml)	45 (15–120)	37.5 (10–100)	0.207
Urge threshold (ml)	80.5 (25–230)	71.5 (20–140)	0.358
Maximum threshold (ml)	140.5 (50–275)	117 (50–238)	0.476
Anal electrosensation (mA)	8.2 (3.8–75)	10.2 (2.1–17)	0.633
Rectal electrosensation (mA)	22.5 (3.1–46)	23.8 (9–42)	0.764
EAS defect (number of patients)	15 (23%)	1 (8%)	0.441
Starck's (11) score (range: 0–16)	3 (0–12)	0 (0–12)	0.262

*As measured over a 2-week bowel habit diary card period.
†Urgency score measuring ability to defer: 1, >15 min; 2, 5–15 min; 3, 1–5 min; 4, <1 min; 5, unable to defer defaecation.
EAS, external anal sphincter; EAUS, endoanal ultrasonography; SF-36, short form 36; FI, faecal incontinence.

stimulation being similar between those with evidence of sphincter trauma [seven (15%) patients] and those with intact sphincters [five (16%) patients; $P = 0.914$].

Operative data of temporary screening were available in 77 patients. Some patients had placement of bilateral temporary screening wires and in these the side that gave the greatest efficacy of treatment was recorded. Temporary screening was performed in 40 subjects on the right side and 37 patients on the left side. The foramen used was documented as S3 in 69 patients, S2 in four patients and S4 in the remaining four subjects. Patients were significantly more likely to fail temporary screening if the S2 or S4 foramen was documented as the site of electrode placement ($P = 0.019$).

Motor responses to stimulation were documented in 61 patients. Eighteen patients (29.5%) did not exhibit toe

or forefoot flexion with the anal contraction. The presence or absence of toe flexion did not predict the outcome of temporary screening ($P = 0.974$).

The threshold required to obtain a motor response during temporary lead insertion was documented in 27 patients. The median (range) voltage was significantly lower in those who were subsequently eligible for permanent implantation when compared with the noneligible group [3 volts (1–10) *vs* 5 volts (3–5); $P = 0.048$]. Spearman correlation showed a significant relationship between the motor threshold for anal contraction obtained during temporary lead insertion and the sensory threshold obtained at the commencement of the temporary screening phase ($r = 0.523$, $P = 0.015$). The median (range) sensory threshold was also lower in the eligible group [1.95 volts (0.2–6.0)] compared with the noneligible group [3.0 volts (0.5–5.0)]; ($P = 0.324$). Those with a sensory threshold of ≤3 volts appeared more likely to have successful outcome from stimulation when compared with those with a sensory threshold of >3 volts ($P = 0.093$).

Stepwise logistic regression (univariate and multivariate) was used to assess the predictive value of the number of temporary procedures together with the sensory threshold during temporary stimulation. Repeating the screening procedure in those who failed their initial temporary stimulation trial was an independent predictive factor of poor outcome ($P = 0.019$; OR 10.91 (95% CI: −1.47 to 80.59). By multivariate analysis sensory threshold was not found to be a significant independent predictive factor of outcome ($P = 0.401$; OR 2.06 (95% CI: 0.37–11.28).

Correlation between the outcome from temporary screening and permanent implantation

At the time of analysis, 11 of the 69 patients were awaiting implantation of the permanent device leaving 58 implanted subjects for analysis. Of the 58 permanently implanted patients, follow-up data was available in 48 (83%) subjects with a median follow-up of 29 months (range: 3–106). In these 48 patients, the results of permanent stimulation were stratified into one of four groups; 100% reduction of incontinent episodes (cure), 75–99% reduction, 50–74% reduction and ≤50% reduction of incontinent episodes. Outcome was also stratified into 'success' (≥50% improvement in symptoms) and 'failure' (those with <49% improvement in symptoms). Only six patients (12.5%) failed to have any improvement in symptoms (defined as <25% improvement) at latest follow-up.

The percentage improvement of incontinent episodes from temporary screening and permanent stimulation at most recent follow-up was compared (Table 2). There was no correlation on Spearman analysis between the percentage reduction in total episodes of incontinence during the screening period and that recorded at latest follow-up [median of 23 months (range: 1–106) ($r = 0.14$; $P = 0.412$)]. It was noted that one patient had undergone permanent implantation despite not meeting the entry criteria. On the most recent follow-up this patient had over 75% improvement in symptoms.

Table 2 Relationship between temporary screening and chronic stimulation in 39 patients implanted with a permanent neurostimulator. Outcome is measured by the percentage reduction of symptoms during screening and latest follow-up compared with prestimulation baseline data (cure = 100% reduction in incontinent episodes).

	Permanent stimulation				
	Cure	75–99%	50–74%	<50%	Total
Temporary stimulation					
Cure	9	4	5	1	19
75–99%	4	4	2	4	14
50–74%	2	2	0	1	5
Fail PNE	0	1	0	0	1
Total	15	11	7	6	39

$P = 0.480$. PNE, peripheral nerve evaluation.

Predictors of outcome for permanent stimulation

There were no significant differences between baseline demographics and outcome of permanent stimulation. Physiological parameters of rectal threshold and urge sensation to volume distension appeared to be lower in those who had achieved 50–74% reduction of incontinent episodes ($P = 0.042$ and $P = 0.023$ respectively). There were no significant predictors of outcome from baseline SF-36 scores, but depression and negative self-perception as measured by the Rockwood FIQL score was greater in those that achieved successful outcome from stimulation. The median baseline FIQL score, where the minimum score of one is equal to poor quality of life and the maximum score of four is equal to good quality of life, was 1.93 (range: 1.0–3.28) in those with >50% improvement in symptoms *vs* a median of 3.0 (range: 2.0–3.43) in those with <50% improvement in symptoms ($P = 0.040$). That is, a good quality of life before treatment was associated with an increased chance of improved symptoms with treatment.

There was no significant difference in clinical outcome between idiopathic, obstetric, postsurgical and miscellaneous causes (imperforate anus and scleroderma) of FI ($P = 0.109$).

Table 3 Clinical outcome of permanent sacral nerve stimulation compared with number of patients with and without endoanal ultrasonographic evidence of trauma to the anal sphincter mechanism ($n = 45$).

	Evidence of sphincter trauma	No evidence of sphincter trauma
>50% improvement	22 (76%)	16 (100%)
<50% improvement	7 (24%)	0 (0%)

$P = 0.040$.

Patients with endoanal ultrasonographic evidence of damage (scarring or defect) to the IAS and/or EAS muscles were significantly more likely to have poor outcome from chronic stimulation when compared with those with structurally intact sphincters (Table 3; $P = 0.040$). This was reflected by the Starck score that was median zero (range: 0–12) for all patients with over 50% improvement in symptoms *vs* median three (range: 0–11) in those with <50% improvement ($P = 0.893$). Of the 45 patients studied, 29 patients had evidence of sphincter injury of which 18 had undergone previous sphincteroplasty. There was no significant difference between the median number of episodes of FI, soiling or ability to defer defaecation between those with a sphincter disruption and those with intact sphincter muscles. Physiological findings were also comparable although the maximum tolerated volume to rectal distension was significantly lower in those with no evidence of sphincter injury [median 100 (range: 50–270) *vs* median 150 (range: 55–275); $P = 0.018$].

Isolated external sphincter disruption may be associated with a better outcome than those with injuries to both muscles. Kaplan–Meier curves were performed to compare the clinical outcome over time in patients with >30°, full-length EAS disruption against those with no evidence of sphincter trauma (Fig. 1). Regardless of the presence of EAS disruption, approximately 80% of subjects in both groups had over 50% reduction of incontinent episodes at up to 80 months postimplantation ($P = 0.819$).

Radiology of permanent lead placement was available for analysis in 30 (62.5%) of the 48 patients with clinical data. Twenty-two patients (73.3%) had lead placement in the S3 foramen, six patients (20%) lead placed in the S4 foramen, one patient in the S2 (3.3%) and one patient (3.3%) in the S5 foramen. There was no significant difference in clinical outcome between leads placed in the S3 foramen and those placed in different foramina ($P = 0.457$). Lead angle and depth below the anterior sacral cortex was measured in those with leads placed in the S3 foramen. There were no significant differences between the depth of lead and clinical outcome ($P = 0.785$). In the S3 foramen, the median angle of the lead in relation to the cortex was 67.50° (range: 50–105) in those with over 50% benefit *vs* 90 (range: 60–100) in those with <50% benefit ($P = 0.653$). The median amplitude of stimulation required to obtain sensory threshold appeared to be lower in those patients with the greatest reduction in symptoms (Table 4).

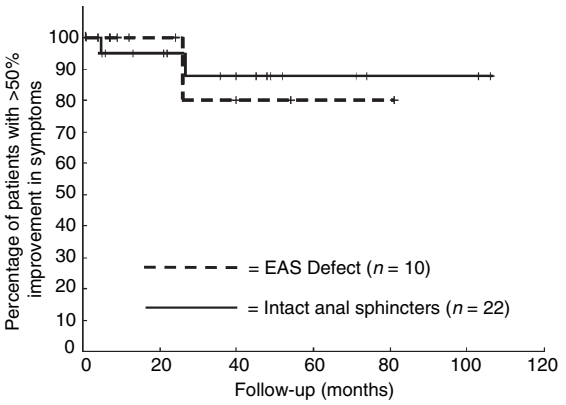

Figure 1 Kaplan–Meier curves comparing the clinical outcome of chronic sacral nerve stimulation in those with external anal sphincter disruption against those with intact sphincter muscles with time. Survival is determined by maintenance of >50% improvement in incontinent episodes when compared with a pretherapeutic baseline, the end-point measured as a 49.9% or less reduction of incontinent episodes (log rank test, $P = 0.819$).

Discussion and conclusion

One benefit of SNS over alternative surgical therapies is the ability to assess the efficacy and acceptability of treatment prior to implantation of the definitive neurostimulator. In order for PNE and temporary stimulation to be valuable assessment tools, the results of screening

Table 4 Comparison of the percentage reduction of incontinent episodes with chronic stimulation and the median (range) sensory threshold (volts) recorded at initial programming of the permanent neurostimulator and at latest follow-up.

	Cure	75–99%	50–74%	<50%	*P*-value
Initial	1 (0.2–3.1)	0.9 (0.1–1.4)	1.7 (0.9–3.5)	1.5 (0.2–2.5)	0.06
Latest	1.4 (0.3–5.0)	1.85 (0.8–3)	1.9 (1.2–3.6)	2.15 (0.5–3)	0.338

Table 5 Summary of factors that may predict the clinical outcome of sacral nerve stimulation in the treatment of faecal incontinence.

Factors not affecting outcome of stimulation
Gender, age and body mass index
Length and severity of symptoms
Absence of toe and/or forefoot plantar flexion on PNE
Angle or depth of the permanent lead
Factors predicting successful stimulation
Low-stimulation amplitude to achieve a motor response
Factors predicting unsuccessful stimulation
Repeat temporary screening procedures

PNE, peripheral nerve evaluation.

should correlate with the outcome of permanent stimulation to avoid unnecessary further surgery to the patient and to justify the ensuing costs to the healthcare provider.

This study has identified predictive factors that can aid the clinician in patient selection and help refine the technique of therapy (Table 5). Multiple attempts at temporary screening, the presence of a high motor threshold with PNE and high sensory threshold during temporary screening appear to be poor prognostic factors. A number of variables do not influence the outcome of temporary or permanent neurostimulation. Patients should not be excluded for treatment on the basis of sex, age, BMI, severity of incontinence, presence of an anal sphincter defects or anorectal physiological findings.

There are possible limitations that could have influenced the results of this study. Outcome was measured by a subjective reduction of symptoms with stimulation that was compared with baseline pre-treatment data. Quantitative data collected by this method are difficult to interpret as they can be influenced by variables such as stool consistency, medication use and patient activity. Assessment using diary cards over a 2-week period aims to eliminate these daily variations, but in all patients 'good' and 'bad' weeks can occur. Patient perception of symptoms can change with time, for example descriptions of soiling and passive incontinence are often interchangeable. During screening, behavioural changes can also occur. Because of the presence of an external stimulator box and temporary wire, patients may stay at home, reducing their usual activities of daily living and remaining in close proximity to a toilet. These factors may explain why some patients reported an apparently good response with temporary stimulation, but then failed to have benefit from chronic stimulation. Permanent lead misplacement or subsequent lead migration are further possible considerations.

Despite leading to some impairment in function, structural damage to the sphincter mechanism has been shown not to be a contraindication for therapy. Although full continence may not be achieved, 76% of patients with EAS and/or IAS deficiency will have acceptable medium-term benefit from permanent stimulation. In those with EAS defects medium-term results were comparable with those with intact muscles. This is not entirely surprising as most studies on patients with intact anal sphincters have found no alteration in the resting pressure and squeeze increment with subsensory chronic stimulation [12–16]. It is likely that the stimulation of sacral nerve roots does not directly affect sphincter motor function at normal therapeutic stimulation amplitudes.

Tolerability to rectal volume distension was significantly lower in patients who had a poor response to chronic stimulation (50–74% reduction of incontinent episodes) when compared with those with a better response (>75% reduction of incontinent episodes). This finding suggests that alteration of rectal volume and compliance may be an important part of the mechanism by which SNS has its effect. Changes in rectal sensation to volume distension has been observed in other studies of patients undergoing successful temporary and permanent stimulation [17,18]

Electrode placement in the S3 foramen during temporary screening was associated with improved outcome when compared with S2 or S4 placement. However, this finding was not reciprocated with chronic stimulation. This incongruity may be secondary to an underpowered, smaller sample size of patients with permanent implants. Alternatively, the placement of temporary screening wires was not assessed radiologically and therefore reporting errors regarding the correct site used may exist.

In this study, patients that required high-stimulation amplitudes to achieve a motor response during PNE were significantly less likely to achieve successful clinical outcome during the temporary screening period. Toe or forefoot plantar-flexion was not a prerequisite for success.

The motor response of the pelvic floor and EAS, observed under general anaesthetic during PNE, is a reflex response mediated by stimulation of afferent fibres within the sacral nerve root [19]. Direct motor contraction of the external sphincter may also occur at higher amplitudes. Normal EAS electromyography has previously been shown to be a significant predictive factor for successful outcome in the treatment of FI by SNS [20]. It has also been suggested that the amplitude required to elicit a reflex response is dependent on the proximity of the electrode to the nerve [6]. However, in some patients asymmetry in the innervation of the pelvic floor could account for a higher stimulation amplitude required to elicit a motor response [21]. Alternatively, the afferent outflow from the pelvis may be confined to a single level

or root accounting for those who fail to respond to stimulation [22]. PNE is a valuable assessment tool to ascertain the optimal site for electrode insertion, but it cannot always predict a successful outcome.

The significant correlation between the amplitude required to obtain the motor threshold during PNE and the amplitude required to obtain sensory threshold during temporary screening suggests that the sensory threshold is also important in predicting the outcome of stimulation. However, in this study, despite a trend being apparent, the amplitude required to obtain the sensory threshold during temporary screening was not found to be a significant independent predictive factor of outcome.

In conclusion, in the absence of major anatomical deformity such as a cloacal injury requiring surgical reconstruction, any patient with FI who has failed conservative treatment may be offered a trial of SNS unless medically contraindicated. Further studies need to be performed to determine whether SNS should be offered as an alternative to sphincter repair in those patients with external sphincter disruption that would normally be treated by sphincteroplasty.

A clinical S3 response should be used to determine the correct foramen for stimulation although this may not correlate with placement of the electrode in the S3 foramen. Flexion of the hallux or forefoot is not imperative for successful outcome. PNE should be achieved at the lowest amplitude required to elicit a motor or sensory response. This will result in the placement of the cathode in close proximity to the nerve root.

In the absence of obvious electrode dislocation, patients who have poor efficacy with temporary stimulation should not undergo repeated procedures. In those who have a successful response, it may be useful to acquire a plain film x-ray prior to wire removal to ascertain the foramen in which the temporary electrode is placed. This can guide the insertion of the permanent electrodes into the same foramen as that used during screening. With permanent lead insertion, obtaining a motor or sensory response at low amplitudes of stimulation is of greater importance than the angle or depth of the permanent lead.

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Original article

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Is a morphologically intact anal sphincter necessary for success with sacral nerve modulation in patients with faecal incontinence?

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Abstract

Objective Sacral nerve modulation (SNM) for the treatment of faecal incontinence was originally performed in patients with an intact anal sphincter or after repair of a sphincter defect. There is evidence that SNM can be performed in patients with faecal incontinence and an anal sphincter defect.

Method Two groups of patients were analysed retrospectively to determine whether SNM is as effective in patients with faecal incontinence associated with an anal sphincter defect as in those with a morphologically intact anal sphincter following anal repair (AR). Patients in group A had had an AR resulting in an intact anal sphincter ring. Group B included patients with a sphincter defect which was not primarily repaired. Both groups underwent SNM. All patients had undergone a test stimulation percutaneous nerve evaluation (PNE) followed by a subchronic test over 3 weeks. If the PNE was successful, a permanent SNM electrode was implanted. Follow-up visits for the successfully permanent implanted patients were scheduled at 1, 3, 6 and 12 months and annually thereafter.

Results Group A consisted of 20 (19 women) patients. Eighteen (90%) had a positive subchronic test stimulation. Twelve patients had a successful SNM implant during middle-term follow-up. Group B consisted of 20 women. The size of the defect in the anal sphincter varied between 17% and 33% of the anal circumference. Fourteen (70%) had a positive subchronic test stimulation. Twelve patients had a successful SNM implant during middle-term follow-up. In both groups, the mean number of incontinence episodes decreased significantly with SNM (test *vs* baseline: $P = 0.0001$, $P = 0.0002$). There was no significant difference in resting and squeeze pressures during SNM in group A, but in group B squeeze pressure had increased significantly at 24 months. Comparison of patient characteristics and outcome between groups A and B revealed no statistical differences.

Conclusion A morphologically intact anal sphincter is not a prerequisite for success in the treatment of faecal incontinence with SNM. An anal sphincter defect of <33% of the circumference can be effectively treated primarily with SNM without repair.

Keywords Sacral nerve modulation, anal sphincter repair, anal sphincter defect, faecal incontinence

Introduction

The incidence of faecal incontinence is probably underestimated. Daily or weekly involuntary loss of liquid or solid stool occurs in about 2% of the adult population and in about 7% of healthy adults aged over 65 years. Few patients report incontinence of faeces spontaneously and they have often suffered several years before the first presentation [1–4].

Faecal continence depends on several factors including intact anorectal sensation, motor innervation and an anatomically intact sphincter complex [5]. It mainly affects women after childbirth. Pudendal nerve damage and/or damage to the anal sphincter is thought to be the main cause of faecal incontinence [6,7]. Surgical treatment is an option when conservative treatment, such as dietary modification, anti-diarrhoeal agents, colonic lavage and biofeedback fails. Patients with a sphincter defect are usually treated by an overlapping sphincteroplasty

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with satisfactory short-term results in 47–100% of the cases [8], but long-term results are less satisfactory after repair of a defect [9] or after total pelvic repair and postanal repair in patients with no structural defects [8,10].

Sacral nerve modulation (SNM) has been used in patients with urinary dysfunction for more than 15 years [11]. In 1995, Matzel *et al.* [12] published their results of SNM applied to faecal incontinence. Since then, many studies demonstrated the efficacy of SNM for the treatment of faecal incontinence [13–15].

Hitherto, an intact anal sphincter ring was a prerequisite for treatment by SNM, but promising results were reported in a small group of patients with a sphincter defect treated by SNM alone [16]. In this study, the results of SNM for the treatment of faecal incontinence in patients with and without an anal sphincter defect were compared.

Table 1 Exclusion criteria.

1	Congenital anorectal malformation
2	Previous rectal surgery (rectopexy and rectal resection)
3	Previous/present external rectal prolapse
4	Chronic inflammatory bowel disease
5	Chronic diarrhoea, unmanageable by drugs or diet
6	Severe constipation
7	Stoma
8	Neurological disease, diabetic neuropathy, Parkinson's disease, multiple sclerosis
9	Bleeding complications
10	Pregnancy
11	Anatomical limitations which would prevent successful placement of an electrode
12	Skin and tissue disease with the risk of infection
13	Psychiatric or physical inability to comply with the study protocol

Method

Forty patients with faecal incontinence treated by SNM between 2000 and 2005 were included in the study. Two groups of patients were compared retrospectively. Patients in group A had initially undergone an anal repair (AR) to create an intact anal ring, but despite this they continued to be incontinent. Group B included patients with faecal incontinence associated with an anal sphincter defect, who were treated by SNM alone. Data were prospectively collected and all patients underwent full preoperative investigation including defaecography, endo-anal ultrasound (SDD 2000; Multiview, Aloka, Japan; 7.5 MHz endo-anal transducer), measurement of pudendal nerve terminal motor latency (PNTML) (St Mark's pudendal electrode) and anal manometry using a Konigsberg-catheter (Konigsberg Instrument Inc. Pasadena, California, USA) connected to a polygraph (Synectics Medical, Stockholm, Sweden). The sensation, urge and maximum tolerated volumes were assessed using an inflatable balloon. Patients with a baseline bowel habit diary showing more than one incontinence episode per week were included. The exclusion criteria are shown in Table 1.

The test stimulation (PNE) followed by a subchronic test during 3 weeks and definitive SNM implantation were performed as previously described [17]. The settings used during the screening and follow-up of the implant were a pulse width of 210 μs and a frequency of 16 Hz. The patients themselves were able to adjust the voltage to the level of sensory response in a preset range. The position of the PNE and definitive electrodes was confirmed by X-ray after the procedure. The main criterion to proceed to a permanent implant was a 50% or more decrease in the number of incontinence episodes or days.

Follow-up after the permanent implantation was scheduled at 1, 3, 6 and 12 months and annually thereafter. The bowel habit diary was collected and anorectal function tests were performed. Failure was defined as return of symptoms to baseline values. A study flow chart is presented in Fig. 1.

Data were analysed using the paired-samples *t*-test or Wilcoxon signed rank test for nonparametric samples in SPSS 13.0 (SPSS, Chicago, Illinois, USA). Results are presented as mean values with standard deviation or range. Statistical significance was set at $P < 0.05$.

Results

There were 20 patients in group A and 20 in group B. Five (33%) patients in group B had had an unsuccessful AR with a persisting sphincter defect demonstrated on physical examination and endo-anal ultrasound. The groups were comparable regarding sex, age and duration of incontinence (Table 2).

Group A

The median follow-up period was 29.2 months (range 6.5–60.0) and the median period between the last AR and the PNE was 3 years (range 1–20). All had an intact anal sphincter determined by endo-anal ultrasound. Twelve patients had a pudendopathy (PNTML > 2.4 ms), which was bilateral in nine [mean latency times were 2.7 ms (range 1.4–4.8) and 2.6 ms (range 1.7–4.6) on right and left sides respectively]. Eighteen (90%) patients had a successful PNE and 16 underwent a

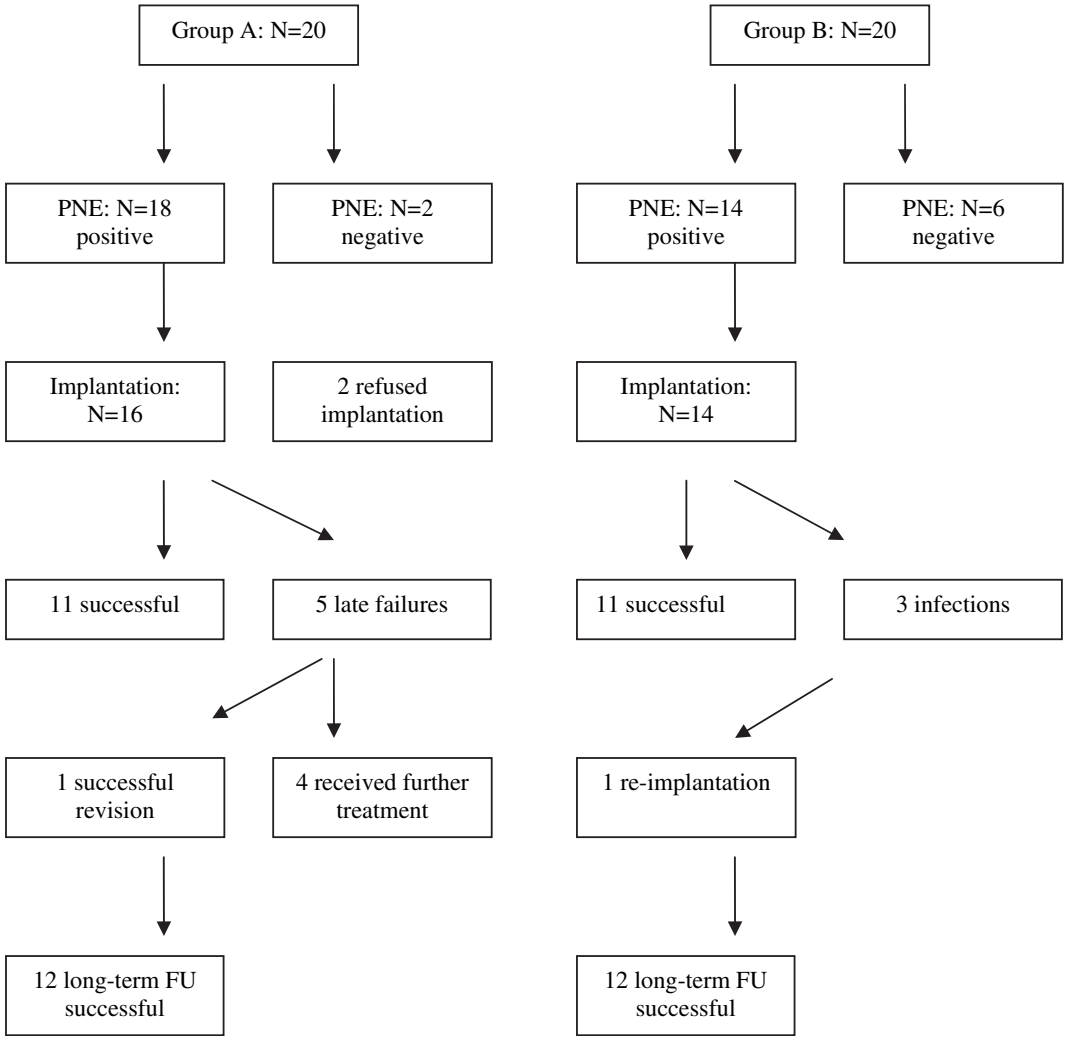

Figure 1 Study flow chart.

Table 2 Patient characteristics.

	Group A	Group B	*P*-value
Characteristics			
Age (years)	55.8 (39.5–78.6)	52.1 (30.7–74.1)	$P = 0.35$
Years of incontinence	13.8 (3.0–43.0)	7.9 (1.0–47.0)	$P = 0.08$
Women/men	19/1	20/0	
Follow-up (months)	29.2 (6.5–60.0)	22.6 (4–41.9)	$P = 0.36$ (Mann–Whitney)

Data are expressed as the mean value with range.

definitive implantation (two patients who would have been suitable declined). Five (31.3%) of the 16 patients were considered late failures and received further treatment which included a permanent electrode at the contra-lateral side in one patient. One patient died of an unrelated cause.

The mean number of baseline incontinence days during 3 weeks of 11.8 ± −5.4 was significantly reduced to 2.5 ± 2.7 ($P < 0.001$) during the test stimulation. At 24 months, the effect remained stable at 4.9 ± 6.9 ($P = 0.02$) incontinence days (Table 3). The mean number of incontinence episodes during 3 weeks also

Table 3 Incontinence days/3 weeks, urgency (minutes) and voltage.

	Baseline	24 months	*P*-value
Group A			
Incontinence days/ 3 weeks (±SD)	11.8 (5.4)	4.9 (6.9)	0.02
Urgency (min) (±SD)	2.4 (6.9)	6.4 (5.8)	0.008
Voltage (V) (±SD)	1.8 (0.9)	2.2 (1.3)	0.16
Group B			
Incontinence days/ 3 weeks (±SD)	12.5 (4.9)	2.6 (3.2)	0.008
Urgency (min) (±SD)	1.3 (2,0)	27.6 (38.8)	0.008
Voltage (V) (±SD)	1.7 (1.0)	1.8 (1.0)	0.63

Data are expressed as the mean value (±SD).

decreased significantly after test stimulation. The effect was sustained during follow-up [baseline: 26.6 ± 21.1, test: 4.8 ± 8.1, (test *vs* baseline: $P = 0.0001$), 24 months: 12.5 ± 19.7, (24 months vs. baseline: $P = 0.001$); Fig. 2]. There was a significant increase in the time of deferment of defaecation which was sustained during follow-up (Table 3). There was no significant difference between the pre- and postoperative anal resting pressures (Fig.3), squeeze pressures (Fig. 4), first sensation, urge and maximum tolerable volume (Table 4).

Group B

The mean follow-up period was 22.6 months (range 4.0–41.9). All patients had a defect in the external anal sphincter varying from 17% to 33% of the circumference determined by endo-anal ultrasound. In one patient, the lesion extended throughout the full length of the anal canal. In all other patients, it involved the upper and middle part of the anal canal with the most distal part intact. Three patients had an internal anal sphincter defect in addition.

Ten patients had a pudendopathy which was bilateral in five (mean latency times were 2.6 (range 1.7–5.0) and 2.6 (range 1.3–5.7) on right and left sides respectively).

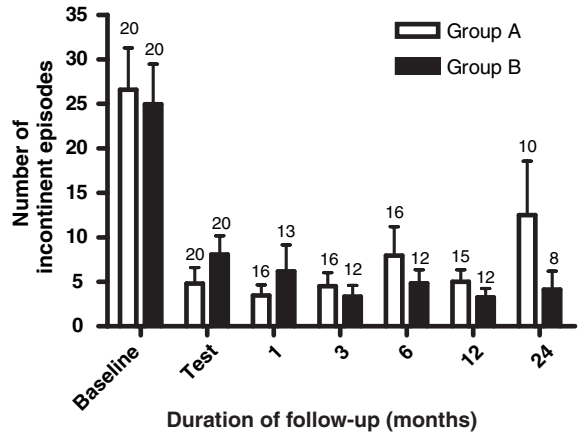

Figure 2 Incontinence episodes per 3 weeks (mean, SD). Numbers represent patients at indicated follow-up.

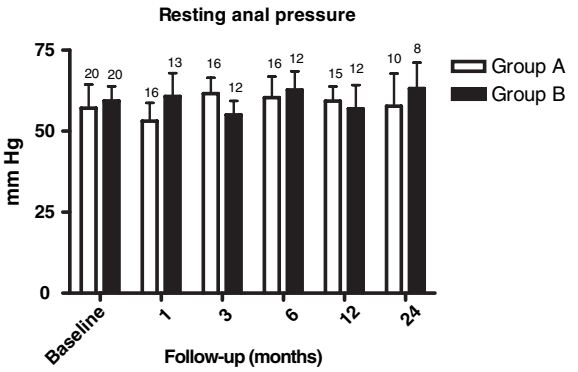

Figure 3 Resting pressures (mean, SD).

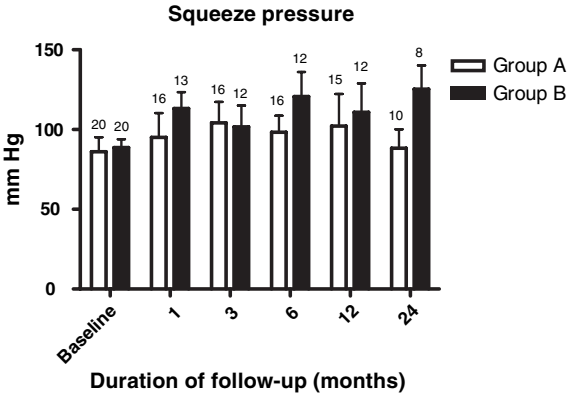

Figure 4 Squeeze pressures (mean, SD).

Table 4 Rectal volumetry (balloon volumes).

Rectal balloon testing			
	Baseline	12 months	*P*-value
Group A			
Sensation (ml)	50.8 (44.9)	38.9 (31.3)	*0.06*
Urge (ml)	96.1 (64.9)	83.3 (40.9)	*0.31*
Maximal tolerable (ml)	164 (87,6)	153.3 (38.1)	*0.36*
Group B			
Sensation (ml)	35.5 (29.0)	25.0 (11.4)	*0.16*
Urge (ml)	59.8 (31.6)	75.0 (33.5)	*0.06*
Maximal tolerable (ml)	125.5 (59.5)	139.1 (44.2)	*0.37*

Data are expressed in mean (±SD) with *P*-value.

Fourteen (70%) patients had a successful test stimulation period. Three (23.1%) patients had an infection and required subsequent removal of the device. One patient received a second implant that is still functioning well. After the test stimulation, the mean number of incontinence days during 3 weeks decreased significantly [baseline: 12.5 ± 4.9, test: 4.3 ± 5.2 ($P < 0.001$)]. At 24 months, the effect remained stable (Table 3). The mean number of baseline incontinence episodes during 3 weeks decreased significantly after test stimulation. The effect was sustained during follow-up [baseline: 24.9 ± 20.2, test: 8.1 ± 9.4 (test *vs* baseline: $P = 0.002$), 24 months: 4.1 ± 5.9 (24 months vs. baseline: $P = 0.008$); Fig. 2]. A significant improvement in defaecation postponement time was observed (Table 4).

No significant difference was observed between the pre-and postoperative anal resting pressures (Fig. 3). The squeeze pressure has risen significantly by 24 months of follow-up [baseline: 88.6 ± 23.6 mmHg, 24 months: 125.3 ± 42.1 mmHg ($P = 0.03$) fig. 4]. The first sensation, urge and maximum tolerable volume were not significantly altered (Table 4).

Comparison between the Groups

There was no significant difference between the baseline number of incontinence episodes ($P = 0.61$) indicating that the severity of the incontinence was similar. The reduction in incontinence episodes after stimulation was also similar (test: $P = 0.14$) and remained stable during follow-up (24 months: $P = 0.63$) in each group.

Although the anal sphincter was disrupted in patients in group B, there was no significant difference in the resting and squeeze pressure compared with group A during baseline ($P = 0.36$ respectively; $P = 0.49$). At 24 months of follow-up, there was no significant change in the resting and squeeze pressures ($P = 0.94$ respectively; $P = 0.08$). There was no significant difference between the groups in the baseline first sensation volume ($P = 0.13$), which remained the same at follow-up of 12 months ($P = 0.31$). Baseline urge volume and maximum tolerable volume were significantly higher in group A ($P = 0.024$ and $P = 0.012$ respectively.). After implantation, the difference in urge and maximum tolerable volumes disappeared (12 months: $P = 0.81$ and $P = 0.82$ respectively).

Discussion

Faecal incontinence is not merely due to the sphincter disruption. Although defects after childbirth are related to faecal incontinence [18], traction and damage to the pudendal nerve [19] and rectal sensory and motor dysfunction are also contributing factors [20]. Twenty per cent of women with an occult anal sphincter defect after delivery report symptoms of faecal incontinence [21]. Treatment of incontinence is also multi-factorial and is not solely based on repairing the sphincter defect. This is supported by the fact that biofeedback therapy can improve faecal incontinence in patients with ultrasound evidence of a sphincter defect [22].

Enhancement of residual functional capacity after biofeedback therapy may be one of the factors to explain the success of SNM, but the mechanism is still not understood. In the beginning, it was thought that SNM directly stimulated the anal sphincter. As with dynamic graciloplasty, it was thought that stimulation induced the transformation of fast-twitch, fatigable muscle fibers (type II) into slow-twitch, fatigue-resistant fibers (type 1) resulting in higher resting and squeeze pressures [12], and indeed several studies showed significant changes in resting and squeeze pressures [23,24]. There is evidence that the effect of SNM is not only motor but also sensory. Uludag *et al.* [25] showed that rectal volumes of first sensation, urge and maximum tolerated volume decreased significantly after SNM with no change in rectal compliance. In the present study, there was a tendency towards a decrease in rectal volumes but this did not reach statistical significance, probably because of the population size.

Sacral nerve modulation can reduce cortico-anal excitability in patients with faecal incontinence, but there is no evidence that a reduction in cortico-anal excitability improves faecal incontinence and there are no long-term data available. SNM possibly drives dynamic brain changes that play a role in influencing anal continence [26].

Koch *et al.* [27] demonstrated that the therapeutic threshold is lower or equal to the sensory threshold and that the resting and squeeze pressures remain unaffected during the stimulation period. In the present study, there was no significant change in the resting and squeeze pressure in both groups during the follow-up.

As this study was not a randomized controlled trial, it is difficult to draw significant conclusions. Almost all the ARs of patients in group A were performed in other hospitals. It is possible that these were different in size from the anal sphincter defects of patients in group B.

Our treatment strategy for patients with faecal incontinence and an anal sphincter defect has changed as a result of the present study. We now start with a PNE and subchronic test stimulation regardless of the morphological state of the anal sphincter complex. If the test is positive, we proceed to the implantation of a permanent system. The data indicate that an intact anal sphincter complex is not necessary for success. A randomized

controlled trial should however be carried out to be certain of this strategy.

Conclusion

The results of this study demonstrate that faecal continence acquired later in life not only depends on an anatomically intact anal sphincter. The action of SNM does not rely solely on the motor effect on the anal sphincter complex. Faecal incontinence associated with an anal sphincter defect up to 33% of the anal circumference can be directly treated with SNM with a success rate comparable to SNM after sphincter repair.

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Original article

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Pilot study of two new injectable bulking agents for the treatment of faecal incontinence

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Abstract

Objective The use of injectable bulking agents for passive faecal incontinence appears to provide reasonable short-term results. However experience with different agents is limited. We report on the outcome of injections with new bulking agents.

Method Each patient received injections of either Bulkamid™ (hydrogel cross-linked with polyacrylamide) or Permacol™ (porcine dermal collagen). Assessment included clinical evaluation, anorectal physiological testing, endoanal ultrasonography and questionnaires including the St Mark's Incontinence Score, one week bowel diary card, the Faecal Incontinence Quality of Life Scale and the Short Form-36 (SF-36) health survey. Follow up was at 6 weeks and 6 months, with a further telephone review at a median of 19 months (range 14–22).

Results Ten patients (nine female), median age 68 years (range 45–79), were enrolled. St Mark's incontinence score (0 = best, 24 = worst) was 15 (range 11–24) at baseline, 12.5 (range 3–18) at 6 weeks and 14 (range 6–22) at 6 months. A 1-week bowel diary and SF-36 forms also showed temporary improvement but this was not sustained beyond 6 weeks.

Conclusion Bulkamid™ and Permacol™ injections did not have a major effect on faecal incontinence.

Keywords Passive faecal incontinence, injection, hydrogel, polyacrylamide, porcine dermal collagen

Introduction

The treatment of passive faecal incontinence due to internal anal sphincter (IAS) dysfunction continues to be a challenge. Degeneration or disruption of this muscle characteristically leads to passive faecal incontinence or soiling. The IAS is not amenable to surgical repair and medical management remains limited. The use of injectable bulking agents as alternative treatment for passive incontinence is attractive in its simplicity and minimal invasiveness.

Since the first report of the use of polytetrafluroethylene paste (Teflon) in 1993 [1], different materials have been injected into the anal canal, including autologous fat [2], bovine glutaraldehyde cross-linked collagen [3] and carbon-coated zirconium beads [4]. PTQ™ implants (Uroplasty BV, Geleen, The Netherlands), a silicone biomaterial, have been used most extensively [5–7]. However the reported results are usually short term; efficacy appears less well maintained in the long term [8].

Bulkamid™ (Contura International A/S, Soeborg, Denmark) is a synthetic, nonparticulate hydrogel consisting of 97.5% water and 2.5% cross-linked polyacrylamide. It is biocompatible but not biodegradable. Bulkamid™ is said to be nonresorbable, resistant to migration and known to cause little reaction in the surrounding tissue. All 21 patients injected with Bulkamid™ for stress urinary incontinence in one study showed a significant reduction in urine leakage at 12 months [9].

Permacol™ (Tissue Science Laboratories Plc, Aldershot, United Kingdom) is a biological material containing large particles of porcine dermal collagen and in its sheet form it has been implanted in over 75 000 patients in a variety of repair procedures over last 6 years. It is biocompatible and nonallergenic. An injectable form of Permacol™ has been developed and has been implanted in over 600 urology patients. In one study, of 32 female with stress urinary incontinence receiving Permacol™ injections 63% had good to excellent results at 12 months [10]. In addition, the majority of patients (88%) required only one treatment.

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Bulkamid™ creates a simple mechanical bulk whilst Permacol™ has the potential to cause revascularization and cell ingrowth from surrounding tissues. We report on the outcome of 10 patients who underwent injections of either Bulkamid™ or Permacol™ for passive faecal incontinence.

Method

Patients

Ten patients with passive faecal incontinence due to IAS dysfunction were recruited. Patient selection criteria included:

1 passive faecal incontinence to solid or liquid stool due to IAS dysfunction;

2 failure of standard conventional treatments such as antidiarrhoeal medication and/or behavioural therapy (biofeedback).

Patients were excluded if they had malignancy, perianal sepsis, marked scarring, immunosuppression or diabetes. Patients who were pregnant at the time of screening or had been previously treated with other injectable bulking agents were also excluded.

Method

After providing written informed consent, each patient underwent clinical assessment, anorectal physiological testing, endoanal ultrasonography and was asked to complete questionnaires. Anorectal physiological testing included anal manometry measurement, rectal volume thresholds and anal and rectal electrosensory thresholds. The St Mark's Incontinence Score [11], a 1-week bowel diary card [11], the Faecal Incontinence Quality of Life Scale [12], and Short Form-36 (SF-36) health survey questionnaire [13] were also completed. These assessments were repeated at 6 weeks and 6 months except for the endoanal ultrasound which was only repeated at 6 weeks and the SF-36 which was only repeated at 6 months. Telephone review was conducted at median of 19 months (range 14–22).

All injections were performed under general anaesthesia in the prone jack-knife position. The patients were given gentamicin 160 mg and metronidazole 500 mg i.v. immediately prior to the procedure. A spinal needle was introduced 2 cm from the anal verge and tracked transsphincterically to the submucosal plane under digital guidance [5]. Bulkamid™ injections were performed with a 20-gauge, 90 mm needle and Permacol™ injections with 18-gauge, 90 mm needle.

The materials were sited at or just above the level of the dentate line and placed circumferentially at sites corresponding to the three physiological anal cushions at 3, 7 and 11 o'clock positions [5]. The volume of the material injected was that required to create adequate sized cushions to achieve closure of the anal canal. Oral cephalexin 500 mg q.d.s. and metronidazole 400 mg t.d.s. were given for 7 days after the procedure. Patients were also given lactulose 15 ml t.d.s. for 2 days before and 7 days after the procedure. In addition, they received oral paracetamol and diclofenac for analgesia.

Statistical analysis

The 10 patients were prospectively randomized to have either Bulkamid™ or Permacol™ injections, five patients being enrolled for each material. A simple randomization method was used, and the randomization schedule was predetermined prior to the recruitment process to ensure equal distribution of patients.

Statistical analysis was performed using unpaired *t*-test for normally distributed data and otherwise using the Wilcoxon signed rank test, Kruskal–Wallis test or Mann–Whitney *U*-test. For variables measured on categorical scales, the Fisher's test was used. As this was a small randomized, uncontrolled, prospective, single blind pilot study the results are also presented in full.

Local Ethical Committee approval for the study was obtained prior to commencement.

Results

Ten patients (nine female), aged 45–79 (median 68) years, participated in the study. Details of the patients, including the endoanal ultrasonographic findings are shown in Table 1. All had either IAS weakness or an internal sphincter defect with passive faecal leakage. Eight patients had intact external anal sphincter muscles and two had a discrete defect in this muscle. All patients completed the study.

Overall, a median total volume of 12 ml (range 8–17.5) was required to create sufficient anal cushions. The median volume of Bulkamid™ required to achieve closure of the anal canal under direct vision was 9 ml (range: 8–9) whereas the median volume of Permacol™ injected was 15 ml (range: 15–17.5), $P < 0.05$.

Clinical assessment

All patients commented that they had experienced a temporary improvement in their passive incontinence symptoms from immediately after the injections but lasting <6 weeks.

Table 1 Table showing the demographics and the endosonographic findings before and after treatment.

				Anal ultrasonography				
					At 6 weeks			
					Injection sites			
	Age	Sex	Cause of faecal incontinence	Preinjection	3	7	11	Total
Bulkamid								
1	45	M	Anal dilatation, lateral sphincterotomy	Discrete IAS defect	−	+	−	1
2	72	F	Idiopathic degeneration	IAS normal	−	+	−	1
3	75	F	Posthaemorrhoidectomy	Fragmented IAS	+	−	−	1
4	52	F	Obstetric trauma	IAS normal	+	+	−	2
5	72	F	Idiopathic degeneration	Thin atrophic IAS	+	−	+	2
Permacol								
6	71	F	Posthaemorrhoidectomy	Discrete IAS defect	+	+	+	3
7	79	F	Idiopathic degeneration	Attenuated IAS	+	−	−	1
8	63	F	Obstetric trauma	Discrete IAS defect	+	−	+	2
9	64	F	Idiopathic degeneration	Thin atrophic IAS	+	−	+	2
10	59	F	Idiopathic degeneration	IAS normal	−	+	+	2

+, visible implant; −, no implant; IAS, internal anal sphincter.

Anorectal physiological testing

The maximum resting pressure appeared to deteriorate during the follow up. The median pressure was 28 cmH_2O (range 15–58) at baseline, 27 cmH_2O (range 19–56) at 6 weeks and 22 cmH_2O (range 10–38) at 6 months ($P < 0.05$, baseline *vs* 6 months). The maximum squeeze increment, five-second squeeze increment, involuntary squeeze increment, rectal sensory volumes and electrosensitivity did not change. The median maximum squeeze increment was 36 cmH_2O (range 16–109) at baseline, 44 cmH_2O (range 13–102) at 6 weeks and 38 cm H_2O (range 15–186) at 6 months ($P < 0.32$, baseline *vs* 6 months).

Endoanal ultrasonography

Six weeks after the injections, one patient had three visible implants, five patients had two, four patients had one visible implant within the vicinity of the IAS (Table 1). Patients in the Bulkamid^{TM} group had a median of one implant (range 0–2) visible in the original sites injected whilst patients in the Permacol^{TM} group had median of two implants (range 1–3) in these sites. This was not a significant difference ($P = 0.222$). There was no correlation between sphincter pathology and the persistence of the material at the original injection sites ($P = 0.682$).

St Mark's Incontinence Score

The median St Mark's incontinence score at baseline was 15 (range 11–24), where 0 is equal to perfect continence and 24 is equal to the worst possible incontinence. Six weeks after the injection, the median score was 12.5 (range 3–18), $P < 0.05$. At 6 months the median was 14 (range 6–22) (Fig. 1). Clinically, the change in score reflected improvement in incontinence episodes from daily to a few times a week.

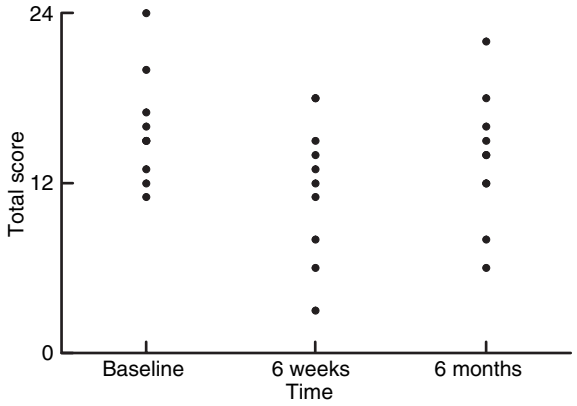

Figure 1 St Mark's Incontinence Score at baseline, at 6 weeks and 6 months after injection with the bulking agents.

In the Bulkamid^{TM} group, the continence score improved and was maintained up to 6 months; 15 (12–17) *vs* 12 (6–15) *vs* 12 (6–18) [baseline *vs* 6 weeks *vs* 6 months, median (range)]. In the Permacol^{TM} group, the incontinence score improved at 6 weeks, then deteriorated at 6 months: 16 (11–24) *vs* 14 (3–18) *vs* 15 (8–22) [baseline *vs* 6 weeks *vs* 6 months, median

(range)]. However, the median change in scores was the same in both groups.

Bowel diaries

In the bowel diary, each positive answer results in a numerical score and the maximum score per day is 10, being worst incontinence. The median baseline score was four (range: 0.5–8.5) improving to a median of 2 (0.0–7.5) at 6 weeks ($P < 0.05$) and deteriorating to median of 3.3 (range 0.0–8.5) at 6 months. There was no difference seen between the Bulkamid™ and Permacol™ groups.

Faecal Incontinence Quality of Life Scale

The lifestyle, coping, depression and embarrassment subscales all showed continuous improvement throughout the 6-month follow-up period. Each subscale range from 1 to 4; with a 1 indicating a lower functional status of quality of life. Overall lifestyle score improved from a median of 3.10 to 3.50 ($P < 0.05$), coping score increased from 2.36 to 2.75 ($P < 0.05$), depression significantly improved from 2.42 to 3.70 ($P < 0.005$) and embarrassment score from 1.67 to 1.84 ($P < 0.05$). There was no difference observed between the Bukamid™ and Permacol™ groups.

SF-36

There was significant improvement in the role of physical score, median 29 (0–100) at baseline rising to 100 (0–100) after the injections ($P < 0.05$). Other mental and physical scores showed no significant change.

Telephone review

Nine of 10 patients were contactable at a median of 19 months follow up (range 14–22 months). Five patients said their condition had improved and four of these were injected with Bulkamid. Two patients said their condition remained the same, both of them had been injected with Permacol. Two patients felt their symptoms had worsened after the injections, one from each group. Two of the five patients who felt they had benefit from the injections noted a decrease in the amount of leakage. Two patients felt improvement despite a lack of change in their leakage. One of the two patients who felt the condition had worsened was satisfied with the treatment as she had received greater attention to her problems at the tertiary centre.

No complications were recorded during this study.

Discussion

Since the first report of the use of injections of bulking agents for faecal incontinence in 1993 various materials have been used with some short-term success. Durability remains an important question and we have recently reported poor long-term results following the injections of silicone biomaterial [8]. Despite the lack of evidence, the use of these treatments has become widespread. In the meantime the search for ideal agent continues.

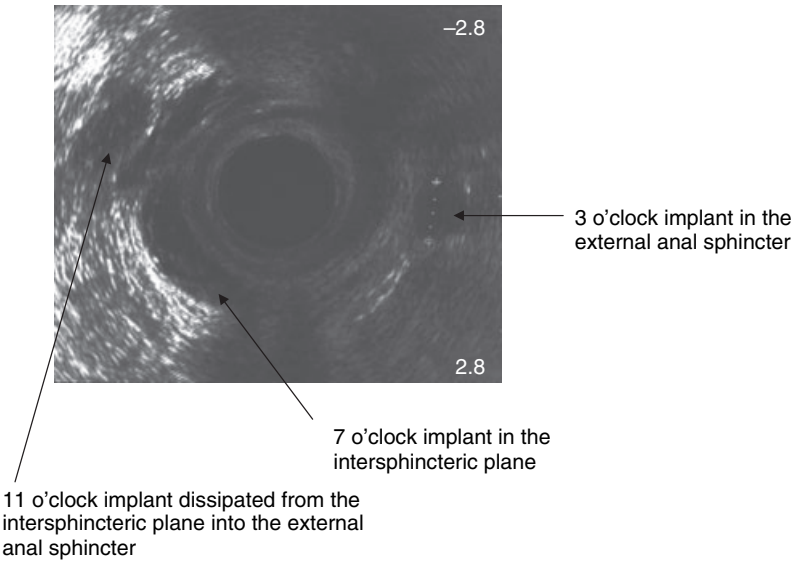

Figure 2 Ultrasound of patient 2, 6 weeks after injection with Bulkamid™. The implants at 3 and 11 o'clock have leaked outside the intersphincteric plane.

Bulkamid™ and Permacol™ injections appear to be less successful than they have been in urology. In this trial, any improvement was not sustained beyond 6 weeks either subjectively or objectively.

Both materials were easy to inject through a syringe and spinal needle. The relatively low viscosity could have resulted in leakage or migration into a deeper plane or beyond external anal sphincter, leading to suboptimal placement of some of the material (Fig. 2). Bulkamid produced a visible bulging of the mucosa at a lower volume of implant than Permacol. This could, in part, explain the different appearances on ultrasound at 6 weeks.

The use of trans-sphincteric injections under digital guidance has been successful in our previous studies in terms of placement of the bulking agent. The needle is withdrawn slowly to prevent immediate back leakage of the material. In a further four patients injected with silicone biomaterial using the same technique we observed optimal placement of the material on endoanal ultrasonography at 6-weeks.

In this study, we were not able to show that perianal injection of bulking agents increases resting or squeeze pressures [6,7]. The temporary improvement in symptoms combined with the endosonographic follow up may suggest that the materials dissipate over a short period of time.

No bulking agent studies have been randomized in faecal incontinence. A previous randomized control trial in urinary incontinence comparing autologous fat and saline (placebo) injections similar improvements were observed in both groups [14]. This suggests that an intervention, rather than the injection material itself, may contribute to a subjective improvement. Further evidence for this may be the continued improvement in quality of life in this study in the absence of ongoing objective improvement. The patients' comments at telephone review also suggest that medical attention and care led to a subjective improvement.

Selection of patients may be a key factor in success of this treatment. Our patients all had moderate to severe incontinence, and this treatment may have limitations in such group. Previous studies have shown better results for those patients with a lesser degree of incontinence [6,7]. A recent trial of PTQ™ implants suggest that this treatment might work better for patients with gutter deformity rather than faecal soiling with intact degenerative sphincters [15]. We have recently followed up a patient who underwent PTQ™ injection 8 years ago and on rectal examination we could palpate three large implants at the original injection sites. However, the patient's symptoms were worse than before treatment.

The treatment of patients with passive faecal incontinence remains challenging. There may be no ideal bulking agent available at this time.

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