Operative Nd:YAG laser plus postoperative hyperbaric oxygen reduces surgical morbidity after radical head and neck cancer surgery and complex reconstruction

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ABSTRACT

Complications after radical head and neck cancer surgery in irradiated patients are frequent and life-threatening. Hemorrhage, salivary fistulas, wound infections that expose the carotid sheath, among others, make these patients difficult management challenges in the ICU.

We studied the effects of Nd:YAG laser surgery plus hyperbaric oxygen (HBO_2) therapy on radical head and neck resections and complex reconstruction as a means of reducing postoperative morbidity and mortality.

Methods: 43 head and neck cancer patients were reviewed. Eight (STD) had standard surgery; 35 (YAG:HBO_2) had Nd:YAG laser and postoperative HBO_2.

Results: Age, staging, primary tumor site, sex, reconstruction procedure and transfusion did not differ between STD and YAG/HBO_2. All STD and Nd:YAG/HBO_2 patients were irradiated, median dosages 5,000 centi-Gray (cGy) and 7,000 cGy, respectively (p=0.073). Median blood loss was 1,000 ml STD and 700 ml YAG/HBO_2 (p=0.046). There were no postoperative deaths.

Major surgical site complications developed in 63% of the STD and 17% of the YAG/HBO_2 patients (p=0.017). All STD and 62% of YAG/HBO_2 cancers recurred within 28 months of surgery (p=0.152). Within the STD and YAG/HBO_2 groups, 100% and 77% of deaths, respectively, were due to cancer.

Conclusions: Combined Nd:YAG laser surgery and HBO_2 reduces morbidity in radical head and neck cancer surgery. Recurrent disease and poor cancer survival remain common in this high-risk population.

INTRODUCTION

Treatment of advanced operable squamous cell carcinoma of the head and neck now commonly includes preoperative chemotherapy and high-dose external beam radiotherapy [1,2,3]. When curative surgery is required in these highly irradiated patients, postoperative complication rates are very high [4,5,6]. Morbidities include wound infections, orocutaneous fistulas in the neck, flap necrosis and osteoradionecrosis of the mandible and maxilla.

Secondary to these surgical site-related problems, events such as subsequent aspiration pneumonia, acute malnutrition, non-healing wounds, the need for multiple reconstructive salvage surgeries and fatal events such as carotid artery rupture and tracheo-innominate fistula increase mortality as well as ICU and hospital stays.

We have explored possible methods of reducing these complications after head and neck surgery and the critical illnesses that ensue. Two such modalities may be the use of lasers during surgery and the perioperative application of hyperbaric oxygen (HBO_2) therapy. The Nd:YAG laser in the contact mode as an operative scalpel theoretically reduces tissue damage and thereby improves healing after surgery. [7-11]. A preliminary review of our experience with the Nd:YAG laser in irradiated head and neck patients suggested that it lowered the complication rates [7], but, nevertheless, it was not tested in larger numbers of patients undergoing more radical resections and complex reconstruction. Hyperbaric oxygen (HBO_2) therapy is standard of care for osteoradionecrosis of the mandible [12,13] and for placing dental implants in irradiated bone [14,15].

HBO_2 has been effective as well in managing failed myocutaneous flaps and free tissue transfer reconstruction in head and neck surgery. [16]. However, the healing efficacy of HBO_2 has not been evaluated as an adjuvant to surgery during the physiologically important days directly following surgery.

While Nd:YAG laser and HBO_2 have been well studied in the management of benign disease in irradiated patients [13], and in treating complications following head and neck surgery [16], their effects in the immediate perioperative period on healing of fresh surgical wounds and on postoperative local and distant morbidity are unknown. Based on the results in the published surgical literature, on our previous experience with the Nd:YAG laser in head and neck cancer surgery, and on the established efficacy of HBO_2 in osteoradionecrosis of the mandible and in saving failed tissue transfer flaps, we hypothesized that the combination of the Nd:YAG laser, used as a surgical scalpel during surgery, and postoperative HBO_2 as adjuvant might have synergistic beneficial effects on healing or irradiated tissue in the head and neck. Such a symbiosis at the tissue level could reduce operative tissue damage and maximize microcirculatory oxygenation, leading to improved wound healing and reduced morbidity in highly irradiated head and neck cancer patients.

The present study evaluated our experience with this regimen of operative Nd:YAG laser and postoperative HBO_2 in patients who received high-dose radiation therapy followed by radical curative surgery and complex tissue transfer reconstruction in the treatment of advanced operable squamous cell carcinoma of the head and neck.

METHODS

Under a protocol approved by the Institutional Research Board of Cooper University Hospital, Camden , N.J., we reviewed the medical records of 43 patients who underwent composite resections of advanced operable head and neck cancers, and complex reconstruction with myocutaneous flaps and/or free tissue transfer (free flap).

Eight patients (STD) were operated upon using standard surgical techniques but without the Nd:YAG laser. STD patients did not undergo HBO_2. Selection of surgical management for each patient was determined by the head and neck surgical oncologist. Two different staff surgeons performed the cancer resections in the STD group.

The excellent healing observed in the first several patients receiving Nd:YAG laser plus HBO_2 caused both waiting patients and surgeons to become reluctant to continue with STD techniques and no-HBO_2 technology. This resulted in the small STD group. All resections in the Nd:YAG laser plus HBO_2 group were carried out by a single surgeon (GJS). For all 43 patients in this study, reconstructive surgery was performed by the same surgeons (MM and LF).

A total of 35 patients (YAG:HBO_2) underwent surgery using the Nd:YAG laser supplemental to conventional surgical techniques. During radical resections of primary tumors and indicated neck dissections, all tissue cutting was done after the skin incision with the Nd:YAG laser in the contact mode at 25 watts of continuous power. All YAG:HBO_2 operations were carried out under frozen section pathology control, with all resection margins negative for residual cancer. Reconstruction using myocutaneous flaps, free flaps or both, as indicated for each patient, was performed using established microsurgical techniques for each procedure.

Patients were transferred from the operating room to the intensive care unit for the first postoperative night at the least.

Beginning on the first postoperative day, and continuing daily for 10 days, patients were transferred from Cooper University Hospital in Camden, N.J., to the Hyperbaric Medicine Unit of the University of Pennsylvania in Philadelphia, Pa., where they underwent a two-hour HBO_2 treatment at 3 atmospheres of pressure while breathing 100% oxygen (O_2). After each HBO_2 session, patients were returned to Cooper University Hospital for continued acute postoperative care.

Data collected retrospectively on each patient included age, sex, medical co-morbidities, tobacco and alcohol use, tumor/nodal/metastasis scoring (TNM) and stage data, primary tumor site, chemotherapy and radiotherapy information, date of surgery, survival status, tumor recurrence, reconstructive procedures, operative time, estimated blood loss in the operating room (EBL transfusions, serum electrolytes, CBC, prothrombin time (PT), partial thromboplastin time (PTT), international normalized ratio (INR) and liver function profile, hospital length of stay (LOS) and postoperative complications.

Data is expressed as mean with standard deviation, median and range. Categorical data were analyzed using the Chi-squared test, or using the Fisher's exact test modification when indicated by cell size [17].

TABLE 1 – *Demographics and Preoperative Treatment*

	Age *(median)*	Male/Female	Radiotherapy Dosage *(median)*	>6,000 cGy RT
Standard	51 (34-63)	6/2 (75% / 25%)	5,000 cGy	2/8 (25%)
YAG/HBO_2	59 (37-73)	26/6 (81% / 19%)	7,000 cGy	21/35 (60%) p=0.073
PREOPERATIVE CHEMOTHERAPY				
Standard		2/8 (25%)		
YAG/HBO_2		29/32 (91%)		p=0.001

TABLE 2 – *Primary Tumor Site and Stage*

	SITE				STAGE		
	Oral Cavity	**Oropharynx**	**Hypopharynx**	**Larynx**	**II**	**III**	**IV**
Standard	5	0	0	4	1	0	7
YAG/HBO_2	24	2	7	2	0	2	33

	T Category			N Category			
	T2	***T3***	***T4***	***N0***	***N1***	***N2***	***N3***
Standard	1	0	7	2	3	3	0
YAG/HBO_2	2	11	22	15	6	9	5

RESULTS

Demographics, co-morbidities and preoperative cancer treatments are listed in Table 1 *(above)*. Of the STD group, 2/8 (25%) of the patients received greater than 6,000 cGy irradiation before surgery, versus 21/35 (60%) for YAG:HBO_2 patients. Preoperative chemotherapy was given to 2/8 (25%) STD and 29/32 (91%) YAG:HBO_2 patients. (p=0.001)

Primary tumor site and staging information is listed in Table 2 *(above)*. The distribution of tumor site, TNM classification and cancer stage was equal statistically between the STD and YAG:HBO_2 groups.

Operative data is displayed in Table 3 *(Page 164)*. In the STD group, 88% had EBL over 800 ml, versus 43% for YAG:HBO_2 patients (p=0.046). Among STD patients, 62.5% received two units of packed red cell transfusions, versus 26% for YAG:HBO_2 patients (p=0.045; p=0.089 Fisher's exact test).

Postoperative results are tabulated in Table 4 *(Page 164)*. Mortality was zero. Major surgical site-related complications developed in 63% of STD patients and in 17% of YAG:HBO_2 patients (p=0.017). Minor site-related complications (superficial wound infection or localized flap edge ischemia) occurred in 14% of YAG:HBO_2 and none of the STD group.

Long-term results are listed in Table 5 *(Page 164)*. Recurrent cancer developed in 86% of STD patients and in 70% of the YAG:HBO_2 group. With a maximum follow-up of 80 months, all STD patients died, six (86%) having succumbed to recurrent or metastatic cancer. Among the YAG:HBO_2 patients, five (15%) were long-term survivors, and 28 (85%) expired, 21 (75%) of the latter dying from recurrent and/or metastatic disease.

DISCUSSION

The results of this study suggest that the combination of Nd:YAG laser during surgery and HBO_2 postoperatively reduces major surgical site-related complications after composite resections for head and neck cancer, with complex reconstruction, among patients who previously had received high-dose external beam radiotherapy.

Major complications developed in 63% of STD patients, compared with only 17% of the YAG:HBO_2 group. This was accomplished in YAG:HBO_2 patients who had received higher doses of external beam radiation therapy before undergoing surgery than did the

TABLE 3 – *Operative Data*

	EBL *(median)*	EBL > 800 ml	Blood Transfusion	>2 Units Transfused
Standard	1000ml	7/8 (88%)	6/8 (75%)	5/8 (62.5%)
YAG/HBO_2	700ml	15/35 (43%)	18/35 (51%)	9/35 (26%)
		p= 0.023	*p=0.045*	

RECONSTRUCTION

Myocutaneous Flap	*Free Flap*	*Both*
6	1	1
18	12	5

TABLE 4 – *Postoperative Results*

SITE-RELATED MORBIDITY

	Mortality	Major *(fistula, flap failure, wound infection)*	Minor
Standard	0	5/8 (63%)	0
YAG/HBO_2	0	6/35 (17%)	4/32 (13%)
		p=0.008	

Two (2) STD and four (4) YAG/HBO_2 patients had pulmonary and/or cardiac morbidities, unrelated to the surgical site.

TABLE 5 – *Long-Term Results After Head and Neck Surgery*

RECURRENT/METASTATIC CANCER

	Local	Second Primary	Distance Metastases	Total
Standard	4	1	1	6/7 (86%)
YAG/HBO_2	17	2	5	23/33 (70%)

	Survival	Died of Disease
Standard	0 %	6/7 (86%)
YAG/HBO_2	5/33 (15%)	21/28 (75%)

STD group (7,000 cGy versus 5,000 cGy, respectively). The Nd:YAG laser reduced operative blood loss and the need for multiple transfusions, suggesting limited surgical tissue damage and reduced transfusion-induced immunocompromise.

Our review of the literature indicates that the significant reductions in postoperative morbidity achieved here by the YAG:HBO_2 regimen among heavily pre-irradiated head and neck cancer patients undergoing radical surgery and reconstruction have not been reported previously and are important findings of this study.

Major complications at the surgical site affect up to 65% of patients [4-6] who endure extensive curative surgery for head and neck cancer. Fistulas, deep tissue infections and carotid artery rupture are life-threatening. The risk for these problems increases after full-dose radiation therapy in excess of 7,000 cGy, which now is emerging as the standard of care in head and neck cancer. [1-3. However, in the present study, major post-operative morbidity was reduced from 63% in the STD group, to 17% among patients treated with YAG:HBO_2. As a result of these findings, we have in YAG:HBO_2 a

surgical approach to extirpative head and neck cancer surgery that may enable the most radical curative resections and complex reconstructions to be performed safely.

The purported beneficial effects of lasers on local tissues in head and neck cancer surgery include reducing edema, limiting blood loss and lowering the probability of postoperative infection [8]. The Nd:YAG contact laser has been used to treat colorectal cancers [10], breast cancer [11], burn excision [9], multiple urologic [18] and gynecologic [19] procedures, and even lumbar diskectomy [20]. We have reported significantly ameliorated post-surgical morbidity in small groups of previously irradiated patients who underwent moderately complicated head and neck cancer surgery with the Nd:YAG laser, compared with standard techniques only [7]. From the nearly fourfold reduction in postoperative complications with YAG:HBO_2 in the present investigation, one might speculate that Nd:YAG treatment effects on operative results in irradiated head and neck fields may be more than theoretical.

Decreased operative blood among Nd:YAG patients minimized the need for multiple blood transfusions, which, in turn, may have contributed to the optimized postoperative course. Exposure to multiple units of banked blood is linked to increased infection rates among trauma patients [21], increased complications after major surgery [22, and progression of disease following resections of solid cancers [23]. One might speculate that post-transfusion systemic immune suppression contributed also to the present results, leading to high STD complication rates. Conversely, by preventing the need for massive transfusions, the Nd:YAG laser during radical head and neck cancer surgery may have improved wound healing by maintaining immunologic homeostasis.

Since Marx's pioneering report in 1983 [12], HBO_2 has been a central treatment modality in the management of osteoradionecrosis complicating radiation therapy for head and neck cancer. More recently, HBO_2 has improved outcomes of dental implant placement in irradiated bone [14,15] and of microvascular reconstruction for advanced osteoradionecrosis [13]. Neovius and co-workers [16] reported accelerated healing of soft-tissue wounds which complicated curative head and neck surgery in irradiated cancer patients. We hypothesized that if HBO_2 was beneficial for non-healing irradiated wounds and effective prophylaxis in surgery for osteoradionecrosis, then, when administered postoperatively, as an adjuvant to surgery, it should optimize the results of radical head and neck cancer operations with complex reconstructions. The data in this paper supports that hypothesis. In fact, at only 17%, the rate of major surgical site-related morbidity in our highly irradiated patient population was lower than the 43% complication frequency reported by Gal *et al.* [13] after microvascular surgery for benign disease in non-irradiated patients.

Preoperative chemotherapy was administered more frequently to YAG:HBO_2 patients in this study than to STD patients (91% versus 25%, respectively; p=0.001). Our review of the literature did not identify a specific risk for complications following head and neck cancer surgery among patients who received chemotherapy before operation. In breast cancer after mastectomy and immediate reconstruction, Peled and co-workers observed significantly increased infections in the group who received neoadjuvant chemotherapy, but no difference in the rate of re-operation for complications [24]. Similarly, neoadjuvant chemotherapy followed by radical hysterectomy was not accompanied by increased postoperative morbidity [25]. If pre-surgical chemotherapy did increase the risk of morbidity in head and neck cancer surgery, then dramatically reduced major complication rates in the YAG:HBO_2 group of this study, who received chemotherapy significantly more often than did STD patients, are quite promising.

In spite of the excellent results in the immediate postoperative period, in long-term follow-up, most of the patients in this study developed recurrent cancer. Nearly all of those with recurrent disease and/or metastatic spread of cancer succumbed to their tumors. These findings are not surprising, with the advanced operable malignancies that were treated surgically in this high-risk oncologic population. However, when surgery is the only hope for such head and neck cancer patients who have failed high-dose radiation therapy, this study confirms that YAG:HBO_2 adjuvant to state-of-the-art operative techniques can bring them safely through radical resections and complex reconstructions.

There are several limitations of this study. First, while the concept of combining the Nd:YAG laser with postoperative HBO_2 has not been evaluated previously in a population of irradiated head and neck cancer patients undergoing radical curative surgery and complex reconstructions, the present study itself still is a retrospective review of our experience with using two established treatment modalities. Thus, the findings here should be validated in prospective, randomized clinical trials that include not only STD versus YAG:HBO_2, but also arms with STD plus HBO_2, as well as Nd:YAG laser without HBO_2.

Secondly, the STD control group was disproportionately small compared with the YAG:HBO_2 cohort. This statistical discrepancy occurred because after the success we experienced in our initial group of YAG:HBO_2 patients, our team was reluctant to return to STD methodology. Obviously a larger number of control patients would have improved the statistical power of this investigation. The dramatically greater number of patients in the YAG:HBO_2 group raises the specter of statistical bias in the results. This limitation again points to the need for further prospective evaluation of YAG:HBO_2 in head and neck cancer surgery. Nevertheless, the results of this pilot study are encouraging.

Thirdly, while our previous experience with the Nd:YAG laser in head and neck surgery suggested beneficial effects, those operations were not as radical as in the present study, and complex reconstruction was not required in most cases. Therefore, clinically, we were not confident that the laser tissue benefits alone would suffice to reduce the known high post-surgical morbidity among irradiated head and neck cancer patients. Thus, in this current report, two new adjuvant therapies, the Nd:YAG laser and HBO_2, were added together and compared to standard methodologies. While the preliminary results here are promising for YAG:HBO_2, adding two therapeutic variables at once does make it difficult to determine which technique is responsible for the results observed. Again, a prospective clinical trial should include HBO_2 alone and Nd:YAG laser alone, versus YAG:HBO_2 and STD.

Finally, although the distribution of free tissue transfer reconstruction was statistically equal in the STD and YAG:HBO_2 groups, the small numbers of free flaps in the STD group may have masked their contribution to successful wound healing in the numerically larger YAG:HBO_2 cohort.

This retrospective investigation identifies YAG:HBO_2 as a possible means of reducing major site-related complications following radical head and neck cancer operations with complex tissue transfer reconstruction among highly irradiated patients. During surgery, the Nd:YAG laser reduced operative blood loss and blood transfusions, possibly optimizing systemic immune function and wound healing. Salubrious tissue effects of laser surgery combined with the microcapillary benefits of HBO_2 resulted in a fourfold reduction in major surgical complications. Unfortunately, in this oncologic high-risk group, long-term cancer-free survival remains low. Nevertheless, the beneficial treatment effects of YAG:HBO_2 seen here represent clinically valuable new knowledge that may improve the care of head and neck cancer patients.

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