

# Surgery for adult laryngeal papillomatosis ☆,☆☆,★



Adi Primov-Fever, MD<sup>a,b</sup>, Ory Madgar, MD<sup>a,b</sup>

From the <sup>a</sup>Department of Otolaryngology and Head and Neck Surgery, Sheba Medical Center, Tel Hashomer, Israel

<sup>b</sup>The Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

## KEYWORDS

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Recurrent laryngeal papillomatosis is a viral (human papillomavirus) disease that causes the growth of epithelial verrucous lesions. Patients with laryngeal papillomatosis undergo multiple surgeries due to the tendency of the lesions to reoccur and cause recurrent voice and breathing problems. The goal of the surgical treatment is to remove the lesions while protecting the delicate layered structure of the vocal folds in order to prevent scarring and permanent damage to the mucosa. This is a review of the currently performed operative procedures for treating recurrent adult laryngeal papillomatosis. They involve the use of cold instruments, lasers, and microdebriders. There is a trend towards preferential use of microdebriders and office-based laser procedures in compliant patients. There is no consensus on any surgical method of choice, and further investigations and long-term results of the ones in current use are warranted to provide more clear-cut guidelines for optimal management.

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## Introduction

Recurrent laryngeal papillomatosis (RLP) is a rare disease caused by human papillomavirus (HPV), primarily types 6 and 11. The larynx is the most common site of recurrent papillomatosis, although papillomas may present anywhere along the upper aerodigestive tract (Figure 1).<sup>1</sup> Derkay et al estimated an incidence rate of 1.8 per 100,000 for adult-onset recurrent papillomatosis.<sup>2,3</sup> The first presentation in adults is usually in the third and fourth decades of life.<sup>4,5</sup> A malignant transformation incidence of 2% has been observed in RLP patients.<sup>6,7</sup> HPV has been detected

not only in the lesions but also in otherwise normal adjacent epithelium. Moreover, the virus can remain dormant in the laryngeal epithelial cells with no visible papillomas.<sup>8,9</sup> The course of the disease is unpredictable, ranging from spontaneous remission to aggressive disease progression that requires multiple surgical procedures to maintain airway and voice function.<sup>10,11</sup>

Surgical resection is the current standard of care in the management of RLP.<sup>12,13</sup> The objectives of the surgery are to preserve adequate voice quality and airway patency. Complete eradication is not necessarily the goal since the virus is present in adjacent epithelial cells and tissues that do not macroscopically develop papillomas.<sup>13,14</sup> Subtotal and staged resection is required if the lesions involve the anterior and/or posterior commissure in order to limit scar formation or airway obstruction. Another goal of surgery is to prevent distal spread of papillomas to the lower respiratory tract.<sup>7,15</sup> Prior to the availability of advanced general anesthesia techniques, endolaryngeal procedures for RLP were performed indirectly (transorally) in awake patients.<sup>16</sup>

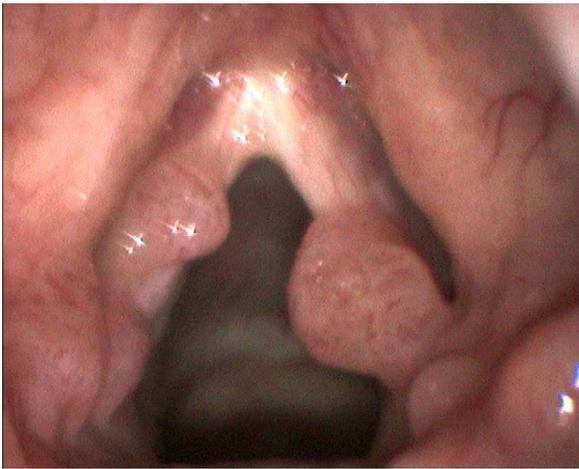
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**Address reprint requests and correspondence:** Adi Primov-Fever, MD, Department of Otolaryngology and Head & Neck Surgery, Sheba Medical Center, Tel Hashomer 52621, Israel.

E-mail address: [adi.primov-fever@sheba.health.gov.il](mailto:adi.primov-fever@sheba.health.gov.il)



**Figure 1** Recurrent laryngeal papillomatosis involving the true vocal cords.

Advances in general anesthesia enabled surgical management of RLP to the operating room where direct microlaryngoscopic procedures were performed. On the other hand, advancement in fiberoptics, channeled endoscopes, and laser technology made over the past decade, resulted in growing numbers of endolaryngeal surgeries performed as office-based procedures.<sup>16</sup>

This article reviews the surgical techniques currently available and in use for the treatment of RLP in the OR as well as office-based procedures.

## Techniques

### OR procedures

Microlaryngoscopic procedures have been a long-standing and effective therapy for RLP, but their use requires an operating suite and general anesthesia. The need for repeated procedures increases the cumulative risks associated with general anesthesia, as well as the post-operative recovery period which can have negative social and financial consequences for the patient.<sup>16</sup> A number of ventilation approaches are commonly employed, among them jet ventilation, apneic techniques, and spontaneous ventilation techniques. Surgeons and anesthesiologists also have personal preferences for various types of standard endotracheal tubes or laser safe endotracheal tubes.

OR procedures include the use of an operating microscope, as well as suspension laryngoscopy with an appropriately sized rigid laryngoscope for optimal exposure of the larynx and comfort for the surgeon. Safety precautions, such as moist patches and drapes and the limitation of inspired oxygen delivery to under 30%, are essential to reduce laser injuries. Safety procedures are also required to protect the staff whenever laser surgery is performed.<sup>17</sup> Surgical instruments have evolved from nonpowered (cold) to lasers and microdebriders that can be used separately or in combination, with excellent surgical outcomes.<sup>8</sup>

### Cold instruments

Resection of RLP evolved from an indirect mirror-guided procedure in the 19th century, into a direct laryngoscopic procedure in the OR under general anesthesia, in the 20th century.<sup>18</sup> The magnification of the microscope and the refined hand-held instruments, such as forceps and scissors, provided better surgical outcomes.<sup>12,18</sup> The introduction of the CO<sub>2</sub> laser enhanced the precision of microlaryngeal surgery by virtue of its hemostatic cutting properties and by providing a stable delivery system.<sup>12</sup> However, the combination of cold instruments with laser is still preferred in selected cases of laryngeal papillomatosis. The introduction of subepithelial dissection by injection of saline with epinephrine, combined with microflap elevation techniques for anterior commissure papillomas, encouraged surgeons to return to the use of cold instruments in selected cases of limited disease.<sup>12,17,18</sup>

### Laser surgery

Laser surgery offers several advantages as well as disadvantages in the removal of RLP. Lasers have better hemostatic properties and longer working distance than cold instruments, but the procedures require more personnel and more safety measures, and involve greater installation and costs.<sup>12</sup> CO<sub>2</sub> laser has been the primary type used for laryngeal pathologies since 1972. Since the CO<sub>2</sub> laser can be delivered through the operating microscope, it allows for hemostatic removal of small lesions precisely and efficiently. The use of CO<sub>2</sub> laser in microlaryngoscopic cases, however, carries the potential risk of scarring of the superficial lamina propria and webbing of the anterior commissure.<sup>16</sup> The use of the 585-nm pulsed dye laser (PDL) was first established in the setting of microlaryngeal surgery. It involved a 1-mm fiber being carried through a malleable aluminum cannula and introduced through the laryngoscope. Later on, the PDL was adapted for office-based procedures.<sup>19</sup>

Despite the drawbacks of associated safety concerns and complications, the CO<sub>2</sub> laser is still the most commonly used laser for vocal pathologies, including RLP, therefore surgeons are more familiar with its use, capabilities, and limitations.<sup>13,20</sup> During laser surgery, the entire operating team needs to be familiar with the potential complications and safety precautions in order to prevent heat-related injuries. It is important to avoid transmission of repeated laser energy to the same location because it can result in deep tissue injury. It is recommended to use the shortest pulse and lowest possible power.<sup>8,20</sup> The safety concerns and complications include proper tube insertion (to prevent endotracheal tube fire), tracheal injury, tracheoesophageal fistula formation, and airway tract burns. Technology has expanded the options of devices and calibrations in performing laser surgeries and as well as for choosing the appropriate laser for each procedure, which should be done on a case-to-case basis.<sup>20</sup>



**Figure 2** Removal of papillomas from the left true vocal cord with a microdebrider.

### Microdebriders

Microdebriders are widely used by otolaryngologists for the removal of tissue in the nasal cavity and sinuses, especially polyps. The microdebrider gained popularity in the treatment of RLP due to the potential risks associated with the use of lasers. Microdebriders have rapidly rotating blades and selective suctioning that enables the debridement of the affected tissue. When papillomas are simultaneously present in the larynx and trachea, the microdebrider is an efficient instrument for their removal, without repositioning the patient. The microdebrider is difficult to use in the mid-to-distal trachea of adults, however, because the blade is too short to reach beyond the upper trachea. Microdebriders can be used in combination with lasers or cold instruments. The surgeon first removes the bulky papillomatous lesion with the microdebrider (Figure 2), followed by lasers or cold instruments in order to provide both hemostasis and superior precision. The advantages of microdebriders over lasers include shorter operating time and the absence of thermal injury which results in reduced damage to the underlying tissue and greater preservation of normal epithelium.<sup>8,9</sup>

### Transoral robotic surgery

Tan Wan Sheng et al described successful transoral robotic surgery for the excision of laryngeal papillomas in a 36-year-old Chinese female with poor laryngeal exposure and impending airway.<sup>21</sup> Using a Flex robotic system, the authors claimed to have achieved a better surgical exposure than that achievable by suspension direct laryngoscopy. The papillomas were completely excised with grasping forceps and monopolar diathermia.<sup>21</sup>

### Office-based procedures

Office-based procedures for RLP satisfactorily address some of the limitations of operative microlaryngoscopy. Advances in technology over the last 10 years have made office-based laryngeal surgery feasible for a variety of

pathologies. Sophisticated fiberoptics with distal chip technology, improved laser mechanics, and flexible channeled endoscopes have endorsed the consideration of office-based surgery for RLP.<sup>19,22</sup>

The first case series that described the treatment of unsedated patients with RLP demonstrated that the 585-nm dye laser (ie, PDL) could be successfully used in an office-based setting.<sup>19,22</sup> The patients in that study were able to tolerate the procedure, and it was possible to offer them treatment for small lesions that would otherwise be delayed until hospital admission.<sup>19</sup> The reported improvement in patients' tolerance, and the potential for time and cost savings, made office-based management of RLP an appealing option.<sup>8,19</sup>

Patient selection, counseling, and joint patient-physician decision-making are essential for the success of office-based laryngeal surgery. Informed consent should be signed taking into consideration the patient's ability to cooperate with an awake procedure. Patients with a substantial gag reflex or who are anxious and cannot tolerate flexible laryngoscopy may not tolerate an unsedated laryngeal procedure.<sup>8,16</sup> In addition, anatomical issues and the extension of the disease must be addressed. Patients with an inadequate nasal passage, a high burden of papillomas, airway compromise, papillomas extending into the laryngeal ventricle and subglottis, as well as patients with coagulopathies and those on anticoagulant therapy, are not good candidates for office-based procedures.<sup>16</sup>

Other disadvantages of office-based procedure lies in the fact that it is difficult to operate on an awake patient with a flexible laryngoscope since the target tissue is mobile. There are also unavoidable tangential vectors for visualization and laser delivery that cannot be overcome since there is no availability for bimanual tissue retraction, as in direct laryngoscopy.<sup>23</sup> In addition, while office-based procedures were described as cost-saving in several studies, they are potentially less complete, whereupon there can be a compensatory increase in the frequency of procedures. Such need for more subsequent procedures may lead to an overall cost that ends up being roughly the same as for surgery in the OR.<sup>16,23</sup>

The key for a successful office-based procedure is laryngeal anesthesia. Appropriate anesthesia can be achieved by transoral application of topical anesthetic agents (eg, 4% lidocaine) to the mucosa of the base of the tongue, the supraglottis, and the glottis via a curved cannula. This can also be achieved by application of the anesthetic agents transnasally by means of the working channel port of the endoscope.<sup>19,24</sup> Prior to that application, the nasal cavity should be provided with local anesthesia and decongestants, and additional nebulized lidocaine can be administered as well, bearing in mind the maximum safe dose. A superior laryngeal nerve block can be performed if necessary.<sup>19,24,25</sup>

Photodynamic lasers offer disease-specific treatment for RLP. These lasers target the vascular system of the papilloma through a specific wavelength absorbed by oxyhemoglobin. The specific wavelength and the pulsed delivery

of the energy reduces the damage to the surrounding tissue.<sup>19</sup>

The PDL was first used in microlaryngoscopic surgery. The possibility for fiberoptic transmission of this laser enhanced its use in both the office and the OR. One disadvantage of the PDL is the difficulty to accurately quantify the amount of energy delivered, and the real-time tissue effect.<sup>19</sup> A shorter wavelength and longer pulsed (532 nm) potassium titanyl phosphate (KTP) laser was investigated and found to be acceptable for the management of RLP.<sup>26</sup> The increased pulsed length and the better absorption by oxyhemoglobin provides the KTP laser with better intravascular coagulation, decreased bleeding, and less damage to the surrounding epithelium.<sup>26</sup> Given its superiority to the PDL, the KTP laser has gained considerable popularity for the treatment of RLP in microlaryngeal and office-based procedures, becoming the preferred laser for office-based management of RLP.<sup>16,26</sup>

The invention of the flexible CO<sub>2</sub> laser delivery system has expanded its use to the office as well. The flexible system's better control over laser angulation was reported to potentially result in decreased thermal damage to the surrounding tissue.<sup>20</sup>

### Tracheostomy

Tracheostomy is sometimes unavoidable in the treatment of patients with RLP, especially when the diagnosis had been postponed and the patient presents with upper airway obstruction.<sup>10,17,27</sup> The need for tracheostomy is more prominent in children. Compared to nontracheostomised patients, there is a higher risk for tracheal spread of the papillomas following a tracheostomy. The risk factors include the presence of subglottal disease at the time of tracheostomy and prolonged cannulation. As a result, many authors recommend that tracheostomy should be avoided in RLP patients whenever possible, and that decannulation should be performed as soon the airway is considered to be stable, when it is unavoidable.<sup>10,13,15,17,27,28</sup>

### Discussion

RLP is rare disease frequently associated with substantial morbidity and occasional mortality. It is managed by surgical excision, both in the OR and in the office setting. The use of cold instruments has been the method of choice for years, and it is still employed in selected cases. Surgical removal by CO<sub>2</sub> laser remains the most important single modality, with an intraoperative complication rate of 0%-12.5%.<sup>29</sup> The majority of reported complications were minor, and they included mucosal tear, teeth injuries, and tracheal edema.<sup>29</sup> The reported incidence of delayed soft tissue complications that included scarring, stenosis, and web formation, particularly in the anterior glottis, was 0%-41%.<sup>29,30</sup> The total number of repeated surgeries, the location of the lesion, and the instrumentation used, were related to the soft tissue complications outcomes.<sup>29,30</sup> In

addition to the CO<sub>2</sub> laser, photoangiolytic lasers, such as the KTP, are useful for precise targeting of lesions.

The advent of the flexible laser delivery systems and topical anesthesia techniques established the office-based procedures as an alternative to OR procedures in selected cases. The value of this option is a matter of controversy: several authors have reported that office-based procedures reduce the cost by 5000-9000 USD per procedure, while others refute that claim and note that patients require 3 times more procedures than patients undergoing a OR procedures.<sup>24</sup> Office-based procedures performed under topical anesthesia require the patient's tolerance, but they minimize the risks associated with general anesthesia and shorten the postoperative recovery.

The CO<sub>2</sub> laser offers advantages over cold instrument surgery, however, the indications and use of CO<sub>2</sub> laser have been challenged in recent years due to the higher risk of respiratory burns scarring and stenosis.<sup>29</sup> This led to the growing use of microdebriders in the OR.

Tatar et al found no sex or age differences between patients who were treated in the office compared to patients treated in the OR. Adult patients with greater disease burden, younger age at diagnosis of RLP, and coexisting diabetes were more likely to be treated in the OR.<sup>31</sup>

### Alternatives to surgery and laser therapy

Although it is beyond the scope of this article to discuss the medical treatment for RLP, it is important to mention that pharmacological agents are administered when surgery is unsatisfactory to control the course of the disease.<sup>8</sup> Several medical protocols have been evaluated for the treatment of RLP, but the effectiveness of those treatments remains unclear. Systemic use and local injections of interferon-alpha showed contradictory results with short- and long-term adverse effects that included neurologic disorders, leukopenia, rash, alopecia, fatigue, and liver dysfunction. The antiviral agent, cidofovir, has been added to RLP treatment mostly by local injection to the infected area after surgical excision of the papillomas. The mechanism of action of cidofovir is not well understood. Its use in combination with surgical treatment showed good remission rates, but caution must be exercised because cidofovir was assumed to induce dysplastic changes in HPV-infected epithelium.<sup>4,8,32</sup> Other pharmacologic agents, such as bevacizumab (an angiogenesis inhibitor used as adjuvant to chemotherapy in metastatic cancer patients), celecoxib (a nonsteroidal anti-inflammatory drug), methotrexate, and others agents were reported to change the natural course of the disease and reduce the need for surgery. However, comprehensive multicenter trials are required to assess the true benefit of these agents.<sup>4,8,32</sup> The quadrivalent vaccine, Gardasil, has activity against HPV types 6, 11, 16 and 18. Although vaccination is currently considered only for patients not infected by HPV and for prevention, it has also been studied for patients with RLP and was shown in several studies to increase the intervals between surgeries and decrease recurrence

in RLP patients. Furthermore, the vaccination reportedly increases anti-HPV6 and anti-HPV11 antibodies in RLP patients.<sup>8,32</sup> Those studies are either case reports or small series, but their results are nevertheless encouraging.

## Summary

There is no consensus regarding the superiority of one surgical approach or one adjuvant therapy over another for the treatment of RLP. Recent trends are towards the use of microdebriders in the OR and angiolytic fiberoptic laser as office-based procedures. The HPV vaccination reduces the incidence of RLP, but a cure for this chronic and debilitating disease remains elusive.

## Conflicts of interest

There are no financial or personal conflicts of interest to declare.

## Disclosure

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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