



Clinical Presentation

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Overview of Fecal Incontinence (FI)

- The frequency of FI ranges from 7 to 22% among women.
- The etiology of FI is often multifactorial.
- Loss of control over bowel movements has a major impact on social interactions and is associated with shame, embarrassment and social phobia leading to a significant deterioration in quality of life.
- Symptoms are often hidden by patients resulting in low rates of self-reporting and therapy-seeking behavior.

Overview of Fecal Incontinence

- The most common etiologies for FI are obstetrical trauma leading to anal sphincter disruption and dysfunction of the puborectalis muscle resulting in a loss of the obtuse anorectal angle.
- Non-surgical therapies for FI include the use of anti-diarrhea drugs, antispasmodic drugs, an increase in fiber intake and biofeedback training.
- Surgical intervention should only be considered for selected patients who have failed conservative measures.
- Anal sphincter repair may result in up to a 50% to 80% symptom improvement, although benefit gradually decreases over years and incontinence may recur.

TRANSFORM Study

- Study - multi-center, single arm, open label, two stage adaptive study
- Purpose - to evaluate the safety and effectiveness of the TOPAS System for women with FI who have failed at least two other conservative therapies (dietary modifications, pharmacological intervention and pelvic floor muscle training)
- Primary effectiveness objective:
 - More than 50% of the study subjects would achieve a $\geq 50\%$ reduction in the number of FI episodes in a 14 day bowel diary at 12 months compared to baseline
 - Referred to as the Responder50 Rate

TRANSFORM Study

Secondary endpoints:

- Long term effectiveness at 24, 36, 48, and 60 months
- Reduction in incontinent days
- Reduction in urge FI episodes
- Reduction in FI symptom severity as measured by the Wexner symptom severity score

Wexner Symptom Severity Score

- Wexner score - most widely used instrument in assessing the efficacy of surgical therapies for FI
- Wexner score measures the degree and frequency of incontinence as well as its impact on daily life
- Correlates closely with subjective perception and clinical assessment
- Other FI device studies have used a Wexner score of at least 10 as an inclusion criteria

Selected Enrollment Criteria

- Inclusion:
 - Female patients >18 years
 - FI episodes ≥ 4 in 14 day period
 - Failed at least two modalities of conservative therapies such as dietary modification, pharmacologic Intervention, or pelvic floor muscle training
- Exclusion:
 - Pelvic prolapse ≥ 1 cm beyond the hymen (Stage III & IV)
 - Had a hysterectomy ,sphincteroplasty,or posterior surgery within six months
 - Pregnant or planning a future pregnancy

Subject Disposition

- 207 subjects enrolled
- 152 subjects implanted
- 55 subjects not implanted

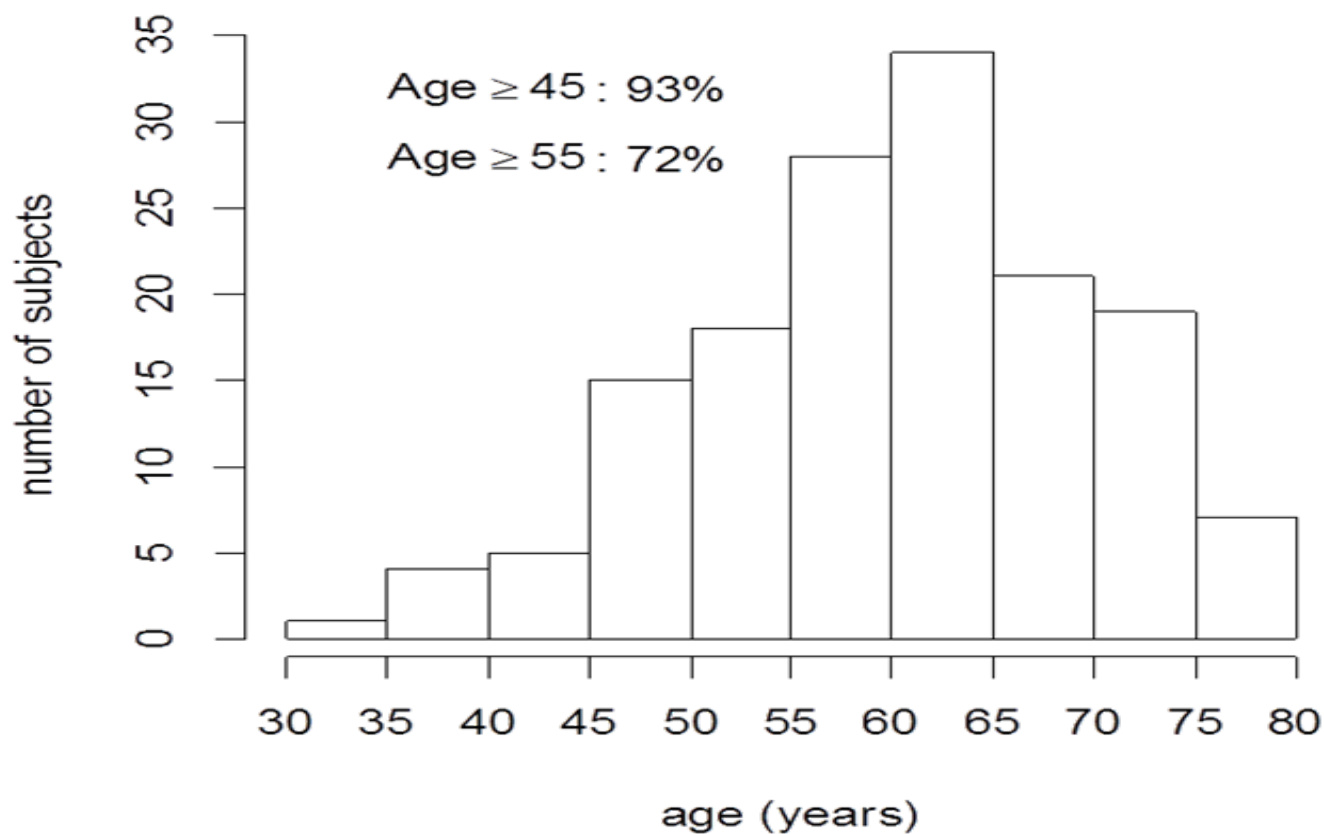
Study Completion

- 145 completed the 12 month visit
- 132 completed the 24 month visit
- 115 completed the 36 month visit

Study Population

- Mean age: 60 years, Caucasian: 90%
- Mean number of vaginal deliveries: 2.4
- Mean number of FI episodes/14 days: 22 (median of 18) at baseline
- Based on the subject's bowel diaries, the majority of FI episodes were small (mean of 12, median of 10)
- Mean number of incontinent days/14 days was 10 at baseline
- Mean Wexner score was 14 at baseline

Subject Age Histogram



Prior History

- 49% of subjects had previous hysterectomy and/or oophorectomy
- 46% of subjects had previous pelvic organ prolapse and/or urinary incontinence surgical repair
- 20% of subjects had a previous anal sphincter repair
- 52% of subjects had an EAS defect on endosonography
- 57% of subjects had obstetric trauma as the etiology for their FI etiology

Anorectal Manometry

- Mean max. resting pressure: 32 mmHg
 - Normal: 62-74 mmHg*
- Mean max. squeeze pressure: 60 mmHg
 - Normal: 150-178*
- Mean first sensation: 43 cc
 - Normal: 17-23 cc*
- Mean max. tolerated volume: 125 cc
 - Normal: 218-266 cc

*From: Rao SSC, et al. Am J Gastroenterol 1999;94:773–783.

FI Medication Use

- Baseline: 60 (40%) subjects
 - 20% opioid-receptor agents (e.g., loperamide, atropine/diphenoxylate)
 - 15% bulking agents
 - 4% anti-cholinergic agents (e.g., hyoscyamine, dicyclomine)
- 12 months
 - No difference between treatment responders or non-responders in FI medication use

Summary

- FI may have a substantial impact on a person's quality of life
- Sphincter disruption secondary to obstetric trauma comprises the largest proportion of FI causes in women
- Device was implanted in 152 female subjects with a minimum of 4 FI episodes over 14 days at baseline.
- At baseline, the mean number of FI episodes/14 days was 22 (median of 18).
- The primary effectiveness objective was to show that more than 50% of the study subjects would achieve at least a 50% reduction in the number of FI episodes at 12 months compared to baseline