NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia

Benign prostatic hyperplasia is a non-cancerous enlargement of the prostate. It can block or narrow the tube (urethra) that urine passes through to leave the body, causing urination problems. In this procedure, a tiny wire device is inserted into the urethra. It expands to create new permanent channels in the lining of the urethra. It stays in place for 5 to 7 days and is then removed. The aim is to increase the flow of urine.

Contents

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in April 2018.

Procedure name

- Prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia

Specialist societies

- British Association of Urological Surgeons (BAUS)
- Royal College of Surgeons
- British Prostate Group.

Description of the procedure

Indications and current treatment

Lower urinary tract symptoms caused by benign prostatic hyperplasia commonly affect men over 50. Stromal and epithelial cells increase in number, causing the prostate to increase in size. It often occurs in the periurethral region of the prostate, with large discrete nodules compressing the urethra. Symptoms include hesitancy during micturition, interrupted or decreased urine stream (volume and flow rate), nocturia, incomplete voiding and urinary retention.

Mild symptoms are usually managed conservatively. Drugs may also be used, such as alpha blockers and 5-alpha-reductase inhibitors. If other treatments have not worked, there are a range of surgical options that may be considered including transurethral resection of the prostate (TURP), transurethral vaporisation, holmium laser enucleation, insertion of prostatic urethral lift implants, prostatic artery embolisation or prostatectomy (see the NICE guideline

on lower urinary tract symptoms in men). Potential complications of some of these surgical procedures include bleeding, infection, urethral strictures, incontinence and sexual dysfunction.

What the procedure involves

Prostatic urethral temporary implant insertion aims to relieve symptoms of benign prostatic hyperplasia by creating new channels in the urethra that increase the flow of urine, without having the complications of an implant left in situ.

Using local anaesthesia or light sedation, a folded device made from nitinol is inserted into the prostatic urethra with a cystoscope under direct visualisation. The device opens in the urethra. Over the following days, the pressure applied by struts in the device creates areas of ischaemia in the prostatic urethra and bladder neck. This makes new longitudinal channels through which urine can flow. After 5 to 7 days lidocaine gel and a flexible silicone extraction catheter are inserted into the urethra and the device is removed. Insertion and removal of the device are both done as a day case procedure and take about 5 minutes.

Outcome measures

International Prostate Symptom Score (IPSS)

The IPSS is a validated questionnaire often used to assess symptoms of benign prostatic hyperplasia (BPH). It is also referred to as the American Urological Association BPH Symptom Score Index. It includes questions on 7 dimensions during the previous month (feeling of incomplete bladder emptying, frequency, intermittency, urgency, weak stream, straining and nocturia) scored from 1 to 5. Higher scores represent worse symptoms. An IPSS score of 0 to 7 indicates mild symptoms, 8 to 19 indicates moderate symptoms and 20 to 35 indicates severe symptoms. An additional question asks men how they feel about their BPH symptoms and the response yields a score for quality of life (ranging from 0 to 6, with 0 representing ‘delighted’ and 6 representing ‘terrible’).

Efficacy summary

International prostate symptom score (IPSS)

In a prospective case series of 32 patients, the median IPSS statistically significantly reduced from baseline (19; interquartile range [IQR] 14 to 23) to 1 year after the procedure (9 [IQR 7 to 13]) and improvement was sustained after 3 years (IQR 12 [6 to 24]) ($p<0.05$).[1,2]

Maximum urinary flow (Qmax)

In the prospective case series of 32 patients, the mean (± standard deviation [SD]) Qmax statistically significantly increased from baseline (7.6 ± 2.2) to 1 year after the procedure (11.9 ± 4.7) and improvement was sustained after 3 years (10.1) ($p<0.05$).[1,2]

Quality of life

In the prospective case series of 32 patients, the median IPSS quality of life index statistically significantly reduced from 3 (IQR 3 to 4) at baseline to 1 (IQR 1 to 2) at 1 year, and improvement was sustained 3 years after the procedure (2 [IQR 1 to 4]) ($p<0.05$).[1,2]

Patient satisfaction

In the prospective case series of 32 patients, 82% (26/32) were 'satisfied' or 'extremely satisfied' with the procedure, 15% (5/32) of patients were uncertain about their satisfaction and 1 patient was 'dissatisfied' 12 months after the procedure.[1,2]

BPH medications

In the prospective case series of 32 patients, all patients were able to stop medical therapy for lower urinary tract symptoms 3 months after the procedure, but 9% (3/32) of patients needed treatment again within 12 or 24 months of the procedure.[1,2]

Reoperation

In the prospective case series of 32 patients, no patients needed surgical therapy for BPH during the 3-year follow-up.[1,2]

Safety summary

Pain

In a case series of 32 patients, median visual analogue score 6 hours after the procedure was 2 (IQR 2 to 4) and median paracetamol use after surgery was one 1,000 mg vial per patient.[1,2]

Urinary retention

Urinary retention was reported in 1 patient on the day of the implantation in the case series of 32 patients. The bladder was voided using a small catheter, which was immediately removed, and the patient was able to urinate spontaneously.[1,2]

Urinary incontinence

Urinary incontinence caused by device displacement was reported in 1 patient in the case series of 32 patients. The device was removed 1 day after the procedure. After device removal, the patient reported no urine leakage.[1,2]

Prostatic abscess

Prostatic abscess was reported in 1 patient in the case series of 32 patients. This was complicated by sepsis, atrial fibrillation and uncontrolled glycaemia. The patient was readmitted 4 weeks after implantation and their symptoms treated with medications.[1,2]

Urinary tract infection

Urinary tract infection was reported in 1 patient in the case series of 32 patients. It was diagnosed 2 weeks after implantation and successfully treated with antibiotics.[1,2]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, specialist advisers listed the following anecdotal adverse events: device displacement. They considered that the following were theoretical adverse events: transient worsening of lower urinary tract symptoms, retrograde ejaculation and erectile dysfunction.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia. The following databases were searched, covering the period from their start to 27 April 2018: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with lower urinary tract symptoms caused by benign prostatic hyperplasia.
Intervention/test	Prostatic urethral temporary implant insertion.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 32 patients from 1 case series[1,2].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) are listed in the appendix.

Table 2 Summary of key efficacy and safety findings on prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia

Study 1 and 2 Porpiglia F (2015 and 2018)

Details

Study type	**Prospective case series**
Country	Italy (single centre)
Recruitment period	2010-13
Study population and number	n= **32** men with lower urinary tract symptoms secondary to benign prostatic hyperplasia
Age and sex	Mean 69 years
Patient selection criteria	Inclusion criteria: Age >50 years, IPSS of ≥10, Qmax of ≤12 mL/s, prostate volume assessed by transrectal ultrasound of <60 mL. Exclusion criteria: Previous prostate surgery, prostate cancer, urethral stricture, bladder stones, obstructing median lobe, a history of significant medical comorbidity, haemostatic disorder or suspected neurological conditions that could potentially affect voiding function.
Technique	The TIND device was used. The procedure was done under light intravenous sedation. In addition, as antibiotic prophylaxis, a single intravenous dose (500 mg) of levofloxacin was administered. The device was removed after 5 days. Paracetamol (1,000 mg) was administered intravenously after surgery per local protocol, and then if needed by the patients.
Follow-up	**3 years**
Conflict of interest/source of funding	The authors declared that they had no conflicts of interest.

Analysis

Follow-up issues:

- Patients had follow-up at 5 days (removal day), 3 and 6 weeks, and 3, 6, and 12, 24 and 36 months after the implantation.
- Data from 31 patients were available for the 36-month analysis because 1 patient died during follow-up.

Study design issues:

- The primary endpoint of the study was to evaluate the feasibility and safety of the procedure; the secondary endpoint was to evaluate the functional results of the procedure based on the IPSS and uroflowmetry.
- Follow-up visits included uroflowmetry, IPSS and IPSS QoL assessments. Sexual dysfunction (retrograde ejaculation) in sexually active patients was investigated at 12, 24 and 36 months after the surgery. Patient satisfaction with the surgical intervention was assessed by posing Question 32 of the EPIC questionnaire to the patients during the follow-up visits.
- During the follow-up visits, any need for medical therapy or surgical intervention due to recurrent/persistent LUTS, was recorded. Complications were recorded during the entire follow-up period. Early complications (<30 days) were classified according to the Clavien–Dindo classification. Treatment failure during follow-up was defined as the need for any surgical treatment for LUTS related to BPH.
- This was the first clinical study using the TIND device.

Study population issues:

- All patients were on alpha-blocker therapy at the time of the procedure, with 46% (15/32) regularly using 5 alpha-reductase inhibitors.
- Mean prostate volume (SD) before the procedure: 29.5 (±7.4) ml

Other issues: The device used for this study was the TIND device (the first generation of the iTIND device).

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 32

Procedure outcomes
• All the implantations were successful.
• Mean operative time (SD) from introduction of the implant until withdrawal of the delivery system: 5.8 (±2.5) min
• Median (IQR) postoperative stay: 1 (1–2) day
• From the 20th procedure, patients were discharged on the same day as the surgery.
• None of the patients was readmitted before device removal.
• All but 1 of the devices (96%) were removed 5 days after implantation.

Functional results and overall satisfaction of patients
<table>
<tr><th></th><th>Before surgery</th><th>3 weeks</th><th>6 weeks</th><th>3 months</th><th>6 months</th><th>12 months</th><th>p*</th><th>36 months (n=31)</th></tr>
<tr><td>Qmax, mL/s[c]</td><td>7.6 (2.2)</td><td>10.0 (4.4)</td><td>12.5 (4.1)</td><td>11.7 (4.7)</td><td>11.4 (4.2)</td><td>11.9 (4.7)</td><td><0.01</td><td>10.1</td></tr>
<tr><td>IPSS[b]</td><td>19 (14–23)</td><td>10 (8–11)</td><td>8 (7–10)</td><td>8 (6–10)</td><td>9 (7–12)</td><td>9 (7–13)</td><td>0.18</td><td>12 (6–24)</td></tr>
<tr><td>IPSS QoL index[b]</td><td>3 (3–4)</td><td>2 (1–2)</td><td>1 (1–2)</td><td>1 (1–2)</td><td>1 (1–2)</td><td>1 (1–2)</td><td>0.45</td><td>2 (1–4)</td></tr>
<tr><td>EPIC index question 32[a, b]</td><td>-</td><td>5 (4–5)</td><td>5 (4–5)</td><td>5 (4–5)</td><td>5 (4–5)</td><td>5 (4–5)</td><td>1</td><td>-</td></tr>
</table>
[a]'Overall, how satisfied are you with treatment you received for your prostate disease intervention?' (1: extremely dissatisfied; 2: dissatisfied; 3: uncertain; 4; satisfied; 5: extremely satisfied).
*p value for the differences in results among the different time points during the follow-up.
[b] median (IQR)
[c] mean (SD)
There were statistically significant differences in the IPSS, QoL score and Qmax when comparing pre- and postoperative results at every time point (p<0.05).

EPIC score
12-month follow-up: 26 patients (82%) were 'satisfied' or 'extremely satisfied' with the intervention, 5 (15%) patients were uncertain about their satisfaction and only 1 (3%) patient was 'dissatisfied'.

BPH treatment
• All patients were able to discontinue LUTS-related medical therapy 3 months after the implantation, but 3 patients (9%) needed treatment again within 12 or 24 months of the procedure.
• No patients needed surgical therapy for BPH during the 3-year follow-up.</td><td>No intraoperative complications recorded.

Pain after the procedure
- Median (IQR) VAS score at 6 h after the procedure: 2 (2–4)
- Median paracetamol use after surgery: one 1,000 mg vial per patient

Complications: 12.5% (4/32)
- Urinary retention on the day of the implantation: 3% (1/32)
The bladder was voided using a small catheter, which was immediately removed, and the patient was then able to urinate spontaneously.
- Urinary incontinence due to device displacement: 3% (1/32)
The device was removed 1 day after the procedure. After device removal, the patient reported no urine leakage.</td></tr>
</table>

IP overview: Prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia

	- **Prostatic abscess: 3%** (1/32) This was complicated by sepsis, atrial fibrillation and uncontrolled glycaemia. The patient was readmitted 4 weeks after implantation and treated with medications. - **Urinary tract infection: 3%** (1/32) It was diagnosed 2 weeks after implantation and was successfully treated with antibiotics. No late complications were reported. None of the 19 patients reporting preoperative sexual activity reported any ejaculatory dysfunction during the 3-year follow-up period. One patient died 26 months after implantation from causes that were unrelated to the surgical treatment.
Abbreviations used: BPH, benign prostatic hyperplasia; EPIC, expanded prostate cancer index composite; IPSS, international prostate symptom score; IQR, interquartile ranges; IV, intravenous; LUTS, lower urinary tract symptoms; Qmax, maximum urinary flow rate; QoL, quality-of-life: SD, standard deviation.	

Validity and generalisability of the studies

- The longest follow-up was 3 years.
- In studies 1 and 2, the first generation of the iTIND device was used.
- No data reporting on the new generation of the iTIND device is included in the overview.
- No randomised controlled trial is included in table 2.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia. NICE interventional procedures guidance in development**.**
- Transurethral water vapour ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia. NICE interventional procedures guidance 625 (2018)**.** Available from http://www.nice.org.uk/guidance/IPG625
- Prostate artery embolisation for lower urinary tract symptoms caused by benign prostatic hyperplasia. NICE interventional procedures guidance 611 (2018)**.** Available from http://www.nice.org.uk/guidance/IPG611
- Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia. NICE interventional

procedure guidance 475 (2014). Available from http://www.nice.org.uk/guidance/IPG475

- Laparoscopic prostatectomy for benign prostatic obstruction. NICE interventional procedures guidance 275 (2008) Available from https://www.nice.org.uk/guidance/ipg275
- Holmium laser prostatectomy. NICE interventional procedure guidance 17 (2003). Available from http://www.nice.org.uk/guidance/IPG17
- Transurethral electrovaporisation of the prostate. NICE interventional procedure guidance 14 (2003). Available from https://www.nice.org.uk/guidance/ipg14

Medical technologies guidance

- GreenLight XPS for treating benign prostatic hyperplasia. NICE medical technologies guidance 29 (2016). Available from https://www.nice.org.uk/guidance/mtg29
- UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia. NICE medical technologies guidance 26 (2015). Available from https://www.nice.org.uk/guidance/mtg26

NICE guidelines

- Lower urinary tract symptoms in men: management. NICE clinical guideline 97 (2010; last updated: June 2015). Available from http://www.nice.org.uk/guidance/CG97

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed

questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Three Specialist Advisor Questionnaires for prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Company engagement

A structured information request was sent to 1 company who manufactures a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

Ongoing studies:

- Pivotal Study to Assess the Safety and Effectiveness of the iTIND Device NCT02506465. MT03. 12-month follow-up. Estimated study completion date: December 2018. RCT. 172 patients. USA and Canada.

- Study to Assess the Tolerability, Safety and Efficacy of (iTIND) NCT03239951. MT04. 3-month follow-up. Male with acute urinary retention secondary to BPH. Estimated study completion date: November 2019; anticipated start date: January 2018. RCT. Estimated enrollment: 44 patients. UK study (5 sites).

- Study to Assess the Efficacy of the iTind in Subjects With Symptomatic BPH NCT03395522. MT06. 12-month follow-up. Estimated study completion date: August 2021. Single arm study. Estimated enrollment: 200 patients. Italy, Spain.

References

1. Porpiglia F, Fiori C, Bertolo R et al. (2015) Temporary implantable nitinol device (TIND): a novel, minimally invasive treatment for relief of lower urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (BPH): feasibility, safety and functional results at 1 year of follow-up. BJU international 116(2), 278-87
2. Porpiglia F, Fiori C, Bertolo R et al. (2018) 3-Year follow-up of temporary implantable nitinol device implantation for the treatment of benign prostatic obstruction. BJU international 122: 106-112

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane)	27/04/2018	Issue 4 of 12, April 2018
HTA database (Cochrane)	27/04/2018	Issue 4 of 4, October 2016
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane)	27/04/2018	Issue 3 of 12, March 2018
MEDLINE (Ovid)	27/04/2018	1946 to April 26, 2018
MEDLINE In-Process (Ovid)	27/04/2018	April 26, 2018
MEDLINE Epubs ahead of print (Ovid)	27/04/2018	April 26, 2018
EMBASE (Ovid)	27/04/2018	1974 to 2018 April 26
BLIC (British Library)	27/04/2018	n/a

Trial sources searched 16th January

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched 16th January

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 Prostatic Hyperplasia/
2 Lower Urinary Tract Symptoms/
3 Urinary Bladder Neck Obstruction/
4 (Prostat* adj2 (hyperplas* or urethra* or enlarg*)).tw.
5 ((bladder* or urinat* or urinar*) adj4 (neck* or obstruct* or block*)).ti.
6 ((bladder* or urinat* or urinar*) adj4 (neck* or obstruct* or block*)).ab. /freq=2
7 (LUTS or (low* adj2 urinar* adj2 tract* adj2 symptom*)).tw.
8 (BPO or BPH or BPH-relat* or BPE).tw.

9 or/1-8
10 minimally invasive surgical procedures/
11 ((minimall* or non) adj2 invasive adj2 (surg* or treatment* or technolog* or procedure* or technique*)).tw.
12 "prostheses and implants"/
13 ((temporary or removable) adj4 (implant* or nitinol* or device*)).tw.
14 or/10-13
15 9 and 14
16 (TIND or itind or Medi-tate).tw.
17 15 or 16
18 animals/ not humans/
19 17 not 18

Appendix

No additional papers were identified.