The Journal of Laryngology & Otology (2006), ***120***, *32–37.*

doi:10.1017/S0022215105006456
Printed in the United Kingdom

Main Article

Nitinol stents in the treatment of benign proximal tracheal stenosis or tracheomalacia

A Y Isa, C Macandie, B W Irvine

Abstract

Nitinol stents have been used in the treatment of benign tracheal stenosis. A retrospective review of five patients treated at Stobhill Hospital over the last six and a half years is presented. Age at presentation ranged from 17 to 76 years. The minimum follow-up period was 23 months and the maximum was 78 months. All our patients were successfully decannulated, with none requiring recannulation. Four patients developed granulation tissue related to the stent at intervals ranging from three weeks to 41 months post stenting. Topical mitomycin C application has been useful after resection of granulations using the carbon dioxide (CO_2) laser. Stent migration occurred in one patient three weeks after insertion. Nitinol stents are easy to insert and effective in the treatment of tracheal stenosis, but can have associated morbidity. Their use should be considered carefully, as insertion should be regarded as permanent. Publications reporting experience and outcome with the use of Nitinol stents in the trachea are reviewed.

Key words: Nitinol; Stents; Tracheal Stenosis; Tracheomalacia; Mitomycin C

Introduction

Nitinol stents, composed of a nickel–titanium alloy, have been used successfully in the treatment of benign tracheal stenosis. Nitinol's inertness, superelasticity, fatigue resistance and shape memory effect, in addition to its physiological response profile to imposed stress, which closely matches structures of the human body, has been thought to account for its excellent biocompatibility with human tissue,[1] thus avoiding the complications that have plagued other metal stents. Previous authors have reported minimal complications with its use in benign tracheobronchial stenosis.[1–5] Here we present the results of the use of these stents in five patients with benign causes of proximal tracheal stenosis.

Material and methods

Stents and insertion

Nitinol stents are cylindrical mesh stents made of a nickel and titanium alloy. They are compressed on to a plastic rod introducer and are released either proximally or distally by pulling a thread once the stent is in position. In our practice we use the distal releasing stents.

The length of stenosis was assessed by pre-operative CT (computed tomography) or MRI (magnetic resonance imaging) if available, and also endoscopically under general anaesthesia. The stent used extended 1 cm above and below the stenosis where possible.

Stent insertion was performed under general anaesthesia using jet ventilation of the patient. The area of stenosis is visualized directly via a laryngoscope. The stenotic lesion is first treated with CO_2 laser prior to insertion of the stent under direct vision. Once in position the stent is released, and can be repositioned for up to a minute after release to optimize positioning.

Mitomycin C

For the treatment of granulation tissue, pledgets are soaked in a 0.4 mg/ml concentration of mitomycin C for three to four minutes prior to application to CO_2-lasered surfaces. The area is then irrigated with 50 ml normal saline.

Collation of results

This was a retrospective review of the clinical notes of all patients having undergone Nitinol stent insertion at Stobhill Hospital over the last six and a half years. In addition, all our patients were asked to fill in the Glasgow Benefit Inventory (GBI) questionnaire as a measure of outcome. This is a post-interventional questionnaire measuring change in general health status as a result of a surgical

From the Department of Otolaryngology, Head and Neck Surgery, Stobhill Hospital, Glasgow, UK.
Accepted for publication: 28 June 2005.

TABLE I

SITE AND DEGREE OF LESION AND PREVIOUS TREATMENTS

Patient	Sex	Age	Site	Percent stenosis	Length of stenosis	Stent size	Previous treatment (no. of treatments)
1	M	17	Proximal tracheal stenosis	100%	2 cm	18 mm × 4 cm	CO_2 laser (4) CO_2 laser + Montgomery T tube (2) Laryngotracheoplasty (1)
2	F	19	Proximal tracheal stenosis	100%	2 cm	14 mm × 4 cm	None
3	M	76	Proximal tracheal stenosis	70%	4 cm	16 mm × 6 cm	CO_2 laser (3)
4	F	75	Subglottic tracheomalacia	70%	3 cm	14 mm × 4 cm 14 mm × 4 cm	CO_2 laser (1)
5	M	60	Proximal tracheal stenosis	100%	2.5 cm	16 mm × 4 cm	None

intervention. There are 18 questions and the answers are on a five-point Likert scale, from worst change to best change. The GBI is scored into a total score plus three subscales: general, social support and physical health. Each of these scores ranges from +100 to −100, with 0 meaning no benefit from the intervention. This is a validated questionnaire which was used to evaluate benefit from five different ORL procedures retrospectively (middle-ear surgery to improve hearing, provision of a cochlear implant, middle-ear surgery to eradicate ear activity, rhinoplasty and tonsillectomy) in the original paper.[6]

Patients

Five patients underwent Nitinol stent insertion at our institution over a period of six and a half years. All were secondary to prolonged intubations and all patients had had tracheostomies. Four had been referred from other institutions. There were three males and two females. Age at presentation ranged from 17 to 76 years. The degree of stenosis ranged from 70 per cent (two patients) to 100 per cent (three patients). Four patients had proximal tracheal stenosis and one subglottic tracheomalacia. Three patients had had failed previous treatments. Patient details are shown in Table I.

Results

All our patients were successfully decannulated and have good voice quality. One patient died 23 months post treatment from unrelated causes.

The complications encountered with Nitinol stenting were granulation tissue formation and stent migration. Four patients suffered from varying amounts of granulation tissue formation. The onset of this varied from three weeks to 41 months post stenting. Granulation tissue was found to form through the stent and at its proximal and distal aspects, in two, one and three patients, respectively. These were treated with a combination of CO_2 lasering with or without oral antibiotics and steroids, or CO_2 lasering with topical mitomycin C application.

Of the four patients suffering from granulation tissue formation, it was most troublesome in patient 2 (Figure 1). She was readmitted with stridor three weeks post stent insertion and found to have granulation tissue at the distal end of her stent, which was obstructing her airway by 80 per cent. This was removed by CO_2 laser but rapidly reformed, requiring further endoscopic laser removal. Adjuvant antibiotics and oral steroids were ineffective. In the nine months after stent insertion the patient underwent 13 endoscopic procedures for removal of tracheal granulations. At this point, topical mitomycin C application was started after the CO_2 lasering. This resulted in a marked reduction in granulation tissue formation. In the following nine months she only underwent four endoscopic procedures and has since healed well, requiring no further intervention in the last 31 months. The other three patients all responded to topical mitomycin C following CO_2 lasering.

Patient 4's stent was found to have migrated distally three weeks after insertion. She had a second stent inserted proximally with some distal overlap with the first stent (Figure 2), and remained symptom free up to her death from unrelated causes.

On the GBI questionnaire all patients except number 3 reported an improvement following Nitinol stent insertion. Surprisingly, however, he required very little intervention after stent insertion. Although he had granulation tissue formation following insertion, that has settled and his trachea is now well healed, with no granulation tissue. His GBI score was negative in all subscales except social support score. His continued dyspnoea is due to longstanding chronic obstructive airways disease, which pre-dates his intensive care admission. These results are summarized in Table II.

Discussion

The treatment of subglottic and tracheal stenosis following prolonged intubation and tracheostomy remains challenging. The incidence of benign tracheal stenosis is reported in 31–65 per cent of patients following tracheostomy and in 19 per cent following endotracheal intubation.[7,8] Various methods of dealing with this include repeated endotracheal dilatation, laser resection of stenotic lesions, and surgical excision of the stenosis with primary anastomosis or laryngotracheoplasty with interpositional grafts. Stenting was widely used in the past for malignant stenotic lesions of the trachea, and more recently in benign strictures. Stents can be divided into two types, metal and non-metal. Non-metallic stents are most often composed of silicon. Various designs are available and have been used. The advantage of silicon stents lies

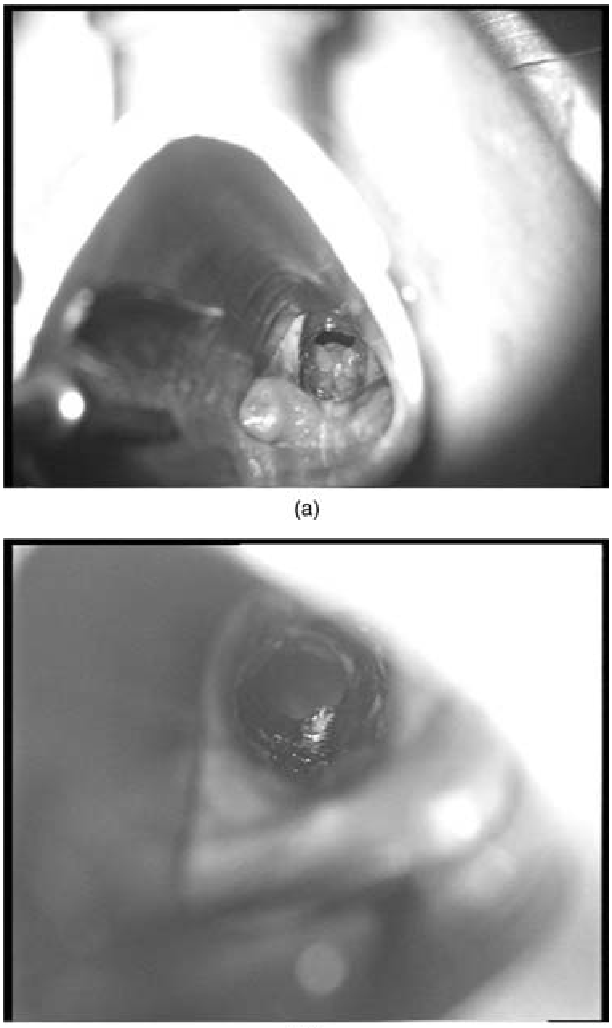

FIG. 1

(a) Patient 2 three months after Nitinol stent insertion and before CO_2 lasering. (b) Patient 2 three months after Nitinol stent insertion and after CO_2 lasering.

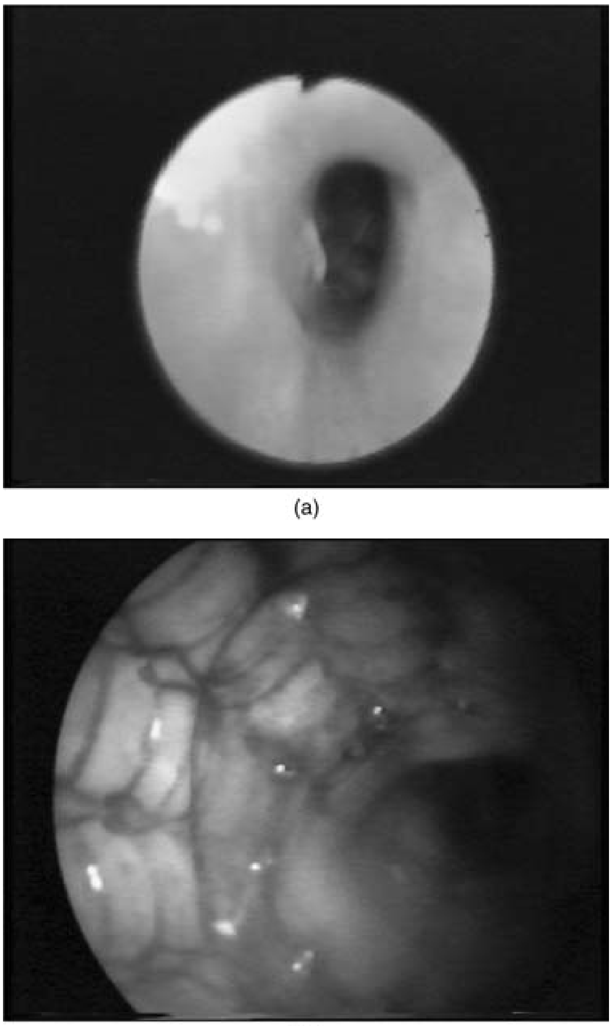

FIG. 2

(a) Patient 4: distal stent migration tracheomalacia is seen proximal to the stent. (b) Patient 4 restented with the two stents overlapping.

in their ease of removal, hence their availability as a temporary measure. Unfortunately, silicon stents are rigid and disrupt ciliary clearance of airway secretions, leading to infection or bacterial colonization of mucus and retention of secretions. Granulation tissue formation has also been problematic. Also, as the stents are rigid and do not integrate with the airway mucosa, they have been prone to migration.[9]

Metal stents cause less disruption to ciliary clearance of airway secretions and integrate into the mucosa. They are therefore less likely to migrate.

TABLE II

STENT COMPLICATIONS AND OUTCOME

	Complications	Treatments post stenting (no. of treatments)	GBI TS	GBI GSS	GBI SSS	GBI PHS	Follow up (months)
1	Recurrent granulations	CO_2 laser + Top Mit C (3)	47.22	50	33.33	−50	60
2	Recurrent granulations	CO_2 laser +/− oral antibiotics and steroids (13) CO_2 laser + Top Mit C (4)	50	66.7	0	33.33	32
3	Granulation tissue	CO_2 laser (2) CO_2 laser + Top Mit C (1)	−8.33	−16.67	0	−33.33	26
4	Stent migration 3 weeks post insertion	Second stent inserted with overlap (1)	25	37.5	0	0	14
5	Granulation tissue	CO_2 laser + Top Mit C	91.67	95.83	100	66.67	6

Top Mit C = topical mitomycin C application; GBI = Glasgow Benefit Inventory; TS = total score; GSS = general subscale score; SSS = social support score; PHS = physical health score

However, complications reported with metal stents include erosion into adjacent structures, ingrowth of tumour through the mesh, and granulation tissue formation. They are also very difficult to remove once integrated, and hence should be thought of as permanent. Because of this, Colreavy *et al.*[1] advised caution with the use of Nitinol stents in benign tracheal stenosis.

Previous published series of treatment of benign stenosis with Nitinol stents have reported minimal complications. Ducic *et al.*[2] experienced no complications in six patients with benign stenosis, with a minimum follow-up period of six months. Of the two patients with benign stenosis reported by Colreavy *et al.*, only one suffered complications. This patient developed a rash six weeks post insertion, which the authors attributed to Nitinol, and four months later her stent was found to have migrated. It was removed piecemeal, with great difficulty.[1] Sasano *et al.*[5] treated three patients with benign stenosis. One died from unrelated causes, but the other two had no complications.

Interestingly, the only series reporting granulation tissue formation was in children. Nicolai *et al.*[4] used a combination of Titan and Nitinol stents in seven patients with central airway obstruction, six of whom suffered from benign stenosis. All the patients were observed to have some granulation at the ends of the stents; however, pronounced granulation formation occurred in two patients with benign stenosis after Nitinol stent insertion. Endoscopic granulation removal was required in one. One of them died from severe peripheral bronchial hypoplasia and obstruction seven weeks following stent insertion. The other died one year after stent insertion from a ventilator-associated complication. At postmortem his airways were patent and his stents were in a satisfactory position.[4] Prasad *et al.*[3] inserted Nitinol stents in two children with previously failed laryngotracheoplasty for benign tracheal stenosis as a temporary measure while awaiting tracheal growth for definitive tracheal resection. They reported stent migration in one patient. A summary of these publications is given in Table III.

We report granulation tissue formation in four of our five patients, with the time of onset ranging from three weeks to 41 months post stent insertion, and are the first to do so in adults. The site most commonly affected by granulations was the distal aspect of the stent, although granulation also grew at the proximal aspect and through the stents. The application of topical mitomycin C to the granulations after CO_2 treatment has been useful.

Mitomycin C, an antineoplastic antibiotic most commonly used as a chemotherapeutic agent, has been shown to inhibit fibroblastic growth *in vitro*[10] and granulation formation *in vivo*.[11] Experimental topical use on antrostomies in rabbit maxillary sinuses has shown successful delay in closure. Topical mitomycin C was also shown to damage cilia on rabbit respiratory epithelium, although ciliary regeneration was seen two weeks post insult on electron microscopy.[12] In ophthalmology, mitomycin C has been successfully used to decrease scarring and improve patency rates in glaucoma surgery.[13]

Experience of topical mitomycin C in otolaryngology is limited. Ward *et al.*[14] reported on its successful use in five paediatric patients with severe recurrent granulations and scarring post laryngotracheal reconstruction when used as an adjunct to bronchoscopy and laser treatment. All patients were successfully decannulated. In a prospective non-controlled study of eight patients, Rahbar *et al.*[15] reported improvement in seven patients with subglottic or posterior glottic stenosis treated with topical mitomycin C following radial incisions with the CO_2 laser and dilation of the stenotic segment (one patient was lost to follow up). However, a randomized double-blind placebo-controlled trial of

TABLE III

SUMMARY OF RESULTS OF CASE SERIES OF NITINOL STENT INSERTION IN BENIGN TRACHEAL/SUBGLOTTIC/BRONCHIAL STENOSIS

Authors	No. of patients (site of stenosis)	Age in years (mean)	Follow-up period	Stent-related complications (*n*)
Ducic *et al.*[2]	6 Benign (subglottic/ tracheal)	27–55 (44.8)	Minimum of 6 months	None
Colreavy *et al.*[1]	2 Benign 4 Malignant (tracheobronchial/ subglottic)	24–82 (53.3)	Maximum of 18 months	Stent migration (1) Rash (1) Pneumothorax (note previous laser and chemoradiotherapy to malignant site) (1)
Nicolai *et al.*[4*]	6 Benign 1 Malignant (tracheobronchial)	0.25–9 (2.8)	7 weeks–6 years	Pneumomediastinum post balloon dilatation and Titan stent insertion (1) Suboptimal positioning (5) Pronounced granulations (2)
Prasad *et al.*[3]	2 Benign (tracheal/ subglottic)	5–15 (10)	25–26 months	Suboptimal stent diameter (1) Stent migration (1)
Sasano *et al.*[5]	3 Benign (proximal trachea)	56–82 (68)	401–746 days	None

*Combination of Titan and Nitinol stents used.

topical mitomycin C after laryngotracheal reconstruction failed to show benefit with its use. In this study a paediatric population who had grades 3 and 4 Myer–Cotton stenosis were treated with either laryngotracheoplasty or cricotracheal resection and post-operative stenting. On removal of the stent the patients were randomized to either topical mitomycin C or normal saline. Results at one year revealed no significant difference in the two arms and the study was terminated.[16] It is interesting to note that previous publications reporting success with topical mitomycin C involved laser incision or excision prior to topical application of the drug.

In our experience, mitomycin C has been useful in the treatment in post-stent granulation formation. Doses used in ophthalmology varied from 0.1 to 0.5 mg/ml, with various times of application (1–5 min).[13] Our decision to use 0.4 mg/ml over 3–4 min was based on the use of mitomycin C in the adult trachea by Rahbar *et al.*[15] Three of the four patients requiring CO_2 laser treatment with adjunctive mitomycin C application remain symptom free. Despite the use of mitomycin C, one patient has had a further episode of stridor.

The only patient to suffer from stent migration was severely kyphoscoliotic (Figure 3), and we feel that this was a major contributory factor. Interestingly, it was not necessary to remove the first stent, as by overlapping and telescoping the second stent was inserted proximal to the first.

Overall, we found Nitinol stents easy to insert. All our patients were successfully decannulated, with excellent voice quality and without any requiring recannulation. We feel that Nitinol stents should be considered in difficult cases where previous surgical interventions have failed, or where open surgery is contraindicated. This should be done with the awareness of the possible complication of granulation tissue formation. However, CO_2 laser combined with topical mitomycin C application has been effective. Once inserted, stents should be regarded as permanent, as mucosal integration makes them very difficult to remove.

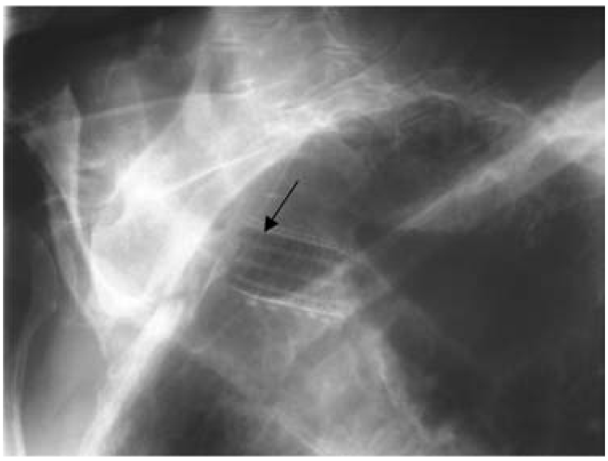

FIG. 3

Lateral cervical X-ray of patient 4 showing severe kyphosis and the displaced stent (arrowed).

- **Tracheal stenosis occurs in 31–65 percent of patients post tracheostomy and in 19 percent post endotracheal intubation**
- **Treatments include repeated tracheal dilatation, laser resection of stenosis, surgical excision with primary anastomosis, and laryngotracheoplasty with interpositional grafts**
- **Nitinol stents are successful in treatment but can be associated with granulation formation and stent migration**
- **Mitomycin C is useful in the treatment of post tracheal stent granulations**

References

1 Colreavy MP, Keogh I, Hone S, Lacy PD, Gaffney RJ, Walsh MA. Nitinol stents: their value in tracheobronchial obstruction. *Clin Otolaryngol Allied Sci* 2000;**25**:233–9

2 Ducic Y, Khalafi RS. Use of endoscopically placed expandable nitinol tracheal stents in the treatment of tracheal stenosis. *Laryngoscope* 1999;**109**:1130–3

3 Prasad M, Bent JP, Ward RF, April MM. Endoscopically placed nitinol stents for pediatric tracheal obstruction. *Int J Pediatr Otorhinolaryngol* 2002;**66**:155–60

4 Nicolai T, Huber RM, Reiter K, Merkenschlager A, Hautmann H, Mantel K. Metal airway stent implantation in children: follow-up of seven children. *Pediatr Pulmonol* 2001;**31**:289–96

5 Sasano S, Onuki T, Adachi T, Oyama K, Ikeda T, Kanzaki M, *et al.* Nitinol stent for the treatment of tracheobronchial stenosis. *Jpn J Thorac Cardiovasc Surg* 2001;**49**:311–16

6 Robinson K, Gatehouse S, Browning GG. Measuring patient benefit from otorhinolaryngological surgery and therapy. *Ann Otol Rhinol Laryngol* 1996;**105**:415–22

7 Norwood S, Vallina VL, Short K, Saigusa M, Fernandez LG, McLarty JW. Incidence of tracheal stenosis and other late complications after percutaneous tracheostomy. *Ann Surg* 2000;**232**:233–41

8 Stauffer JL, Olson DE, Petty TL. Complications and consequences of endotracheal intubation and tracheotomy. A prospective study of 150 critically ill adult patients. *Am J Med* 1981;**70**:65–76

9 Vergnon JM, Costes F, Polio JC. Efficacy and tolerance of a new silicone stent for the treatment of benign tracheal stenosis: preliminary results. *Chest* 2000;**118**:422–6

10 Khaw PT, Doyle JW, Sherwood MB, Grierson I, Schultz G, McGorray S. Prolonged localized tissue effects from 5-minute exposures to fluorouracil and mitomycin C. *Arch Ophthalmol* 1993;**111**:263–7

11 Spector JE, Werkhaven JA, Spector NC, Huang S, Page RN, Baranowski B, *et al.* Preservation of function and histologic appearance in the injured glottis with topical mitomycin-C. *Laryngoscope* 1999;**109**:1125–9

12 Ingrams DR, Volk MS, Biesman BS, Pankratov MM, Shapshay SM. Sinus surgery: does mitomycin C reduce stenosis? *Laryngoscope* 1998;**108**:883–6

13 Wilkins M, Indar A, Wormald R. Intra-operative mitomycin C for glaucoma surgery. *Cochrane Database Syst Rev* 2001:CD002897

14 Ward RF, April MM. Mitomycin-C in the treatment of tracheal cicatrix after tracheal reconstruction. *Int J Pediatr Otorhinolaryngol* 1998;**44**:221–6
15 Rahbar R, Valdez TA, Shapshay SM. Preliminary results of intraoperative mitomycin-C in the treatment and prevention of glottic and subglottic stenosis. *J Voice* 2000;**14**:282–6
16 Hartnick CJ, Hartley BE, Lacy PD, Liu J, Bean JA, Willging JP, *et al.* Topical mitomycin application after laryngotracheal reconstruction: a randomized, double-blind, placebo-controlled trial. *Arch Otolaryngol Head Neck Surg* 2001;**127**:1260–4

Address for correspondence:
Mr BW Irvine,
Department of Otolaryngology, Head and Neck Surgery,
Stobhill Hospital,
133 Balornock Road,
Glasgow G21 3UW, UK.

Miss A Isa takes responsibility for the integrity of the content of the paper.
Competing interests: None declared

https://doi.org/10.1017/S0022215105006456 Published online by Cambridge University Press