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Biodegradable braided poly(lactic-co-glycolic acid) urethral stent combined with dutasteride in the treatment of acute urinary retention due to benign prostatic enlargement: a pilot study

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Study Type – Therapy (case series)
Level of Evidence 4

OBJECTIVE

To evaluate, in a pilot study, the efficacy and safety of combining a braided poly(lactic-co-glycolic acid) (PLGA, a copolymer of L-lactide and glycolide) urethral stent and dutasteride in the treatment of acute urinary retention (AUR) due to benign prostatic enlargement (BPE).

PATIENTS AND METHODS

Ten men with AUR due to BPE were treated as outpatients. A biodegradable braided PLGA urethral stent was inserted into the prostatic urethra, using a specially designed insertion device under visual control. Dutasteride treatment was started and the patients were followed up for 3 months after insertion of the stents.

RESULTS

In all patients the stents were placed successfully with the new insertion device. All men were able to void after inserting the stent. At 1 month five patients voided freely with a low residual urine volume (<150 mL), two voided but had a high residual urine volume and a suprapubic catheter was placed, and three needed a suprapubic or an indwelling catheter before 1 month, due to AUR or comorbidities. At 3 months five patients were voiding with no problems.

CONCLUSIONS

We have developed a new and effective insertion device for biodegradable braided prostatic stents. The new braided-pattern stent overcomes the earlier problems of migration and sudden breakage into large particles associated with biodegradable spiral stents. However, the mechanical properties of the new stent need to be improved and tested in a longer follow-up. We consider that this new biodegradable braided-pattern urethral stent could provide a new option in the future treatment of AUR.

KEYWORDS

bioabsorbable, prostatic stents, 5α-reductase inhibitors, urinary retention

INTRODUCTION

Benign prostatic enlargement (BPE) is a frequent cause of LUTS, with a prevalence of 50% by the sixth decade of life [1]. Acute urinary retention (AUR) is the predominant complication of BPE and is the indication for surgery in 25–30% of patients undergoing TURP [2]. TURP resulting from AUR is associated with an increased risk of morbidity and death during and after surgery [3]. Dutasteride, as an inhibitor of both type 1 and 2 5α-reductase subtypes, decreases very effectively the concentration of dihydrotestosterone both in the serum and in the prostatic tissue, resulting in decreased prostate volume, increased maximum urinary flow rate (Q_{max}), improvement in symptoms, and decreased risk of AUR and need for surgical intervention [1]. Although many minimally invasive treatment options for BPE have become everyday clinical practice, including transurethral microwave therapy or photoselective vaporization of the prostate, the problem of AUR remains.

The treatment of urinary obstruction with temporary stenting has been a challenge for urologists. A second-generation temporary stent (ProstaCoil, originally Instent, Inc. Eden Prairie, MN, USA) has been used with good results in releasing obstruction due to BPE [4], as well as during hormonal therapy given for prostate cancer [5].

Biodegradable urological stents have long been the interest of our research group in Finland. We previously developed a spiral configuration biodegradable prostatic stent [6]. Due to the problems of their tendency to migrate from the correct location, and the sudden breakdown of the stent structure, they have not gained extensive use in clinical urological practice [7]. To overcome these problems we have now changed the configuration pattern of the stents and developed the tubular-mesh urethral stent. These novel stents have already been

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FIG. 1. The biodegradable braided-pattern PLGA-80/20 stent.

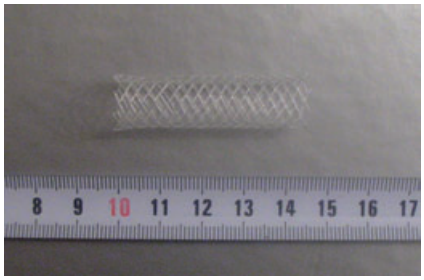


FIG. 2. The specially designed stent insertion device with 25° cystoscope.

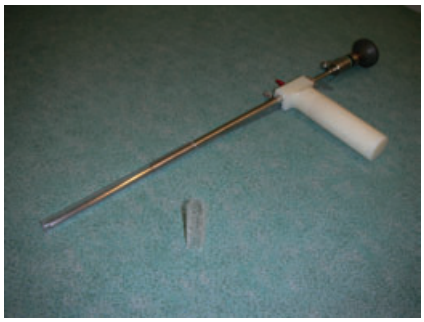
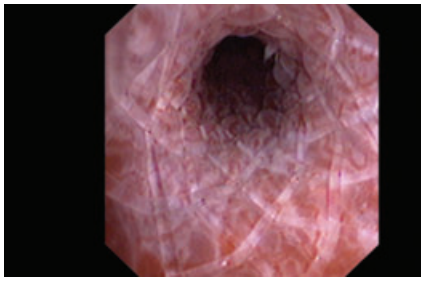


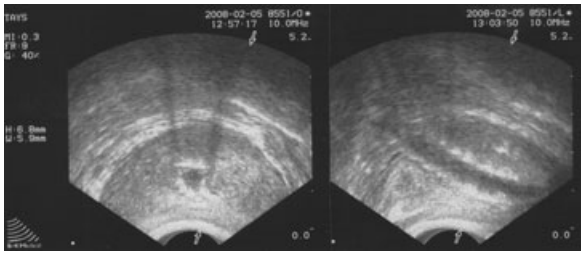
FIG. 3. The braided-pattern PLGA stent released in the prostatic urethra.



confirmed as safe and effective in animal studies [8,9].

The aim of the present study was to evaluate clinically the efficacy and safety of the new biodegradable braided poly(lactic-co-glycolic acid) (PLGA) prostatic stent combined with dutasteride in the treatment of AUR. In this approach, the stent is intended to keep the obstructed prostatic lumen open until dutasteride reduces the prostatic volume and thus alleviates BOO. We also tested a new insertion device developed for the braided-pattern urethral stents.

FIG. 4. A TRUS image of the PLGA stent in the prostate.



PATIENTS AND METHODS

The study included 10 men (mean age 75 years, range 62–85) with AUR who were referred to the Department of Urology, Tampere University Hospital, for surgery. The mean (range) prostatic volume was 59.6 (35.4–114) mL. Patients were excluded if they had a small prostate (<30 mL), bladder or prostate cancer, a neurogenic bladder or severe renal insufficiency. The study was conducted in an outpatient setting and all patients were discharged on the same day as surgery.

The biodegradable braided PLGA stents were designed and manufactured at the Institute of Biomaterials, Tampere University of Technology, Finland. The PLGA had an initial monomer ratio of 80/20; the medical grade, low monomer content polymer for melt-spinning was obtained from Purac Biochem b.v. (Gorinchem, the Netherlands). The stent monofilament was melt-spun using a single-screw extruder (Extrudex, Mühlacker, Germany), after which the internal orientation of the filament fibrils was achieved by drawing in a three-step process, obtaining a final monofilament diameter of 0.4 mm. The stents were manufactured by braiding 16 melt-spun PLGA 80/20 monofilaments on a metallic mandrel (diameter 12 mm) in a 1-over-1 pattern using a 32-carrier braiding machine (Pick Master, Germany) (Fig. 1). The structure was stabilized by thermal treatment and the stents were cut from the braid to a length of 45 mm. Finally the stents were sterilized by a commercial service-provider using γ-irradiation at 25 kGy and at <42 °C.

The stent-insertion device consisted of a specially designed delivery tube that was combined with 25° cystoscope optics (Fig. 2). Xylocaine 2% gel (AstraZeneca plc, UK) was used to anaesthetise the urethra in the same way as done routinely before cystoscopy.

The stents were delivered into the prostatic urethra under visual control (Fig. 3), and the location was always verified using TRUS (Fig. 4). After the stent insertion procedure the patients were followed as outpatients until spontaneous voiding was verified. Dutasteride (Avodart®, GlaxoSmithKline, UK) 0.5 mg daily was started on the same day and was maintained throughout the follow-up. The patients were assessed at 1 and 3 months after inserting the stent, with a measurement of the postvoid residual urine volume (PVR), TRUS and cystoscopy, if needed.

RESULTS

The new stent-delivery device worked correctly, and after being released all the stents stayed firmly in place. However, if needed, it was possible to slightly correct the position of the stent by pushing it with the tip of the cystoscope or by pulling it with grasping forceps. TRUS was used to ensure that the lumen of the stent had expanded to a sufficient diameter to allow voiding.

After stent placement, all the patients started to void spontaneously on the same day and their bladders emptied fully. At 1 month after placing the stents, five patients were able to void freely with no PVR or of <150 mL. The stent was still located correctly in the prostatic urethra when assessed by TRUS. Two patients were voiding spontaneously but still had a significant PVR; on TRUS the structure of these stents was apparently in place but on cystoscopy the stent lumen was found be compressed. These two patients had a suprapubic catheter placed. Three patients in pilot study group needed a suprapubic or indwelling catheter placed before the 1-month follow-up, one for recurrent AUR 5 days after stenting and two due to comorbities needing a measurement of daily diuresis.

At 3 months five patients were still voiding with no problems, and on TRUS the stent was seen to have started to degrade. These patients reported no local discomfort from the stent during the follow-up. The two patients with a high PVR at the first follow-up were still unable to void properly and had a TURP. None of the patients had any migration of the stent or incontinence due to the stent.

DISCUSSION

This new biodegradable braided PLGA stent could be inserted successfully in all 10 patients with AUR using the new insertion device, and patients were able to void immediately after the procedure. However, the mechanical strength of the stent was insufficient, especially in patients with the large prostates.

Although it has been shown that dutasteride reduces the incidence of AUR [10], alone it has no role in treating AUR because of its slow effect on the size of the prostate and the BOO caused by BPE. However, the Q_{max} starts to improve significantly after 1 month [11]. The biodegradation time of our new PLGA braided prostatic stents is 2–3 months, and thus the idea of combining the biodegradable stent in the prostatic urethra with dutasteride treatment is realistic. We hypothesized that the stent would keep the prostatic lumen open long enough to allow dutasteride to reduce the prostatic volume, resulting in a reduction of BOO. The degradation time of the braided PLGA stent is shorter than our previous spiral self-reinforced poly L-lactic acid stents [6], aiming to cause less tissue reaction, and the stent material is completely degraded by the third month; the total degradation time of these stents was 1 year.

The first problem faced during the development programme before the pilot study was inserting the stent. We devised a special insertion device that uses ordinary 25° cystoscope optics to make the insertion possible under visual control. The insertion device was engineered to be as simple as possible to use. We have now managed to release the stents exactly in the prostatic urethra, and due to its braided pattern it stays firmly in place after being released from the device. In the present study there was no migration or displacement of the stent. In case of slight mis-positioning during insertion, correcting the position was relatively easy by pushing or pulling the stent.

Although five patients were voiding with no problems throughout the study we remain dissatisfied with the present results. We performed both TRUS and video-cystoscopy in all patients who had a high PVR or who had needed additional means of bladder catheterization. By using the braided PLGA stent we overcame the previous problem of stent migration. More importantly, the stent structure degraded smoothly and no large broken particles were seen to obstruct the urethral lumen. The negative finding was that in two patients who had problematic voiding, the stent structure had collapsed. The major reason for this is probably insufficient radial compressive stiffness of the stents. We also noted that the stent structure tended to collapse at the distal end, where it was handled using compression to place it into the insertion device. We are planning to correct the insertion technique to overcome this possible factor of stent collapse. Another explanation could be prostate size; in the present study we used stents of the same length and these did not work sufficiently well in patients with large prostates.

The stents could be improved by adding radial compression stiffness and by using stents of different sizes and lengths according to prostatic volume. The work to further improve the mechanical properties of the stents is ongoing and a larger study is planned by our group. We also speculate that biodegradable stents with a relatively short degradation time could be useful not only for treating AUR but also as an alternative to catheterization after transurethral microwave therapy or brachytherapy in patients with a low Q_{max} before surgery.

In conclusion, we developed a new and effective insertion device for the biodegradable braided prostatic stents; this novel braided-pattern stent overcomes the earlier problem of stent migration and rapid breakdown associated with spiral stents. However, the mechanical properties of the new stent need to be improved and tested in a longer follow-up. We think that the new braided-pattern biodegradable urethral stent could provide an alternative in the treatment of AUR in elderly patients unsuitable for surgical treatment, as well as in combination with treatments which induce prostatic oedema and so cause temporary BOO.

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CONFLICT OF INTEREST

None declared.

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Abbreviations: **PLGA**, poly(lactic-coglycolic acid); **BPE**, benign prostatic enlargement; **AUR**, acute urinary retention; **PVR**, postvoid residual urine volume; $\mathbf{Q}_{max}$, maximum urinary flow rate.